Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

DEC 2 1 2001

Appendix 25 - *revised*
510(k) Summary of Safety and Effectiveness

Vertis Neuroscience, Inc.
Percutaneous Neuromodulation Therapy (PNT) ™ Control Unit and Accessories

K011702

General Information

Classification	Class II
Trade Name	Percutaneous Neuromodulation Therapy (PNT) Nerve Stimulation System
Submitter	Vertis Neuroscience, Inc. 2101 Fourth Avenue, Suite 200 Seattle, Washington, USA 98121
Contact	Lori Glastetter Vice President, Regulatory Affairs/ Quality Assurance

Substantially Equivalent Devices

Manufacturer	Substantially Equivalent devices	510(k)
Empi, Inc. St. Paul, MN	EPIX Tens Device System Model EPIX VT Model EPIX XL	K970203 K951903
Rehabilicare, Inc. New Brighton, MN	SMP-Plus™ Model 4930	K982410
Chattanooga Group, Inc. Hixson, TN	Intelect ® Legend Stim Model IFC2 (catalog #INT002)	K924666
Medtronic, Inc Minneapolis, MN	Mattrix ® Neurostimulation System Receiver model: 3272 Transmitter model: 3210	K982902
TECA Corporation Pleasantville, NY	TECA Disposable Monopolar Needles 902-DMFxx-TP series 892-DMGxx-TP series	K973442
Medtronic, Inc. Minneapolis, MN	DMN™ Disposable Monopolar Needle Electrodes DMFxx series DMNxx series	K950314
Medtronic, Inc. Minneapolis, MN	Resume II Lead Model 3587a	K915540

Intended use

Percutaneous Neuromodulation Therapy (PNT) is indicated for the symptomatic relief and management of chronic or intractable low back pain and/or as an adjunctive treatment in the management of post-surgical low back pain and post-trauma low back pain.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

The PNT Control Unit is to be used with a PNT Safeguide Kit – Lumbar.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

Device Description

The Vertis PNT System is designed for delivering percutaneous electrical stimulation (termed: Percutaneous Neuromodulation Therapy - PNT). The Vertis PNT System is intended to be used in pain management by a physician (e.g., anesthesiologists or physical medicine and rehabilitation physicians) or on the order of a physician (e.g., by a physical therapist) in a clinic environment. It is not intended for patient use. The device system includes 3 major components:

- the *Vertis PNT Control Unit* - a software-driven, five channel, AC powered nerve stimulator which generates the electrical stimulus;
- the sterile *Safeguides* – which are sterile, needle electrodes, and
- the *Patient Cable* - which interconnects the PNT Control Unit to the electrodes

Bench/Animal Testing

Extensive bench and animal was conducted on the Vertis PNT System and included performance and safety testing. The Vertis PNT System conforms to applicable sections of the technical references and FDA-recognized consensus standards noted below. Additionally, the PNT Control Unit software was validated per recognized validation techniques.

Results: All testing of the products yielded acceptable results prior to commercial distribution.

ANSI/AAMI NS4-1985 Transcutaneous Electrical Nerve Stimulators, approved 5-20-86.
ANSI/AAMI ES1 1993 - Safe Current Limits for Electromedical Apparatus, approved 12-2-93
ANSI/AMI NS15-1995 Implantable Peripheral Nerve Stimulators, approved 2-1-95
IEC60601-1:1993 Medical Electrical Equipment, Part 1: General Requirements for Safety and Amendments A1:1991, A2:1995.
IEC 60601-1-2 First Edition 1993-4 Medical Electrical Equipment, - Part 1: General Requirements for Safety: Electromagnetic Compatibility – Requirements and Tests (tested in accordance to the IEC 61000 series).
IEC 60601-1-4:1996 Medical Electrical Equipment, Part 1: General Requirements for Safety, Part 2: Collateral Standard: Programmable electrical medical systems.
IEC 60601-2-10:1987 Medical Electrical Equipment, Part 2: Particular Requirements for the Safety of Nerve and Muscle Stimulators.
EN (CEN) 1441:1997 Medical Devices – Risk Analysis.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

ANSI/AAMI/ISO 15223: 2000 Medical Devices – Symbols to be used with Medical Device Labels, Labeling and Information to be Supplied, approved 3-13-00.
IEC 60601-2-10:1987 Medical Electrical Equipment, Part 2: Particular Requirements for the Safety of Nerve and Muscle Stimulators.
ANSI/AAMI/ISO 11137: 1994 Sterilization of Health Care Products – Requirements for Validation and Routine Control –Radiation Sterilization; using Method 1 as described per AAMI/ISO TIR No. 13409: 1996 Sterilization of Health care Products – Radiation Sterilization – Substantiation of 25kGy as a Sterilization Dose for Small or Infrequent Production Batches.
ANSI/AAMI/ISO 10993-1:1997, Biological Evaluation of Medical Devices - Part 1: Evaluation and Testing.

Clinical Testing

Under the auspices of an Investigational Device Exemption, Vertis conducted a prospective clinical study evaluating the safety and effectiveness of percutaneous neuromodulation therapy.

The Vertis clinical trial was reviewed and approved in November 2000. The trial commenced shortly thereafter at multiple United States clinical sites. The trial was completed in March 2001. During the multi-week investigational protocol, there were a total of 2150 electrode placements in 215 PNT therapy sessions with patients.

Results: The clinical trial demonstrated the safety and effectiveness of the percutaneous neuromodulation therapy.

Summary of Substantial Equivalence

Therefore, due to the similarity of design features, materials, test results, clinical results and indicated use to other predicate devices, Vertis believes the Vertis PNT System does not raise any new safety or effectiveness issues and is substantially equivalent to currently available nerve stimulators, electrodes and accessories that have been determined to be substantially equivalent to devices in commercial distribution prior to May 28, 1976.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

DEC 21 2001

Lori J. Glastetter
Vice President, Regulatory Affairs/Quality Assurance
Vertis Neuroscience, Inc.
2101 Fourth Avenue, Suite 200
Seattle, Washington 98121

Re: K011702/S1
Trade/Device Name: Vertis Percutaneous Neuromodulation Therapy (PNT) Stimulation System (Vertis PNT Control Unit and Vertis PNT Lumbar Safeguard Kit)
Regulation Number: 21 CFR 882.5890 and 21 CFR 882.1350
Regulation Name: Transcutaneous Electrical Nerve Stimulator for Pain Relief and Needle Electrode
Regulatory Class: Class II
Product Code: NHI and GXZ
Dated: September 24, 2001
Received: September 25, 2001

Dear Ms. Glastetter:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 21 CFR Part 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4659. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address
http://www.fda.gov/cdrh/dsma/dsmamain.html

Sincerely yours,

Celia M. Witten, Ph.D., M.D.
Director
Division of General, Restorative
and Neurological Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

510(k) Number (if known): K011702

Device Name: Vertis PNT System

Indications For Use:

Percutaneous Neuromodulation Therapy (PNT) is indicated for the symptomatic relief and management of chronic or intractable low back pain and/or as an adjunctive treatment in the management of post-surgical low back pain and post-trauma low back pain.

The PNT Control Unit is to be used with a PNT Safeguide Kit – Lumbar.

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

(Division Sign-Off)
Division of General, Restorative and Neurological Devices

(Optional Format 3-10-98)

510(k) Number K011702

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

DEPARTMENT OF HEALTH & HUMAN SERVICES — Public Health Service
Food and Drug Administration

Memorandum

Date: 12/27/01

From: DMC (HFZ-401)

Subject: Premarket Notification Number(s): K011702/17'

To: Division Director: NE/DGRND

The attached information has been received by the 510(k) DMC on the above referenced 510(k) submission(s). Since a final decision has been rendered, this record is officially closed.

Please review the attached document and return it to the DMC, with one of the statements checked below.

_____Information does not change the status of the 510(k); no other action required by the DMC; please add to image file. (Prepare K-25) THIS DOES NOT APPLY TO TRANSFER OF OWNERSHIP. PLEASE BRING ANY TRANSFER OF OWNERSHIP TO POS.

_____Additional information requires a new 510(k); however, the information submitted is incomplete; (Noitify company to submit a new 510(k);[Prepare the K30 Letter on the LAN]

_____*Additional information requires a new* 510(k); please process [This information will be made into a new 510(k)

__X__No response necessary (e.g., hard copy of fax for the truthful and accuracy statement, 510(k) statement). Hard Copy of fax

CLIA CATEGORIZATION refers to laboratory test system devices reviewed by the Division of Clinical Laboratory Devices (HFZ-440_

_____Information requires a **CLIA CATEGORIZATION**; *the complexity may remain the same* as the original 510(k) or may change as a result of the additional information (Prepare a CAT letter)

____Additional information requires a **CLIA CATEGORIZATION**; however, the information submitted is incomplete; (call or fax firm)

_____No response necessary

This information should be returned to the DMC within 10 working days from the date of this memorandum.

Reviewed by: Kristen Bamks
Date: 1-9-02

Draft #2 : 9/8/99
Draft #3: 1/3/00

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-4170, Released by CDRH on 09-10-2015

K011702/A1

Vertis Neuroscience

2101 Fourth Avenue, Seattle, WA 98121-2329
Tel 206.728.1497
www.vertisneuro.com

December 21, 2001

Office of Device Evaluation
510(k) Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Blvd.
Rockville, MD 20850

SK-16

Reference: 510(k) Notification K011702 – Additional Information
Vertis Neuroscience, Inc. Nerve Stimulator, Electrodes and Accessories

Dear Document Mail Center Staff:

Regarding the above noted 510(k), Vertis provided information by email to ODE Reviewer Kristen Bowsher, Ph.D.

Dr. Bowsher asked that we send a hard copy of this information to Document Mail Center for addition to the file. It is enclosed with this letter.

Statement of Confidentiality

This information provided is considered by Vertis Neuroscience, Inc. to be confidential information as it relates to our intention to market this product in the future. We have not, to our knowledge, released this information through advertising or any other manner to anyone outside the employ of, or under contract to, Vertis Neuroscience, Inc. Vertis has taken precautions to protect the confidentiality of this information under Section 21CFR 807.95, Confidentiality of Information. We ask that this information be treated as confidential in accordance with the Freedom of Information Act.

Should you have any questions, please do not hesitate to contact me at (206) 902-1902.

Sincerely,

Lori J. Glastetter
Vice President, Regulatory Affairs/Quality Assurance
Vertis Neuroscience, Inc.

Vertis PNT is a trademark of Vertis Neuroscience, Inc.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

Lori Glastetter

From: Lori Glastetter
Sent: Thursday, December 20, 2001 2:41 PM
To: Kristen A. Bowsher Ph. D. (E-mail)
Subject: Vertis 510(k) - Revised Indications form and 510(k) summary

Kristen,

Regarding 510(k) K011702:

Per our conversation just a moment ago, here are the revised Indications form and 510(k) summary - both reflecting the final Indications for Use that FDA has agreed to.

Final 510(k) Summary - revised... Final Indications form - revis...

I will send a hard copy of this email and attached documents to the Document Mail Center.

best regards,

Lori

LORI GLASTETTER
VP, Regulatory Affairs & Quality Assurance
lglastetter@vertisneuro.com

Direct line: 206.902.1902
Fax: 206.902.0140

Vertis Neuroscience
2101 Fourth Avenue, Suite 200
Seattle, WA 98121-2329
www.vertisneuro.com

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

3

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

Appendix 25 - *revised*
510(k) Summary of Safety and Effectiveness

Vertis Neuroscience, Inc.
Percutaneous Neuromodulation Therapy (PNT) ™ Control Unit and Accessories

General Information

Classification	Class II
Trade Name	Percutaneous Neuromodulation Therapy (PNT) Nerve Stimulation System
Submitter	Vertis Neuroscience, Inc. 2101 Fourth Avenue, Suite 200 Seattle, Washington, USA 98121
Contact	Lori Glastetter Vice President, Regulatory Affairs/ Quality Assurance

Substantially Equivalent Devices

Manufacturer	Substantially Equivalent devices	510(k)
Empi, Inc. St. Paul, MN	EPIX Tens Device System Model EPIX VT Model EPIX XL	K970203 K951903
Rehabilicare, Inc. New Brighton, MN	SMP-Plus™ Model 4930	K982410
Chattanooga Group, Inc. Hixson, TN	Intelect ® Legend Stim Model IFC2 (catalog #INT002)	K924666
Medtronic, Inc Minneapolis, MN	Mattrix ® Neurostimulation System Receiver model: 3272 Transmitter model: 3210	K982902
TECA Corporation Pleasantville, NY	TECA Disposable Monopolar Needles 902-DMFxx-TP series 892-DMGxx-TP series	K973442
Medtronic, Inc. Minneapolis, MN	DMN™ Disposable Monopolar Needle Electrodes DMFxx series DMNxx series	K950314
Medtronic, Inc. Minneapolis, MN	Resume II Lead Model 3587a	K915540

Intended use

Percutaneous Neuromodulation Therapy (PNT) is indicated for the symptomatic relief and management of chronic or intractable low back pain and/or as an adjunctive treatment in the management of post-surgical low back pain and post-trauma low back pain.

The PNT Control Unit is to be used with a PNT Safeguide Kit – Lumbar.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

4

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

Device Description

The Vertis PNT System is designed for delivering percutaneous electrical stimulation (termed: Percutaneous Neuromodulation Therapy - PNT). The Vertis PNT System is intended to be used in pain management by a physician (e.g., anesthesiologists or physical medicine and rehabilitation physicians) or on the order of a physician (e.g., by a physical therapist) in a clinic environment. It is not intended for patient use. The device system includes 3 major components:

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Extensive bench and animal was conducted on the Vertis PNT System and included performance and safety testing. The Vertis PNT System conforms to applicable sections of the technical references and FDA-recognized consensus standards noted below. Additionally, the PNT Control Unit software was validated per recognized validation techniques.

Results: All testing of the products yielded acceptable results prior to commercial distribution.

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Under the auspices of an Investigational Device Exemption, Vertis conducted a prospective clinical study evaluating the safety and effectiveness of percutaneous neuromodulation therapy.

The Vertis clinical trial was reviewed and approved in November 2000. The trial commenced shortly thereafter at multiple United States clinical sites. The trial was completed in March 2001. During the multi-week investigational protocol, there were a total of 2150 electrode placements in 215 PNT therapy sessions with patients.

Results: The clinical trial demonstrated the safety and effectiveness of the percutaneous neuromodulation therapy.

Summary of Substantial Equivalence

Therefore, due to the similarity of design features, materials, test results, clinical results and indicated use to other predicate devices, Vertis believes the Vertis PNT System does not raise any new safety or effectiveness issues and is substantially equivalent to currently available nerve stimulators, electrodes and accessories that have been determined to be substantially equivalent to devices in commercial distribution prior to May 28, 1976.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

6

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

510(k) Appendix 27 - *revised*
Indications for Use

Percutaneous Neuromodulation Therapy (PNT) is indicated for the symptomatic relief and management of chronic or intractable low back pain and/or as an adjunctive treatment in the management of post-surgical low back pain and post-trauma low back pain.

The PNT Control Unit is to be used with a PNT Safeguide Kit – Lumbar.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

Brian Cleary
Vertis Neuroscience
2401 Fourth Avenue
Suite 500
Seattle, WA 98121

JUL 15 2003

Re: k022241 – Vertis PNT Control Unit, Model CU 100, PNT Safeguide-Cervical, Model SG 102-XXX
k011702 – Vertis PNT Control Unit, Vertis PNT Safeguide Kit

Dear Mr. Cleary:

We have reviewed your letter, dated May 23, 2003, stating that the rights to the above referenced premarket notifications (510(k)s) have been transferred. Transfer of 510(k) rights alone does not require submission of a new 510(k) under 21 CFR 807.81(a)(3). Consequently, we cannot change the name of the original 510(k) submitter in our database. We suggest that information showing the transfer of the 510(k)s and their current ownership should be maintained in the company's files for review by an FDA investigator. You may contact the Center for Devices and Radiological Health's Office of Compliance at (301) 594-4692 if you have any questions on what information we expect to be maintained in your files.

If you have any other questions regarding this letter, please contact the 510(k) Staff at (301) 594-1190.

Sincerely yours,

Heather S. Rosecrans

Heather S. Rosecrans
Director, Premarket Notification Section
Program Operations Staff
Office of Device Evaluation
Center for Devices and
Radiological Health

cc: RS Medical
14401 S.E. First St.
Vancouver, WA 98684

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service
Food and Drug Administration

Memorandum

Date: 5/17/03

From: DMC (HFZ-401)

Subject: Premarket Notification Number(s): K011702/A2

To: Division Director: NE/DGRND

The attached information has been received by the 510(k) DMC on the above referenced 510(k) submission(s). Since a final decision has been rendered, this record is officially closed.

Please review the attached document and return it to the DMC, with one of the statements checked below.

_____Information does not change the status of the 510(k); no other action required by the DMC; please add to image file. (Prepare K-25) THIS DOES NOT APPLY TO TRANSFER OF OWNERSHIP. PLEASE BRING ANY TRANSFER OF OWNERSHIP TO POS.

_____Additional information requires a new 510(k); however, the information submitted is incomplete; (Noitify company to submit a new 510(k);[Prepare the K30 Letter on the LAN]

_____Additional information requires a new 510(k); please process [This information will be made into a new 510(k)

_____No response necessary (e.g., hard copy of fax for the truthful and accuracy statement, 510(k) statement, change of address, phone number, or fax number).

CLIA CATEGORIZATION refers to laboratory test system devices reviewed by the Division of Clinical Laboratory Devices (HFZ-440

_____Information requires a **CLIA CATEGORIZATION**; the complexity may remain the same as the original 510(k) or may change as a result of the additional information (Prepare a CAT letter)

____Additional information requires a **CLIA CATEGORIZATION**; however, the information submitted is incomplete; (call or fax firm)

_ ___No response necessary

This information should be returned to the DMC within 10 working days from the date of this memorandum.

Reviewed by:_____
Date:_____

Draft #2 : 9/8/99
Draft #3: 1/3/00

POS

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

2

Records processed under FOIA Request # [illegible]; Released by CDRH on 09-10-2015

K011702/A2

Vertis neuroscience

2401 Fourth Avenue, Ste. 500 Seattle, WA 98121-2329
Tel 206.728.1477 Fax 206.728.1497
www.vertisneuro.com

May 23, 2003

Food and Drug Administration
Center for Devices and Radiological Health (HFZ-401)
9200 Corporate Boulevard
Rockville, Maryland 20850

FDA/CDRH/ODE/PMO
2003 MAY 27 A 11:31
RECEIVED

Re: 510(k) #K011702

To Whom It May Concern:

This letter is to inform you that, effective May 20, 2003, Vertis Neuroscience, Inc. has transferred the ownership of 510(k) #K011702 for the **Vertis PNT Control Unit, Vertis PNT Safeguide Kit** to RS Medical (Establishment Registration # 1644243).

RS Medical will be notifying your office that it is assuming ownership of the 510(k) and will make all necessary changes to its device listing information to reflect this change in ownership.

Sincerely,

Brian Cleary
Director of Regulatory Affairs
Vertis Neuroscience, Inc.

3

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

APPENDIX 10

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

Appendix 10
Software Information

Vertis is providing software information for the Vertis PNT Control Unit in accordance with the FDA Guidance for Reviewers and Industry: Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices (released 5-29-98).

Note #1: Vertis contracted the development and testing of the Vertis PNT Control Unit device software to Plexus Corporation (establishment registration # 3031699). Hence Plexus documents are referenced below for some of the software information and are provided as Attachments in this Appendix.

Vertis Development Engineering and Quality Engineering participated in the review and management of the Plexus software development activities and validation testing. Vertis maintains all responsibility for the Device Master Record (including software specifications).

Note #2: For convenience during product development, the project names used for the Vertis PNT Control Unit, Safeguide electrode and Patient Cable were "Telluride", "Edelweiss" and "Powderhorn" respectively. Hence, these project names may be present in the attached documents.

Software Information – per FDA Guidance

Software Aspect	Guidance Description	Vertis Reference/Info – location in this Appendix
Level of Concern	Estimate of the severity of injury that a device could permit or inflict (directly or indirectly) on a patient or operator as a result of latent failures, design flaws, or using the medical device software.	In accordance to the above noted FDA guidance, Vertis believes the software of the PNT Control Unit to be of a Minor level of concern. However, Vertis opted to pursue a conservative development path and developed and tested the software in accordance to the **MODERATE** level of concern.
Software Description	A comprehensive overview of the device features controlled by software, and intended operational environment.	This information is provided in Plexus document 939367 Rev. P3 Telluride Software Design Description, sections one and two (pages 4 through 11) - copy provided as Attachment A in this Appendix.
Device Hazard Analysis	An analysis that takes into account all device hazards associated with intended use, hardware, and software.	This information is provided in Vertis document 10093-001 Rev D, Control Unit/Safeguide Risk Analysis and Plexus document 939340 Rev P2 Report, Software Risk Analysis, Telluride - copies provided as Attachment B and C in this Appendix, respectively.
Software Requiremnts. Specification (SRS)	Document of the requirements for software, including functional, performance, interface, design and development requirements.	This information is provided in Plexus document 939403 Rev P5 Telluride Software Requirements Specification - copy provided as Attachment D in this Appendix.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Software Aspect	Guidance Description	Vertis Reference/Info – location in this Appendix
Architecture Design Chart	A chart depicting the partitioning of the software system into functional subsystems, listing of the functional modules and a description of how each fulfill the requirements.	This information is provided in Plexus document 939367 Rev. P3 Description Software Design, Telluride, sections three and four (pages 12 through 226; software partitioning charts can be found on pages 17-51) - copy provided as Attachment A in this Appendix.
Design Specification	A description of what the program should do and how it should do it. Provides a high level summary of the design and specifications with enough detail to provide direction to programmers.	This information is provided in Plexus document 939402 Rev P7 Telluride Product Requirements Specification - copy provided as Attachment E in this Appendix.
Traceability Analysis	Traceability among requirements, identified hazards, and Verification and Validation testing.	This information is provided in Plexus document 939440 Rev P1 Report, Software Verification & Validation, Telluride, sections A.6 (pages 12 through 16) and B.7 (page 22) - copy provided as Attachment F in this Appendix.
Development	Summary of software life cycle development plan, including a summary of the configuration management and maintenance activities.	This information is provided in Plexus document 939366 Rev P2 Plan, Software Development, Telluride. Configuration management activity is specified in section eight (pages 15 and 16) - copy provided as Attachment G in this Appendix.
Validation, Verification and Testing (VV&T)	Description of VV&T activities at the unit, integration and system level. System level test protocol including pass/fail criteria, and test results.	This descriptive information is provided in Plexus document 939438 Rev. P1 Plan Software Verification/Validation, Telluride - copy provided as Attachment H in this Appendix. This system level validation test protocol is provided in Plexus document 939439 Rev. P2 Procedure, Software Validation Test, Telluride, and test report is provided in Plexus document 939440 Rev P1 Report, Software Verification & Validation, Telluride, are provided as Attachments I and F in this Appendix, respectively. **Results:** Results of system level validation indicate the software meets the requirements of Vertis document 10093-001 Rev C PNT Control Unit Software Requirements Specification.

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Software Aspect	Guidance Description	Vertis Reference/Info – location in this Appendix
Revision Level History	Revision history log documenting all major changes to the software during its development cycle.	This information is provided in "Telluride Change History from Alpha code release to P2" - copy provided as Attachment J in this Appendix. This information has been compiled from Visual Source Safe (VSS), a configuration management tool.
Unresolved Anomalies (bugs)	List of errors and bugs that remain in the device and an explanation how they were determined to not impact safety or effectiveness, including operator usage and human factors.	This information is provided in Access database "Telluride" – copy provided as Attachment K in this Appendix. **Results**: All errors/bugs have been resolved with the exception of the 2 noted. These 2 issues are conditions observed if a user used the Control Unit in an off-label manner (e.g., attached a non-Vertis patient cable to the Control Unit or pressed a non-functioning button in a random sequence, not per User's Guide). These 2 issues do not impact the current functionality of the device. However, to ensure adequate device response (e.g., an error message) if in the unlikely event these occurred, these 2 issues will be resolved in a subsequent software revision and software revalidation completed.
Release Version Number	Version number and date of the software to be included in the marketed device.	Software version number: 1.01 Release date: 3/22/2001

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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PLEXUS®

DESCRIPTION, SOFTWARE DESIGN, TELLURIDE

Drawing Number
939367

(b) (4)

Initial Approval	Date
Engineering Laurence Harris	8/02/00
Manufacturing Engineering	
Quality Assurance Craig Newton	8/01/00
Customer David Himes	3/21/01

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REPORT, SOFTWARE RISK ANALYSIS, TELLURIDE

Drawing Number
939340

(b) (4)

Initial Approval	Date
Engineering Lawrence Harris	6/08/00
Manufacturing Engineering	
Quality Assurance Craig Newton	6/08/00
Customer Kent Leyde	6/08/00

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Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

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SPECIFICATION, SOFTWARE REQUIREMENTS, TELLURIDE

Drawing Number
(b)(4)

(b) (4)

Initial Approval	Date
Engineering Lawrence Harris	6/8/00
Manufacturing Engineering	
Quality Assurance Craig Newton	6/8/00
Customer Kent Leyde	6/8/00

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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SPECIFICATION, PRODUCT REQUIREMENTS, TELLURIDE

Drawing Number
(b)(4)

(b) (4)

Initial Approval	Date
Engineering Allen Stueben	5/25/00
Manufacturing Engineering Jean Rempel	6/08/00
Quality Assurance Jon Olearain	5/25/00
Customer Kent Leyde	5/25/00

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Appendix 10 – Attachment F
Software Validation Report Clarification

(b)(4)

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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REPORT, SOFTWARE VERIFICATION & VALIDATION, TELLURIDE

Drawing Number
(b)(4)

(b) (4)

ORIGINAL

PREPRODUCTION

Initial Approval	Date
Engineering: Laurence Harris	3/28/2001
Manufacturing Engineering	
Quality Assurance: M E	3/29/01
Customer: P. Leonard	3/29/01

30

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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PROCEDURE, SOFTWARE VALIDATION TEST, TELLURIDE

Drawing Number
(b)(4)

(b) (4)

REFERENCE
MAR 13 2001
ONLY

ORIGINAL
PREPRODUCTION

Initial Approval	Date
Engineering Laurence Harris	3/13/01
Manufacturing Engineering	
Quality Assurance T. Reg	3/13/01

53

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

(b)(4) Test Data

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Drawing Number
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Initial Approval	Date
Engineering Laurence Harris	6/28/00
Manufacturing Engineering	
Quality Assurance Craig Newton	6/28/00
Customer Paul Leonard	3/15/01

245

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Drawing Number
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Initial Approval	Date
Engineering Laurence Harris	8/2/00
Manufacturing Engineering	
Quality Assurance Craig Newton	8/1/00
Customer	8/3/00

PREPRODUCTION
ORIGINAL

261

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Drawing Number
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Initial Approval	Date
Engineering Laurence Harris	3/13/01
Manufacturing Engineering	
Quality Assurance Peter Reid	3/13/01
Customer David Himes	3/28/01

203

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DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

AUG 2 9 2001

Lori J. Glastetter
Vice President, Regulatory Affairs/Quality Assurance
Vertis Neuroscience, Inc.
2101 Fourrth Avenue, Suite 200
Seattle, WA 98121-2329

Re: K011702
Vertis Percutaneous Neuromodulation Therapy (PNT™) Control Unit
Dated: May 31, 2001
Received: June 1, 2001

Dear Ms. Glastetter,

We have reviewed your Section 510(k) notification of intent to market the device referenced above and have determined that your submission has major deficiencies. We, therefore, cannot determine if the device is substantially equivalent to a device marketed before May 28, 1976, the enactment date of the Medical Device Amendments, based solely on the information you provided. Because of the significance of the deficiencies identified below, we believe that you cannot adequately respond in 30 days as required by 21 CFR 807.87(l). Therefore, we now consider your premarket notification to be withdrawn and your submission deleted from our system. If you submit the information requested below it will be considered and processed as a new 510(k). All information previously submitted must be resubmitted so that your new 510(k) is complete.

Although you have provided results from a clinical study using your device, due to significant study design flaws, conclusions cannot be drawn with respect to the safety and effectiveness of your device as compared to legally marketed predicate devices. Particularly, the study's design did not attempt to compare the new device to a legally marketed predicate device and did not attempt to differentiate between the device effect and placebo/sham effect, i.e., a sham control was not used. Therefore, you should perform a new clinical study to determine whether your device is as safe and effective as legally marketed predicate devices. We recommend performing a study that directly compares the Vertis PNT device to a legally marketed predicate device to which you are claiming equivalence (e.g., a legally marketed TENS device with surface electrodes) and/or to a sham control. Prior to conducting a future study, we highly recommend that you contact us to discuss your study protocol. The following information should be considered in a new study protocol:

(b) (4)

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

(b) (4)

The deficiencies identified above represent the issues that we believe need to be resolved before our review of your 510(k) submission can be successfully completed. In developing the deficiencies, we carefully considered the statutory criteria as defined in Section 513(i) of the Federal Food, Drug, and Cosmetic Act for determining substantial equivalence of your device. We also considered the burden that may be incurred in your attempt to respond to the deficiencies. We believe that we have considered the least burdensome approach to resolving these issues. If, however, you believe that information is being requested that is not relevant to the regulatory decision or that there is a less burdensome way to resolve the issues, you should follow the procedures outlined in the "A Suggested Approach to Resolving Least Burdensome Issues" document. It is available on our Center web page at: http://www.fda.gov/cdrh/modact/leastburdensome.html.

You may not market this device until you have received a letter from FDA allowing you to do so. If you market the device without conforming to this requirement you will be in violation of the Federal Food, Drug, and Cosmetic Act.

If you have questions concerning the contents of this letter, please contact Kristen A. Bowsher, Ph.D. at (301) 594-1296. If you need information or assistance concerning the Investigational Device Exemption regulations, please contact the Division of Small Manufacturers International and Consumer Assistance at its toll free number (800) 638-2041 or (301) 443-6597, or at its internet address "http://www.fda.gov/cdrh/dsma/dsmamain.html".

Sincerely yours,

for Mark N Melkerson

Celia M. Witten, Ph.D., M.D.
Director
Division of General, Restorative,
and Neurological Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

AUG 2 9 2001

Lori J. Glastetter
Vice President, Regulatory Affairs/Quality Assurance
Vertis Neuroscience, Inc.
2101 Fourrth Avenue, Suite 200
Seattle, WA 98121-2329

Re: K011702
Vertis Percutaneous Neuromodulation Therapy (PNT™) Control Unit
Dated: May 31, 2001
Received: June 1, 2001

Dear Ms. Glastetter,

We have reviewed your Section 510(k) notification of intent to market the device referenced above and have determined that your submission has major deficiencies. We, therefore, cannot determine if the device is substantially equivalent to a device marketed before May 28, 1976, the enactment date of the Medical Device Amendments, based solely on the information you provided. Because of the significance of the deficiencies identified below, we believe that you cannot adequately respond in 30 days as required by 21 CFR 807.87(l). Therefore, we now consider your premarket notification to be withdrawn and your submission deleted from our system. If you submit the information requested below it will be considered and processed as a new 510(k). All information previously submitted must be resubmitted so that your new 510(k) is complete.

Although you have provided results from a clinical study using your device, due to significant study design flaws, conclusions cannot be drawn with respect to the safety and effectiveness of your device as compared to legally marketed predicate devices. Particularly, the study's design did not attempt to compare the new device to a legally marketed predicate device and did not attempt to differentiate between the device effect and placebo/sham effect, i.e., a sham control was not used. Therefore, you should perform a new clinical study to determine whether your device is as safe and effective as legally marketed predicate devices. We recommend performing a study that directly compares the Vertis PNT device to a legally marketed predicate device to which you are claiming equivalence (e.g., a legally marketed TENS device with surface electrodes) and/or to a sham control. Prior to conducting a future study, we highly recommend that you contact us to discuss your study protocol. The following information should be considered in a new study protocol:

(b) (4)



3

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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(b) (4)

[redacted]

The deficiencies identified above represent the issues that we believe need to be resolved before our review of your 510(k) submission can be successfully completed. In developing the deficiencies, we carefully considered the statutory criteria as defined in Section 513(i) of the Federal Food, Drug, and Cosmetic Act for determining substantial equivalence of your device. We also considered the burden that may be incurred in your attempt to respond to the deficiencies. We believe that we have considered the least burdensome approach to resolving these issues. If, however, you believe that information is being requested that is not relevant to the regulatory decision or that there is a less burdensome way to resolve the issues, you should follow the procedures outlined in the "A Suggested Approach to Resolving Least Burdensome Issues" document. It is available on our Center web page at: http://www.fda.gov/cdrh/modact/leastburdensome.html.

You may not market this device until you have received a letter from FDA allowing you to do so. If you market the device without conforming to this requirement you will be in violation of the Federal Food, Drug, and Cosmetic Act.

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Sincerely yours,

Celia M. Witten, Ph.D., M.D.
Director
Division of General, Restorative,
and Neurological Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

FILE COPY

OFFICE	SURNAME	DATE	OFFICE	SURNAME	DATE	OFFICE	SURNAME	DATE
410		8/27/04						
410	Stevens	8/27/04						
410		8/28/04						

☆ U.S. GOVERNMENT PRINTING OFFICE 1991-519-771

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

4

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cc: DMC (HFZ-401)
510(k) Staff (HFZ-404)
DGRND (HFZ-410)
District Office (D.O.)

KXB: 8-27-01

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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DEPARTMENT OF HEALTH & HUMAN SERVICES — Public Health Service
Food and Drug Administration

Memorandum

From: Reviewer(s) - Name(s) KRISTEN BOWSHER

Subject: 510(k) Number K011702

To: The Record - It is my recommendation that the subject 510(k) Notification:

- ☐ Refused to accept.
- ☐ Requires additional information (other than refuse to accept).
- ☐ Is substantially equivalent to marketed devices.
- ☐ NOT substantially equivalent to marketed devices.
  - De Novo Classification Candidate? ☐ YES ☐ NO
- ☒ Other (e.g., exempt by regulation, not a device, duplicate, etc.) CANNOT RESPOND-30DAYS

Is this device subject to Postmarket Surveillance?	☐ YES	☒ NO
Is this device subject to the Tracking Regulation?	☐ YES	☒ NO
Was clinical data necessary to support the review of this 510(k)?	☒ YES	☐ NO
Is this a prescription device?	☒ YES	☐ NO
Was this 510(k) reviewed by a Third Party?	☐ YES	☒ NO
Special 510(k)?	☐ YES	☒ NO
Abbreviated 510(k)? Please fill out form on H Drive 510k/boilers	☒ YES	☒ NO

This 510(k) contains:

Truthful and Accurate Statement ☐ Requested ☒ Enclosed
(required for originals received 3-14-95 and after)

☒ A 510(k) summary OR ☐ A 510(k) statement

N/A ☐ The required certification and summary for class III devices

☒ The indication for use form (required for originals received 1-1-96 and after)

Material of Biological Origin ☐ YES ☐ NO

The submitter requests under 21 CFR 807.95 (doesn't apply for SEs):

☐ No Confidentiality ☐ Confidentiality for 90 days ☐ Continued Confidentiality exceeding 90 days

Predicate Product Code with class: Additional Product Code(s) with panel (optional):

Review: [signature] (Branch Chief) RE DB (Branch Code) 8/27/01 (Date)

Final Review: Mark N Melkerson (Division Director) 8/28/01 (Date)

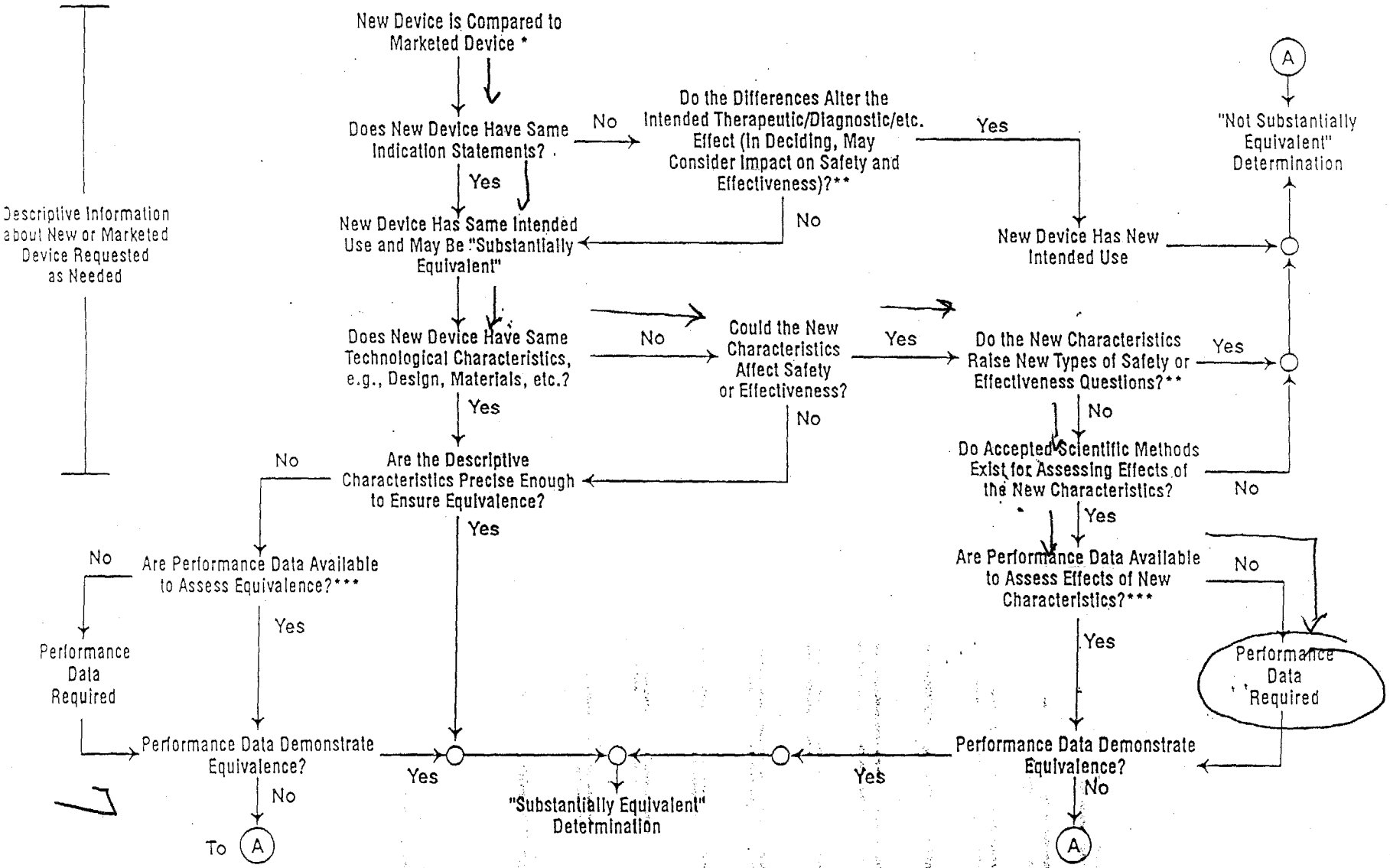
Revised:8/17//99

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

6

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510(k) "Substantial Equivalence" Decision-Making Process (Detailed)



* 510(k) Submiss... Compare New Devices to Marketed Devices. FDA Requests Additional Infor... If the Relationship Between Marketed and Predicate (Pre-Amendments or Reclassified Post-Amendments) Devices is Unclear.

** This Decisio... Normally Based on Descriptive Information Alone, But Limited Te... formation is Sometimes Required.

*** Data May Be ...e 510(k), Other 510(k)s, The Center's Classification Files, or the Literature.

Questions? Contact FDA/CDRH/OCE/DDI at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Screening Checklist
For all Premarket Notification 510(k) Submissions

3-30-01

Device Name:	K
Submitter (Company):	

Items which should be included *(circle missing & needed information)*	SPECIAL YES	SPECIAL NO	ABBREVIATED YES	ABBREVIATED NO	TRADITIONAL YES	TRADITIONAL NO	✓ IF ITEM IS NEEDED AND IS MISSING
1. Cover Letter clearly identifies Submission as: a) "Special 510(k): Device Modification" b) "Abbreviated 510(k)" c) Traditional 510(k)	GO TO # 2,3		GO TO # 2,4,5		GO TO #2, 5		

2. GENERAL INFORMATION: REQUIRED IN ALL 510(K) SUBMISSIONS	NA SPECIALS YES	NA SPECIALS NO	YES ABBREVIATED YES	YES ABBREVIATED NO	NO TRADITIONAL YES	NO TRADITIONAL NO	✓ IF ITEM IS NEEDED AND IS MISSING
Financial Certification or Disclosure Statement for 510(k)s with a Clinical Study 807.87(i) including forms 3454 and/or 3455							
a) trade name, classification name, establishment registration number, device class							
b) OR a statement that the device is not yet classified	FDA-may be a classification request; see coordinator						
c) identification of legally marketed equivalent device	NA						
d) compliance with Section 514 - performance standards	NA						
e) address of manufacturer							
f) Truthful and Accurate Statement							
g) Indications for Use enclosure							
h) SMDA Summary or Statement *(FOR ALL DEVICE CLASSES)*							
i) Class III Certification & Summary *(FOR ALL CLASS III DEVICES)*							
j) Description of device (or modification) including diagrams, engineering drawings, photographs, service manuals							
k) Proposed Labeling:							
i) package labeling (user info)							
ii) statement of intended use							
iii) advertisements or promotional materials							
i) MRI compatibility (if claimed)							
l) Comparison Information (similarities and differences) to named legally marketed equivalent device (table preferred) should include:							
i) Labeling							
ii) intended use							
iii) physical characteristics							
iv) anatomical sites of use							
v) performance (bench, animal, clinical) testing	NA						
vi) safety characteristics	NA						
m) If kit, kit certification							

3. "SPECIALS" - ONLY FOR MODIFICATIONS TO MANUFACTURER'S OWN CLASS II , III OR RESERVED CLASS I DEVICE				
a) Name & 510(k) number of legally marketed (unmodified) predicate device				
b) ***STATEMENT - INTENDED USE AND INDICATIONS FOR USE OF MODIFIED DEVICE AS DESCRIBED IN ITS***			* If no - STOP not a special	

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	LABELING HAVE NOT CHANGED*			
c)	***STATEMENT - FUNDAMENTAL SCIENTIFIC TECHNOLOGY OF THE MODIFIED DEVICE HAS NOT CHANGED****		* If no - STOP not a special	
d)	Design Control Activities Summary			
	i) Identification of Risk Analysis method(s) used to assess the impact of the modification on the device and its components, and the results of the analysis			
	ii) Based on the Risk Analysis, an identification of the verification and/or validation activities required, including methods or tests used and acceptance criteria to be applied			
	iii) A declaration of conformity with design controls. The declaration of conformity should include:			
	1) A statement signed by the individual responsible, that, as required by the risk analysis, all verification and validation activities were performed by the designated individual(s) and the results demonstrated that the predetermined acceptance criteria were met			
	2) A statement signed by the individual responsible, that manufacturing facility is in conformance with design control procedure Requirements as specified in 21 CFR 820.30 and the records are available for review.			

	SPECIALS		ABBREVIATED		TRADITIONAL		✓ IF ITEM IS NEEDED AND IS MISSING
	YES	NO	YES	NO	YES	NO	
4. ABBREVIATED 510(K): SPECIAL CONTROLS/CONFORMANCE TO RECOGNIZED STANDARDS - PLEASE FILL OUT THE STANDARDS ABBREVIATED FORM ON THE H DRIVE							
a) For a submission, which relies on a guidance document and/or special control(s), a summary report that describes how the guidance and/or special control(s) was used to address the risks associated with the particular device type							
b) If a manufacturer elects to use an alternate approach to address a particular risk, sufficient detail should be provided to justify that approach.							
c) For a submission, which relies on a recognized standard, a declaration of conformity to the standard. The declaration should include the following:							
i) An identification of the applicable recognized consensus standards that were met							
ii) A specification, for each consensus standard, that all requirements were met, except for inapplicable requirements or deviations noted below							
iii) An identification, for each consensus standard, of							

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any way(s) in which the standard may have been adapted for application to the device under review, e.g., an identification of an alternative series of tests that were performed						
iv) An identification, for each consensus standard, of any requirements that were not applicable to the device						
v) A specification of any deviations from each applicable standard that were applied						
vi) A specification of the differences that may exist, if any, between the tested device and the device to be marketed and a justification of the test results in these areas of difference						
vii) Name/address of test laboratory/certification body involved in determining the conformance of the device with applicable consensus standards and a reference to any accreditations for those organizations						
d) Data/information to address issues not covered by guidance documents, special controls, and/or recognized standards						

5. Additional Considerations: (may be covered by Design Controls)							
a) Biocompatibility data for all patient-contacting materials, OR certification of identical material/formulation:							
i) component & material							
ii) identify patient-contacting materials							
iii) biocompatibility of final sterilized product							
b) Sterilization and expiration dating information:							
i) sterilization method							
ii) SAL							
iii) packaging							
iv) specify pyrogen free							
v) ETO residues							
vi) radiation dose							
c) Software validation & verification:							
i) hazard analysis							
ii) level of concern							
iii) development documentation							
iv) certification							

Items shaded under "NO" are necessary for that type of submission. Circled items and items with checks in the "Needed & Missing" column must be submitted before acceptance of the document.

Passed Screening ✓ **Yes** ____ **No** **Reviewer:** Kristen Boam

Date: 8-1-01 **Concurrence by Review Branch:** ____

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REVISED:3/14/95

THE 510(K) DOCUMENTATION FORMS ARE AVAILABLE ON THE LAN UNDER 510(K) BOILERPLATES TITLED "DOCUMENTATION" AND MUST BE FILLED OUT WITH EVERY FINAL DECISION (SE, NSE, NOT A DEVICE, ETC.).

"SUBSTANTIAL EQUIVALENCE" (SE) DECISION MAKING DOCUMENTATION

K 011702

Reviewer: KRISTEN BOWSHER

Division/Branch: DGRND /REDB

Device Name: VERTIS PNT

Product To Which Compared (510(K) Number If Known): _____

	YES	NO	
1. Is Product A Device	✓		If NO = Stop
2. Is Device Subject To 510(k)?	✓		If NO = Stop
3. Same Indication Statement?	✓		If YES = Go To 5
4. Do Differences Alter The Effect Or Raise New Issues of Safety Or Effectiveness?			If YES = Stop NE
5. Same Technological Characteristics?		✓	If YES = Go To 7
6. Could The New Characteristics Affect Safety Or Effectiveness?	✓		If YES = Go To 8
7. Descriptive Characteristics Precise Enough?			If NO = Go To 10 If YES = Stop SE
8. New Types Of Safety Or Effectiveness Questions?		✓	If YES = Stop NE
9. Accepted Scientific Methods Exist?	✓		If NO = Stop NE
10. Performance Data Available?		✓	If NO = Request Data
11. Data Demonstrate Equivalence?			Final Decision:

Note: In addition to completing the form on the LAN, "yes" responses to questions 4, 6, 8, and 11, and every "no" response requires an explanation.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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See reviews dated 8/23/01
8/2/01
7/11/01

1. Intended Use:

2. Device Description: Provide a statement of how the device is either similar to and/or different from other marketed devices, plus data (if necessary) to support the statement. Is the device life-supporting or life sustaining? Is the device implanted (short-term or long-term)? Does the device design use software? Is the device sterile? Is the device for single use? Is the device over-the-counter or prescription use? Does the device contain drug or biological product as a component? Is this device a kit? Provide a summary about the devices design, materials, physical properties and toxicology profile if important.

EXPLANATIONS TO "YES" AND "NO" ANSWERS TO QUESTIONS ON PAGE 1 AS NEEDED

1. Explain why not a device:

2. Explain why not subject to 510(k):

3. How does the new indication differ from the predicate device's indication:

4. Explain why there is or is not a new effect or safety or effectiveness issue:

5. Describe the new technological characteristics:

6. Explain how new characteristics could or could not affect safety or effectiveness:

7. Explain how descriptive characteristics are not precise enough:

8. Explain new types of safety or effectiveness questions raised or why the questions are not new:

9. Explain why existing scientific methods can not be used:

10. Explain what performance data is needed:

11. Explain how the performance data demonstrates that the device is or is not substantially equivalent:

ATTACH ADDITIONAL SUPPORTING INFORMATION

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Internal Administrative Form

	YES	NO
1. Did the firm request expedited review?		✓
2. Did we grant expedited review?		✓
3. Have you verified that the Document is labeled Class III for GMP purposes? N/A		
4. If, not, has POS been notified?	✓	
5. Is the product a device?		
6. Is the device exempt from 510(k) by regulation or policy?		✓
7. Is the device subject to review by CDRH?	✓	
8. Are you aware that this device has been the subject of a previous NSE decision?		✓
9. If yes, does this new 510(k) address the NSE issue(s), (e.g., performance data)?		
10. Are you aware of the submitter being the subject of an integrity investigation?		✓
11. If, yes, consult the ODE Integrity Officer.		
12. Has the ODE Integrity Officer given permission to proceed with the review? (Blue Book Memo #I91-2 and Federal Register 90N0332, September 10, 1991.		

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510(k) MEMO

DATE: 8-23-01

FROM: Kristen A. Bowsher, Ph.D., Biomedical and Electrical Engineer KAB
ODE/DGRD/REDB

SUBJECTS: Vertis Neuroscience, Inc. – Percutaneous Neuromodulation Therapy (PNT) Control Unit and Accessories

TO: K011702

Please also review to the attached clinical data review dated August 2, 2001 by Marie A. Schroeder, MS, PT (clinical reviewer, DGRND) and statistical review by Harry Bushar, Ph.D. dated in an email July 11, 2001.

Intended Use
Percutaneous Neuromodulation Therapy (PNT) is indicated for the symptomatic relief and management of chronic, intractable pain and/or as an adjunctive treatment in the management of post-surgical and post-trauma acute pain.

In the "Nerve Stimulator (Control Unit) Comparison Chart" in Appendix 16 the sponsor lists the following as examples of therapy applications for this device: low back pain, cervical pain, thoracic pain, sciatica, shingles (zoster), diabetic neuropathy, headache, and other neuropathies.

Device Description
The Vertis PNT System is designed for delivering percutaneous electrical stimulation (termed: Percutaneous Neuromodulation Therapy - PNT). The device system includes three (3) components:

- the *Vertis PNT Control Unit* - a software-driven, five channel, AC-powered nerve stimulator which generates the electrical stimulus;
- the sterile *Safe guides* — which are sterile, needle electrodes, and
- the *Patient Cable* - which interconnects the PNT Control Unit to the electrodes

The Patient Cables and Safeguide electrodes are provided separately from the Vertis PNT Control Unit; Instructions for Use are provided with these separate accessories.

PNT Control Unit
The device user activates the PNT Control Unit by plugging the device into wall (AC) power and by pressing the on/off switch on the Control Unit's back panel. Both the power cord and the patient cables plug into the AC power cord receptacle and the patient cable receptacle, respectively, on the Control Unit's back panel. When connected with the Patient Cable and Electrodes to a patient, the PNT Control Unit uses text prompts on the device's LCD screen that allows the clinician to:

- Select from a variety of electrical stimulation modes (e.g., 4 Hz, 15/30 Hz, etc.).
- Set the treatment duration (e.g., 30 minutes)

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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- Set the stimulus intensity individually for each of the 5 electrode channels. The device's LCD screen graphically shows these individual stimulation channels using indicator bars
- Initiate delivery of percutaneous electrical stimulation
- Record the progress and completion of therapy (e.g., minutes in session).

	Vertis PNT System
Output Waveform	Charge-balanced, rectangular, biphasic
Pulse Width (μs)	200
Amplitude (mA) @ 500 Ω	15
Frequency (Hz)	4 – 50
Max. Charge/Pulse (μC)	7.2
# of Channels	5

Electrodes

The Safeguide electrodes are supplied as disposable, single use, sterile electrode kits offered in various pack/multi pack configurations (example: 1 pack electrode, 6 pack of electrode kits, etc.). **For device user ease of use and convenience, electrode kits may also be provided as clinical application specific (e.g., a lumbar kit, a cervical kit, etc.).** There are up to 10 Safeguide electrodes in each sterile electrode kit.

Each individual Safeguide electrode assembly is a very small (approximately 1.6" (height) x 0.9" (diameter) cylindrical electrode housing/configuration that has an adhesive patch (approximately 1.8" diameter) attached to its base. The cylinder area of the electrode assembly functions as a sharp-safe housing and contains an extremely fine (0.25 mm diameter) stainless steel needle electrode and range from 0.5 - 3.0 centimeters in length.. The adhesive patch attached to the base of the Safeguide allows for adherence of the electrode assembly to the patient's skin.

The components and materials of the Safeguide electrode are all commonly used medical device materials and are summarized in the following table:

Safeguide component	**Material info**
Electrode (needle)	(b)(4)
Adhesive foam disc (patch) - adhered onto electrode housing base	
Electrode housing — base, slider and retainer	
Electrode housing -sleeve	

In comparison to other percutaneous electrodes, a unique feature of the Safeguide product is the containment of the needle electrode within a protective housing both before and after electrode use. Vertis

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chose to specifically contain the needle of the Safeguide in this sharp-safe design configuration to mitigate the risk of accidental needle-stick injuries that have occurred with other unprotected needles, electrodes, or similar sharps.

The electrodes are provided as a sterile, disposable kit and are intended and labeled for single patient use only (not reusable). The electrodes are packaged in a polystrene tray with tyvek/paper lid. The tray is heat sealed using conventional platen heat sealing technology.

Predicate Devices
The sponsor is claiming substantial equivalence to the following devices:

For the Vertis PNS Control Unit:

- TENS for pain relief (21 CFR 882.5890, GZJ)
- Implanted peripheral nerve stimulator for pain relief (21 CFR 882.5870, GZB)
- Implanted spinal cord stimulator for pain relief (21 CFR 882.5880, GZB)
- Interferential current therapy device for pain relief (unclassified, LIH)

For the percutaneous electrodes:

- Needle electrodes (21 CFR 882.1350, GXZ)
- Electromyograph needle electrodes (21 CFR 890.1385)
- Cutaneous electrodes (21 CFR 882.1320, GXY)
- Implanted peripheral nerve stimulator for pain relief (21 CFR 882.5870, GZB)

Comments
The sponsor is requesting the same indication as for legally marketed TENS devices. The output parameters are similar to those of legally marketed TENS devices but the big difference is that the electrodes for this device are percutaneous. We are not aware of any legally marketed TENS devices with percutaneous electrodes. However, we have cleared through 510(k) electrodes that are placed into the body: Implanted peripheral nerve stimulator for pain relief (21 CFR 882.5870, GZB), Implanted spinal cord stimulator for pain relief (21 CFR 882.5880, GZB) and needle electrodes for EEG recording and stimulating and electromyography. The percutaneous needles used with the Vertis PNS system are only in for the length of a single treatment and are not left in place for a duration of time after or between treatments. This limits the added risk of infection.

In an internal meeting regarding this application on August 2, 2001 a discussion as to whether a 510(k) application was appropriate for this device. Mark Melkerson (Deputy Director, DGRND) determined that this was an appropriate route to market for this device. However, clinical data needs to be provided supporting the safety and effectiveness of this device in relieving pain.

Clinical Data
The sponsor has provided results of a study with use of the Vertis PNS System on patients with low back pain. Refer to the attached clinical and statistical reviews.

Comments
The clinical data provided was not sufficient in demonstrating the safety and effectiveness of this device. This was mainly due to significant study design flaws (as mentioned in attached clinical review) which did not allow for a proper analysis of the safety and effectiveness of the device.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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A meeting was held on August 16, 2001 to decide what type of letter should be sent to the sponsor. Attendees included: Kristen Bowsher, Ph.D. (Lead Reviewer, DGRND/REDB), Marie A. Schroeder, MS, PT (clinical reviewer, DGRND), Ted Stevens (Branch Chief, DGRND/REDB) and Mark Melkerson (Deputy Director, DGRND). It was determined that, since the study design itself was flawed and it could not be determined whether the device was effective or not, a Cannot Respond in 30 Days letter should be sent to the sponsor requesting additional clinical data in the form of a new study.

The clinical study results provided only studied low back pain patients. However, the sponsor is requesting use of this device for other unknown specific indications as demonstrated by the statement on page 10 of the application that, "For device user ease of use and convenience, electrode kits may also be provided as clinical application specific (e.g., a lumbar kit, a cervical kit, etc.)." Additionally, as noted previously in this review in the "Nerve Stimulator (Control Unit) Comparison Chart" in Appendix 16 the sponsor lists the following as examples of therapy applications for this device: low back pain, cervical pain, thoracic pain, sciatica, shingles (zoster), diabetic neuropathy, headache, and other neuropathies. It should be noted to the sponsor that clinical data supporting the use of the device for specific indications would be required.

RECOMMENDATION

(b) (4)



Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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(b) (4)



Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

MEMORANDUM

DATE August 2, 2001

FROM Director, Regulatory Review Officer, DGRND

SUBJECT K011702 – Vertis Percutaneous Neuromodulation Therapy (PNT)

TO Kristen Bowsher, Ph. D., Lead Reviewer, Electrical & Biomedical Engineer

Recommendation

Due to the significant study design flaws mentioned below, conclusions regarding the safety and effectiveness of this device can not be made. I have some concern that this device might actually caused more harm than benefit, since it may be that only 12.8% (5/39) of the patients had clinically meaningful benefit. I would have expected more patients to have clinically meaningful benefit from placebo alone. Note that the sponsor reports that **5** patients reported that they got ***a lot better*** from **massage** which is a non-invasive therapy (it's not clear what the denominator was for this massage group). Only **3** patients reported getting ***very much benefit*** and **2** patients reported ***much benefit*** from the Vertis PNT device. The background information was very well presented and appeared to support the feasibility of effectiveness for this device. However, because of the uncertainties mentioned below, it's hard to say for sure what happened in this trial.

Due to the apparent new design of the needle electrodes with a safety feature to minimize clinician sticks, this electrode design should be reviewed by General Hospital Devices Branch.

Scope of Review

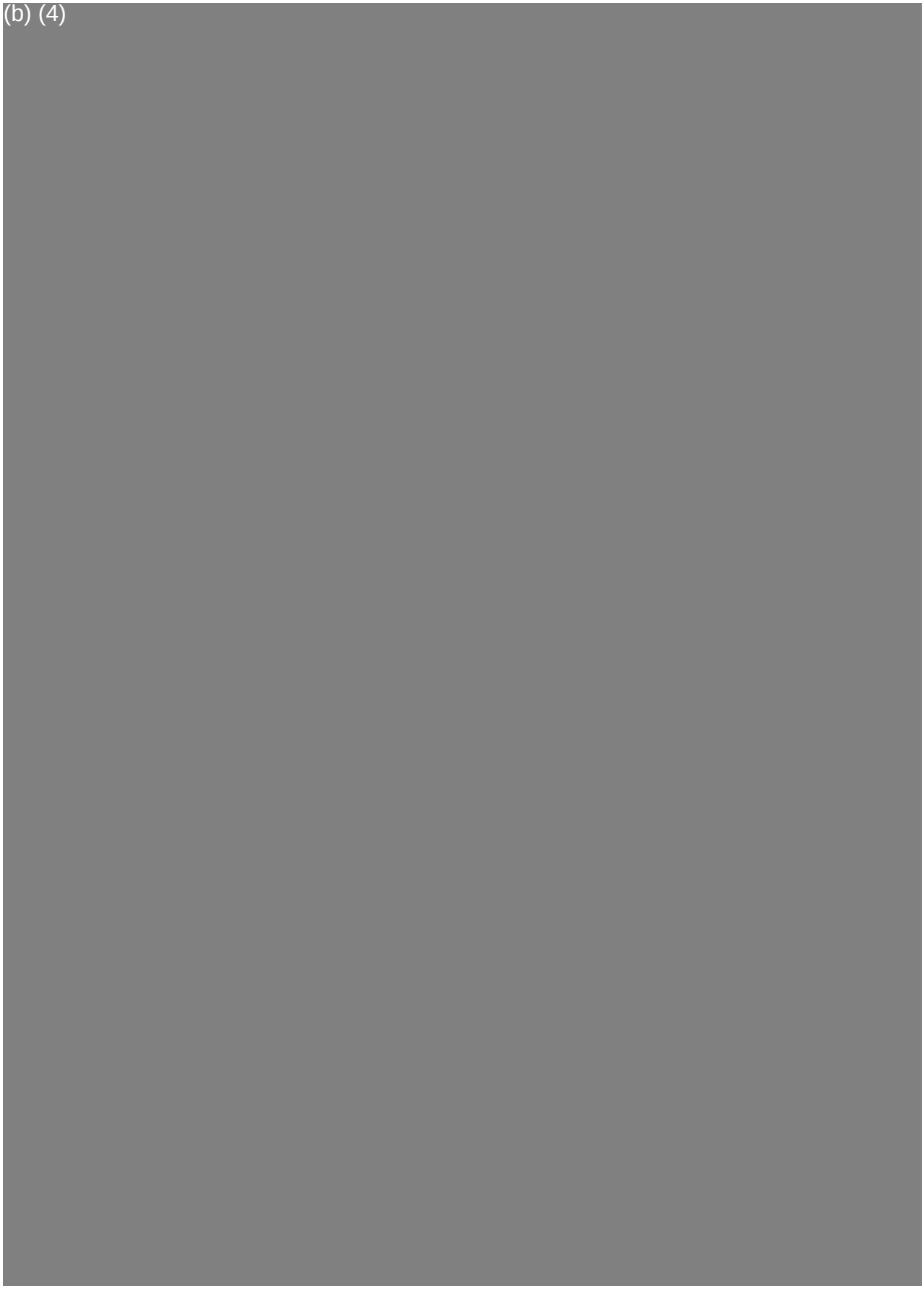
I reviewed Appendix 23, Appendix 24 and Attachment B of Appendix 24.

Comments

(b) (4)

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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(b) (4)

[redacted]

Future Considerations

Prior to conducting a future study, the sponsor should consider submitting a pre-IDE to FDA for comments. Future studies should eliminate the bias mentioned above. Validated and reliable assessment tools should be provided along with the validation data (e.g., peer reviewed literature may be provided). In order to support a general claim of reducing low back pain (LBP), sufficient numbers of patients should be studied in a sufficient number of subsets (with respect to etiology of LBP). Justification as to why the subsets included adequately support a general claim should be provided.

Premarketing applications should include case report forms and individual patient listings of data (actual scores and changes from baseline). The results should include the numbers and percentages of patients who passed unbiased success criteria as well as those who failed, e.g. worsening, no change and improvements should be reported. ITT analyses should be done as per our statistician's recommendation. Justification that the success criteria are clinically meaningful must also be provided.

The statistician was silent regarding the pooling, whether the p-value was appropriate in light of the 3 chances to succeed, and whether there were adequate numbers of patients in the subsets. In light of the most significant deficiencies, it is pointless to address these for this document. However, these issues should be addressed in a future application.

The Vertis PNT device has several modes/output signals. Data should support all output options. Likewise, if multiple body sites are to be treated, data should support multiple sites.

Marie A. Schroeder, MS, PT

Marie A. Schroeder, MS, PT

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

Schroeder, Marie
From: Bowsher, Kristen
Sent: Wednesday, July 11, 2001 11:05 AM
To: Schroeder, Marie
Subject: FW: Statistical Review of 510(k) K011702 for Vertis Neuroscience Percutaneous Neuromodulation Therapy (PNT) Nerve Stimulation System

FYI

-----Original Message-----
From: **Bushar, Harry F.**
Sent: Wednesday, July 11, 2001 9:12 AM
To: Bowsher, Kristen
Cc: Stevens, Ted; Witten, Celia; Campbell, Gregory; Barrick, Mary K.; Roberson, Helen W.
Subject: Statistical Review of 510(k) K011702 for Vertis Neuroscience Percutaneous Neuromodulation Therapy (PNT) Nerve Stimulation System

As requested, I have reviewed 510(k) K011702 for Vertis Neuroscience Percurtaneous Neuromodulation Therapy (PNT) Nerve Stimulation System, which "is indicated for the symptomatic relief and management of chronic, intractable pain and/or as an adjunctive treatment in the management of post-surgical and post-trauma acute pain". (See page 4.) The sponsor conducted a non-significant risk, prospective clinical trial by enrolling 39 patients with low back pain at 3 U.S. clinical sites from 11/00 through 3/01 to evaluate the safety and effectiveness of the Vertis PNT. (See Appendix 24, page 3.)

(b) (4)

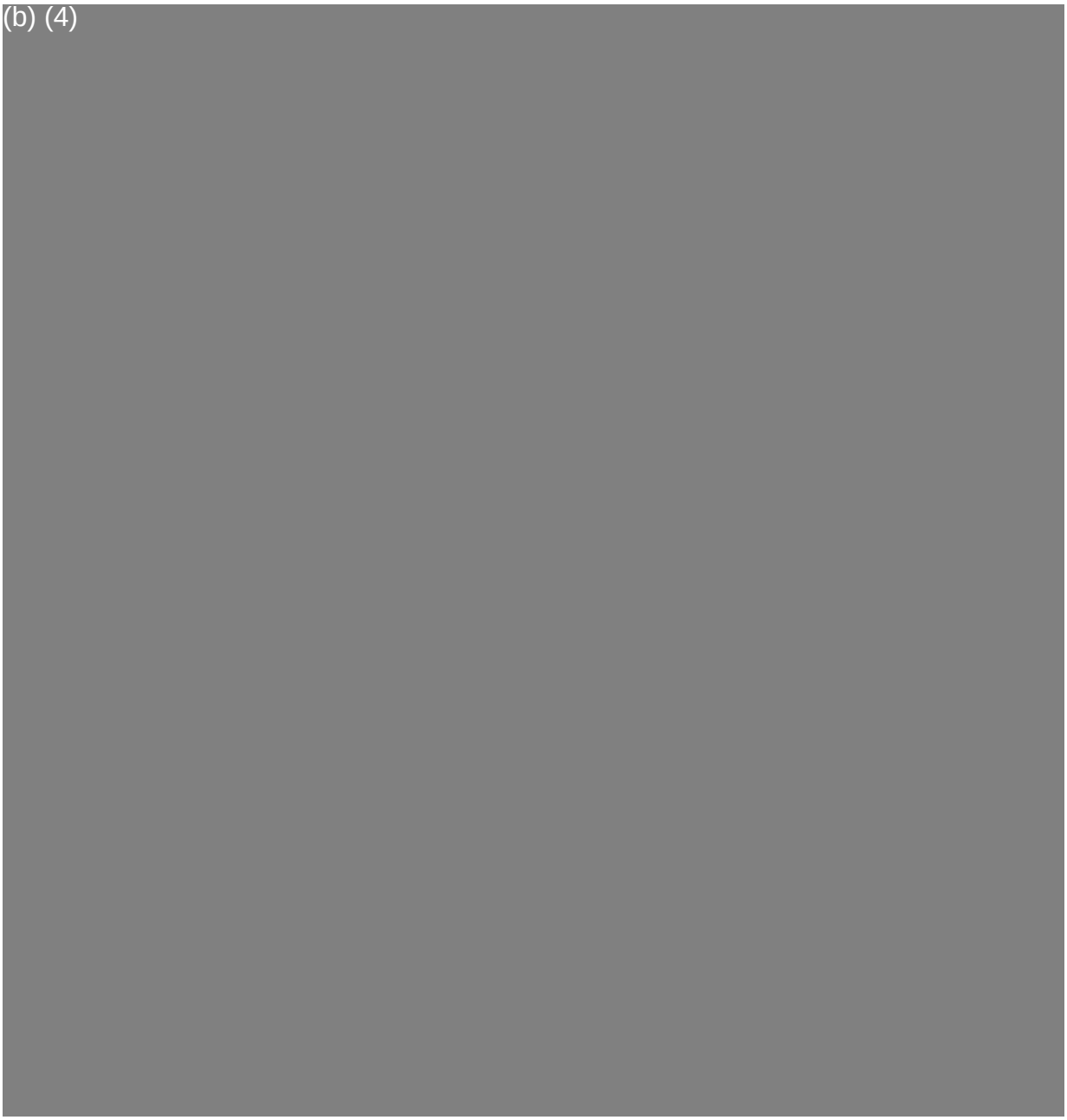


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Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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(b) (4)



Please contact me for any further review of this submission.

Harry F. Bushar, Ph.D.
Mathematical Statistician
Phone: (301) 827-4361
FAX: (301) 443-8559

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

DEPARTMENT OF HEALTH AND HUMAN SERVICES Public Health Service

Food and Drug Administration
Center for Devices and
Radiological Health
Office of Device Evaluation
Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, Maryland 20850

June 01, 2001

VERTIS NEUROSCIENCE INC.
2101 FOURTH AVE STE 200
SEATTLE, WA 98121
ATTN: LORI GLASTETTER

510(k) Number: K011702
Received: 01-JUN-2001
Product: VERTIS PNT CONTROL UNIT, VERTIS PNT SAFEGUIDE KIDS, MODELS CU100, SGXXX

The Center for Devices and Radiological Health (CDRH), Office of Device Evaluation (ODE), has received the Premarket Notification you submitted in accordance with Section 510(k) of the Federal Food, Drug, and Cosmetic Act (Act) for the above referenced product. We have assigned your submission a unique 510(k) number that is cited above. Please refer prominently to this 510(k) number in any future correspondence that relates to this submission. We will notify you when the processing of your premarket notification has been completed or if any additional information is required. YOU MAY NOT PLACE THIS DEVICE INTO COMMERCIAL DISTRIBUTION UNTIL YOU RECEIVE A LETTER FROM FDA ALLOWING YOU TO DO SO.

On January 1, 1996, FDA began requiring that all 510(k) submitters provide on a separate page and clearly marked "Indication For Use" the indication for use of their device. If you have not included this information on a separate page in your submission, please complete the attached and amend your 510(k) as soon as possible. Also if you have not included your 510(k) Summary or 510(k) Statement, or your Truthful and Accurate Statement, please do so as soon as possible. There may be other regulations or requirements affecting your device such as Postmarket Surveillance (Section 522(a)(1) of the Act) and the Device Tracking regulation (21 CFR Part 821). Please contact the Division of Small Manufacturers Assistance (DSMA) at the telephone or web site below for more information.

Please remember that all correspondence concerning your submission MUST be sent to the Document Mail Center (HFZ-401) at the above letterhead address. Correspondence sent to any address other than the Document Mail Center will not be considered as part of your official premarket notification submission. Because of equipment and personnel limitations, we cannot accept telefaxed material as part of your official premarket notification submission, unless specifically requested of you by an FDA official. Any telefaxed material must be followed by a hard copy to the Document Mail Center (HFZ-401).

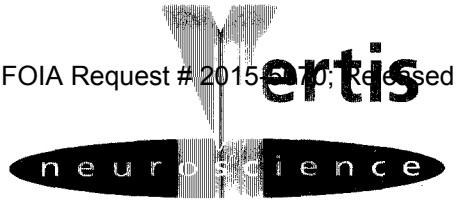
You should be familiar with the manual entitled, "Premarket Notification 510(k) Regulatory Requirements for Medical Devices" available from DSMA. If you have other procedural or policy questions, or want information on how to check on the status of your submission (after 90 days from the receipt date), please contact DSMA at (301) 443-6597 or its toll-free number (800) 638-2041, or at their Internet address http://www.fda.gov/cdrh/dsmamain.html or me at (301) 594-1190.

Sincerely yours,

Marjorie Shulman
Consumer Safety Officer
Premarket Notification Staff

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-2170; Released by CDRH on 09-10-2015



K011702

2101 Fourth Avenue, S[illegible] eattle, WA 98121-2329
Tel 206.728.1[illegible] 206.728.1497
www.[illegible]ro.com

May 31, 2001

Office of Device Evaluation
510(k) Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Blvd.
Rockville, MD 20850

Reference: **510(k) Notification for the Vertis Neuroscience, Inc. Nerve Stimulator, Electrodes and Accessories**

Attention: **Mr. Stephen M. Hinckley**

Dear Device Evaluation Staff:

In accordance with Section 510(k) of the Federal Food, Drug and Cosmetic Act and subsequent Amendments, Vertis Neuroscience, Inc. (Vertis), hereby notifies the Food and Drug Administration of its intention to introduce new products into interstate commerce for commercial distribution on or after issuance of an order of substantial equivalence.

It is Vertis' intention to market nerve stimulators, electrodes and other accessories under the product name of Vertis *Percutaneous Neuromodulation Therapy (PNT)* ™ *Control Unit* and Accessories.

Devices of this generic type have been previously reviewed by the General, Restorative and Neurological Device panels. Regarding this product, Vertis has worked over the past years with Office of Device Evaluation staff member, Mr. Stephen M. Hinckley. Accordingly, as he is knowledgeable regarding this product, we respectfully request that this Notification be forwarded to Mr. Hinckley's attention.

For the convenience of the FDA Document Mail Center and Device Evaluation staffs, Vertis has enclosed (at the front of this binder) the CDRH Premarket Submission Cover Sheet to aid FDA in the rapid processing of this Notification.

NE
II
5K27

25

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

The following information is provided in accordance to 21 CFR 807. Based on the information provided and the supporting Attachments, we believe the Vertis *PNT™ Control Unit* and Accessories to be substantially equivalent to devices in commercial distribution prior to May 28, 1976.

Statement of Confidentiality

The information provided in this Notification is considered by Vertis Neuroscience, Inc. to be confidential information as it relates to our intention to market this product in the future. We have not, to our knowledge, released this information through advertising or any other manner to anyone outside the employ of, or under contract to, Vertis Neuroscience, Inc. Vertis has taken precautions to protect the confidentiality of this information under Section 21CFR 807.95, Confidentiality of Information. We ask that this Notification be treated as confidential in accordance with the Freedom of Information Act.

Should you require any additional information or have any questions regarding this Notification, please do not hesitate to contact me at (206) 902-1902. Your attention to this Notification is sincerely appreciated.

Sincerely,

Lori J. Glastetter
Vice President, Regulatory Affairs/Quality Assurance
Vertis Neuroscience, Inc.

Vertis PNT is a trademark of Vertis Neuroscience, Inc.

CONFIDENTIAL
Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

CDRH SUBMISSION COVER SHEET

Date of Submission: **May 31, 2001** FDA Document Number:

Section A Type of Submission

PMA
- ☐ Original submission
- ☐ Modular submission
- ☐ Amendment
- ☐ Report
- ☐ Report Amendment

PMA Supplement
- ☐ Regular
- ☐ Special
- ☐ Panel Track
- ☐ 30-day Supplement
- ☐ 30-day Notice
- ☐ 135-day Supplement
- ☐ Real-time Review
- ☐ Amendment to PMA Supplement

PDP
- ☐ Presubmission summary
- ☐ Original PDP
- ☐ Notice of intent to start clinical trials
- ☐ Intention to submit Notice of Completion
- ☐ Notice of Completion
- ☐ Amendment to PDP
- ☐ Report

510(k)
- ☒ Original submission:
  - ☒ Traditional
  - ☐ Special
  - ☐ Abbreviated
- ☐ Additional information:
  - ☐ Traditional
  - ☐ Special
  - ☐ Abbreviated

Meeting
- ☐ Pre-IDE meeting
- ☐ Pre-PMA meeting
- ☐ Pre-PDP meeting
- ☐ 180-day meeting
- ☐ Other (specify):

IDE
- ☐ Original submission
- ☐ Amendment
- ☐ Supplement

Humanitarian Device Exemption
- ☐ Original submission
- ☐ Amendment
- ☐ Supplement
- ☐ Report

Class II Exemption
- ☐ Original submission
- ☐ Additional information

Evaluation of Automatic Class III Designation
- ☐ Original submission
- ☐ Additional information

Other Submission

Describe submission:

Section B Applicant or Sponsor

Company/Institution name: **Vertis Neuroscience, Inc.** Establishment registration number: **Not Yet Assigned**

Division name (if applicable): **N/A** Phone number (include area code): **(206) 902-1902**

Street address: **2101 Fourth Avenue, Suite 200** FAX number (include area code): **(206) 728-1497**

City: **Seattle** State/Province: **WA** Country: **USA**

Contact name: **Lori Glastetter**

Contact title: **Vice President, RA/QA** Contact e-mail address: **lglastetter@vertisneuro.com**

Section C Submission correspondent (if different from above)

Company/Institution name: **Same as above** Establishment registration number:

Division name (if applicable): Phone number (include area code): ( )

Street address: FAX number (include area code): ( )

City: State/Province: Country:

Contact name:

Contact title: Contact e-mail address:

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

Section D1 Reason for Submission—PMA, PDP, or HDE

- ☐ New device
- ☐ Withdrawal
- ☐ Additional or expanded indications
- ☐ Licensing agreement
- ☐ Process change
  - ☐ Manufacturing
  - ☐ Sterilization
  - ☐ Packaging
  - ☐ Other (specify below)
- ☐ Response to FDA correspondence:
  - ☐ Request for applicant hold
  - ☐ Request for removal of applicant hold
  - ☐ Request for extension
  - ☐ Request to remove or add manufacturing site
- ☐ Other reason (specify):
- ☐ Change in design, component, or specification:
  - ☐ Software
- ☐ Color Additive
  - ☐ Material
  - ☐ Specifications
- ☐ Other (specify below)
- ☐ Labeling change:
  - ☐ Indications
  - ☐ Instructions
  - ☐ Performance Characteristics
- ☐ Shelf life
- ☐ Trade name
- ☐ Other (specify below)
- ☐ Location change:
  - ☐ Manufacturer
  - ☐ Sterilizer
  - ☐ Packager
  - ☐ Distributor
- ☐ Report submission:
  - ☐ Annual or periodic
  - ☐ Post-approval study
  - ☐ Adverse reaction
- ☐ Device defect
- ☐ Amendment
- ☐ Change in ownership
  - ☐ Change in correspondent

Section D2 Reason for Submission—IDE

- ☐ New device
- ☐ Addition of institution
- ☐ Expansion / extension of study
- ☐ IRB certification
- ☐ Request hearing
- ☐ Request waiver
- ☐ Termination of study
- ☐ Withdrawal of application
- ☐ Unanticipated adverse effect
- ☐ Notification of emergency use
- ☐ Compassionate use request
- ☐ Treatment IDE
- ☐ Continuing availability request
- ☐ Other reason (specify):
- ☐ Change in:
  - ☐ Correspondent
  - ☐ Design
  - ☐ Informed consent
  - ☐ Manufacturer
  - ☐ Manufacturing process
  - ☐ Protocol – feasibility
  - ☐ Protocol – other
  - ☐ Sponsor
- ☐ Report submission:
  - ☐ Current investigator
  - ☐ Annual progress
  - ☐ Site waiver limit reached
  - ☐ Final
- ☐ Response to FDA letter concerning:
  - ☐ Conditional approval
  - ☐ Deemed approved
  - ☐ Deficient final report
  - ☐ Deficient progress report
  - ☐ Deficient investigator report
  - ☐ Disapproval
  - ☐ Request extension of time to respond to FDA
  - ☐ Request meeting

Section D3 Reason for Submission—510(k)

- ☒ New device
- ☐ Additional or expanded indications
- ☐ Other reason (specify):
- ☐ Change in technology
- ☐ Change in design
- ☐ Change in materials
- ☐ Change in manufacturing process

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

Section E Additional Information on 510(k) Submissions

Product codes of devices to which substantial equivalence is claimed:

1 **GZJ**	2 **GZF**	3 **GZB**	4 **LIH**
5 **GXZ**	6 **IKT**	7 **GXY**	8

Summary of, or statement concerning, safety and effectiveness data:
- ☒ 510(k) summary attached
- ☐ 510(k) statement

Information on devices to which substantial equivalence is claimed:

	510(k) Number	Trade or proprietary or model name	Manufacturer
1	**K970203 K951903**	1 **EPIX TENS Device System**	1 **Empi, Inc.**
2	**K982410**	2 **SMP-Plus™**	2 **Rehabilicare**
3	**K924666**	3 **Intelect® Legend Stim**	3 **Chattanooga Group, Inc.**
4	**K973442**	4 **TECA Disposable Monopolar Needles**	4 **TECA Corporation**
5	**K950314**	5 **DMN™ Disposable Monopolar Needle Electrodes**	5 **Medtronic, Inc.**
6	**K982902 K915540**	6 **Mattrix Neurostimulation System Resume II Lead**	6 **Medtronic, Inc.**

Section F Product Information—Applicable to All Applications

Common or usual name or classification name: **Nerve Stimulator, Peripheral Nerve Stimulator, or Electrical Nerve Stimulator and Accessories**

Trade or proprietary or model name	Model number
1 **Vertis PNT Control Unit**	1 **CU100**
2 **Vertis PNT Safeguide Kits**	2 **SGXXX**
3	3
4	4
5	5

FDA document numbers of all prior related submissions (regardless of outcome):

1 **K970203**	2 **K951903**	3 **K982410**	4 **K924666**	5 **K973442**	6 **K950314**
7 **K982902**	8 **K915540**	9	10	11	12

Data included in submission: ☒ Laboratory testing ☒ Animal trials ☒ Human trials

Section G Product Classification—Applicable to All Applications

Product Code **GZJ GZF** | C.F.R. Section: **21 CFR 882.5890 21 CFR 882.5870**

Device Class: ☐ Class I ☒ Class II ☐ Class III ☐ Unclassified

Classification panel: **General Restorative and Neurological**

Indications (from labeling): **Percutaneous Neuromodulation Therapy (PNT) is indicated for the symptomatic relief and management of chronic, intractable pain and/or as an adjunctive treatment in the management of post-surgical and post-trauma acute pain.**

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

Note: Submission of this information does not affect the need to submit a 2891 or 2891a Device Establishment Registration form.	FDA Document Number:

Section H Manufacturing/Packaging/Sterilization Sites Relating to a Submission

☒ Original ☐ Add ☐ Delete	FDA establishment registration number: (b) (4)	☐ Manufacturer ☒ Contract manufacturer	☐ Contract sterilizer ☐ Repackager / relabeler
Company/Institution name: (b) (4)		Establishment registration number: (b) (4)	
Division name (if applicable):		Phone number (include area code): (b) (4)	
Street address: (b) (4)		FAX number (include area code): (b) (4)	
City: (b) (4)	State/Province: (b)	Country: **USA**	
Contact name: (b) (4)			
Contact title: **Quality/Regulatory Manager**		Contact e-mail address: (b) (4)	

☒ Original ☐ Add ☐ Delete	FDA establishment registration number: (b) (4)	☐ Manufacturer ☒ Contract manufacturer	☐ Contract sterilizer ☐ Repackager / relabeler
Company/Institution name: (b) (4)		Establishment registration number: (b) (4)	
Division name (if applicable):		Phone number (include area code): (b) (4)	
Street address: (b) (4)		FAX number (include area code): (b) (4)	
City: (b) (4)	State/Province: (b	Country: **USA**	
Contact name: (b) (4)			
Contact title: **President**		Contact e-mail address: (b) (4)	

☒ Original ☐ Add ☐ Delete	FDA establishment registration number: (b) (4)	☐ Manufacturer ☐ Contract manufacturer	☒ Contract sterilizer ☐ Repackager / relabeler
Company/Institution name: (b) (4)		Establishment registration number: (b) (4)	
Division name (if applicable):		Phone number (include area code): (b) (4)	
Street address: (b) (4)		FAX number (include area code): (b) (4)	
City: (b) (4)	State/Province: (b	Country: **USA**	
Contact name: (b) (4)			
Contact title: **Manager of Regulatory Affairs and Quality Systems**		Contact e-mail address: (b) (4)	

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Note: Submission of this information does not affect the need to submit a 2891 or 2891a Device Establishment Registration form.	FDA Document Number:

Section H Manufacturing/Packaging/Sterilization Sites Relating to a Submission

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Company/Institution name: (b) (4)		Establishment registration number: (b) (4)	
Division name (if applicable):		Phone number (include area code): (b) (4)	
Street address: (b) (4)		FAX number (include area code): (b) (4)	
City: (b)	State/Province: **UT**	Country: **USA**	
Contact name: (b) (4)			
Contact title: **Manager RA/QS**		Contact e-mail address: (b) (4)	
☒ Original ☐ Add ☐ Delete	FDA establishment registration number: (b) (4)	☐ Manufacturer ☒ Contract manufacturer	☐ Contract sterilizer ☐ Repackager / relabeler
Company/Institution name: (b) (4)		Establishment registration number: (b) (4)	
Division name (if applicable):		Phone number (include area code): (b) (4)	
Street address: (b) (4)		FAX number (include area code): (b) (4)	
City: (b) (4)	State/Province: (b	Country: **USA**	
Contact name: (b) (4)			
Contact title: **QA Manager**		Contact e-mail address: (b) (4)	
☐ Original ☐ Add ☐ Delete	FDA establishment registration number:	☐ Manufacturer ☐ Contract manufacturer	☐ Contract sterilizer ☐ Repackager / relabeler
Company/Institution name: **N/A**		Establishment registration number:	
Division name (if applicable):		Phone number (include area code): ( )	
Street address:		FAX number (include area code): ( )	
City:	State/Province:	Country:	
Contact name:			
Contact title:		Contact e-mail address:	

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

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Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

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Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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510 (k) Notification for the Vertis Neuroscience, Inc.
Vertis PNT Control Unit (Nerve Stimulator) and Accessories

Section I – Vertis PNT Control Unit

Device Name

Common Names: Nerve Stimulator, Peripheral Nerve Stimulator or Electrical Nerve Stimulator

Trade Name: Percutaneous Neuromodulation Therapy (PNT) Nerve Stimulation System

Catalog Numbers:

Catalog/Model Number	Product name
Model CU 100	Vertis PNT™ Control Unit

Establishment Registration

Manufacturing

Product will be manufactured and distributed by Vertis Neuroscience, Inc. Mailing and facility address:

Vertis Neuroscience, Inc.
2101 Fourth Avenue, Suite 200
Seattle, Washington, USA 98121

Vertis PNT Control Unit – contract assembler:
(b) (4)

Establishment Number

In accordance to 21 CFR 807, Vertis Neuroscience, Inc. will file establishment registration documentation (Form 2891) prior to commercial distribution.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Classification and Special Controls

FDA Panel: General, Restorative and Neurological Devices

Class/Regulation/ Product Codes:

Class II - Transcutaneous electrical nerve stimulator for pain relief
21 CFR 882.5890, product code: GZJ

Class II - Implanted peripheral nerve stimulator for pain relief
21 CFR 882.5870, product code: GZF

Class II - Implanted spinal cord stimulator for pain relief
21 CFR 882.5880, product code: GZB

Class II – Interferential current therapy
No CFR reference, product code: LIH

Special Controls: (513/514 compliance)

To date, no Food and Drug Administration special controls (including performance standards) have been established for these devices. However, the nerve stimulator complies with applicable portions of the following technical standards and FDA-recognized consensus standards:

Technical standards:

ANSI/AAMI NS4-1985 Transcutaneous Electrical Nerve Stimulators, approved 5-20-86.

ANSI/AAMI ES1 1993 - Safe Current Limits for Electromedical Apparatus, approved 12-2-93

ANSI/AMI NS15-1995 Implantable Peripheral Nerve Stimulators, approved 2-1-95

ANSI/AMI NS14-1995 Implantable Spinal Cord Stimulators, approved 2-2-95

FDA-recognized consensus standards:

IEC60601-1:1993 Medical Electrical Equipment, Part 1: General Requirements for Safety and Amendments A1:1991, A2:1995.

IEC 60601-1-2 First Edition 1993-4 Medical Electrical Equipment, - Part 1: General Requirements for Safety: Electromagnetic Compatibility – Requirements and Tests (tested in accordance to the IEC 61000 series).

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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IEC 60601-1-4:1996 Medical Electrical Equipment, Part 1: General Requirements for Safety, Part 2: Collateral Standard: Programmable electrical medical systems.

IEC 60601-2-10:1987 Medical Electrical Equipment, Part 2: Particular Requirements for the Safety of Nerve and Muscle Stimulators.

EN (CEN) 1441:1997 Medical Devices – Risk Analysis.

Device Description

Overview

The Vertis PNT System is designed for delivering percutaneous electrical stimulation (termed: Percutaneous Neuromodulation Therapy - PNT). The Vertis PNT System is intended to be used in pain management by a physician (e.g., anesthesiologists or physical medicine and rehabilitation physicians) or on the order of a physician (e.g., by a physical therapist) in a clinic environment. It is not intended for patient use. The device system includes three (3) components:

- the *Vertis PNT Control Unit* - a software-driven, five channel, AC-powered nerve stimulator which generates the electrical stimulus;
- the sterile *Safeguides* – which are sterile, needle electrodes, and
- the *Patient Cable* - which interconnects the PNT Control Unit to the electrodes

  The Patient Cables and Safeguide electrodes are provided separately from the Vertis PNT Control Unit; Instructions for Use are provided with these separate accessories.

An overview system photograph of the PNT Control Unit and its accessories (patient cable and electrodes) is provided in Appendix 1.

In general, the PNT Control Unit is approximately 6 pounds in weight. The overall device dimensions are approximately 5" (height) x 9.7" (width) x 9.5" (depth). The PNT Control Unit was designed with careful consideration of human factors. The top face of the PNT Control Unit is simple, with a few main controls. On the face of the device, there are 5 push buttons for individual electrode channel selection, a "select all" electrodes channels button, and a single therapy control rotating dial for the clinician to set and adjust therapy intensity. Text prompts, therapy delivery parameters and other messages are provided on a backlit liquid crystal display (LCD) screen to provide instructions and therapy delivery information to the clinician throughout device use. Several device function keys are also available for the selection of parameters and other control functions.

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When connected with the Patient Cable and Electrodes to a patient, the PNT Control Unit uses text prompts on the device's LCD screen that allows the clinician to:

- Select from a variety of electrical stimulation modes (e.g., 4 Hz, 15/30 Hz, etc.).
- Set the treatment duration (e.g., 30 minutes)
- Set the stimulus intensity individually for each of the 5 electrode channels. The device's LCD screen graphically shows these individual stimulation channels using indicator bars
- Initiate delivery of percutaneous electrical stimulation
- Record the progress and completion of therapy (e.g., minutes in session).

Engineering drawings of the PNT Control Unit final assembly and subassemblies are provided in Appendix 2. A detailed overview of the PNT Control Unit, including various features and technical characteristics, is documented in the device comparison charts in Appendix 16.

As is common with other commercially available nerve stimulators, Vertis will provide various accessories for the Vertis PNT Control Unit. These accessories, which include such items as electrodes, cables and carrying cases, are listed and described in Appendix 3.

> Note: One of the accessories noted in Appendix 3 that will be offered in conjunction with the PNT Control Unit is percutaneous electrodes. Because of the important nature of these electrodes in the use of the nerve stimulator, detailed information for the Vertis electrodes (model: Safeguides) is enclosed in Section II of this Notification. Please refer to Section II (pages 8-15) for all details and data regarding the electrodes.

Intended Use

Percutaneous Neuromodulation Therapy (PNT) is indicated for the symptomatic relief and management of chronic, intractable pain and/or as an adjunctive treatment in the management of post-surgical and post-trauma acute pain.

This Indications for Use is provided as a separate Statement in this Notification and may be found in Appendix 27.

Operating Controls and Features

The Vertis PNT Control Unit was specifically designed and engineered to make the device simple for the operator to use. For the following "device panel" descriptions and "Description of Operation" section, please refer to the device diagrams in Appendixes 4 and 5 to identify the following various underlined operating controls and features of the Vertis PNT Control Unit.

> **Device front panel/face (diagramed in Appendix 4):** The front panel or face of the PNT Control Unit has all therapy controls (Select All Channels Button, Channel Selection Buttons, Therapy Control Dial, Pause Button and Function Keys) and a LCD screen for display of therapy delivery information and prompts. A fault indicator light is also present on the front panel.
>
> > A detailed description of each of these features/controls is contained in Appendix 4.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Device back panel (diagramed in Appendix 5): The back panel of the PNT Control Unit has the cord receptacles (AC Power cord receptacle; Patient Cable receptacle) locations and the on/off switch.

A detailed description of each of these features/controls is contained in Appendix 5.

Device bottom panels: The bottom (underside) panel of the device contains device labeling only (refer to Appendix 7 for device labeling). There are no additional controls on the device bottom panel.

Device right and left side panels: There are no additional controls or features on the sides of the device.

Description of Operation

To use the Vertis PNT System in a clinical setting, the clinician needs a Vertis PNT Control Unit (includes the AC power cord); a patient cable and a sterile, Safeguide electrode kit.

The device user activates the PNT Control Unit by plugging the device into wall (AC) power and by pressing the on/off switch on the Control Unit's back panel. Both the power cord and the patient cables plug into the AC power cord receptacle and the patient cable receptacle, respectively, on the Control Unit's back panel.

The clinician uses the function keys on the front panel of the PNT Control Unit to adjust a number of therapy-related variables. These include, for example, treatment session duration, selection of treatment (referred to as "modulation") mode, etc.

The Safeguide electrodes are removed from the sterile packaging and placed by the clinician onto the patient by adhering the Safeguide adhesive patches. Each electrode is connected to the patient cable via a "key" on the patient cable. This key mechanically inserts or "keys" into the upper portion of the Safeguide electrode assembly. This key on the patient cable establishes the mechanical and electrical connections between the electrode and the PNT Control Unit. The extremely fine (0.25 mm diameter) needle electrode contained within the electrode housing is deployed percutaneously as the clinician slides/depresses the key down through the electrode assembly. Please refer to Section II of this Notification (pages 8-15) for additional details and technical discussion regarding the Safeguide electrodes.

Once the electrodes are placed, the clinician initiates electrical stimulation (percutaneous neuromodulation therapy) by turning the therapy control dial, which controls the PNT current output. To adjust the stimulation current levels, the clinician uses the "select all" channels button (to adjust all electrode channels simultaneously) or the channel selection buttons (to adjust electrode channels individually). A pause button is available in the event the clinician desires to pause therapy. The fault indicator is for user convenience and when lit indicates that the PNT Control Unit has detected an internal fault condition and requires service (refer to the Control Unit User's Guide, Appendix 6, for details).

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Throughout device use, the LCD Screen displays therapy information (e.g., session time remaining, electrode channel output, etc.) for the clinician's reference. A session timer automatically terminates the delivery of therapy after a designated period of time.

Packaging

Similar to other non-patient contact, electronic medical devices, the Vertis PNT Control Unit is provided non-sterile and will be individually packaged in corrugated cardboard packaging material for shipping.

Proposed Labeling

Labeling for the Vertis PNT Control Unit was designed in accordance to the following industry standards:

ANSI/AAMI NS4-1985 Transcutaneous Electrical Nerve Stimulators, approved 5-20-86.

ANSI/AAMI/ISO 15223: 2000 Medical Devices – Symbols to be used with Medical Device Labels, Labeling and Information to be Supplied, approved 3-13-00.

IEC60601-1:1993 Medical Electrical Equipment, Part 1: General Requirements for Safety and Amendments A1:1991, A2:1995.

IEC 60601-2-10:1987 Medical Electrical Equipment, Part 2: Particular Requirements for the Safety of Nerve and Muscle Stimulators.

Directions for Use
A draft of the proposed Instructions for Use (User's Guide) for the Vertis PNT Control Unit is provided in Appendix 6.

Labels
A draft of the proposed labels for the Vertis PNT Control Unit are provided in Appendix 7. Draft labeling provided in Appendix 7 includes:

- Device labeling: device front, back and bottom panel labeling. There is no labeling on the side panels of the device.
- Shelf/Shipping carton labeling

Advertisements or Promotional Materials
No promotional material or advertisements exist at this time.

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Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-9118

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Performance/Specification/Technical Information

Conformance to FDA-recognized Consensus Standards

Statement of Conformity

In accordance to the FDA Guidance - Use of Standards in Substantial Equivalence Determination (dated 3-12-00), Vertis provides a Statement of Conformity with respect to adherence to FDA-recognized Consensus Standards. Please refer to Appendix 8 for this Statement of Conformity and related information.

> Note: A *Statement* of Conformity, rather than *Declaration* of Conformity is being provided in this 510(k) Notification as per the above noted FDA Guidance ("Summary", page 8), a Statement is the appropriate Conformity mechanism if all test data is not yet completed/on file at Vertis at the time of the 510(k) Notification filing, but will be completed prior to marketing of the device.

Results

The Statement of Conformity specifies that the Vertis PNT Control Unit complies with several specific FDA-recognized Consensus Standards. Adherence to the design and testing requirements of these standards ensures that the PNT Control Unit demonstrates acceptable device performance, as defined by these recognized technical standards.

Specification/Technical Information

Vertis is providing device specification/technical information for the Vertis PNT Control Unit in accordance with the FDA Guidance for TENS 510(k) Content (August 1994). This information is provided in Appendix 9.

Results

Technical and specification information includes detailed information regarding electrical output, electrical safety, compliance to technical standards and software. All information indicates that the device complies with specifications relevant to an electronic medical device and has technical and performance characteristics comparable to the substantially equivalent devices.

Software Information

Vertis is providing software information for the Vertis PNT Control Unit in accordance with the FDA Guidance for Reviewers and Industry: Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices (released 5-29-98). This information is provided in Appendix 10.

Results

System level validation testing has been performed for the Vertis PNT Control Unit. The test protocol and test results are included in Appendix 10. All testing demonstrated acceptable device performance in accordance to the devices' software requirement specifications.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Note: One of the accessories that will be offered in conjunction with the Vertis PNT Control Unit is percutaneous electrodes. Because of the important nature of these electrodes in the use of the nerve stimulator, information for the Vertis electrodes is enclosed in this Notification, rather than a separate Notification

Section II - Electrodes

Device Name

Common Names: Needle Electrodes or Nerve Stimulation Electrodes

Trade Name: Percutaneous Neuromodulation Therapy (PNT) Nerve Stimulation Electrodes

Catalog Numbers:

Catalog/Model Number	Product name
Model SG xxx Series	Vertis PNT Safeguide™ Kit(s)

Establishment Registration

Manufacturing
Product will be manufactured and distributed by Vertis Neuroscience, Inc. Mailing and facility address:

Vertis Neuroscience, Inc.
2101 Fourth Avenue, Suite 200
Seattle, Washington, USA 98121

Safeguide electrodes – contract assembler:
(b) (4)

Safeguide electrodes – alternative contract assembler:
(b) (4)

Establishment Number
In accordance to 21 CFR 807, Vertis Neuroscience, Inc. will file establishment registration documentation (Form 2891) prior to commercial distribution.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

Classification and Special Controls

FDA Panel: General, Restorative and Neurological Devices

Class/Regulation/ Product Codes:

Class II - Needle electrodes
21 CFR 882.1350, product code: GXZ
Class II - Electromyograph needle electrodes
21 CFR 890.1385, product code: IKT
Class II - Cutaneous electrode
21 CFR 882.1320, product code: GXY
Class II - Implanted peripheral nerve stimulator for pain relief
21 CFR 882.5870, product code: GZF

Special Controls: (513/514 compliance)

To date, no Food and Drug Administration special controls (including performance standards) have been established for these devices. However, the electrodes comply with applicable portions of the following technical standards and FDA-recognized consensus standards:

Technical standards:

ANSI/AMI NS15-1995 Implantable Peripheral Nerve Stimulators, approved 2-1-95

FDA-recognized consensus standards:

ANSI/AAMI/ISO 11137: 1994 Sterilization of Health Care Products – Requirements for Validation and Routine Control –Radiation Sterilization; using Method 1 as described per AAMI/ISO TIR No. 13409: 1996 Sterilization of Health care Products – Radiation Sterilization – Substantiation of 25kGy as a Sterilization Dose for Small or Infrequent Production Batches.

ANSI/AAMI/ISO 10993-1:1997, Biological Evaluation of Medical Devices - Part 1: Evaluation and Testing.

EN (CEN) 1441:1997 Medical Devices – Risk Analysis.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Device Description

Intended Use

The Vertis PNT Nerve stimulation electrodes (model: Safeguide) are needle electrodes used in the delivery of percutaneous electrical stimulation from the Vertis PNT Control Unit. The Safeguide electrodes are intended for use only with the Vertis PNT Control Unit and Patient Cables.

Features

The Safeguide electrodes are supplied as disposable, single use, sterile electrode kits offered in various pack/multi pack configurations (example: 1 pack electrode, 6 pack of electrode kits, etc.). For device user ease of use and convenience, electrode kits may also be provided as clinical application specific (e.g., a lumbar kit, a cervical kit, etc.). There are up to 10 Safeguide electrodes in each sterile electrode kit.

Each individual Safeguide electrode assembly is a very small (approximately 1.6" (height) x 0.9" (diameter) cylindrical electrode housing/configuration that has an adhesive patch (approximately 1.8" diameter) attached to its base. The cylinder area of the electrode assembly functions as a sharp-safe housing and contains an extremely fine (0.25 mm diameter) stainless steel needle electrode. The adhesive patch attached to the base of the Safeguide allows for adherence of the electrode assembly to the patient's skin. Please refer to Appendix 11 - Diagram 1 for dimensional diagrams of the top, side and bottom views of the Safeguide electrode.

The components and materials of the Safeguide electrode are all commonly used medical device materials and are summarized in the following table:

Safeguide component	Material info
Electrode (needle)	(b) (4)
Adhesive foam disc (patch) - adhered onto electrode housing base	
Electrode housing – base, slider and retainer	
Electrode housing - sleeve	

Additional details regarding the Safeguide electrodes, including technical characteristics, is documented in the device comparison chart in Appendix 18.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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In comparison to other percutaneous electrodes, a unique feature of the Safeguide product is the containment of the needle electrode within a protective housing both before and after electrode use. Vertis chose to specifically contain the needle of the Safeguide in this sharp-safe design configuration to mitigate the risk of accidental needle-stick injuries that have occurred with other unprotected needles, electrodes, or similar sharps. This design of Safeguide is consistent with the goal of recent sharps safety federal legislation, summarized as follows:

> Passed unanimously by Congress and signed by the President on November 6, 2000, the *Needlestick Safety and Prevention Act* (H.R. 5178, S. 3067) requires that healthcare facilities use "safe medical devices" which are devices that have built-in safety features to prevent blood exposures caused by needlesticks. In the Congressional text contained in this Act, Congress found that "in March 2000, the Centers for Disease Control and Prevention estimated that more than 380,000 percutaneous injuries from contaminated sharps occur annually among health care workers in the United States hospital settings. Estimates for all health care settings are that 600,000 to 800,000 needlestick and other percutaneous injuries occur among health care workers annually".
>
> The Act further ordered specific revisions of Occupational Safety and Health Administration's (OSHA) bloodborne pathogens standard within six months. OSHA responded in 2.5 months and published its revised standard in the Federal Register on January 18, 2001. The revisions to the OSHA bloodborne pathogen standard, which take effect on April 18, 2001, clarify the responsibility of health care employers to provide their workers (estimated to be nearly 6 million personnel) with the safest device technology to reduce employees' risk of bloodborne pathogens exposure. The standard specifically requires employers to evaluate and implement the use of safety-engineered sharp devices as part of the employer's exposure control plan.
>
> This Safeguide electrode design is consistent with the Act's new terminology of a "sharp with engineered sharps injury protections". Specifically, the Safeguide requires a key to deploy the electrode (the sharp) and correspondingly, the use of the key to allow for complete retraction of the electrode into its housing, post use. This design allows the device user to handle the electrode both before and after use, without fear of contacting the sharp (the electrode tip). Overall, the Safeguide electrode design is consistent with the intent of this new federal legislation and will help aid device users in minimizing sharps injuries.

Description of Operation

During clinical use, the clinician selects the Safeguide electrode kit that is appropriate for the intended clinical application. Example: selects a lumbar electrode kit to be used on the patient's lumbar region. Safeguide electrodes are then removed from the sterile packaging and positioned by the clinician by adhering the adhesive patches of the Safeguides onto the patient's skin. Please refer to Appendix 11 - Diagram 1 to show this adhesive patch feature. This adhesive patch allows for secure attachment of the electrode to the skin. Thus, once adhered, electrode deployment and retraction can be performed in a safe manner and prevent device user exposure to any sharp (e.g., the needle tip).

Each electrode is then connected to the patient cable via a "key" on the patient cable. This key mechanically inserts or "keys" into the upper portion of the Safeguide electrode assembly.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Please refer to Appendix 11 - Diagram 2 for a diagram of the key placement into the Safeguide electrode.

This key on the patient cable establishes the mechanical and electrical connections between the electrode and the PNT Control Unit. When the key is placed in the upper portion of the Safeguide, it can be rotated past a detent (a bump within the Safeguide interior which provides tactical feedback to clinician of engagement). Once beyond the detent, the "slider" contained within the interior "sleeve" of the Safeguide can then be pushed downwards by the clinician. This downward, sliding motion deploys the extremely fine needle electrode contained within the housing sleeve. Please refer to Appendix 11 - Diagram 3 for a cross section diagram of the Safeguide showing the "slider" and "sleeve" components and electrode deployment.

As mentioned previously, each Safeguide contains an extremely fine gauge needle which functions as an electrode for the delivery of the PNT therapy. The dimensional information regarding this needle is 0.25 mm diameter and a range of 0.5 – 3.0 centimeters in length. It is important to note that this needle is *very* small. For a clinical frame of reference, a normal injection syringe needle used for intramuscular vaccine delivery is much larger at 0.6 – 1.0 mm diameter and 2.5 – 4.0 centimeters in length. For a general frame of reference, the Safeguide needle is approximately three times the diameter of a human hair. It is extremely pliable and will flex readily upon contact. To aid the needle in penetrating the skin layer, the base of the Safeguide has a small cone-like piece of material (called the distraction tube – diagramed in Appendix 11 - Diagram 1). This tube pushes slightly on the skin, causing it to be taut on the surface. This makes needle penetration of the skin easier. Lastly, the material of this needle is medical grade 304 stainless steel and is identical to other commercially available needle electrodes.

Once the electrodes are placed, the clinician initiates and controls electrical stimulation (percutaneous neuromodulation therapy) by using the PNT Control Unit. Refer to Section I of this Notification (pages 1-7) for all details regarding the PNT Control Unit.

At the completion of therapy, the clinician pulls the key in the Safeguide electrode upwards which automatically completely retracts the electrode up into the sleeve of the Safeguide. Each electrode is then removed by the clinician from the patient without fear of contacting the sharp (the electrode tip). To aid in removal of the electrode, the adhesive patch has a tab on one side that the user can grasp and conveniently "peel" the adhesive patch of the electrode off the patient. Safeguides are designed for single patient, single use and are discarded after each use.

Packaging

The electrodes are provided as a sterile, disposable kit and are intended and labeled for single patient use only (not reusable). The electrodes are packaged in a polystrene tray with tyvek/paper lid. The tray is heat sealed using conventional platen heat sealing technology.

Instructions for Use are provided with the electrodes. For shipping, handling and storage at the user sites, electrode kits are placed in labeled cardboard shelf and shipping cartons.

These packaging materials and sealing methods are identical to currently marketed electrodes and are commonly used in the medical device industry for the packaging of sterile disposable medical devices.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Proposed Labeling

Labeling for the Vertis electrodes was designed in accordance to the following industry standard:

ANSI/AAMI/ISO 15223: 2000 Medical Devices – Symbols to be used with Medical Device Labels, Labeling and Information to be Supplied, approved 3-13-00.

Instructions for Use

A draft of a proposed Instruction for Use for an example Vertis electrode kit (e.g., for lumbar application) is provided in Appendix 12.

Please note, in addition to the Instructions for Use, information is also pre-printed on the lid of the kit tray that contains the electrodes- see below for this tray label text.

Labels

A draft of sample proposed labels for an example Vertis electrode kit (e.g., for lumbar application) is provided in Appendix 13. Draft labeling provided in Appendix 13 includes:

- Device labeling: There is no labeling on each individual Safeguide electrode.
- Electrode kit tray labeling
- Shelf/Shipping carton labeling

Advertisements or Promotional Materials

No promotional material or advertisements exist at this time.

Performance/Specification/Technical Information

Performance/Specification/Technical Information

Vertis is providing device specification/technical information for the Safeguide electrodes in accordance with the FDA Supplementary Guidance on the Content of Premarket Notification (510(k) Submissions for Medical Devices with Sharps Injury Prevention Features (March 1995). This information is provided in Appendix 14.

Testing of Vertis electrodes was performed on electrodes produced in the production (clean room) environment, thus test samples are representative of all production methods/handling. Test electrodes were also subjected to a double gamma radiation sterilization cycle to replicate worst-case double sterilization. Testing performed by Vertis included assessment of design safety criteria (e.g., electrode pull out force, etc.). Test methods, specifications, sample sizes, etc. are discussed in conjunction with the test data provided in Appendix 14.

Results

All testing demonstrates that the electrodes met the product's design specifications.

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Biocompatibility testing

Patient contact components (identified in Appendix 15) used in the Safeguide electrodes are made of materials commonly used in the medical device industry for various applications, including electrodes and skin contact devices. Biocompatibility testing for the patient contact materials is performed in accordance to the following references:

ANSI/AAMI/ISO 10993-1:1997, Biological Evaluation of Medical Devices - Part 1: Evaluation and Testing.

FDA ODE General program memorandum G95-1 (5-1-95), "Use of International Standard ISO-10993, Biological Evaluation of Medical Devices Part 1: Evaluation and Testing".

In accordance to ISO 10993-1 and G95-1, the electrodes are in the device category of "External communicating devices" (Section 4.1.3 of the ISO Standard), "Tissue/bone/dentin" contact (Section 4.1.3 (b) of the ISO Standard) and of a contact duration of "A = limited exposure; <24 hour contact" (Section 4.2 (a) of the ISO Standard). Suggested tests to assess biocompatibility include: Cytotoxicity, Sensitization and Irritation/Intracutaneous reactivity.

Results

Biocompatibility testing is performed on the patient contact materials of the electrodes and is performed on sterilized materials, which is consistent with how the electrodes will be supplied. The patient contact materials will be shown to be biocompatible according to Appendix 15 testing prior to commercial distribution.

Sterilization Information

The Safeguide electrodes are provided to the device user sterile. In accordance to the FDA ODE General program memorandum K90-1 (2-12-90), "510(k) Sterility Review Guidance" information relevant to the sterilization process is provided as follows:

Sterilization method and dose:

Gamma irradiation, production dose: 25 – 35 kGy

Contract sterilizer:

(b) (4)

Alternative contract sterilizer:

(b) (4)

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Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Sterilization validation method:

(b) (4)

SAL: Device will meet a Sterility Assurance Level (SAL) of 10^{-6}.

Packaging:

The electrodes are packaged in a polystrene tray with tyvek/paper lid. The tray is heat sealed using conventional platen heat sealing technology.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Section III- Substantial Equivalence and Statements

Nerve Stimulator

The Vertis PNT Control Unit and accessories are substantially equivalent to the following devices. These devices are currently available nerve stimulators and accessories that have been determined to be substantially equivalent to devices in commercial distribution prior to May 28, 1976.

Manufacturer	Substantially Equivalent devices	510(k)
Empi, Inc. St. Paul, MN	EPIX Tens Device System Model EPIX VT Model EPIX XL	K970203 K951903
Rehabilicare, Inc. New Brighton, MN	SMP-Plus™ Model 4930	K982410
Chattanooga Group, Inc. Hixson, TN	Intelect ® Legend Stim Model IFC2 (catalog #INT002)	K924666
Medtronic, Inc Minneapolis, MN	Mattrix ® Neurostimulation System Receiver model: 3272 Transmitter model: 3210	K982902

Comparison Charts to Substantially Equivalent Devices and Device Literature

A comparison chart that summarizes the similarities and differences of the Vertis nerve stimulator versus the currently marketed substantially equivalent devices is provided as Appendix 16.

Product literature for the substantially equivalent devices is provided in Appendix 17.

Electrodes

The Vertis Safeguide electrodes are substantially equivalent to the following devices. These devices are currently available nerve stimulation electrodes that have been determined to be substantially equivalent to devices in commercial distribution prior to May 28, 1976.

Manufacturer	Substantially Equivalent devices	510(k)
TECA Corporation Pleasantville, NY	TECA Disposable Monopolar Needles 902-DMFxx-TP series 902-DMGxx-TP series	K973442
Medtronic, Inc. Minneapolis, MN	DMN™ Disposable Monopolar Needle Electrodes DMFxx series DMNxx series	K950314
Medtronic, Inc. Minneapolis, MN	Resume II Lead Model 3587a	K915540

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Comparison Charts to Substantially Equivalent Devices and Device Literature

A comparison chart that summarizes the similarities and differences of the Vertis Safeguide electrodes versus the substantially equivalent devices is provided as Appendix 18.

Product literature for the substantially equivalent devices is provided in Appendix 19.

Substantial Equivalence Discussion and Rationale

A discussion of substantial equivalence is provided in Appendix 20 and includes a decision tree for the "Substantial Equivalence" determination.

Conclusion

Based on the information provided and the supporting Appendices, we believe the Vertis PNT Control Unit and accessories to be substantially equivalent in intended use, materials, design and function to currently available nerve stimulators, electrodes and accessories that have been determined to be substantially equivalent to devices in commercial distribution prior to May 28, 1976.

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Section III (continued) - Summary and Statements

510(k) Summary of Safety and Effectiveness

A Summary of Safety and Effectiveness is provided in Appendix 25.

Premarket Notification Truthful and Accurate Statement

The Premarket Notification Truthful and Accurate Statement is provided in Appendix 26.

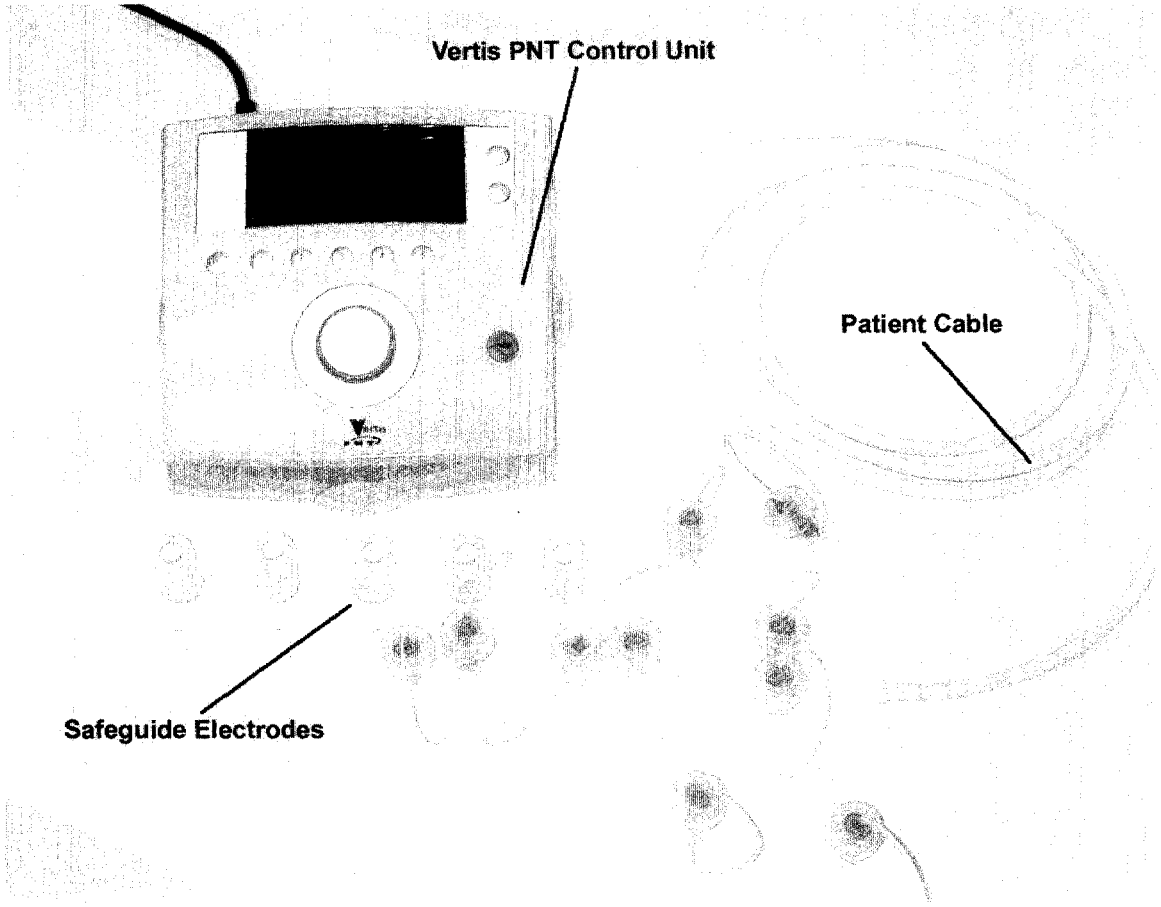
Indications for Use Statement

The Indications for Use Statement is provided in Appendix 27.

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Appendix 1
Vertis PNT Control Unit and Accessories – System photograph



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Appendix 2
Vertis PNT Control Unit - Engineering Drawings

Note #1: Vertis contracted some of the development and testing of the Vertis PNT Control Unit device to Plexus Corporation (formerly SeaMED Corporation), establishment registration # 3031699. Plexus will also serve as the contract manufacturer for the Vertis PNT Control Unit. Hence, Plexus documents are referenced below and are provided as Attachments in this Appendix. Vertis maintains all responsibility for the Device Master Record (including all engineering drawings and specifications).

Note #2: For convenience during product development, the project name used for the Vertis PNT Control Unit was "Telluride". Hence, this project name is present in the attached engineering drawings.

Engineering Drawings enclosed in this Appendix

Drawing 936719 – PNT Control Unit - Final Assembly 4 pages
Shows the top level assembly for the PNT Control Unit

Drawing 939793 – PNT Control Unit -- Console Assembly 8 pages
Shows the exploded assembly, including subassemblies that are part of the PNT Control Unit. Includes bill of materials.

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Appendix 3
Vertis PNT Control Unit – Accessories

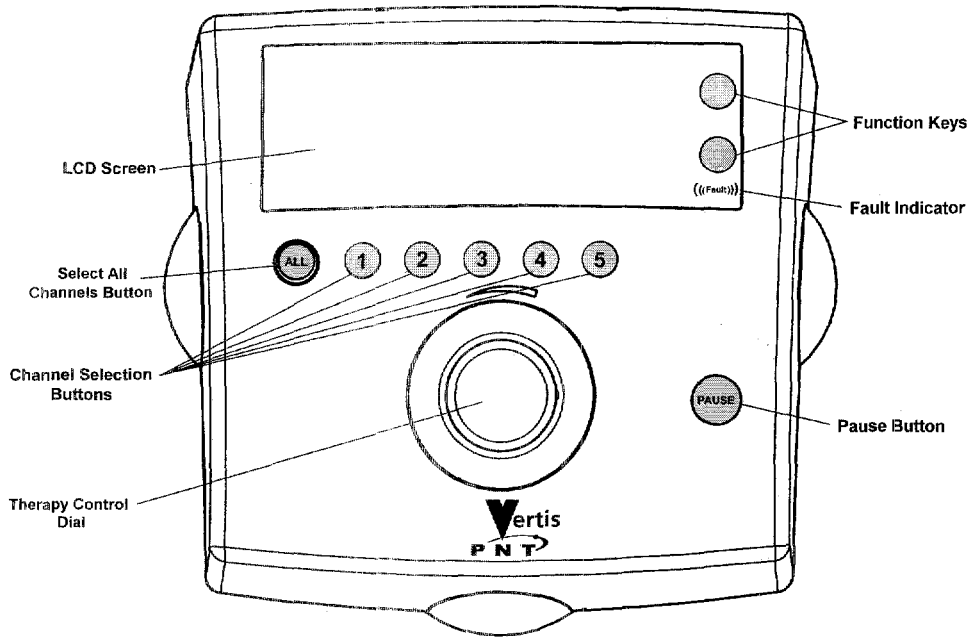
Accessory	Description
Electrodes	Disposable, sterile, percutaneous electrodes will be offered in various pack/multi pack configurations (example: 1 pack electrode, 6 pack of electrode kits, etc.). For device user ease of use and convenience, electrode kits may also be provided as clinical application specific (e.g., a lumbar kit, a cervical kit, etc.).
Patient cables	Reusable, non-sterile cables that interconnect the PNT Control Unit to the electrodes. Cables offered may be multipurpose (e.g., in various lengths such as 6 foot, 10 foot, etc.), of varying designs, or may also be clinical application specific. Example: a "lumbar" cable is configured long enough to reach from the PNT Control Unit to a patient's back in a normal clinical setting.
AC Power cord	Reusable, non-sterile replacement power cords for the PNT Control Unit (e.g., in the event a power cord is damaged in use).
Fuses	Replacement fuses for the PNT Control Unit.
Carrying Cases	Various carrying cases will be offered and are designed to accommodate the Vertis PNT Control Unit. These cases provide protection and user convenience in transporting and/or storing the device. Soft-sided cases and hard-sided cases will be offered, depending upon user preference.
Hardware/Carts	Hardware (e.g., brackets) for mounting of the PNT Control Unit on a wall or shelf or a cart to be used for holding/transporting the PNT Control Unit.
Training Video	Video to familiarize device user on how to properly use the Vertis PNT Control Unit and Accessories.
Mannequin - Training aid	Mannequin/Training dummy or poster to help device users train personnel on how to properly use the Vertis PNT Control Unit and Accessories.
User's Guides, Instructions for Use Quick Reference Cards	Extra copies (in addition to those shipped with the devices) of the PNT Control Unit User's Guide or Safeguide electrode Instructions for Use – to be used for clinician's reference or training of their clinic staffs. Includes "quick reference cards", example: a laminated card of the electrode placement diagram (same diagram from the electrode Instructions for Use), etc.
Patient brochures/ information	Brochures/information regarding PNT to be provided by the clinician to the patient – for patient education purposes.
Skin marking pen	For skin marking of electrode positioning, if desired by the clinician. Note: Vertis does not intend to be the specification developer or manufacturer for this product – we will simply distribute an existing commercially available product.

Note: Vertis intends to offer the above noted accessories. Vertis may choose to market additional or variations to these accessories (for example: a 10 pack of electrodes) as warranted by clinician's requests. Any accessory additions or changes will be evaluated in accordance to 21CFR807 with respect to the requirements to file a new 510(k) Notification.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Appendix 4
Vertis PNT Control Unit – Front Panel Diagram



LCD Screen

The LCD Screen displays therapy delivery and event information including the selected modulation mode, the selected session time, the session time remaining, active channel output information, and various text prompts. The LCD backlight is on whenever the Control Unit is turned on.

Select All Channels Button

The Select All Channels Button is used to select *all* of the electrode channels for simultaneous adjustment of stimulation current levels.

Channel Selection Buttons

The Channel Selection Buttons are used to select *individual* electrode channels for therapy adjustment. They also are used to make selections for various default Control Unit options when the device is in Setup mode.

Therapy Control Dial

The Therapy Control Dial controls the stimulation current output of selected electrode channels. The dial turns clockwise to increase intensity and counter-clockwise to decrease intensity.

Function Keys

The Function Keys are used to perform a number of actions including selection of session time, adjustment of session time, and adjustment of default settings. Text prompts or icons on the LCD Screen indicate the function of the keys.

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Fault Indicator

A lit amber LED illuminating the word "FAULT" indicates that the Control Unit has detected an internal fault.

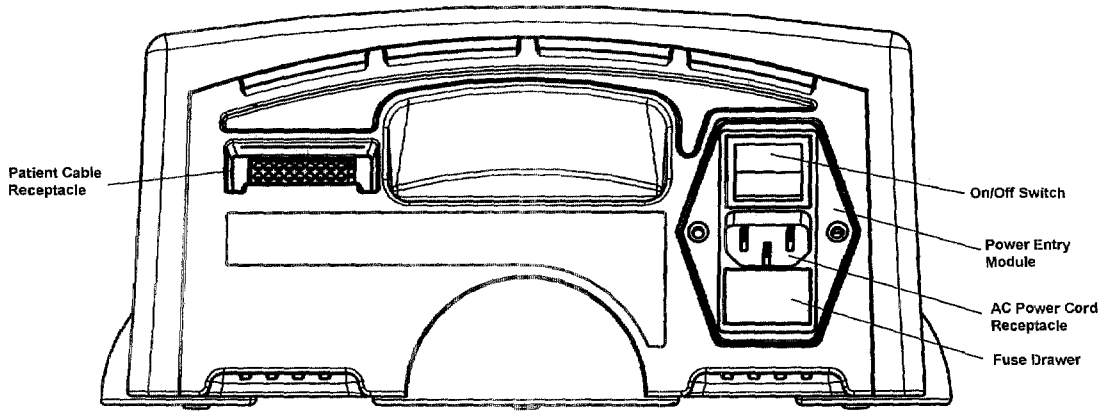
Pause Button

The Pause Button pauses the delivery of therapy.

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Appendix 5
Vertis PNT Control Unit – Back Panel Diagram



Power Entry Module

The Power Entry Module houses the On/Off Switch, the AC Power Cord Receptacle, and the Fuse Drawer/Line Voltage Selector.

On/Off Switch

The On/Off Switch controls power to the Control Unit.

AC Power Cord Receptacle

The AC Power Cord Receptacle is where the AC Power Cord, which connects into the wall power source, is connected to the Control Unit.

Fuse Drawer

The Fuse Drawer houses the fuses and provides line voltage selection.

Patient Cable Receptacle

The Patient Cable Receptacle is where the Patient Cable is connected to the Control Unit.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Appendix 6
Vertis PNT Control Unit User's Guide (draft)

User's Guide: The draft PNT Control Unit User's Guide (10070-001) is enclosed –52 pages

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Vertis PNT Control Unit

User's Guide

For

Model CU 100

Draft

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Published in the U.S.A.

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Patents pending.

Vertis Neuroscience, Inc.

Seattle, WA 98121

www.vertisneuro.com

For Customer Service: 1-800-597-2695

Vertis PNT Control Unit User's Guide

PN: 10070-001, Rev. A 05/01

DRAFT

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Introduction

This User's Guide provides information about using and maintaining the Vertis PNT™ Control Unit, Model CU 100. This chapter presents general information and should be read before using the PNT Control Unit.

Indications

Percutaneous Neuromodulation Therapy (PNT) is indicated for the symptomatic relief and management of chronic, intractable pain and/or as an adjunctive treatment in the management of post-surgical and post-trauma acute pain.

Contraindications

- PNT should not be used on patients with a demand-type implanted pacemaker or defibrillator.
- Electrode placement should be avoided over the carotid sinus region (anterior neck) or transcerebrally (through the head).
- PNT should not be used with undiagnosed pain.

Complications

The following are possible complications with PNT:

- Tissue irritation or burns at the electrode insertion site
- Superficial bleeding or hematoma
- Infection
- Allergic reaction to the electrode materials
- Reaction to electrode use or possible use (e.g., vaso-vagal reaction)
- Localized discomfort (e.g., ache, stiffness, etc.) from tissue penetration by the electrode or from electrical stimulation
- Electrode dislodgment
- Nerve irritation

Warnings and Precautions

See *Appendix A: Warnings and Precautions* for a list of warnings and precautions. These warnings and precautions are used throughout this User's Guide or on the Vertis PNT Control Unit.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Product Description

The Vertis PNT Control Unit is a five-channel, AC-powered console for delivering Percutaneous Neuromodulation Therapy (PNT). Individual Channel Selection Buttons, a Select All Channels Button, and a single Therapy Control Dial are used to set and adjust therapy intensity. A Session Timer automatically terminates the delivery of therapy after a designated period of time.

Text prompts, therapy delivery parameters, and other messages are provided on a backlit liquid crystal display (LCD) screen to provide instructions and therapy delivery information to the clinician throughout the treatment session. Adjacent Function Keys are used for the selection of parameters and other control functions.

The Vertis PNT Control Unit is designed for use with Vertis PNT Safeguide Kits and a Vertis PNT Patient Cable. Patient Cables and Safeguide Kits are provided separately. Instructions for Use are provided with these separate accessories.

Operating Controls and Features

Review the location of these operating controls and features on the Vertis PNT Control Unit prior to initiating therapy. Figure 1 shows the Vertis PNT Control Unit front panel, which includes the LCD Screen, Select All Channels Button, Channel Selection Buttons, Therapy Control Dial, Function Keys, Fault Indicator, and Pause Button.

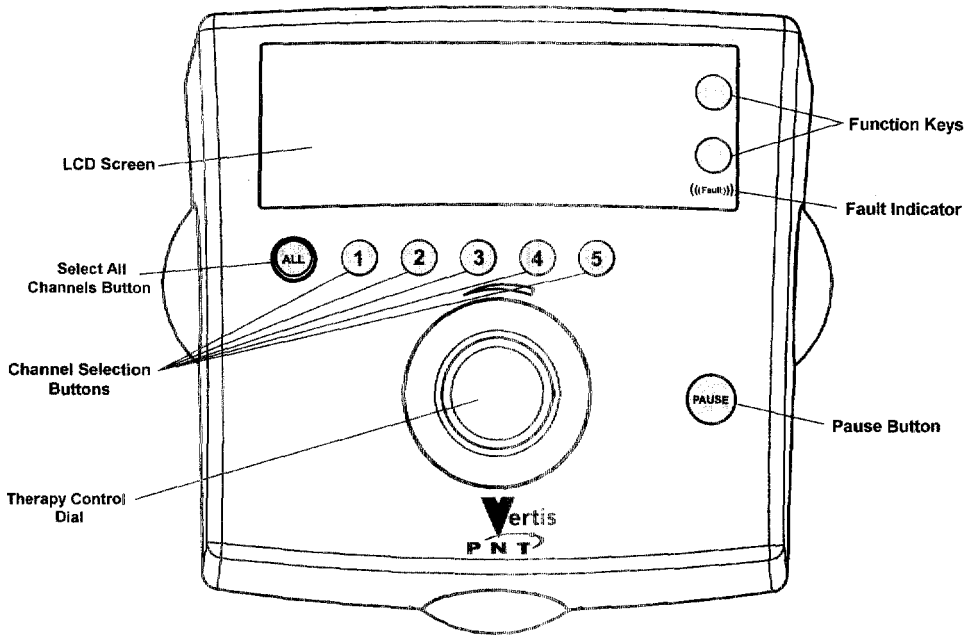


Figure 1: Vertis PNT Control Unit Front Panel

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LCD Screen

The LCD Screen displays therapy delivery and event information including the selected modulation mode, the selected session time, the session time remaining, active channel output information, and various text prompts. The LCD backlight is illuminated whenever the PNT Control Unit is "On".

Select All Channels Button

The Select All Channels Button is used to select *all* of the electrode channels for simultaneous adjustment of stimulation current levels.

Channel Selection Buttons

The Channel Selection Buttons are used to select *individual* electrode channels for therapy adjustment. They also are used to make selections for various default PNT Control Unit options when the device is in Setup mode.

Therapy Control Dial

The Therapy Control Dial controls the stimulation current output of selected electrode channels. The dial turns clockwise to increase intensity and counter-clockwise to decrease intensity.

Function Keys

The Function Keys are used to perform a number of actions including selection of session time, adjustment of session time, and adjustment of default settings. Text prompts or icons on the LCD Screen indicate the function of the keys.

Fault Indicator

A lit amber LED illuminating the word "FAULT" indicates that the PNT Control Unit has detected an internal fault.

Pause Button

The Pause Button pauses the delivery of therapy.

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Figure 2 shows the back panel of the PNT Control Unit, which includes the Power Entry Module, On/Off Switch, AC Power Cord Receptacle, Fuse Drawer, and Patient Cable Receptacle.

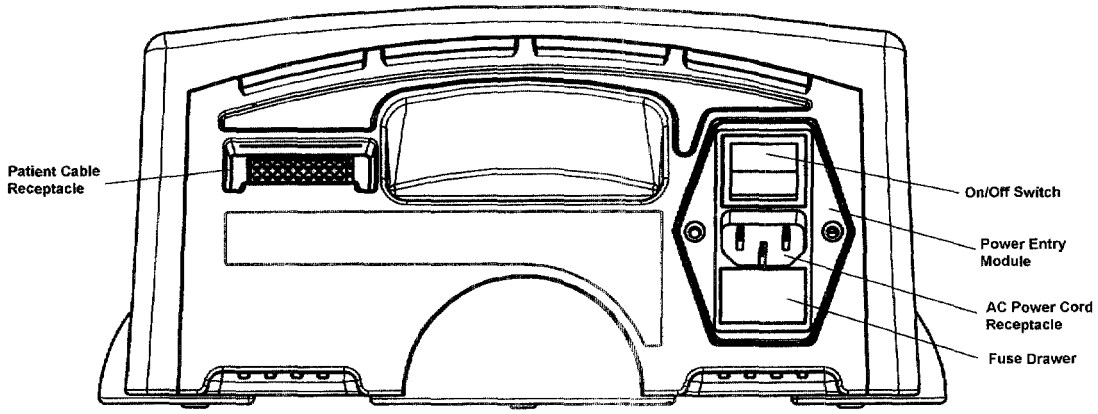


Figure 2: Vertis PNT Control Unit Back Panel

Power Entry Module

The Power Entry Module houses the On/Off Switch, the AC Power Cord Receptacle, and the Fuse Drawer/Line Voltage Selector.

On/Off Switch

The On/Off Switch controls power to the PNT Control Unit.

AC Power Cord Receptacle

The AC Power Cord Receptacle is where the AC Power Cord, which connects into the wall power source, is connected to the Control Unit.

Fuse Drawer

The Fuse Drawer houses the fuses and provides line voltage selection.

Patient Cable Receptacle

The Patient Cable Receptacle is where the Patient Cable is connected to the PNT Control Unit.

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Putting the Vertis PNT Control Unit Into Service

Four items are required to put the Vertis PNT Control Unit into service:

- The PNT Control Unit;
- The AC Power Cord;
- A Patient Cable; and
- A Safeguide Kit.

1. Carefully remove the PNT Control Unit from it packaging. Confirm that the PNT Control Unit is undamaged. Ensure the wall line voltage is compatible with the PNT Control Unit. For standard 120 volts AC power, no PNT Control Unit voltage adjustments are necessary. For line voltage that is not 120 volts AC, see *Vertis PNT Control Unit Setup Options: Changing the Line Voltage Setting.*

   ⚠**Warning: Damage**—Do not use the PNT Control Unit if it appears to be damaged.

   ⚠ **Warning**: **Line Voltage Selection**—Improper voltage selection may cause damage to the PNT Control Unit.

2. Connect the Patient Cable to the PNT Control Unit by inserting the plug into the PNT Control Unit Patient Cable Receptacle (Figure 2). Be sure that the plug is in the proper orientation with the cable angled downward, and firmly seated.

3. Plug the AC Power Cord into the PNT Control Unit and wall receptacle.

4. Place the PNT Control Unit On/Off Switch (Figure 2) in the "On" position. When the PNT Control Unit is turned "On," it automatically runs a self test for approximately 10 seconds. A self-test progress bar appears on the LCD Screen (Figure 3) to indicate that a self test is in progress. If the PNT Control Unit passes the self tests, the LCD Screen temporarily displays a "Self tests passed" message.

   If a fault is detected, it is indicated by a lit amber LED illuminating the word "FAULT" on the PNT Control Unit front panel (Figure 1).

   Note: It is normal for the fault indicator light to flash briefly at power up.

   ⚠**Warning: Failed Self Test**—Do not use the PNT Control Unit if it fails any self tests. Remove the PNT Control Unit from service and contact Vertis Neuroscience Customer Service.

7. Upon satisfactory completion of self testing, the LCD Screen displays the Vertis PNT Main Screen (Figure 4) and is ready for use.

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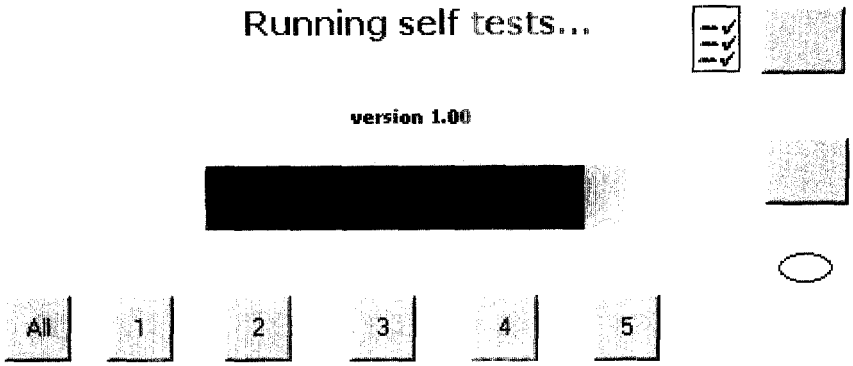


Figure 3: Power-On Self-Test Screen

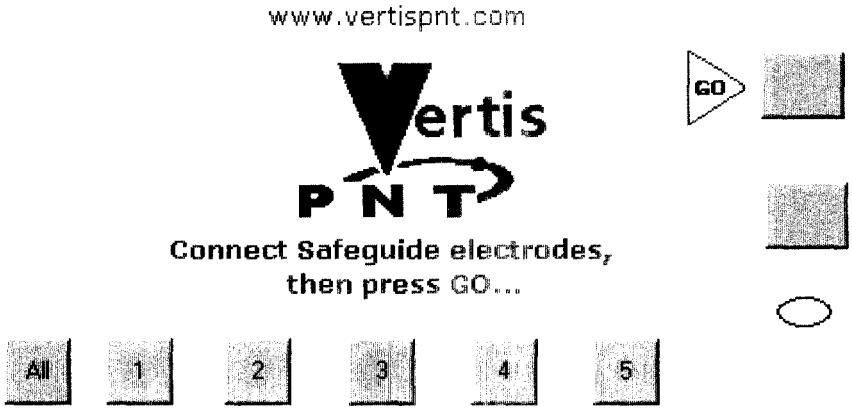


Figure 4: Vertis PNT Main Screen

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Using the Vertis PNT Control Unit

As with any medical procedure, clinicians are advised to use appropriate clinical judgment and discuss the nature of PNT with their patients prior to treatment. For example, this may include answering patients' questions, addressing patients' concerns, and setting patients' expectations about the therapy. See *Appendix C: Patient Education Information* for more information.

Please become acquainted with device operating instructions, as well as the indications, contraindications, warnings, and precautions, before administering any treatment to a patient.

> ⚠**Warning: Proper Use**—The safety and efficacy of PNT depends on the proper use and handling of the PNT Control Unit and accessories. The PNT Control Unit has potentially hazardous electrical output that, if used improperly, may cause injury to the patient or clinician.
>
> **Precaution: Accessory Use**—Do not use Safeguide Kits or Patient Cables other than those supplied or recommended by Vertis Neuroscience, Inc. The safety of other products or accessories has not been established and their use could result in injury to the patient or damage to the Vertis PNT Control Unit or accessories.

Positioning the Patient

Place the patient in a comfortable position using pillows or other supports as necessary. To minimize patient discomfort, the patient should remain stationary for the duration of the treatment session. Refer to the *Safeguide Kit Instructions for Use* for patient positioning recommendations.

Take care to position the patient, the PNT Control Unit, and the Patient Cable to minimize tension on the Patient Cable and to protect the Patient Cable from inadvertent motion. This helps avoid pulling the PNT Control Unit off the tabletop surface or accidental electrode dislodgment or disconnection due to the Patient Cable pulling on the Safeguides.

Identifying Sites for Safeguide Electrode Placement

Select the appropriate Safeguide Kit for the anatomical location requiring therapy. Selecting the sites for applying Safeguide electrodes should be based on clinician judgment. Refer to the *Safeguide Kit Instructions for Use* for Safeguide placement montage recommendations.

Preparing the Skin

To ensure proper electrode adhesion verify that the area where the Safeguide electrodes are to be applied is clean and dry. For patients with excessive body hair, consider shaving the appropriate areas or applying additional adhesive taping. Refer to the *Safeguide Kit Instructions for Use* for more information.

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Applying the Safeguide Electrodes and Connecting the Patient Cable

Refer to the *Safeguide Kit Instructions for Use* for instructions on applying the Safeguide electrodes and connecting the Patient Cable to the Safeguides. Instruct the patient to minimize all movement once the electrodes are in position.

Initiating Therapy and Adjusting the Treatment Settings

After the Safeguide electrodes have been connected to the Patient Cable, press the "GO" Function Key on the Vertis PNT Main Menu Screen (Figure 4). The Initiating Therapy Screen (Figure 5) displays Output Indicator Bars for each of the five channels.

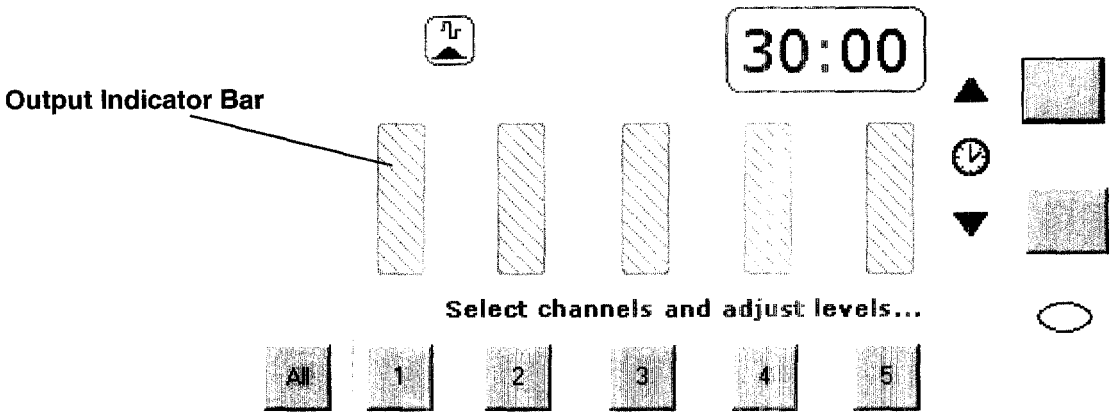


Figure 5: Initiating Therapy Screen

Due to variable patient sensitivity to stimulation at different electrode sites, Vertis Neuroscience recommends adjusting the therapy levels for each individual channel. For example, press Channel Selection Button 1, which highlights the corresponding Output Indicator Bar with a high-contrast (dark colored) rectangle (Figure 6). Use the Therapy Control Dial (Figure 1) to adjust the delivery of therapy to this channel. Turn clockwise to increase intensity, counter-clockwise to decrease intensity.

As the intensity level is slowly increased, ask the patient to identify the maximum level of current that is within the patient's comfort zone. If muscle contractions are observed, decrease the stimulation intensity to a level where contractions subside. Once the optimum stimulation level is achieved where discomfort is minimized and there is an absence of muscle contractions, repeat for each subsequent active channel.

Some patients may be anxious or apprehensive when experiencing the initial sensation of electrical current. If the patient is extremely apprehensive, set the intensity at a level where the patient feels a minimal sensation. Allow the patient to become accustomed to the sensation before increasing the intensity.

If the patient experiences marked discomfort with an individual electrode when current is applied, consider removing the Safeguide and replacing it with a new Safeguide in a slightly different

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location. Moving the insertion point of the electrode by as little as a few millimeters is often enough to relieve discomfort associated with a particular electrode insertion site. Refer to the *Safeguide Kit Instructions for Use* with regard to electrode removal and replacement.

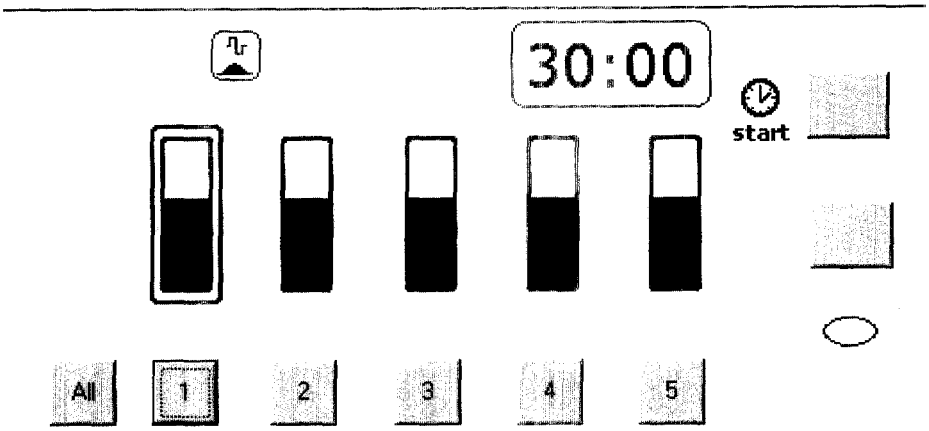


Figure 6: Adjusting Individual Channels Screen

If the PNT Control Unit detects that a Safeguide electrode has not been deployed while attempting to adjust the therapy level for that electrode channel, the inactive Output Indicator Bar is displayed with lower contrast (light colored) and is filled with a single hatch pattern (Figure 7). In addition, a chime sounds and an Alert icon momentarily flashes in the inactive Output Indicator Bar. See *Responding to Channel Alerts* later in this chapter.

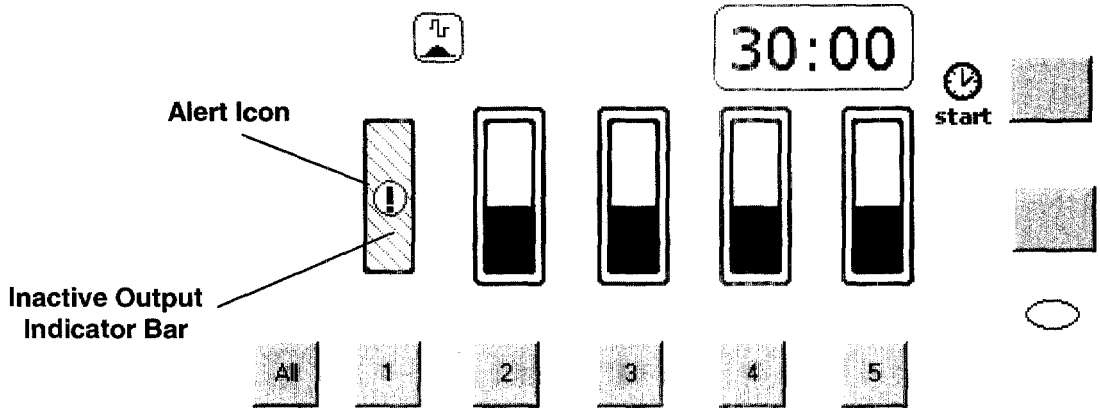
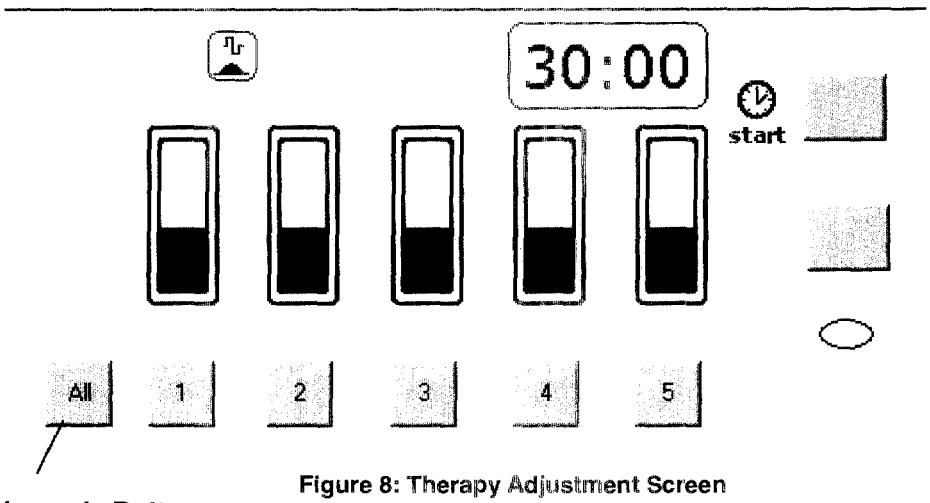


Figure 7: Channel Alert at Start of Therapy Session Screen

An alternative therapy adjustment method is to press the Select All Channels Button (Figure 1), which highlights all active Output Indicator Bars with a high-contrast (dark colored) rectangle (Figure 8). Use the Therapy Control Dial (Figure 1) to simultaneously begin the delivery of therapy to all active channels. Turn clockwise to increase intensity, counter-clockwise to decrease intensity. Query the patient to identify the maximum level of current that is within the patient's comfort zone. Therapy adjustment may then proceed channel by channel, if desired.

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Select All Channels Button

Figure 8: Therapy Adjustment Screen

Beginning the Session Timer

The Session Timer (Figure 9) displays the time remaining in the session. The therapy session is ready to begin once the therapy levels are set. To begin the Session Timer, press the "Start Clock" Function Key (Figure 9).

> **Note:** After stimulation is initiated at any therapy level, the Session Timer automatically starts if the PNT Control Unit does not sense any adjustments to operating controls for 30 seconds.

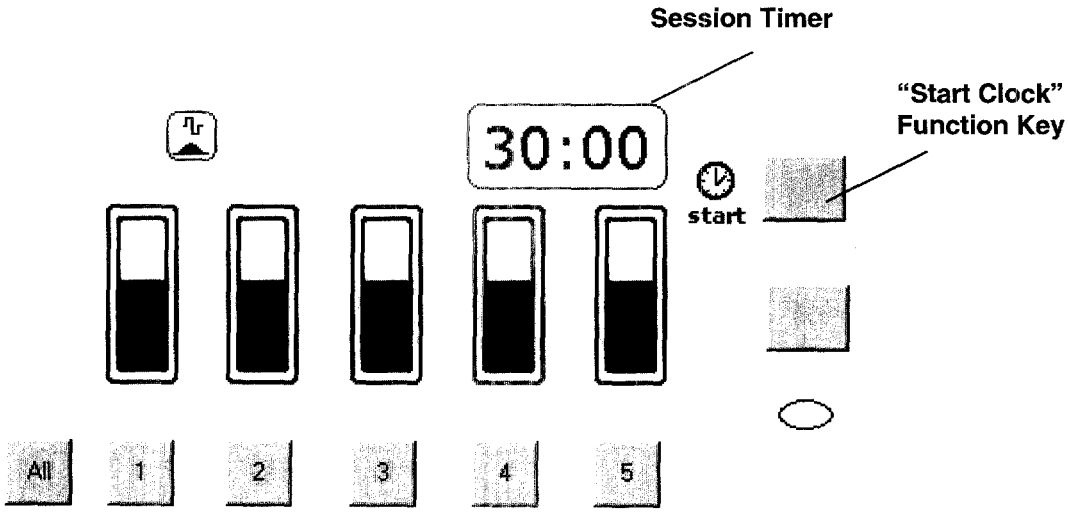


Figure 9: Starting the Session Timer Screen

Once the Session Timer is running, it can be increased (to a maximum total session time of 45 minutes) or decreased in one-minute increments. Press the "Clock Up" Function Key (Figure 10)

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to manually increase the Session Timer. Press the "Clock Down" Function Key (Figure 10) to manually decrease the Session Timer.

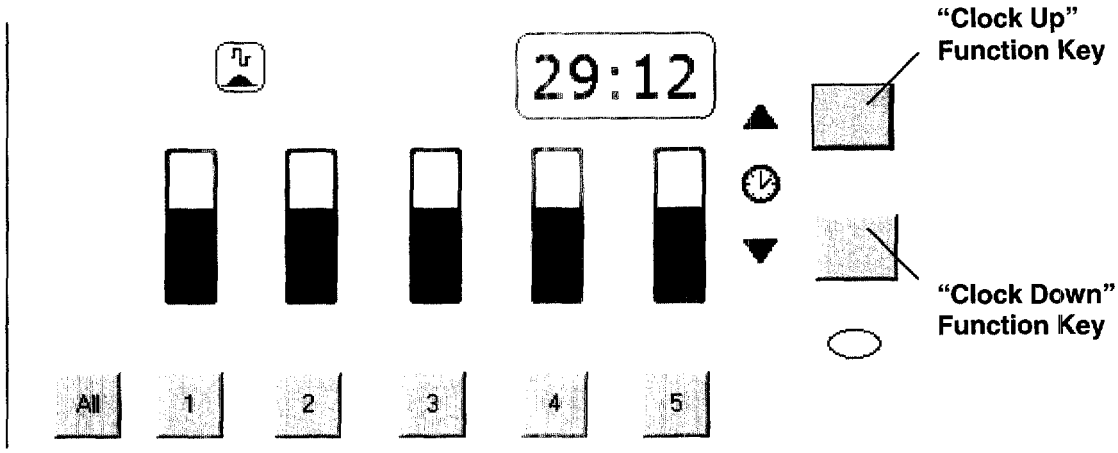


Figure 10: Adjusting the Session Timer Screen

The PNT Control Unit ships from the factory with a Session Timer default of 30 minutes. The default therapy time can be altered in the PNT Control Unit Setup Screen. See *Vertis PNT Control Unit Setup Options: Adjusting the Default Therapy Time.*

Monitoring the Patient During the Treatment Session

Monitor the patient during the therapy session to ensure that the patient remains comfortable and therapy continues without interruption.

Several minutes into the therapy session, some patients may be able to comfortably tolerate higher therapy intensity levels. Conversely, others may want the intensity decreased. If adjustment is desired, press the individual Channel Selection Buttons or the Select All Channels Button and adjust the intensity level up or down using the Therapy Control Dial. See *Initiating Therapy and Adjusting the Treatment Settings* earlier in this chapter for instructions on adjusting settings. The Session Timer continues to run while adjustments are made to the therapy settings.

Ending the Treatment Session

A chime sounds and the therapy session automatically terminates when the Session Timer reaches zero. The LCD Screen displays a completion message, the elapsed session time, and the modulation mode used during the session (Figure 11). The intensity of each active channel automatically resets to zero when the therapy session ends.

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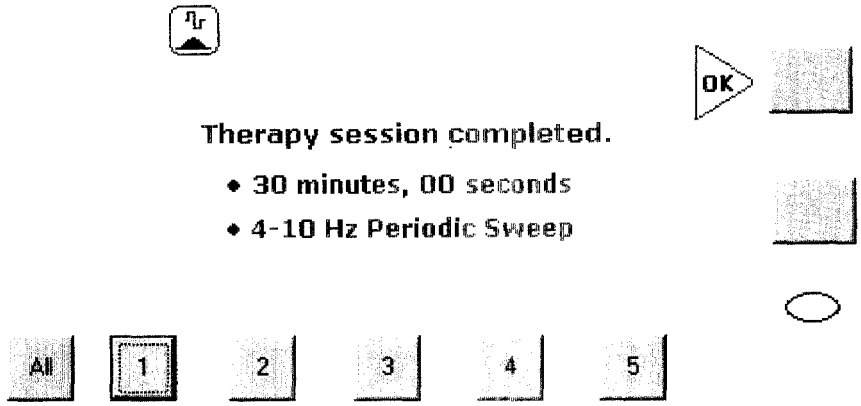


Figure 11: Therapy Session Completed Screen

To manually terminate a therapy session, press the Pause Button (Figure 1). The output for all active channels rapidly drops to zero, the Session Timer halts, and an instructional message appears on the LCD Screen (Figure 12). Press the "X" Function Key to end the therapy session. The LCD Screen displays a discontinued therapy message, the elapsed session time, and the modulation mode used during the session (Figure 13). The intensity of each active channel automatically resets to zero when the therapy session is terminated.

See *Pausing the Treatment Session* later in this chapter for instructions on continuing therapy following a pause during a treatment session.

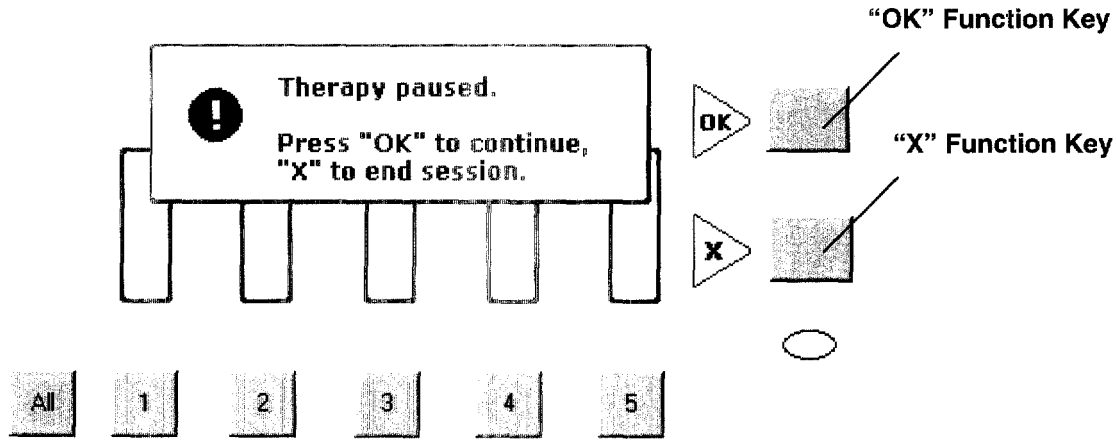


Figure 12: Therapy Paused Screen

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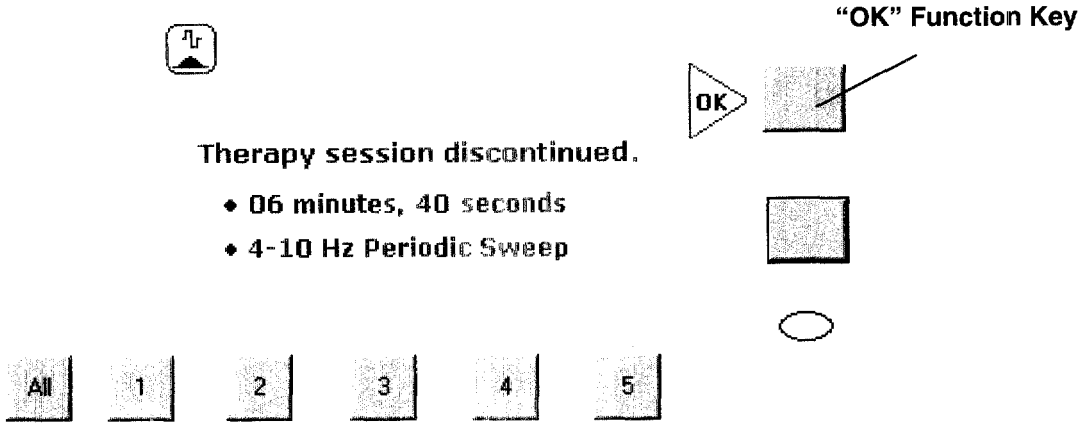


Figure 13: Therapy Session Discontinued Screen

From either the Therapy Session Completed Screen or the Therapy Session Discontinued Screen, press the "OK" Function Key to return to the Vertis PNT Main Screen (Figure 4) to begin the next therapy session. The PNT Control Unit automatically returns to the Vertis PNT Main Screen if no adjustments to operating controls are made for 10 minutes.

Disconnecting the Patient from the Patient Cable and Removing the Safeguides

At the completion of therapy, turn the Vertis PNT Control Unit "Off" and disconnect the Patient Cable keys from the Safeguide electrodes as soon as practical to minimize patient discomfort. Once all keys have been removed, take the Key Manager off the patient. The Safeguides should then be removed from the patient. Refer to the *Safeguide Kit Instructions for Use* for information about the disconnection of the Patient Cable from the Safeguide electrodes and subsequent removal of the Safeguides.

Pausing the Treatment Session

The therapy session can be paused at any time during the delivery of therapy by pressing the Pause Button on the front panel of the PNT Control Unit (Figure 1). When the Pause Button is pressed, the output for all active channels rapidly drops to zero, the Session Timer halts, and an instructional message appears on the LCD Screen (Figure 12).

The therapy session can either be continued or terminated following a pause:

- To continue the therapy session, press the "OK" Function Key. The PNT Control Unit displays the Therapy Screen. To resume therapy, adjust the output of each channel as if initiating a new session. An indicator line appears in each Output Indicator Bar showing the output level of each active channel at the time the pause was initiated (Figure 14). Use the indicator lines to facilitate returning the channels to the desired output level. See *Initiating Therapy and Adjusting the Treatment Settings* earlier in this chapter for instructions on adjusting therapy settings.

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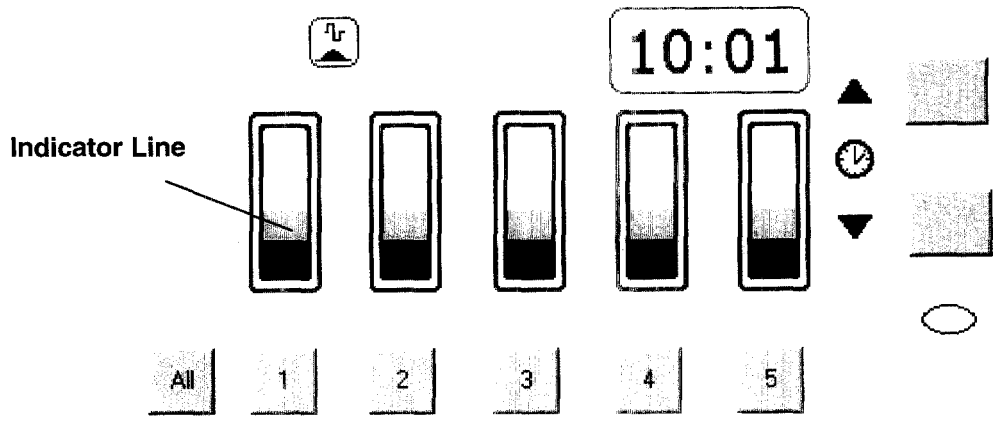


Figure 14: Indicator Lines

- To terminate the therapy session, press the "X" Function Key. The LCD Screen displays the Discontinued Therapy Screen (Figure 13).

Responding to Channel Alerts

Each channel of the PNT Control Unit provides stimulation current to a pair of Safeguide electrodes. A Channel Alert occurs when the PNT Control Unit senses that either a Safeguide is not connected to the Patient Cable or a Safeguide has become dislodged from the patient.

If fewer than five electrode pairs are attached at the start of the therapy session (e.g., an electrode accidentally becomes dislodged or a Safeguide pair is intentionally omitted), a chime sounds and a flashing Channel Alert icon appears in the corresponding Output Indicator Bar as the current level is adjusted upward (Figure 7).

If the Safeguide pair was omitted intentionally, therapy can continue and the flashing Channel Alert icon ceases after a few seconds. If the alert is unexpected, press the Pause Button. The output for all active channels rapidly drops to zero and the LCD Screen displays an instructional text prompt (Figure 15). See *Troubleshooting and Repair: Troubleshooting* for instructions on troubleshooting the problem. Press the "OK" Function Key to continue the therapy session or the "X" Function Key to end the session.

Should an electrode become dislodged during a therapy session, a repeating chime sounds and a Channel Alert icon appears in the corresponding Output Indicator Bar. The PNT Control Unit automatically pauses the delivery of therapy, reduces the current level indicator to zero for all channels, halts the Session Timer, and provides an instructional text prompt (Figure 15). See *Troubleshooting and Repair: Troubleshooting* for instructions on troubleshooting the problem. Press the "OK" Function Key to continue or the "X" Function Key to end the therapy session.

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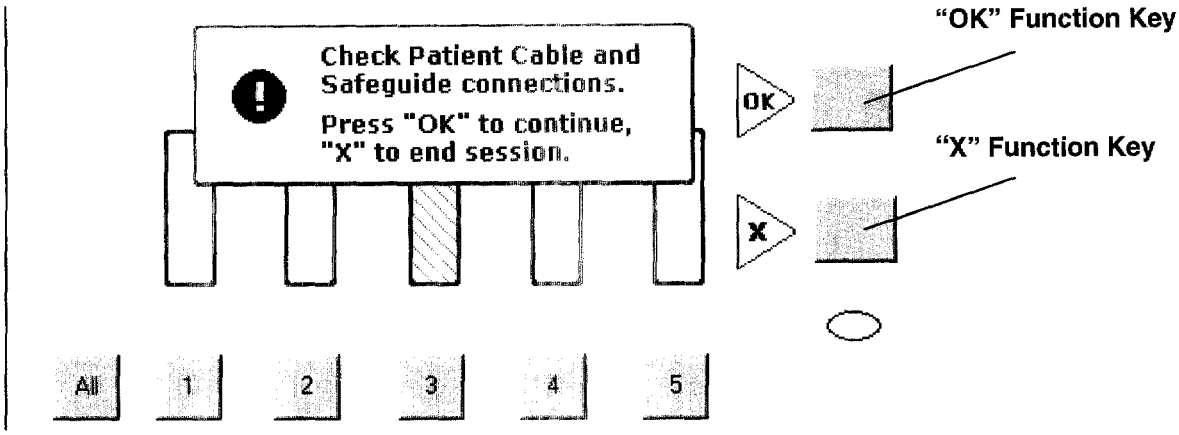


Figure 15: Channel Alert During a Therapy Session Screen

If therapy is resumed after a Pause initiated by a Channel Alert, adjust the output of each channel as if initiating a new session. An indicator line appears in each Output Indicator Bar showing the output level of each active channel at the time the pause was initiated (Figure 14). Use the indicator lines to facilitate returning the channels to the previous output level, if desired. An indicator line may not appear in the Output Indicator Bar for the channel(s) that triggered the alert. See *Initiating Therapy and Adjusting the Treatment Settings* earlier in this chapter for instructions on adjusting therapy settings.

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Vertis PNT Control Unit Setup Options

Several default PNT Control Unit options may be configured by the clinician. These include the LCD Screen contrast, the default therapy time, the default modulation mode, and the line power setting. The first three features are adjusted by accessing the PNT Control Unit Setup Main Menu Screen. The line power setting is changed at the Power Entry Module.

Accessing the PNT Control Unit Setup Main Menu Screen

Access the Setup Main Menu Screen to change the software default settings in the Vertis PNT Control Unit, including the LCD Screen contrast, the default therapy time, and the default modulation mode. To access the Setup Main Menu Screen:

1. Turn the PNT Control Unit "Off".
2. Pause at least five seconds while the PNT Control Unit powers down.
3. Turn the PNT Control Unit "On".
4. Press the "Setup Screen" Function Key while the PNT Control Unit performs its power-on self-test (Figure 16) to reach the Setup Main Menu Screen (Figure 17).
5. To exit the Setup Main Menu Screen and return to the Power-On Self-Test Screen (Figure 3), select "Exit" by pressing Channel Selection Button 5. The PNT Control Unit continues running its self tests. If the PNT Control Unit passes the self tests, the LCD Screen automatically displays the Vertis PNT Main Screen (Figure 4) and is ready for use.

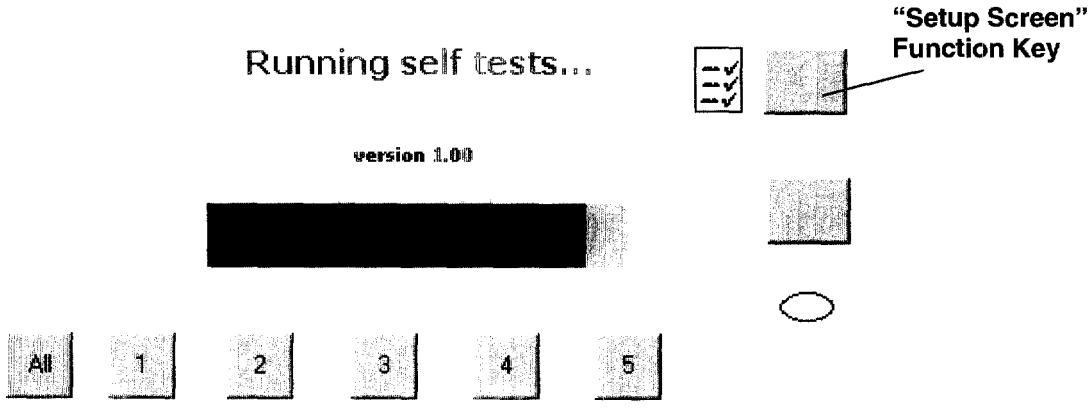


Figure 16: "Setup Screen" Function Key

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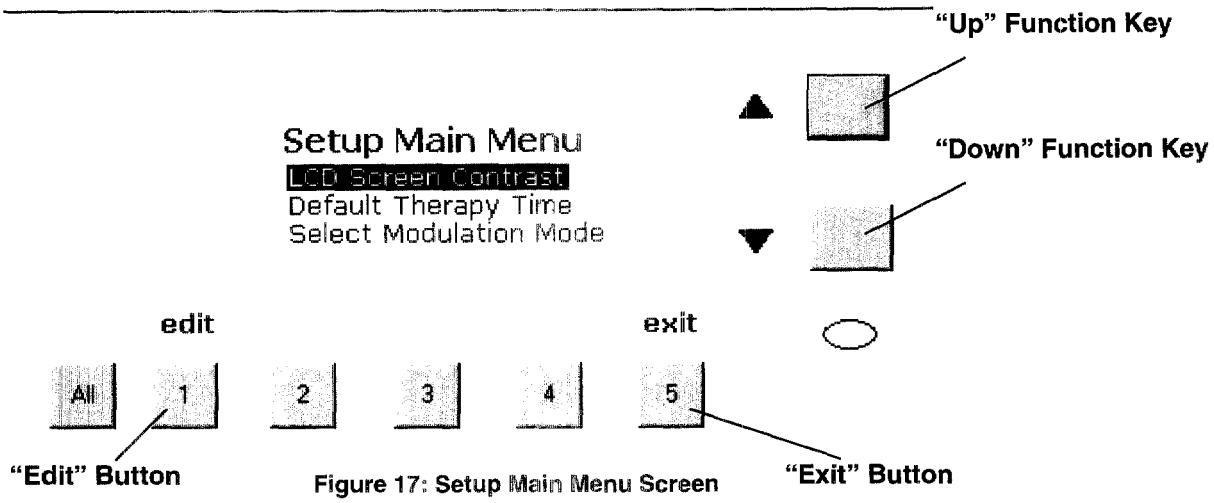


Figure 17: Setup Main Menu Screen

Adjusting the LCD Screen Contrast

The PNT Control Unit ships from the factory with the LCD Screen contrast adjusted for typical indoor lighting. In the Setup Screen Main Menu, press the "Up" or "Down" Function Key (Figure 17), as necessary, to highlight LCD Screen Contrast. Select "Edit" by pressing Channel Selection Button 1. The PNT Control Unit displays the LCD Screen Contrast Screen (Figure 18). Increase or decrease the LCD Screen contrast by pressing the "Up" or "Down" Function Keys, respectively.

Once the desired LCD Screen contrast is reached, select "accept" by pressing Channel Selection Button 2 and return to the Setup Main Menu Screen. Press Channel Selection Button 5 to "cancel" and return to the Setup Main Menu Screen without adjusting the LCD Screen contrast.

Press Channel Selection Button 5 to "exit" the Setup Main Menu Screen or use the "Up" and "Down" Function Keys to select another option for adjustment.

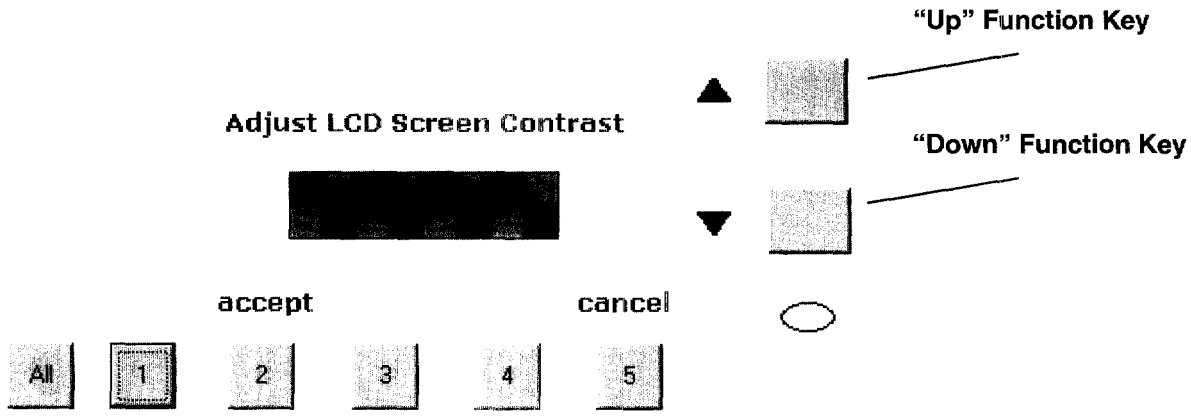


Figure 18: Adjusting the LCD Contrast Screen

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Adjusting the Default Therapy Time

The PNT Control Unit ships from the factory with a Session Timer default of 30 minutes. In the Setup Main Menu Screen, press the "Up" or "Down" Function Key, as necessary, to highlight Default Therapy Time (Figure 17). Select "edit" by pressing Channel Selection Button 1. The PNT Control Unit displays the Default Therapy Time Screen (Figure 19). Select the desired default therapy time ranging from 0 minutes to 45 minutes by pressing the "Up" or "Down" Function Keys to increase or decrease the default therapy time.

Once the desired default therapy time is reached, select "accept" by pressing Channel Selection Button 2 and return to the Setup Main Menu Screen. Press Channel Selection Button 5 to "cancel" and return to the Setup Main Menu Screen without adjusting the default therapy time.

Press Channel Selection Button 5 to "exit" the Setup Main Menu Screen or use the "Up" and "Down" Function Keys to select another option for adjustment.

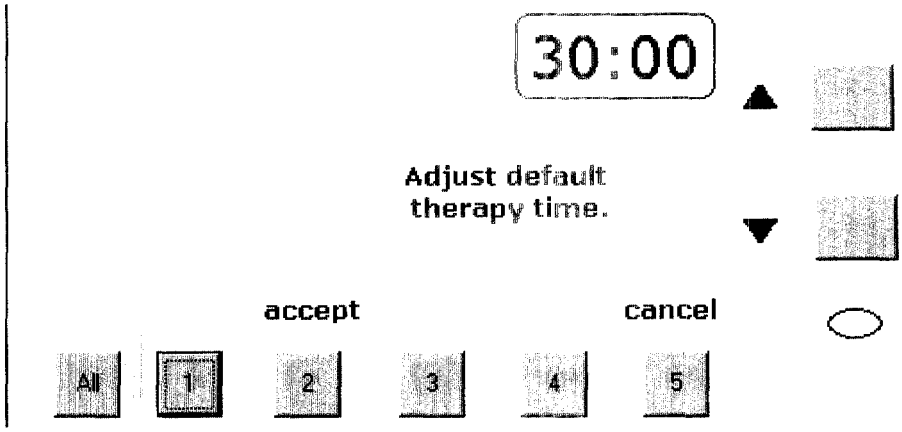


Figure 19: Adjusting the Default Therapy Time Screen

Changing the Default Modulation Mode

The PNT Control Unit ships from the factory with the default modulation mode set to the 4-10 Hz Periodic Sweep Modulation Mode. In the Setup Main Menu Screen, press the "Up" or "Down" Function Key, as necessary, to highlight Select Modulation Mode (Figure 17). Select "edit" by pressing Channel Selection Button 1. The PNT Control Unit displays the Select Modulation Mode Screen (Figure 20). Select from five pre-programmed modulation modes by pressing the "Up" and "Down" Function Keys to scroll through the options.

The Vertis PNT Control Unit has five pre-programmed modulation modes. These modulation modes were designed to deliver therapy that varies over a range of frequencies. If a patient does not respond to a particular modulation mode after several sessions, clinicians should consider selecting a different modulation mode.

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4-10 Hz Periodic Sweep Modulation Mode

When the 4-10 Hz Periodic Sweep Modulation Mode is selected, the PNT Control Unit produces a pulse train that gradually varies from 4 Hz to 10 Hz, then back down to 4 Hz in a periodic manner. Thus, the patient feels a periodic sweep from a relatively slow rate of pulses to a more moderate rate of pulses.

4 Hz Continuous Modulation Mode

When the 4 Hz Continuous Modulation Mode is selected, the PNT Control Unit produces a continuous pulse train of 4 Hz pulses. The patient feels a relatively slow, continuous rate of pulses.

15/30 Alternating Modulation Mode

When the 15/30 Hz Alternating Modulation Mode is selected, the PNT Control Unit produces a pulse train sequence consisting of 3 seconds of 15 Hz pulses followed by 3 seconds of 30 Hz pulses. The patient feels pulses alternating between a moderately slow rate and a moderately fast rate.

50 Hz Continuous Modulation Mode

When the 50 Hz Continuous Modulation Mode is selected, the PNT Control Unit produces a continuous pulse train of 50 Hz pulses. The patient feels a relatively fast, continuous rate of pulses.

4-50 Hz Aperiodic Sweep Modulation Mode

When the 4-50 Hz Aperiodic Sweep Modulation Mode is selected, the PNT Control Unit produces 3-second intervals of fixed frequency pulse trains that vary aperiodically from 4 to 50 Hz. The PNT Control Unit produces a sweep of frequencies as one fixed frequency pulse train transitions to the next. The patient feels pulses that vary from a relatively slow rate to a relatively fast rate in an aperiodic pattern.

The selected modulation mode icon remains on the LCD Screen in the upper left-hand corner throughout the therapy session. The modulation mode also is displayed at the end of a therapy session on both the Therapy Completed and Therapy Discontinued Screens (Figure 11 and Figure 13 respectively) to facilitate entering into patients' records.

Once the desired default modulation mode is reached, select "accept" by pressing Channel Selection Button 2 to return to the Setup Main Menu Screen. Press Channel Selection Button 5 to "cancel" and return to the Setup Main Menu Screen without changing the default modulation mode.

Press Channel Selection Button 5 to "exit" the Setup Main Menu Screen or use the "Up" and "Down" Function Keys to select another option for adjustment.

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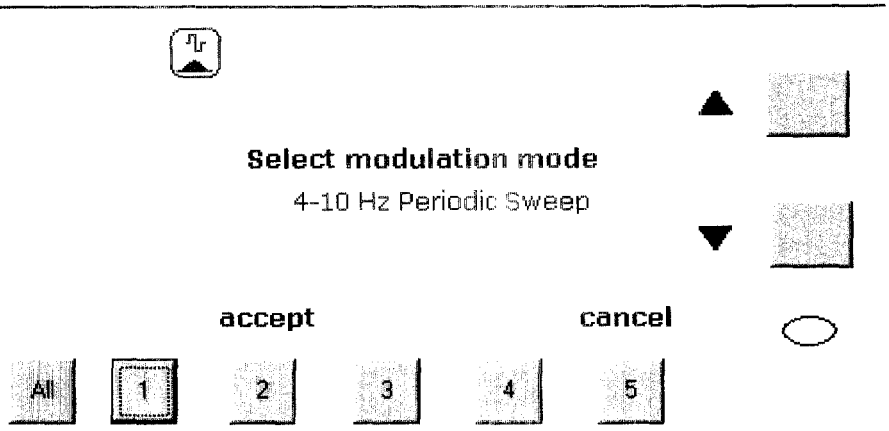


Figure 20: Select Modulation Mode Screen

Changing the Line Voltage Setting

The PNT Control Unit ships from the factory with the default line power set for 120 volt AC. Line input can be changed to accommodate 240 volt AC within the Power Entry Module. To make this change, disconnect the AC Power Cable from the PNT Control Unit. Remove the fuse drawer located directly below the AC Power Cord Receptacle on the Power Entry Module (Figure 21). Orient the fuse drawer so that the appropriate line power is selected and reinsert.

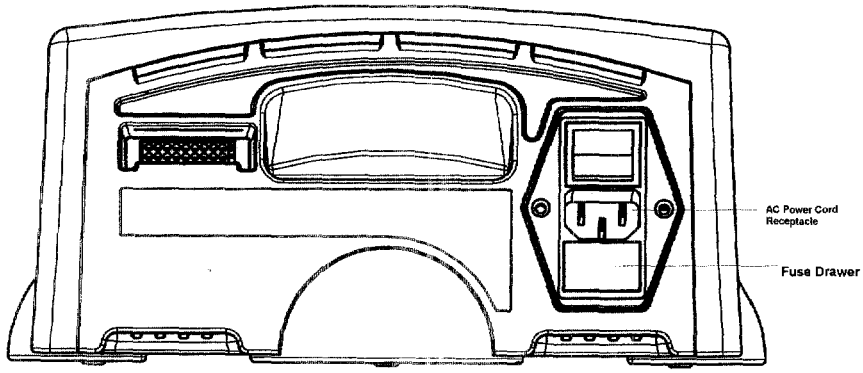


Figure 21: Fuse Drawer

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Maintaining the Vertis PNT Control Unit

Self Tests

The Vertis PNT Control Unit performs a variety of self tests during normal use. A power-on self-test ("POST") is performed when the device is powered on (Figure 3). Upon successful completion of the POST, the PNT Control Unit enters its normal operating mode.

Once in normal operating mode, the PNT Control Unit performs both continuous and periodic tests to ensure that the device is operating properly. These tests are automatic and do not interfere with the routine operation of the PNT Control Unit. The fault indicator light illuminates if a self test fails.

Fault Indicator Light

The fault indicator light is an amber LED visible on the front panel of the PNT Control Unit, just below the Function Keys (Figure 1). If the PNT Control Unit fails certain self tests, the fault indicator light illuminates. Turn the PNT Control Unit "Off", pause at least five seconds, and then turn it "On". Do this only *one* time. This process causes the PNT Control Unit to rerun its POST to either confirm the fault or verify that the fault cleared. If the fault persists, disconnect the patient immediately (if connected) and contact Vertis Neuroscience Customer Service.

> ⚠**Warning: Failed Self Test**—Do not use the PNT Control Unit if it fails any self tests. Remove the PNT Control Unit from service and contact Vertis Neuroscience Customer Service.

Power Fuse

The Vertis PNT Control Unit contains power fuses within the Power Entry Module (Figure 2). These fuses may be inspected by removing the Fuse Drawer located below the AC Power Cord Receptacle in the Power Entry Module. Ensure that fuses are replaced appropriately, in accordance with *Appendix B: Technical Specifications*. If the PNT Control Unit blows fuses repeatedly, disconnect the patient immediately (if connected) and contact Vertis Neuroscience Customer Service.

Maintenance Schedule

The recommended interval between field safety tests (such as leakage tests) for the PNT Control Unit is one year. A qualified technician should perform these checks. See *Appendix B: Technical Specifications* for the information needed to perform these tests.

Cables eventually wear out. Check the AC Power Cable and Patient Cables regularly for signs of wear or damage, such as cracked insulation, and replace these items as needed.

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Cleaning

Observe the following guidelines to clean the Vertis PNT Control Unit and Patient Cables:

- Use a soft, damp cloth with soapy water, or a 70% isopropyl alcohol solution, or a 10% bleach solution. Do *not* use abrasive materials, cleaners, or strong solvents, such as acetone or acetone-based cleaners.
- Do *not* splash or immerse the PNT Control Unit or Patient Cables in water or other liquids.

  ⚠**Warning: Water Immersion**—Do not immerse any portion of the Vertis PNT Control Unit in water or other fluids. Avoid spilling any fluids on the Vertis PNT Control Unit or accessories as an electrical fault may occur, potentially causing injury to the patient or clinician.

Storage

Store the PNT Control Unit and Patient Cables in a cool, dry location.

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Troubleshooting and Repair

Troubleshooting

Error Condition	Possible Causes	Corrective Actions
PNT Control Unit does not turn "On".	• Fuses open. • AC Power Cord not properly installed. • Power switch not "On". • PNT Control Unit not plugged into wall power. • Incorrect voltage selected.	• Remove fuse drawer and replace with like fuses. • Check to see that AC Power Cord is fully inserted into PNT Control Unit. • Confirm power switch is in the "On" position. • Plug PNT Control Unit into wall receptacle. • Check Power Entry Module for proper line voltage selection.
Amber "fault" indicator light stays illuminated and/or message on LCD Screen states that an internal fault was detected.	• An internal fault condition has been detected in the PNT Control Unit.	• Disconnect the device from the patient. Cycle the PNT Control Unit power switch (turn the Unit "Off", pause at least 5 seconds, and turn it "On") to trigger the internal self tests. If the fault condition persists, the PNT Control Unit must be serviced. See *Repair*.
"Patient Cable error detected. Check cable." error message on LCD Screen.	• Patient Cable not installed properly. • Patient Cable damaged.	• Check to see that the Patient Cable is fully inserted into PNT Control Unit. • Check to see that the Patient Cable plug is in the proper orientation with the cable angled downward. • Check Patient Cable for damage. If damaged, replace cable.
Channel Alert icon on Output Indicator Bar(s); "Check Patient Cable and Safeguide connections" message on LCD Screen.	• Safeguide electrodes not deployed properly. • Missing or dirty Safeguide key connector.	• Verify that the Safeguide electrodes corresponding to the Output Indicator Bar(s) with the Channel Alert icon(s) are applied properly and that they have been fully deployed. • Check metallic contact in key for dirt or other contamination. Clean with dry cotton swab.

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Repair

With the exception of the power fuse, there are no user serviceable parts inside the PNT Control Unit. Do not use the PNT Control Unit on a patient if it appears damaged or presents a fault. Remove the PNT Control Unit from service and call Vertis Neuroscience Customer Service at 1-800-597-2695 for instructions.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Appendix A: Warnings and Precautions

This Appendix includes a list of warnings and precautions.

⚠Warnings

Conditions, hazards, or unsafe practices that can result in serious personal injury or death.

Precautions

Conditions, hazards, or unsafe practices that can result in minor personal injury or damage to the device.

⚠Warnings and Precautions

Percutaneous Neuromodulation Therapy (PNT)

- ⚠**Warning: Pregnancy**—The safety of PNT for use during pregnancy or delivery has not been established.
- ⚠**Warning: Central Pain**—PNT has not been tested on pain of central origin (i.e., appendicitis, hepatitis, etc.).
- ⚠**Warning: Symptomatic Treatment and Medical Supervision**—PNT is a symptomatic treatment and as such, suppresses the sensation of pain that would otherwise serve as a protective mechanism. Therefore, PNT should only be used under the medical supervision of a physician or a medical practitioner to whom the patient is referred by the physician.
- ⚠**Warning: Non-curative**—PNT has no known curative value for the underlying conditions causing pain.
- ⚠**Warning: Interference with Electronic Patient Monitoring Equipment**—Electronic monitoring equipment (i.e., ECG monitors and ECG alarms) may not operate properly when PNT equipment is being utilized.
- **Precaution: Patient Selection**—The efficacy of PNT is dependent upon patient selection by a clinician qualified in the management and treatment of pain. PNT may or may not be efficacious for an individual patient.
- **Precaution: Drugs or Mental State**—PNT treatment outcome may be influenced by the patient's psychological state and use of drugs.
- **Precaution: Sensitivity to Stimulation**—Patients who react negatively to the PNT after an adequate trial period or who find stimulation intolerable, should not undergo further PNT treatment.

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- **Precaution: Heat and Cold**—The use of heat or cold producing devices, such as electric heating blankets, heating pads, or ice packs, may impair the performance of PNT or alter the patient's circulation/sensitivity and increase the risk of injury to the patient.

Vertis PNT Control Unit

- ⚠**Warning: Damage**—Do not use the PNT Control Unit if it appears to be damaged.
- ⚠**Warning: Line Voltage Selection**—Improper voltage selection may cause damage to the PNT Control Unit.
- ⚠**Warning: Failed Self Test**—Do not use the PNT Control Unit if it fails any self tests. Remove the PNT Control Unit from service and contact Vertis Neuroscience Customer Service.
- ⚠**Warning: Proper Use**—The safety and efficacy of PNT depends on the proper use and handling of the PNT Control Unit and accessories. The PNT Control Unit has potentially hazardous electrical output that, if used improperly, may cause injury to the patient or clinician.
- ⚠**Warning: RF Diathermy**—Do not use shortwave or microwave therapy equipment in close proximity (e.g., 1 meter) to the PNT Control Unit as diathermy equipment may interfere with the PNT Control Unit output, possibly causing patient injury.
- ⚠**Warning: External Defibrillators**—Remove the Vertis PNT Control Unit and Safeguide electrodes before patient monitoring or the delivery of external defibrillation shocks.
- ⚠**Warning: RF Surgical Equipment**—Do not use RF surgical equipment in conjunction with the PNT Control Unit. Simultaneous use of RF surgical equipment may cause burns at the electrode sites or may cause damage to the PNT Control Unit.
- ⚠**Warning: Water Immersion**—Do not immerse any portion of the Vertis PNT Control Unit in water or other fluids. Avoid spilling any fluids on the Vertis PNT Control Unit or accessories as an electrical fault may occur, potentially causing injury to the patient or clinician.
- **Precaution: Accessory Use**—Do not use Safeguide Kits or Patient Cables other than those supplied or recommended by Vertis Neuroscience, Inc. The safety of other products or accessories has not been established and their use could result in injury to the patient or damage to the Vertis PNT Control Unit or accessories.
- **Precaution: Cellular (Wireless) Telephones and Two-Way Radios**—Avoid operation in close proximity (e.g., < 1 meter) to transmitting cellular (wireless) telephones or two-way radios. This equipment may interfere with the Vertis PNT Control Unit output, possibly causing patient injury.

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Appendix B: Technical Specifications

Specifications are subject to change without notice. All specifications are nominal unless otherwise indicated.

Physical Dimensions

Category	Specification/Description
Size (H x W x D)	5 inches (12.7 cm) x 10 inches (25.4 cm) x 10 inches (25.4 cm)
Weight	Approximately 7.0 pounds (3.18 kg)

Input Power and Fusing

Category	Specification/Description
Input Voltage Ranges	Configurable for 115 volts AC (97-132 VAC) or 240 VAC (204-265 VAC)
Input Voltage Range Selection	Via fuse drawer position
Input Line Frequency	50 Hertz or 60 Hertz
Input Power	20 Watts
Fuse Type	250 mA, type AT, 5x20mm, slow blow

Environmental Conditions

Category	Specification/Description
Operating Temperature/Humidity	10 to 35°C (50 to 95°F), 30% to 90% Relative Humidity (non-condensing)
Storage Temperature/Humidity (when packaged for shipment)	-20 to 60°C (-4 to 140°F), 10% to 95% Relative Humidity (non-condensing).

Classification

Category	Specification/Description
Type of protection against electrical shock	Class I Equipment

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Degree of protection against electrical shock	Type BF Applied Part
Degree of protection against harmful ingress of water	Ordinary Equipment
Degree of safety of application in the presence of a flammable anesthetic mixture with air or with oxygen or nitrous oxide	Equipment not suitable for use in the presence of a flammable anesthetic mixture with air or with oxygen or nitrous oxide
Mode of Operation	Continuous Operation

Patient Outputs

Category	**Specification/Description**
Patient Connection Type/Leakage current performance	Type BF Applied Part 
Output Type	Five independently controllable, charge-balanced, rectangular biphasic, current outputs
Phase Duration	200 uSec per phase, ±5%
Output Amplitude	±15 mA max @ 4 Hz PRF ±15%, into 500 Ohm load
Output Amplitude/Pulse Repitition Frequency (PRF) Compensation	100 % @ 4 Hz PRF, reduced to 68% @ 50 Hz PRF
Output Modulation Modes	User selectable: 4-10 Hz Periodic Sweep PRF  4 Hz Continuous PRF  15/30 Hz Alternating PRF  50 Hz Continuous PRF  4-50 Hz Aperiodic Sweep PRF 

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Maximum Output Charge	7.2 uC per biphasic pulse (500 ohm load)
Output Protection	Automatic channel disable for open-circuit load condition

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Typical Output Waveforms and Modulation Modes

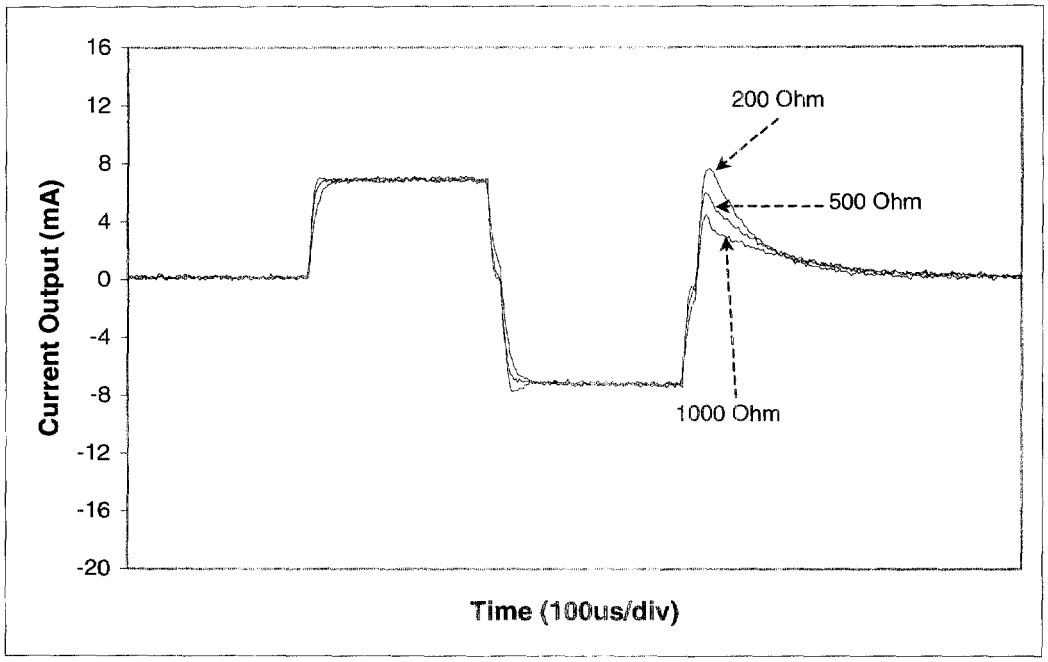


Figure 22: Output Current Using AAMI Standard Loads

Typical current pulses delivered at 50% of maximum current (7.5 mA) to AAMI loads consisting of 200, 500, and 1,000 Ω in series with the parallel combination of 2,700 Ω and 1 μF.

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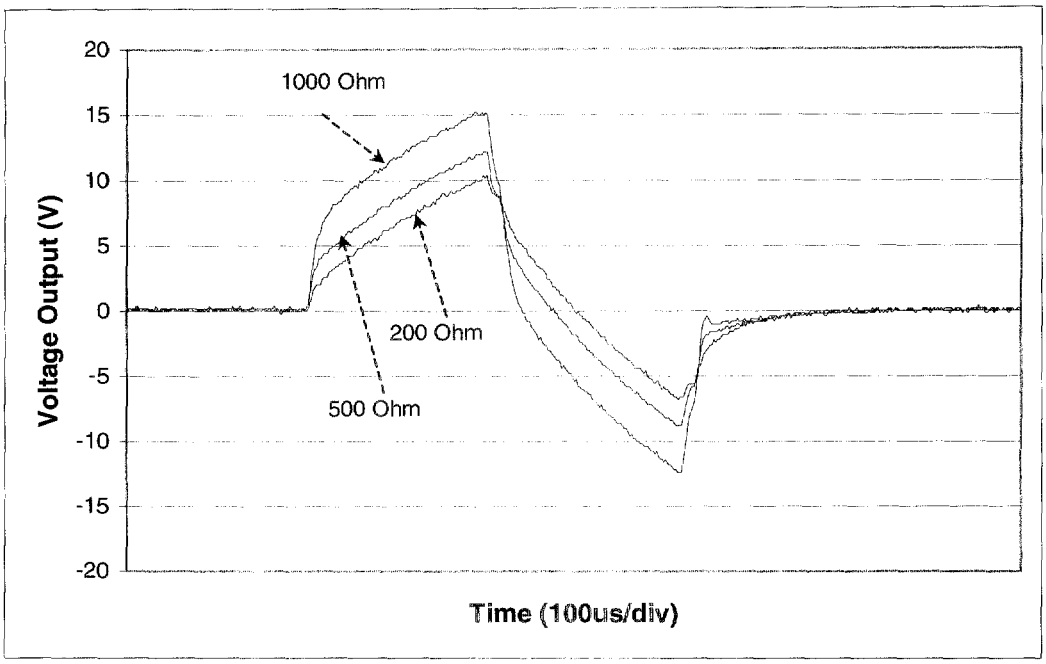


Figure 23: Output Voltage Using AAMI Standard Loads

Typical voltage pulses delivered at 50% of maximum current (7.5 mA) to AAMI loads consisting of 200, 500, and 1,000 Ω in series with the parallel combination of 2,700 Ω and 1 μF.

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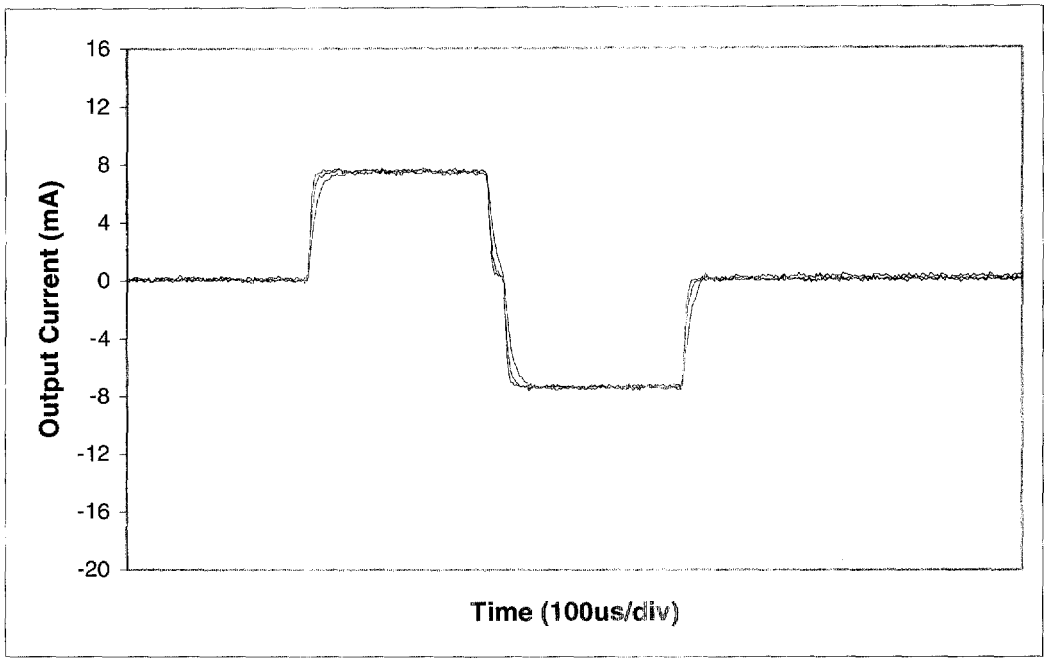


Figure 24: Output Current Using Resistive Loads

Typical current pulses delivered at 50% of maximum current (7.5 mA) to resistive loads of 200, 500, and 1,000 Ω.

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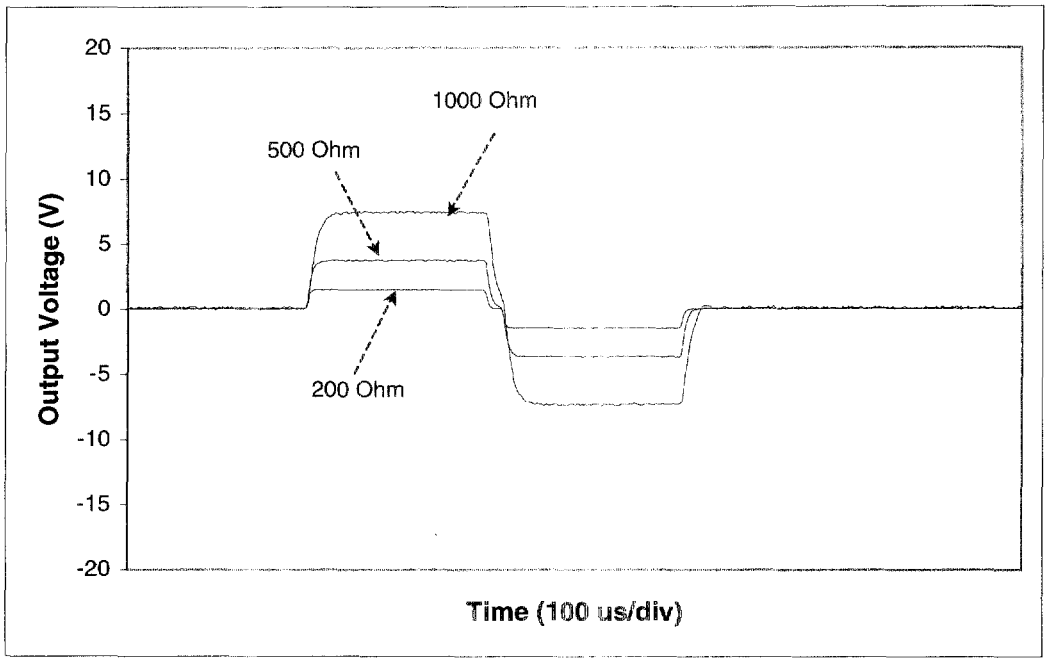


Figure 25: Output Voltage Using Resistive Loads

Typical voltage pulses delivered at 50% of maximum current (7.5 mA) to resistive loads of 200, 500 and 1,000 Ω.

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4-10 Hz Periodic Sweep Modulation Mode

When the 4-10 Hz Periodic Sweep Modulation Mode (Figure 26) is selected, the PNT Control Unit produces a pulse train from 4 to 10 Hz Pulse Repitition Frequency (PRF) varying the pulse repetition frequency as follows.

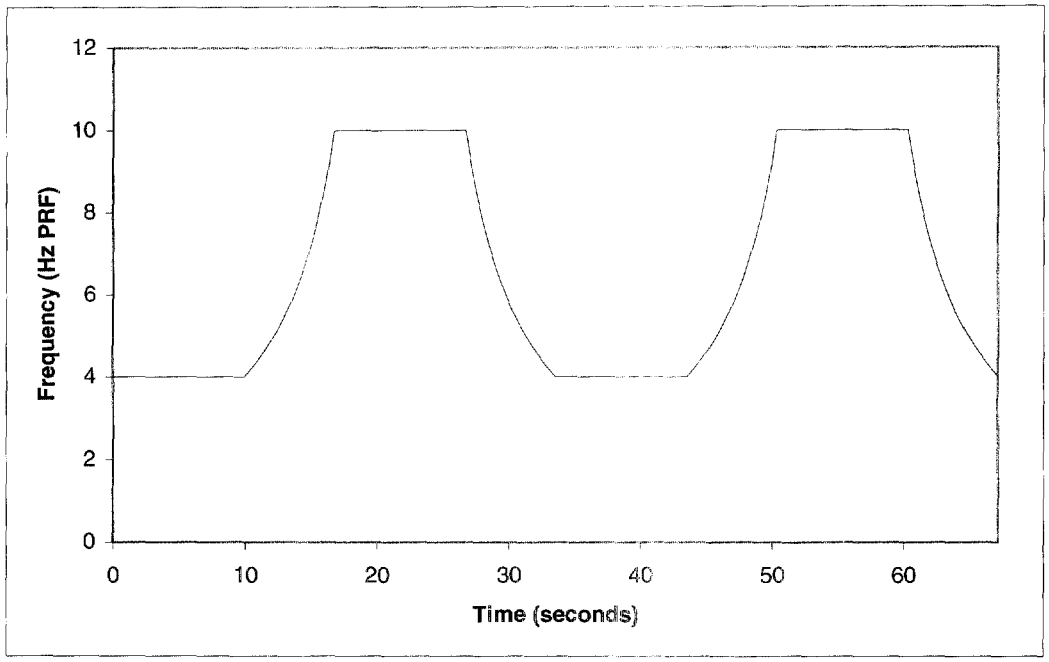


Figure 26: Profile of the 4-10 Hz Periodic Sweep Modulation Mode

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4 Hz Continuous Modulation Mode

When the 4 Hz Continuous Modulation Mode (Figure 27) is selected, the PNT Control Unit produces a continuous pulse train of 4 Hz PRF pulses.

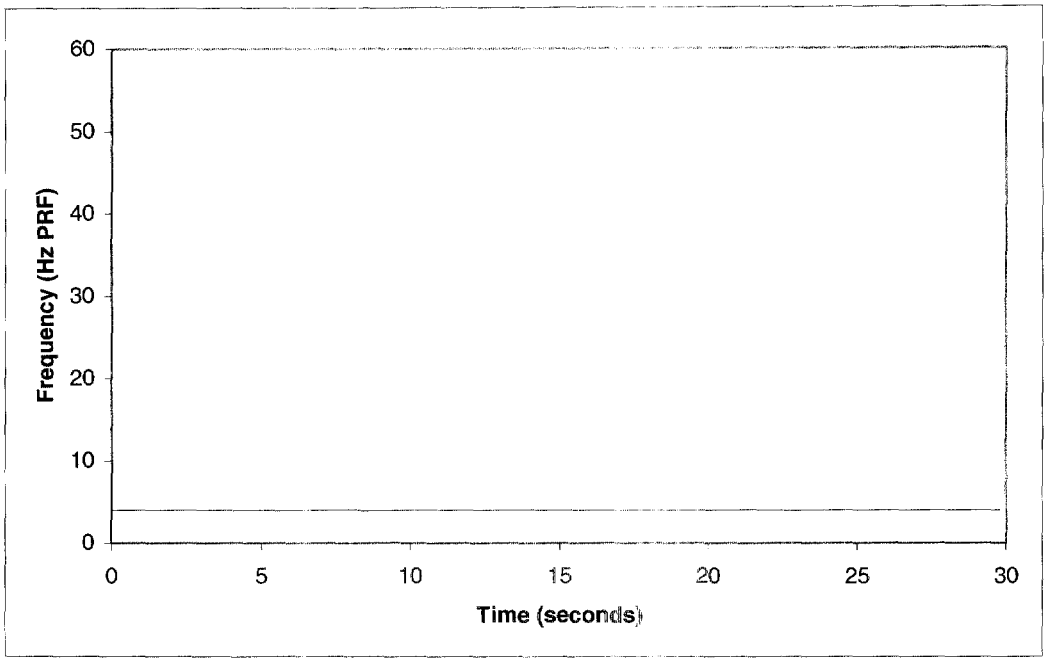


Figure 27: Profile of the 4 Hz Continuous Modulation Mode

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15/30 Hz Alternating Modulation Mode

When the 15/30 Hz Alternating Modulation Mode (Figure 28) is selected, the PNT Control Unit produces a pulse train sequence consisting of 3 seconds of 15 Hz PRF pulses followed by 3 seconds of 30 Hz PRF pulses.

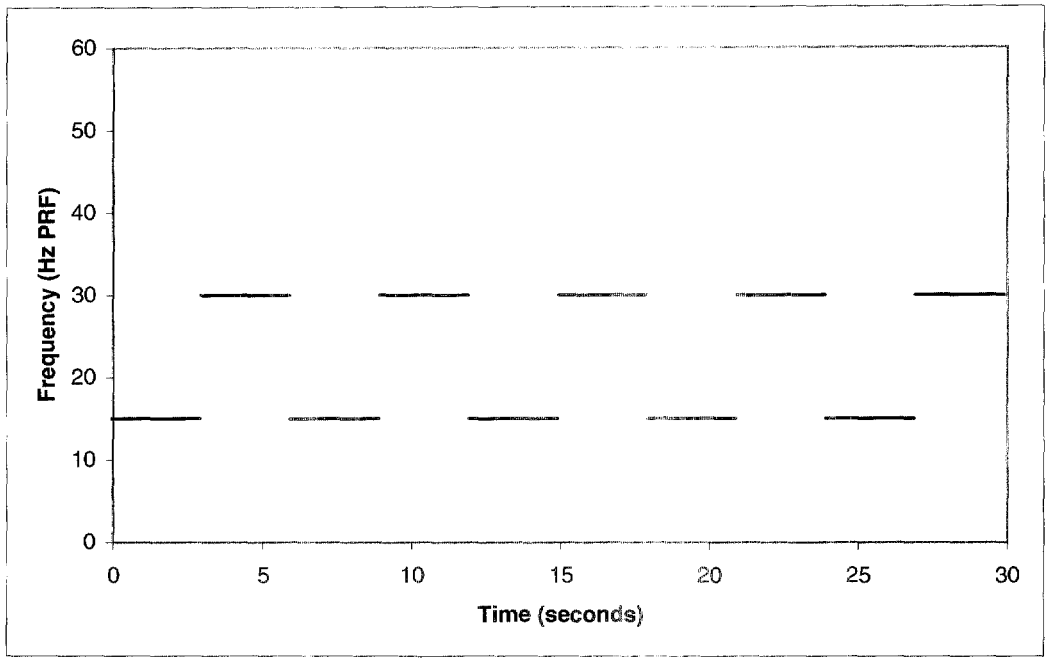


Figure 28: Profile of the 15/30 Hz Alternating Modulation Mode

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50 Hz Continuous Modulation Mode

When the 50 Hz Continuous Modulation Mode (Figure 29) is selected, the PNT Control Unit produces a continuous pulse train of 50 Hz PRF pulses.

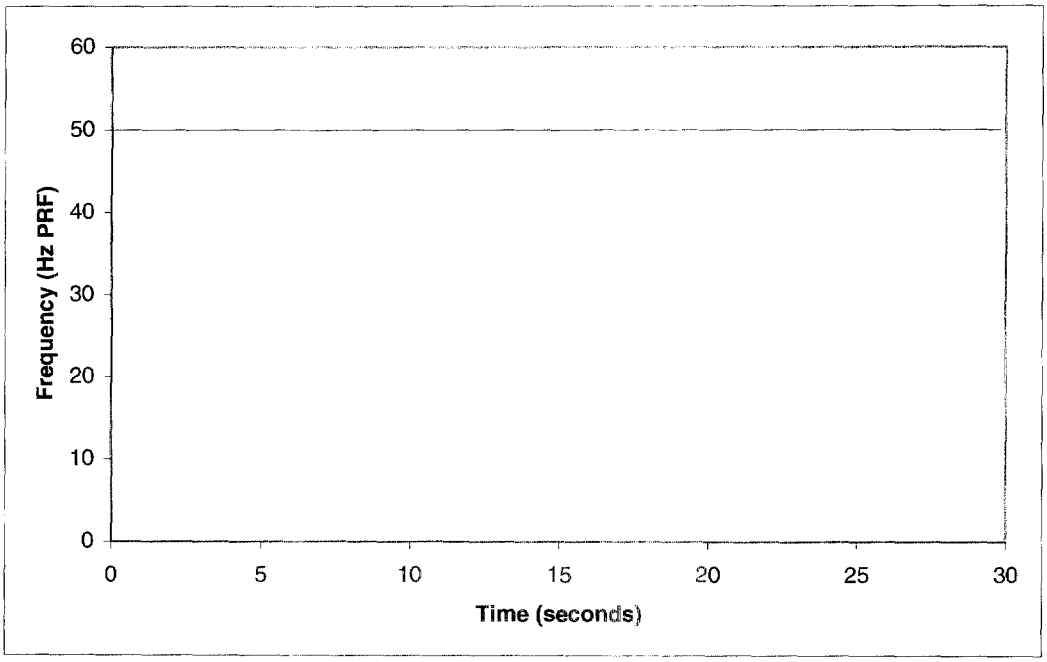


Figure 29: Profile of the 50 Hz Continuous Modulation Mode

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4-50 Hz Aperiodic Sweep Modulation Mode

When the 4-50 Hz Aperiodic Sweep Modulation Mode (Figure 30) is selected, the PNT Control Unit varies the output pulse repetition frequency aperiodically as follows:

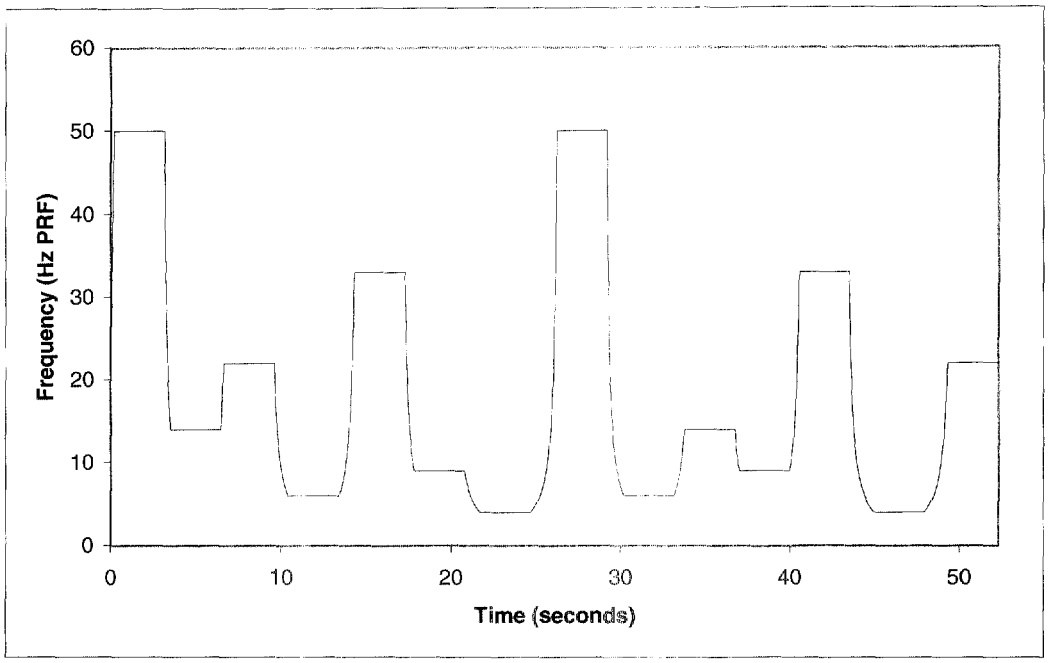


Figure 30: Profile of the 4-50 Hz Aperiodic Sweep Modulation Mode

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Appendix C: Patient Education Information

Patient education is an important component of PNT. As with any medical procedure, clinicians are advised to use appropriate clinical judgment and discuss the nature of PNT with patients prior to treatment

Addressing Questions and Concerns

It is important that patients are both physically comfortable and emotionally relaxed during the entire PNT session. Taking time to position the patient and ensuring the ambient room temperature is comfortable will help the patient feel physically at ease.

Patients may express fear or concern regarding various aspects of the PNT procedure. Taking time to listen to patients and address their concerns or to calm anxious patients may reduce anxiety and increase patients' emotional comfort level during the PNT session.

Setting Realistic Expectations

Typically, patients who are candidates for PNT will have suffered from pain for some period of time and will have tried a range of other pain relief therapies with limited or no success. While these patients may be eager to experience PNT, it is not uncommon for patients to develop unrealistic expectations about trying a new therapy.

It is the role of clinicians to clearly communicate with patients to explain PNT and to help set realistic expectations about the pain relief they may derive from PNT. Patients may hear about PNT from other patients or news reports. While many patients experience a significant reduction in pain, there is the possibility that for some patients PNT will provide a minimal reduction or no reduction at all.

> **Precaution: Patient Selection**—The efficacy of PNT is dependent upon patient selection by a clinician qualified in the management and treatment of pain. PNT may or may not be efficacious for an individual patient.

Helping patients develop realistic expectations about PNT and treatment outcomes will contribute to patients' satisfaction with the therapy. For example, discuss with patients that:

- Few patients will experience immediate pain relief from PNT. Three to four treatment sessions are typically required before patients begin to experience relief. Some patients may experience no reduction in pain even after several treatments.
- Some patients may develop some stiffness following the PNT procedure because they have been in a stationary position for an extended period of time.
- Some patients may experience stiffness or a dull ache post-treatment that may last from a few minutes to up to 24 hours, but generally not beyond.

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- Some patients may feel an immediate analgesic effect following a PNT session, whereas other patients may experience a cumulative analgesic effect over the first several treatments.

- Some patients may experience an exacerbation of pain commonly known as a "rebound response." The rebound response usually lasts 24 to 48 hours but may not occur until after the patient has left the office. Educating the patient about this possibility prior to initiating therapy can help alleviate anxiety and patient concern that "the treatment made me worse."

- After the first several treatments, if a patient has not begun to demonstrate a response to the therapy, the course of treatment should be discontinued.

- For certain patients, the delivery of PNT may not be well tolerated. For example, for some patients, the delivery of even low levels of stimulation may produce an unpleasant stinging sensation. For these patients, therapy should be discontinued and other treatment options should be considered.

  Precaution: Sensitivity to Stimulation—Patients who react negatively to the PNT after an adequate trial period or who find stimulation intolerable, should not undergo further PNT treatment.

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Appendix D: Glossary of Symbols

Vertis PNT Control Unit—LCD Screen Symbols

Icon	Description
"Setup Screen" icon 	Function Key icon used to select Setup Mode during power-on self-test.
"Go" icon 	Function Key icon used to commence a therapy session.
"!" in a circle 	Indicates an alert condition.
"4-10 Hz Periodic Sweep Modulation Mode" icon 	Indicates selection of 4-10 Hz Sweep Modulation Mode.
"4 Hz Continuous Modulation Mode" icon 	Indicates selection of 4 Hz Continuous Modulation Mode.
"15/30 Hz Alternating Modulation Mode" icon 	Indicates selection of 15/30 Hz Alternating Modulation Mode.
"50 Hz Continuous Modulation Mode" icon 	Indicates selection of 50 Hz Continuous Modulation Mode.
"4-50 Hz Aperiodic Sweep Modulation Mode" icon 	Indicates selection of 4-50 Hz Aperiodic Sweep Modulation Mode.

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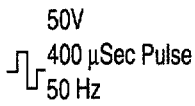
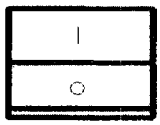
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"Start Clock" icon 	Function Key icon used to start Session Timer.
"Clock Up" and "Clock Down" icons 	Icons indicating Function Keys are active for control of Session Timer.
"X" icon 	Function Key icon used to terminate therapy session after an alert message or pause.
"OK" icon 	Function Key icon used to continue therapy session after an alert message or pause.

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Vertis PNT Control Unit—Front and Back Panel Symbols

Icon	Description
"!" in triangle icon 	Refer to User's Guide.
"Type BF output" icon 	Patient outputs are type BF applied parts
"Patient conn/max output" icon 	Patient connection, maximum electrical output.
Channel Selection Button 	Used to select an individual electrode channel for adjustment.
Select All Channels Button 	Used to select all electrode channels for simultaneous adjustment.
Pause Button 	Used to cause the cessation of the delivery of therapy.
Function Key 	Used to perform a number of functions. LCD Screen icons or text prompts indicate function.
"Fault Indicator" icon 	Indicates that the PNT Control Unit has detected an internal fault.
"On/Off" icons 	The "| " indicates the PNT Control Unit is "ON" and the "O" indicates the PNT Control Unit is "OFF."

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PN: 10070-001, Rev. A 05/01
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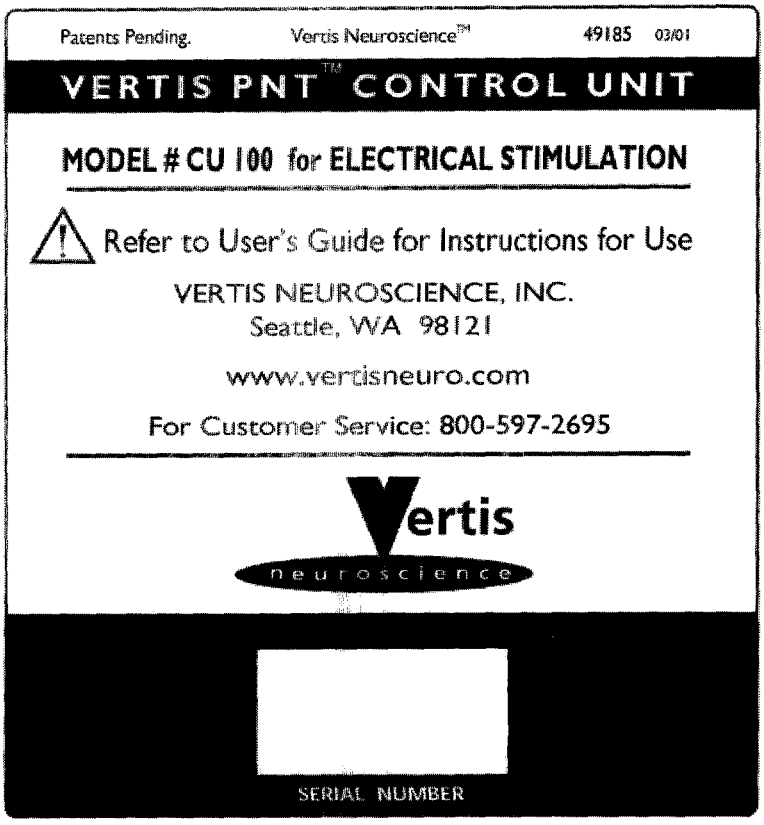
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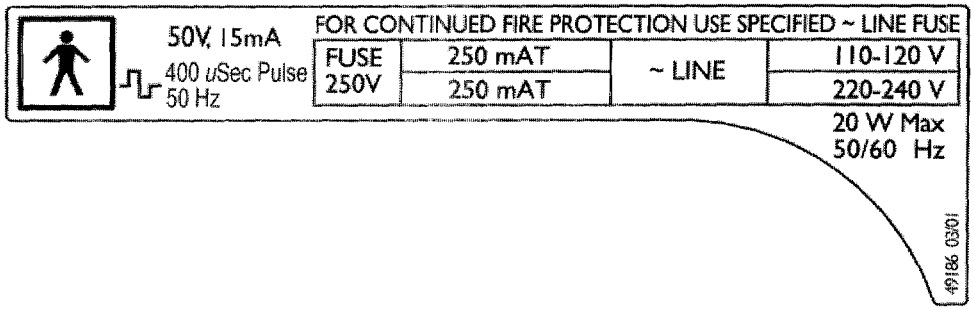
Appendix 7
Vertis PNT Control Unit – Device and Carton labeling (draft)

Device labeling

Label on the bottom panel of the PNT Control Unit



Label on the back panel of the PNT Control Unit

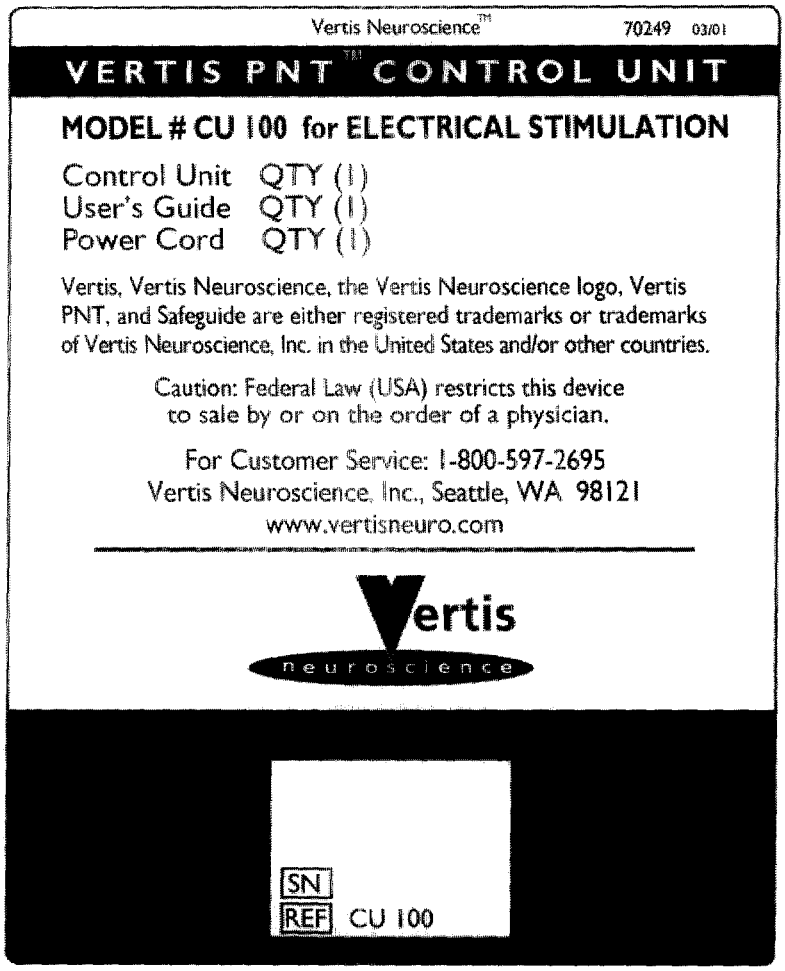


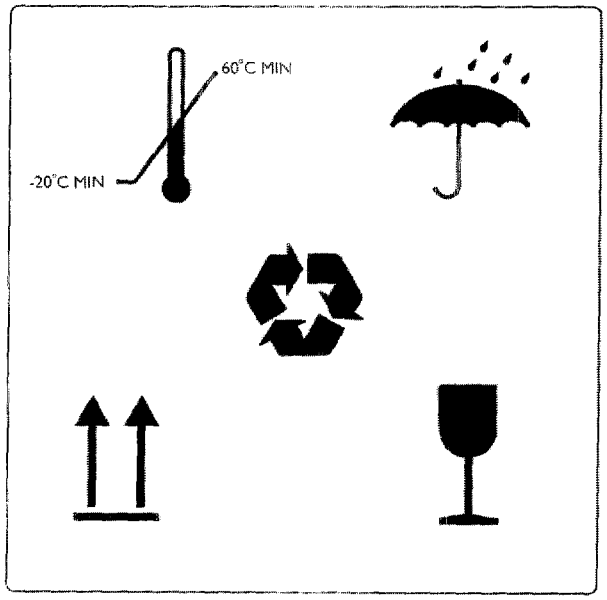
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Shelf/Shipping carton labeling





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Appendix 8
Conformance to FDA-Recognized Consensus Standards

Statement of Conformity: The Vertis PNT Control Unit is designed, developed and tested in accordance to the applicable FDA-recognized Consensus Standards noted below. Vertis certifies that we will have all testing performed, with satisfactory results, prior to marketing of the device.

Kent Leyde
Director, Engineering
Vertis Neuroscience, Inc.

Lori Glastetter
Vice President, RA/QA
Vertis Neuroscience, Inc.

In accordance to the above FDA Guidance, the following information is provided regarding the above Statement of Conformity.

Statement of Conformity - component	**Information**
Applicable recognized standards	IEC60601-1: 1993 Medical Electrical Equipment, Part 1: General Requirements for Safety and Amendments A1: 1991, A2: 1995. IEC 60601-1-2 First Edition 1993-4 Medical Electrical Equipment, - Part 1: General Requirements for Safety: Electromagnetic Compatibility – Requirements and Tests (tested in accordance to the IEC 61000 series). IEC 60601-1-4:1996 Medical Electrical Equipment, Part 1: General Requirements for Safety, Part 2: Collateral Standard: Programmable electrical medical systems. EN (CEN) 1441:1997 Medical devices – Risk Management.
Requirements met:	All requirements of the above noted standards will be met prior to marketing of this device, with no exceptions.
Standard adaptations for application to the device	The requirements of the above noted standards applied to the PNT Control Unit. These standards were not adapted in order to apply to the Control Unit.
Standard requirements that did not apply to the device	The requirements of the above noted standards applied to the PNT Control Unit. There were not any requirements that did not apply to the Control Unit.
Deviations from the	The requirements of the above noted standards were

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Standards applied	adhered to (no deviations) for the PNT Control Unit.
Differences between the test device and the device to be marketed	None. Testing in accordance to these standards is conducted on a PNT Control Unit produced in the production environment. This test device is identical to the devices to be marketed.
Test laboratory/ Certification body used	Testing to assess EMC (per IEC 60601-1-2) and other testing to IEC 60601-1 is performed at: Plexus Corporation 21621 30th Ave., S.E. Bothell, WA 98021 Establishment registration number: 3031699 Northwest EMC 22975 NW Evergreen Parkway, Suite 400 Hillsboro, OR 97124 Establishment registration number: None (contract test laboratory)

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Appendix 9
Specification/Technical Information

(b) (4)

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(b) (4)

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Appendix 10
Software Information

(b)(4)



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Appendix 12
Instructions for Use (draft)

Instructions for Use: The draft Vertis PNT Safeguide electrode kit Instructions for Use (b)(4) enclosed –13 pages

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Vertis PNT™ Safeguide™ Kit—Lumbar
Instructions for Use



Vertis PNT Safeguide Kit—Lumbar
For Use with the Vertis PNT Control Unit

For single use only.

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Introduction

These instructions provide information about using Vertis PNT™ Safeguide™ electrodes for the treatment of lumbar spinal pain. Safeguide Kits are indicated for use only with the Vertis PNT Control Unit and Vertis PNT Lumbar Patient Cable.

Each lumbar kit contains 10 Safeguide electrodes. Each Safeguide consists of a fine-diameter, stainless steel, filament electrode housed within a plastic assembly providing engineered sharps protection for both clinicians and patients. The Safeguide is designed to prevent the sharp electrode from being inadvertently exposed during handling or disposal. When an electrode deployment key is not in the Safeguide, the electrode is locked in a position that prevents sharps exposure.

The highly polished stainless steel electrode is manufactured with a proprietary sharpening process that produces an extremely sharp tip. Additional product features include tactile distraction at the point of electrode insertion to minimize patient discomfort, and a mechanism to help prevent accidental dislodgment of the electrode during therapy.

Vertis PNT for the Treatment of Lower Back Pain

Vertis PNT is a minimally invasive pain management therapy. Lumbar Safeguide kits are designed to be used in conjunction with the Vertis PNT Control Unit for the treatment of lower back pain (LBP).

Few patients experience immediate pain relief from their initial PNT session. Three to four treatment sessions are typically required before patients begin to experience meaningful relief. For patients who derive benefit from this initial series of treatments, PNT may be continued on a periodic basis based on clinical judgment and patient feedback.

For those patients who do not derive benefit from the first three to four treatment sessions, other pain therapies should be considered.

Indications and Contraindications

Vertis PNT Safeguide Kits are indicated for use only with the Vertis PNT Control Unit. Refer to the *Vertis PNT Control Unit User's Guide* for complete operating instructions on the use of the Vertis PNT Control Unit, as well as indications, contraindications, warnings, and precautions relevant to delivering PNT.

Using Vertis PNT Safeguide Electrodes

⚠**Warning:** Do not use a Safeguide electrode if it appears damaged.

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Positioning the Patient

To minimize patient discomfort, the patient should remain stationary for the duration of the treatment session. It is therefore important that the patient be comfortable and relaxed throughout the treatment session. Taking time to position the patient and ensuring the ambient room temperature is comfortable will help the patient feel physically at ease.

Prone Position

Clinicians are encouraged to use the prone position when treating patients in the lumbar region with Vertis PNT. The use of pillows, towels, blankets, and additional padding to position the patient more comfortably may be helpful. With the patient lying in the prone position on an exam table or similar flat surface (Figure 1), place pillows under the patient to support the chest, hips, and feet.



Figure 1: Lying in prone position.

Though the clinician is encouraged to use this position, the following are other positions to consider for patients for whom the prone position is not an option.

The On-One-Side Position

With the patient lying on one side (Figure 2), place a pillow under the patient's head to support the neck. Place another pillow between the knees to support the hips.

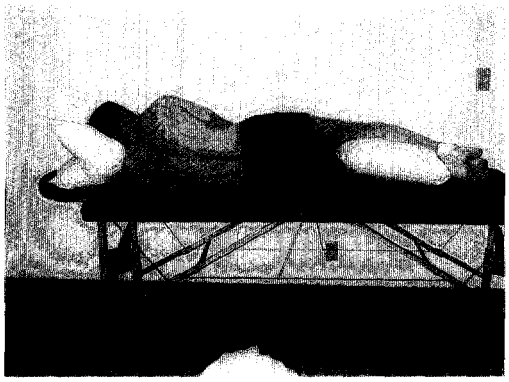


Figure 2: Lying on one side.

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The ¾ Position

Have the patient lay at a ¾ position (Figure 3). Start with the patient lying on one side; slowly roll towards prone position to a position of maximum comfort. Place a pillow under the patient's head and another pillow under the patient's chest to support the arms and chest. Place another pillow between the knees to support the hips.

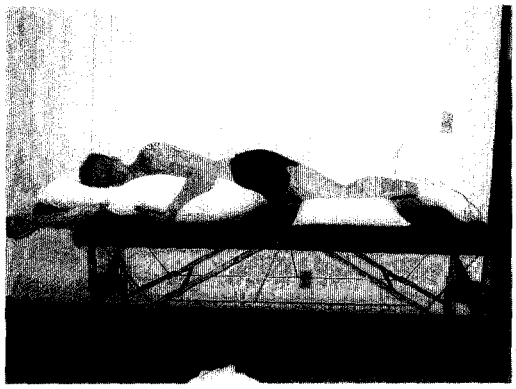


Figure 3: Lying at ¾ position.

Identifying Sites for Safeguide Electrode Placement

Percutaneous Neuromodulation Therapy (PNT) treats pain based upon the delivery of electricity directly to the soft paraspinal tissues near the level of the involved dermatomes. Selecting the sites for applying Safeguide electrodes should ultimately be based on clinician judgment. Vertis recommends a placement montage for the Safeguide electrodes (Figure 4) developed from Vertis' clinical work and previous studies on percutaneous electrical therapy for the treatment of lower back pain.

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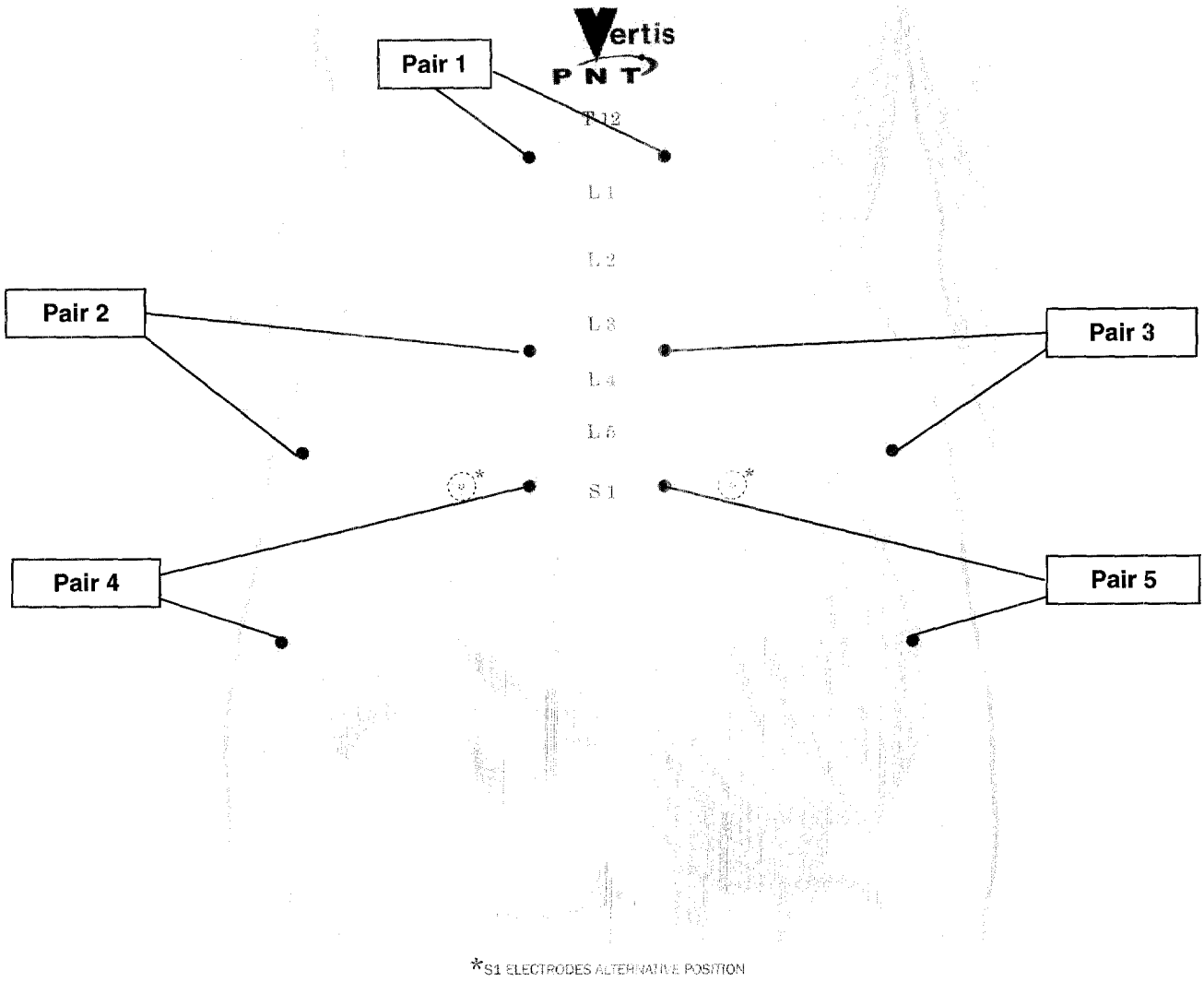


Figure 4: Placement montage for Safeguide electrodes.

There are five (5) Safeguide electrode pairs supplied in each kit. Table 1 describes the placement montage depicted in Figure 4.

Table 1: Placement montage recommendations

Safeguide Electrode Pair	Placement Recommendation	Placement Alternatives
Pair 1	Spans vertebral level T12-L1 with the center of each Safeguide approximately 3 cm from the spinous process.	
Pairs 2 & 3	Medial Safeguide placed approximately 3 cm from the spinous process at vertebral level L3-L4. Lateral Safeguide placed approximately 12 cm from the midline to just above the highest point of the iliac crest as shown.	

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Pairs 4 & 5	Medial Safeguide at vertebral level L5-S1 approximately 3 cm from the spinous process. Lateral Safeguide placed two-thirds along the line from the posterior superior iliac spine to the greater trochanter.	Medial Safeguide at vertebral level L5-S1 approximately 6 cm from the spinous process to avoid the medial border of the ilium.

If a patient is particularly sensitive in one area, consider using fewer than 10 electrodes in the montage. If the clinician determines that it is appropriate to use fewer than 10 electrodes, care should be taken to understand which electrodes function as pairs to ensure that both electrodes corresponding to a channel pair are eliminated. Clinicians should use appropriate clinical judgment in varying the montage.

⚠**Warning: Safeguide Use**—Each Safeguide is designed to deploy a small gauge needle electrode into the tissue to a depth of 3 cm. To avoid patient injuries or complications, use appropriate clinical judgment in patient selection (e.g., body morphology) and tissue/site selection for electrode placement. For example, in extremely thin patients, consider repositioning the electrode to a location of sufficient tissue mass or possibly exclude the patient from treatment.

Preparing the Skin

To ensure proper electrode adhesion verify that the area where the Safeguide electrodes are applied is clean and dry. For patients with excessive body hair, consider shaving the appropriate areas or applying additional adhesive taping.

⚠**Warning: Skin Preparation**—Failure to adequately prepare the skin may cause improper adhesion of the Safeguide electrodes, resulting in possible electrode dislodgment and/or reduced effectiveness.

Applying the Safeguide Electrodes

Peel each Safeguide electrode from the adhesive liner (Figure 5) and apply it to the prepared location on the patient's back. Firmly press the adhesive around the Safeguide to ensure that it is well adhered to the patient's skin (Figure 6). Do not use a Safeguide electrode if the adhesive is dry or if the electrode shelf life date (on package) has expired, as the adhesive may not adhere well.

⚠**Warning: Safeguide Application**—Do not insert the Patient Cable keys until the Safeguides are applied to the patient. An electrode will deploy from the Safeguide upon key insertion, possibly causing injury to the patient or clinician if the Safeguide is not secured to the patient.

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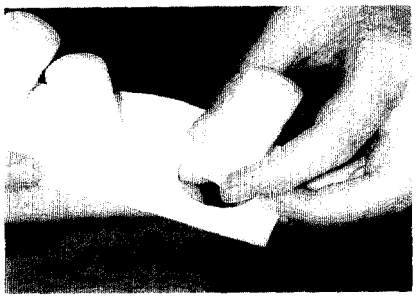


Figure 5: Peel Safeguide from adhesive liner.

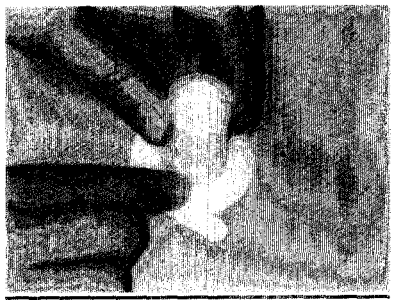


Figure 6: Press Safeguide electrode firmly on patient's back.

Connecting the Lumbar Patient Cable to the Safeguide Electrodes

The Lumbar Patient Cable is designed to maximize the time efficiency for the set-up of PNT. The Patient Cable consists of a connector, which inserts into the Vertis PNT Control Unit, a length of cable, and the "Key Manager," which organizes the 10 key connectors and is designed for placement on the patient's back. The Key Manger helps prevent electrode leads from becoming entangled, and serves as a guide for the correct electrical connection of each Safeguide electrode.

Place the Key Manager on the patient's back along the vertebrae approximately spanning from the lower thoracic to upper sacral area (Figure 7). For reference purposes, align the arrows on the Key Manager to approximately vertebral level L5-S1. For patients not in the prone position, consider using adhesive tape to secure the Key Manager in the appropriate location.

Remove each key from the Key Manager and insert into the corresponding Safeguide (Figure 8). Note that keys are color coded, and that all keys of like color belong on one side of the patient's mid-line. Ensure that both pegs at the end of each key are completely seated in the Safeguide. Rotate the key clockwise. The key will pass over a small bump and stop after approximately $\frac{1}{8}^{th}$ of a turn (Figure 9). After completing the rotation, gently push the key down to deploy the electrode (Figure 10). As each key is gently depressed, the electrode is inserted to a depth of 3 cm with a trajectory that is approximately perpendicular to the plane of the skin. Do *not* force the key or electrode.

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⚠**Warning: Patient Response**—Safeguides deploy a needle electrode. As with other medical procedures involving a needle, in rare cases, some patients may experience a vaso-vagal response to the insertion or the proposed use of a needle. The reaction is termed "needle shock" and can manifest itself as lightheadedness, cold perspiration, nausea, hypotension, and very rarely, a decrease in or loss of consciousness. In the event this occurs, discontinue therapy and take appropriate clinical action.

Note: A vaso-vagal response can be alarming to both patients and clinicians and patients should be informed of such a possibility in advance. In susceptible patients, the reaction usually occurs within the first few sessions.

Should a vaso-vagal response occur, clinicians are advised to reassure the patient and terminate the procedure. Remove and dispose of the Safeguide electrodes as indicated. Further care for the patient should follow standard clinical protocols for vaso-vagal reaction.

Consistent with any electrode insertion procedure, some patients may experience mild discomfort during electrode placement. If the patient experiences marked discomfort or pain with the application of an individual electrode, consider removing the Safeguide and replacing it with a new Safeguide in a slightly modified location. Moving the insertion location of the electrode by as little as a few millimeters is often enough to relieve discomfort associated with a particular electrode insertion site. See *Replacing a Safeguide Electrode*.

⚠**Warning: Safeguide Reuse**—Safeguide electrodes are designed for single use only. Do not reuse the Safeguide once the electrode has been deployed. Reuse may cause injury to the patient, as electrode damage may have occurred during the previous use.

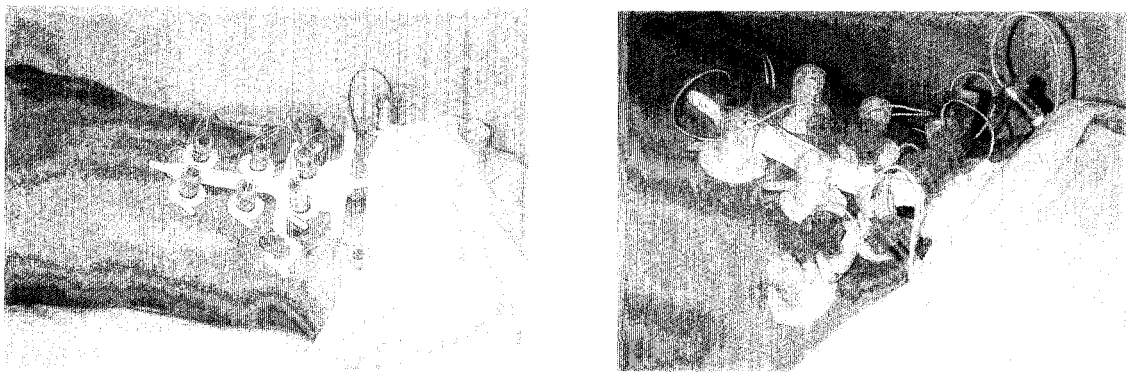


Figure 7: Key Manager placed on patient's back.

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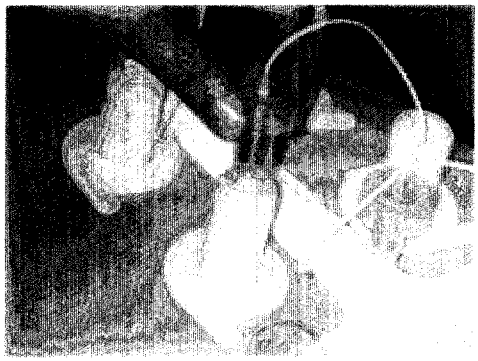


Figure 8: Remove key from Key Manager and insert into a Safeguide.



Figure 9: Place key into Safeguide and rotate clockwise.

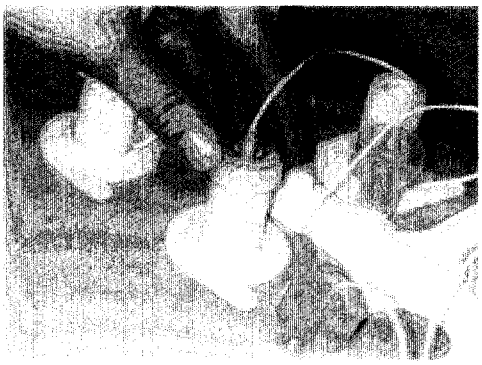


Figure 10: Gently push the key down to deploy the electrode.

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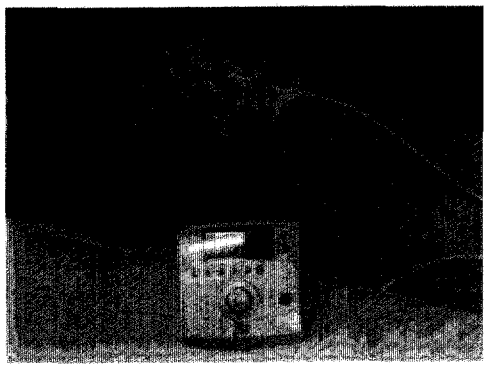


Figure 11: Fully deployed Vertis PNT System including the Vertis PNT Control Unit, Lumbar Patient Cable, and Safeguide electrodes.

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Delivering Vertis PNT Therapy

Once the Safeguides have been applied and the electrodes are deployed, the patient is ready to receive therapy. Refer to the *Vertis PNT Control Unit User's Guide* for instructions on initiating therapy.

Disconnecting the Patient from the Lumbar Patient Cable

At the completion of therapy, turn the Vertis PNT Control Unit "Off" and disconnect the Patient Cable keys from the Safeguide electrodes as soon as practical to minimize patient discomfort. Remove each electrode by pulling up the key until it stops and then rotating the key counter-clockwise approximately $\frac{1}{8}^{th}$ of a turn (Figure 12). Removing the key retracts and locks the electrode into the Safeguide. Place each key in the corresponding holder in the Key Manager. Once all keys have been removed, remove the Key Manager from the patient.

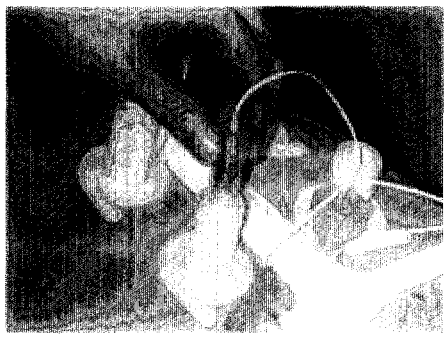


Figure 12: Pull up and rotate counter-clockwise to remove key from Safeguide.

⚠**Warning: Safeguide Removal**—Do not remove the Safeguide from the patient unless the electrode is fully retracted and the key is removed. Removal of the Safeguide prior to electrode retraction may cause irritation or injury to the patient or may pose a hazard to the patient or clinician.

Removing and Disposing Safeguide Electrodes

Remove each Safeguide electrode from the patient's skin by peeling up the tab of the Safeguide's adhesive ring (Figure 13). Discard used Safeguide electrodes.

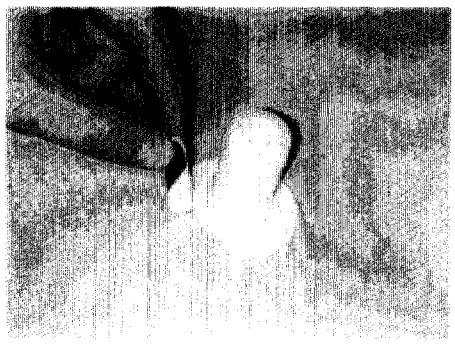


Figure 13: Hold tab and peel adhesive ring around bottom of Safeguide.

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Replacing a Safeguide Electrode

To replace a Safeguide electrode during therapy, press the Pause Button on the Vertis PNT Control Unit. The output for all active channels rapidly diminishes to zero and the Session Timer is halted. Disconnect the key from the Safeguide electrode. See *Disconnecting the Patient from the Lumbar Patient Cable* above for instructions. Remove the Safeguide electrode from the patient's skin. See *Removing and Disposing of the Safeguide Electrodes* above for instructions.

Each box of electrode kits contains several single-packaged Safeguides. These Safeguides are to be used if a Safeguide is damaged during handling prior to use, or if an electrode must be replaced during use due to patient discomfort.

Remove a single Safeguide electrode from its packaging (Figure 14) and place in the desired location on the patient's back. Reconnect the key to the Safeguide electrode. See *Connecting the Lumbar Patient Cable to the Safeguide Electrodes* for more details.

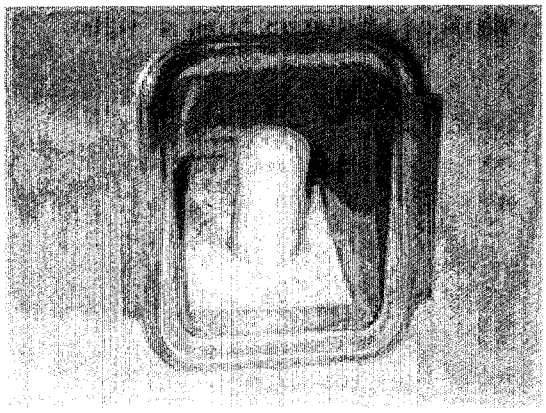


Figure 14: Single Safeguide electrode.

⚠**Warning: Safeguide Reuse**—Safeguide electrodes are designed for single use only. Do not reuse the Safeguide once the electrode has been deployed. Reuse may cause injury to the patient, as electrode damage may have occurred during the previous use.

Refer to the *Vertis PNT Control Unit User's Guide* for instructions following a pause during a therapy session.

Sterility

Safeguide Kits are supplied sterile. As with all sterile medical products, use appropriate technique in handling sterile Safeguides in order to avoid contaminating the product and to minimize the risk of infection.

Do *not* use if package has been previously opened or damaged. Do *not* resterilize. Reprocessing or resterilization will not extend the indicated shelf life.

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Reuse

Safeguide electrodes are designed for single use only. Discard the Safeguides after use. Do *not* reuse Safeguides, as reuse could result in injury or infection.

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Specifications are subject to change without notice.

Published in the U.S.A.

Caution: Federal law (USA) restricts this device to sale by or on the order of a physician.

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www.vertisneuro.com
For Customer Service: 1-800-597-2695

Patents pending.
Model Number: SG 101
PN: 10071-001 05/01

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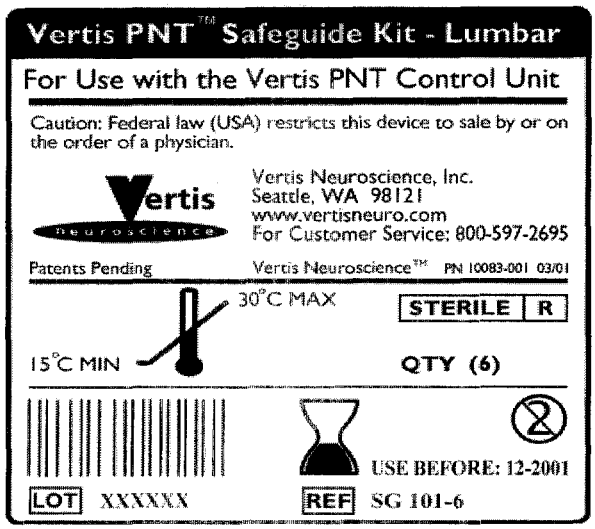
Appendix 13
Vertis Safeguide – Tray and Box Labeling (draft)

Tray labeling

Label on the tray of the Safeguide



Label on the Safeguide Box



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Appendix 14
Performance/Specification/Technical Information

(b) (4)

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APPENDIX 14

ATTACHMENT B

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Appendix 14 – Attachment B
Electrode Performance Testing and Data

(b)(4)



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Tests performed and test results:

(b)(4)

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Appendix 16
Nerve Stimulator (Control Unit) Comparison Chart

Company	**Vertis Neuroscience, Inc. Seattle, WA**	**Empi, Inc. St. Paul, MN**	**Rehabilicare, Inc. New Brighton, MN**	**Chattanooga Group, Inc. Hixson, TN**	**Medtronic, Inc Minneapolis, MN**
Product	**Vertis PNT System**	**EPIX TENS Device**	**SMP-Plus™**	**Intelect® Legend Stim**	**Mattrix® Neurostimulation System**
Model/Catalog No(s)	Model: CU 100	Model: EPIX VT Model: EPIX XL	Model 4930	Model IFC2 (catalog no. INT002)	Receiver model: 3272 Transmitter model: 3210
510(k) References	N/A – This submission	K970203, K951903	K982410	K924666	K982902
Indications for Use	Indicated for the symptomatic relief and management of chronic intractable pain and/or as an adjunctive treatment in the management of post-surgical and post-trauma acute pain.	Indicated for the symptomatic relief and management of chronic, intractable pain and/or adjunctive treatment for post-surgical and post-trauma acute pain.	Indicated for the symptomatic relief and management of chronic intractable pain and/or as an adjunctive treatment in the management of post-surgical and post-traumatic pain.	Indicated for symptomatic relief of chronic, intractable pain and management of pain associated with post-traumatic or post-operative conditions.	Indicated for spinal cord stimulation and for peripheral nerve stimulation. Indicated for treatment of chronic, intractable pain of the trunk or limbs.
Intended User	Clinician (e.g., physician, physical therapist) use.	Clinician use or patient use under the supervision of a clinician.	Clinician use or patient use under the supervision of a clinician.	Clinician use.	Implant procedure: Clinician Ongoing use: patient with clinician supervision.
Examples of Therapy Applications	Low back pain Cervical pain Thoracic pain Sciatica Shingles (zoster) Diabetic neuropathy Headache Other neuropathies	Low back pain Arthritis Chronic strains and sprains Neuralgia Reflex sympathetic dystrophy Shingles (zoster) Degenerative joint disease Intractable migraine	Cervical, thoracic, lumbar, and sacral syndromes Neuropathies Causalgias Neuralgias Nerve root/plexus injuries Phantom limb syndromes Spinal stenosis Arthritis Reflex sympathetic dystrophy	Not disclosed in manufacturer's literature.	Chronic limb pain Complex regional pain syndrome Failed back syndrome Arachnoiditis Painful neuropathies

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Company	**Vertis Neuroscience, Inc. Seattle, WA**	**Empi, Inc. St. Paul, MN**	**Rehabilicare, Inc. New Brighton, MN**	**Chattanooga Group, Inc. Hixson, TN**	**Medtronic, Inc Minneapolis, MN**
Product	**Vertis PNT System**	**EPIX TENS Device**	**SMP-Plus™**	**Intelect® Legend Stim**	**Mattrix® Neurostimulation System**
How Therapy Delivered	Percutaneous stimulation of peripheral nerves	Cutaneous stimulation of peripheral nerves	Cutaneous stimulation of peripheral nerves	Cutaneous stimulation of peripheral nerves	Pulses transmitted across skin to receiver and electrodes to stimulate peripheral nerves or spinal cord.
System Components & Accessories	Nerve stimulator Electrodes Patient Cables	Nerve stimulator Electrodes Lead Wires Batteries Battery Charger	Nerve stimulator Electrodes Patient cables Batteries	Nerve stimulator Electrodes Lead	Receiver Transmitter Antenna Electrodes/leads
Specifications					
Physical					
size (H x W x D)	4.7" x 9.65" x 9.5"	3.7" x 2.5" x 0.94"	3.75" x 2.5" x 1"	3" x 8" x 12"	2.75" x 2" x .5"
approximate weight	6.0 lbs.	4.0 oz with battery	4.8 oz with battery	7.0 lbs	Not disclosed in manufacturer's literature.
portable	yes	yes	yes	yes	yes
power supply	AC, configurable to either 115 or 240V	DC, 9V alkaline or rechargeable battery	DC, 9V alkaline or rechargeable battery	AC, configurable to either 120 or 220/240V	DC, 9V alkaline or rechargeable battery
Therapeutic					
waveform	charge-balanced, rectangular biphasic	balanced asymmetrical biphasic, constant current, constant voltage	biphasic asymmetrical with zero net DC	sinusoidal	Not disclosed in manufacturer's literature.
phase duration/pulse width	200 µSec	0-400 µSec	40-300 µSec	NA (with sinusoidal waveform)	50-500 µSec
maximum output amplitude	15 mA into 500 Ohm load	60 mA into 1000 Ohm load (>60 mA into 500 Ohm load – but actual data not disclosed in manufacturer's literature)	60 mA into 500 Ohm load	50 mA into a 500 Ohm load	24 mA into a 500 Ohm load
frequency range	4–50 Hz	2–150 Hz	2-125 Hz	0-200 Hz	5-240 Hz
maximum output charge per pulse	7.2 µC	20 µC	18 µC	NA (with sinusoidal waveform)	12 µC

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Product	**Vertis PNT System**	**EPIX TENS Device**	**SMP-Plus™**	**Intelect® Legend Stim**	**Mattrix® Neurostimulation System**
# of output channels	1 - 5	1 – 2	1 – 2	1-2	2
Features					
on/off activation	button	button	touch pad	touch pad	button
text prompts	on LCD screen	on LCD screen	on LCD screen	on LCD screen	on LCD screen
intensity control	knob/dial	button	touch pad	touch pad	push-button
data recording	Yes (e.g., # of sessions used, therapy mode delivered, length of therapy session, etc.)	Yes (e.g., # of sessions used, therapy mode delivered, length of therapy session, % of sessions with pain relief, etc.)	Yes (e.g., stores parameter setting from most recent session)	Yes (e.g., stores parameters)	Not disclosed in manufacturer's literature.
Safety					
output protection	automatic channel disable for high voltage (open-circuit) load condition	automatic channel disable for high amplitude (open-circuit load) condition	automatic shut off with disconnect of electrode or lead wire	automatic channel disable when excessive current change.	Not disclosed in manufacturer's literature.
patient isolated	yes	yes	yes	yes	yes
safety standards compliance	AAMI NS 4 AAMI NS 15	AAMI NS 4	AAMI NS 4	AAMI NS 4	AAMI NS 15

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APPENDIX 17

EMPI INC.

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Empi

EPIX VT™

■ Dual Channel Transcutaneous Electrical Nerve Stimulator

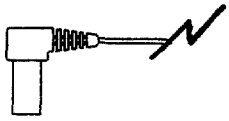
Instruction Manual

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Additional System Information

Epix VT™ requires the use of Empi lead wires with the custom safety connection as pictured below.



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Instruction Manual for the Empi EPIX VT™ TENS Device

Caution: Federal law (USA) restricts this device to sale by or on the order of a physician.

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Introduction

What is Pain?

Pain is an unpleasant sensation that can serve a useful purpose by alerting us to a possible or actual injury or disease. When the body is functioning normally, pain serves as a warning system that something is not right. Without pain a person would not know when to get away from danger or seek medical help. Pain becomes a problem when it continues after treatment has started or long after an injury is healed.

There are two types of pain: acute and chronic. Acute pain is limited in duration. Typical examples are sprains, incisional pain or muscle strain. This type of pain is typically associated with workplace or recreational injuries. Chronic pain, however, is a long-lasting, persistent pain that ceases to serve as a warning system and becomes a problem. TENS was developed to help relieve some types of both chronic and acute pain.

What is TENS?

TENS stands for Transcutaneous Electrical Nerve Stimulation. Pain, whether chronic (long-term) or acute (short-term), can be relieved through a variety of methods, including drugs, topical ointments, surgery and electrical stimulation. TENS devices deliver electrical pulses through the skin to the cutaneous (surface) and afferent (deep) nerves to control pain. Unlike drugs and topical ointments, TENS does not have any known side effects.

How Does TENS Control Pain?

There are two major theories as to how electrical stimulation relieves pain. According to the "gate control theory," pain and non-pain impulses are sent to the brain from the local nervous system. These pulses travel through the cutaneous nerves to the deeper afferent nerves and then to the spinal cord and brain. Along the path are many areas referred to as "gates." These gates control which impulses are allowed to continue to the brain. The gates prevent the brain from receiving too much information too quickly. Since the same nerve cannot carry a pain impulse and a non-pain impulse simultaneously, the stronger, non-pain impulse (from the TENS device) "controls the gate."

According to the second theory, TENS stimulation encourages the body to produce natural pain killers called endorphins. These chemicals interact with receptors, blocking the perception of pain. This is similar to the way the pharmaceutical drug morphine works, but without the side effects associated with morphine.

No matter which pain theory is applied, TENS has been proven useful in pain management. By reading this manual and carefully following the treatment instructions given to you by your clinician, you will attain the maximum benefit from your TENS device.

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Patient Selection

⚠ Indications

TENS devices are indicated for:

- Symptomatic relief and management of chronic, intractable pain.
- Adjunctive treatment for post-surgical and post-trauma acute pain.

⚠ Contraindications

TENS treatments should not be used if the patient has any of the following conditions:

- Undiagnosed pain (until the etiology is established).
- Demand-type implanted pacemaker or defibrillator.
- Transcerebral electrode placements.
- Electrode placements over the carotid sinus (neck) region.

⚠ WARNINGS

Review the following warnings before initiating treatment:

- **Pregnancy** - The safety of TENS devices for use during pregnancy or delivery has not been established.
- **Symptomatic Treatment** - TENS is a symptomatic treatment and, as such, may suppress the sensation of pain that would otherwise serve as a protective mechanism.
- **Central Pain** - TENS is not effective for pain of central origin.
- **Non-curative** - TENS has no known curative value for the conditions for which it is indicated.
- **Medical Supervision** - TENS should only be used under the medical supervision of a physician or a medical practitioner to whom the patient is referred by the physician. TENS is a prescription device and should not be given to other individuals.
- **Children** - Keep out of the reach of children.
- **Electromagnetic Radiation** - The TENS lead wires and electrodes should be removed before using industrial, scientific or medical equipment (Group 2 ISM) that intentionally generates high frequency or high energy electromagnetic radiation. Operation in close proximity (e.g. < 3m) to this equipment may startle the user by producing output instability or improper operation of the stimulator. Simultaneous connection to the TENS user may result in burns and possible damage to the stimulator. Examples of Group 2 ISM Equipment are: radio-frequency (rf) induction heating, cutting or welding equipment and short-wave/microwave therapy and diagnostic equipment such as diathermy or surgical electrocautery units.
- **External Defibrillators** - Remove the TENS electrodes before defibrillation signals are applied. Defibrillation of a person wearing a TENS device can damage the device whether it is turned on or off. Under some circumstances there can be risk of burns under the electrode sites during the defibrillation.
- **Wall Sockets** - Do not plug lead wires into AC power outlets such as wall sockets or line cord receptacles under any circumstances. Doing so could result in severe shock or burns whether or not the lead wires are attached to the stimulator.

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Warnings *continued*

- **Patient Monitoring Equipment** - TENS devices may interfere with the intended operation of electronic monitoring equipment (such as ECG monitors or ECG alarms) if the stimulator is simultaneously connected to the patient being monitored.
- **Safety and Efficacy** - The safety and efficacy of TENS depends on the proper use and handling of the device and accessories. IF USED IMPROPERLY, TENS HAS A POTENTIALLY HAZARDOUS ELECTRICAL OUTPUT. IT MUST BE USED ONLY AS PRESCRIBED. Electrode or lead wire burns may result from misuse. Electrodes and lead wires should be securely fastened to prevent inadvertent disconnection. Electrodes and lead wires will eventually wear out. Check accessories regularly for signs of wear, and replace if needed.

⚠ Precautions

Review the following precautions:

- **Prescribed Conditions** - TENS therapy should not be used for conditions other than those for which the device is prescribed. If there are any changes in an existing condition, or if a new condition develops, the patient should consult a clinician.
- **Patient Selection** - The efficacy of TENS therapy is highly dependent upon patient selection by a person qualified in the management and treatment of pain.
- **Drugs or Mental State** - Treatment outcome will be influenced by the patient's psychological state and use of drugs.
- **Sensitivity to Stimulation** - Patients who react negatively to the stimulation sensation after an adequate trial period or who find stimulation intolerable should not undergo further TENS treatment.
- **Sensory Deprivation** - Due to the risk of adverse skin reactions, electrodes should not be placed on areas of skin with reduced response to normal sensory stimuli.
- **Skin Irritation** - Skin irritation, hypersensitivity and burns beneath electrodes have been reported with the use of TENS. Electrodes should not be left in place for long periods of time without checking or cleaning the skin underneath them. Electrode sites should be rotated with long term use when possible. DO NOT CONTINUE STIMULATION OVER IRRITATED SKIN. Consult a clinician if any skin irritation or reaction develops at the electrode sites following use of the stimulator. The clinician may recommend a different type of electrode.
- **Operating Machinery** - Do not operate hazardous equipment such as automobiles or power tools while using TENS. Abrupt changes in sensation can occur during the use of TENS which could startle the patient and create a hazard.
- **Cellular (Wireless) Telephones and Two Way Radios** - Avoid operation in close proximity (e.g. < 1m) to transmitting cellular (wireless) telephones or two-way radios. This equipment may produce instability in the stimulator output. Sudden, unexpected changes in output could startle the patient and create a hazard.

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Precautions *continued*

- **Water Immersion** - Do not use in the bath or shower. The stimulator should not be submerged in water or other liquids as this may startle the patient and possibly damage the stimulator. If the device should become accidentally immersed in water, do not attempt to use it immediately afterward. Remove the battery and allow the excess water to drain away. Air dry the device thoroughly for at least 48 hours at room temperature before attempting to operate it.
- **Heat and Cold** - The use of heat or cold producing devices, such as electric heating blankets, heating pads or ice packs, may impair the performance of the electrode or alter the patient's circulation/sensitivity and increase the risk of injury to the patient.
- **Sleep** - Do not use while sleeping because the lead wires or the electrodes may become disconnected.
- **Electrodes and Lead Wires** - Do not use electrodes and lead wires other than those supplied with the system or recommended by Empi. The safety of other products has not been established, and their use could result in injury to the patient. NOTE: An electrode active area of no less than 1.6cm (0.25in) is recommended for the Epix VT.
- **Batteries** - Do not carry batteries in a pocket, purse or any other place where the terminals could become short-circuited, e.g. by way of a coin or paper clip. Intense heat could be generated and injury may result.
- **Battery Charger's** - Only the Empi battery charger should be used with Empi rechargeable batteries. Do not attempt to recharge any battery other than the rechargeable battery supplied by Empi for this device. Attempts to charge alkaline or other non-rechargeable batteries could cause the battery to overheat, burst or be permanently damaged.

⚠ Adverse Reactions

Skin irritation and burns beneath the electrodes have been reported with the use of TENS.

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PRODUCT DESCRIPTION

The Epix VT™ is a dual channel TENS device with twelve (12) program options. All the operation modes produce the unique Bi-Sourced® waveform to deliver energy efficiently through the cutaneous tissues.

The Epix VT TENS system components and accessories may include:

- Epix VT TENS Device
- User's Manual
- Electrodes
- Lead Wires
- Batteries (either rechargeable or alkaline)
- 110V/60Hz Battery Charger (if rechargeable batteries are used)

Stimulator Controls and Features

Become familiar with the location of the features of the Epix VT TENS device before initiating treatment. Figure 1 outlines the Channel Output Jacks, the combined Battery Status and ON/OFF Indicator Lights, the Intensity Controls, the Program Option Controls, the Descriptive Pain Scale and the Data Retrieval Controls.

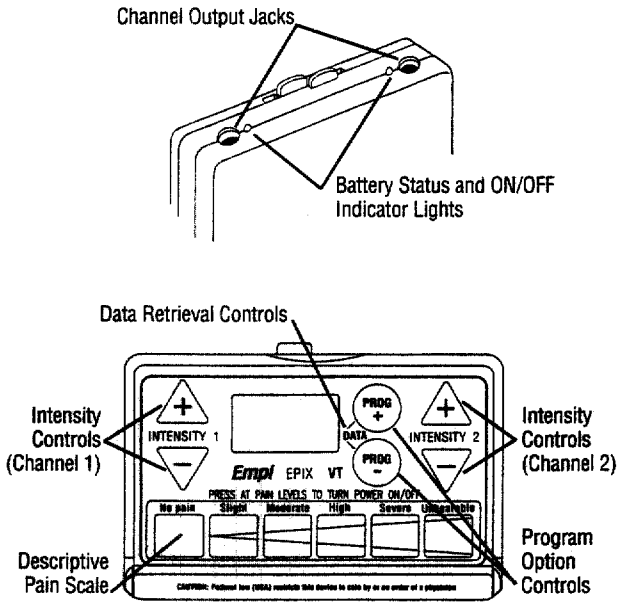


Figure 1.

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Channel Output Jacks

There are two Safety Jacks labeled "1" and "2" (Figure 1). These jacks allow lead wires to be connected to the TENS device. Channels 1 and 2 operate independently.

ON/OFF and Battery Status Indicator Lights

The ON/OFF Indicator Lights indicate that the device is operational. The intensity and rate of flash changes with the output intensity and rate. As the intensity of the stimulation is increased, the intensity of the light also increases. (Above 40 pps the light will appear to be on continuously.) These lights also indicate that the battery voltage is low. The status lights will flash at a different pace if the battery voltage is at or below 7.0 volts. The device will automatically shut off if the battery voltage falls to 5.4 volts. When the battery status light pattern begins, it is recommended that the battery be changed as soon as possible.

Descriptive Pain Scale

The Epix VT device offers a Descriptive Pain Scale for determining the patient's perceived level of pain before and following the TENS application. The device is turned on by depressing the description that best represents the patient's pain. To turn the device off, the level of pain at that time is selected and depressed.

Intensity Controls

Epix VT amplitude is adjustable from 0-60 milliamperes. The intensity (amplitude and pulse duration) of the stimulation available through each of the lead wires attached to either or both of the channels is controlled by the push buttons on the control panel (see Figure 1). Depressing the up-arrow button increases the intensity of the stimulation. When increasing intensity,output will be delivered continuously. Decreasing the intensity level is done by depressing the down-arrow. Increasing or decreasing intensity adjusts amplitude and pulse duration simultaneously.

Note: Audio signal accompanies intensity control adjustment. To disable audio:

1) Turn device off
2) Hold down both Channel 2 Intensity Control buttons
3) Press one of the Descriptive Pain Scale buttons

Repeat process to turn audio on.

Note: THE INTENSITY CONTROLS DO NOT TURN THE DEVICE ON AND OFF. THIS IS ACCOMPLISHED BY DEPRESSING ONE OF THE PAIN LEVELS INDICATED ON THE PAIN SCALE. INTENSITY WILL BE RESET TO ZERO EACH TIME THE DEVICE IS TURNED OFF.

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Program Option Controls

Epix VT offers twelve (12) program options. Selecting a specific program option is done by depressing one of the PROG buttons (Figure 1). The "PROG +" and "PROG –" buttons allow going forward or backward when selecting the program option.
A description of the available program options is described in the Program Options section of this manual.

1	Extremely low frequency	ELF
2	Dual pulse	DP
3	High frequency	HF
4	Bi-modal	BM
5	Ramped burst	RB
6	Alternating ramped burst	ARB
7	Amplitude modulation	MA
8	Random modulation	RM
9	Continuous	C
10	Cycled burst	B
11	Rate modulation	R
12	Multi-modulation	M

Battery Compartment

The Battery Compartment is located under the Front Panel Cover (Figure 2). See Changing the Battery section for instructions on inserting or replacing the battery.

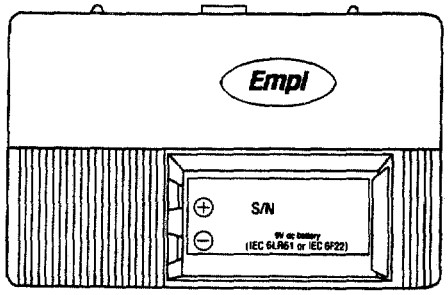


Figure 2. Battery Compartment

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Belt Clip

The Belt Clip allows you to wear the TENS device on a belt or pants top. If the Belt Clip is not already attached, securely attach it to the device. Open the lid past the first stop, slide the Belt Clip on the bottom of the lid to fit the groove, pull it up until it engages on the bottom and snap the top catches over the top of the lid.

Covers

There are two covers for the Epix VT TENS device. The Control Panel Cover rotates on and off the Control Panel (Figure 3). The Belt Clip is attached to this cover to allow the user to open the device and adjust the controls while the device is being worn.

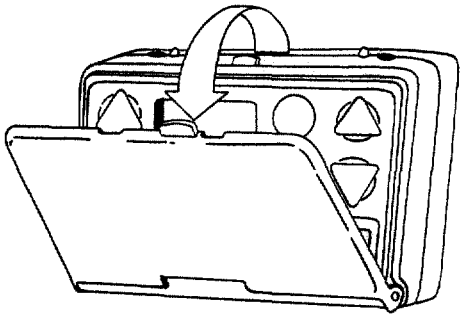


Figure 3. Opening the Control Panel Cover

The Battery Compartment Cover is on the front of the device (Figure 4). It is opened and closed using the "thumb print" depression to slide the cover on and off the device.

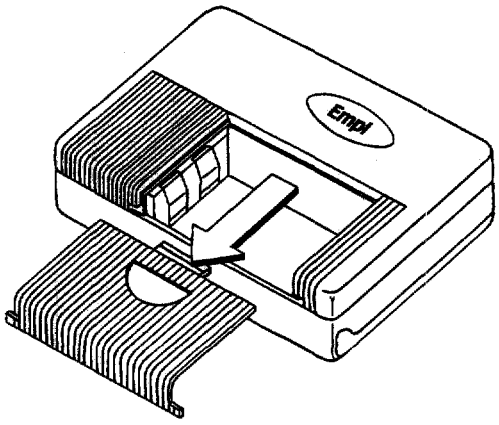


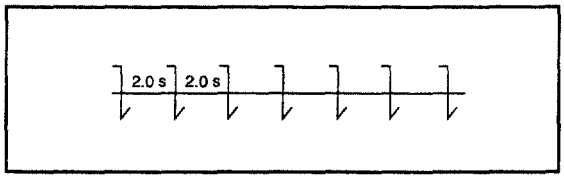
Figure 4. Opening the Battery Compartment Cover

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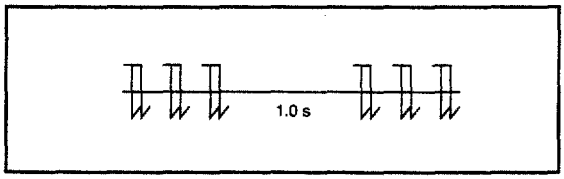
Program Options

1 Extremely Low Frequency (ELF)



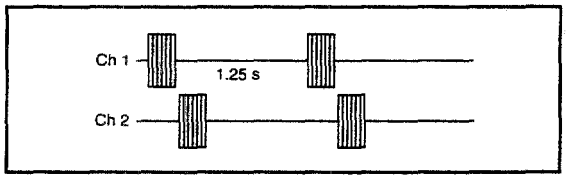
With the Extremely Low Frequency program, the TENS stimulator delivers one pulse every two seconds from both channels simultaneously.

2 Dual Pulse (DP)



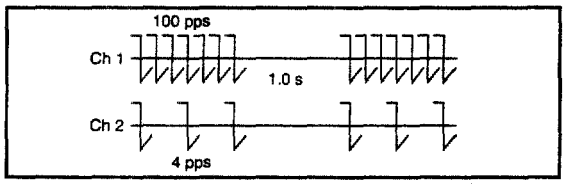
The Dual Pulse program is similar to the conventional burst mode. Two pulses, separated by 3 milliseconds, are delivered at the rate of 20 pps for 1.0 second, followed by no stimulation for 1.0 second. The pulses are delivered through both channels simultaneously.

3 High Frequency (HF)



The High Frequency program is a 2500 pps burst for 0.25 second, followed by 1.25 seconds of no stimulation. Channel 2 alternates with Channel 1.

4 Bi-modal (BM)



In the Bi-modal program, Channel 1 delivers the pulse at 100 pps and Channel 2 delivers the pulse at 4 pps. The stimulation is cycled 1.0 second on, 1.0 second off. Both channels deliver stimulation simultaneously.

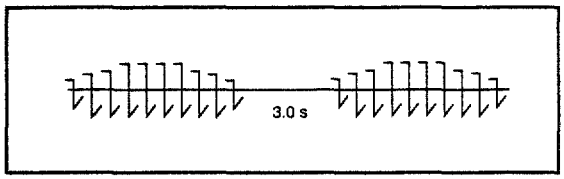
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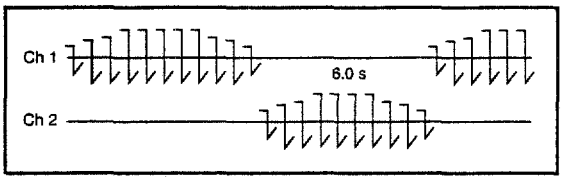
Program Options *continued*

5 Ramped Burst (RB)



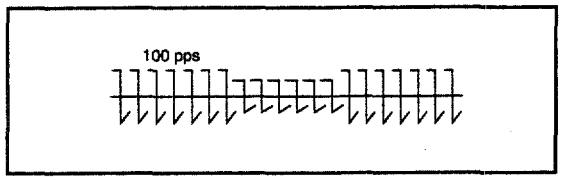
The Ramped Burst program gradually increases the intensity from 0 to the set level over 0.4 second, maintains it at the set level for 1.0 second, and then gradually decreases the intensity over 0.5 second. The device then sends no stimulation for 3.0 seconds. The rate is set at 100 pps. The pulses are delivered through both channels simultaneously.

6 Alternating Ramped Burst (ARB)



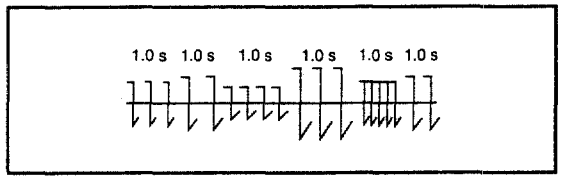
The Alternating Ramped Burst program is the same as the Ramped Burst, but Channel 2 starts after Channel 1 has completed a cycle. Channel 1 gradually increases intensity from 0 to the set level over 0.5 second, holds at the set intensity for 5.0 seconds, and then decreases intensity over 0.5 second. Channel 1 then stays off for 6.0 seconds. As Channel 1 intensity is decreasing, Channel 2 starts increasing intensity, via the same pattern. The set rate is 100 pps.

7 Modulated Amplitude (MA)



In the Modulated Amplitude program, for 0.5 second the intensity is at 100% of the set level and the next 0.5 second, it is at 60%. The cycle is then repeated. There is no off time. The rate is 100 pps. Both channels are used simultaneously.

8 Random Modulation (RM)



Rate is selected pseudo-randomly from 8 rates - 2, 10, 20, 40, 60, 80, 100, 150 pps; pulse duration is selected pseudo-randomly from 7 values between 50% of set pulse duration and set pulse duration. Each combination is on for 1 second.

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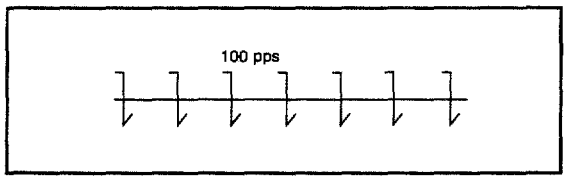
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Program Options *continued*

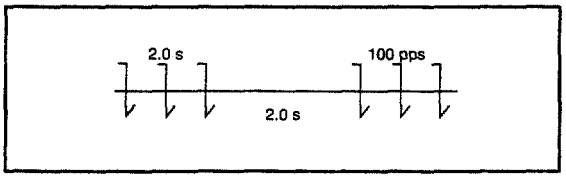
Adjustable Rate Options:
The following program options (9-12) offer adjustable rate. To change rate, press both PROG+ and PROG- buttons at the same time while device is on and set on one of the rate adjustable program options (9, 10, 11, or 12). Display will show the program letter (C, B, R, or M) and the current rate. Use PROG+ or PROG- to go to the next or previous rate. Press PROG+ and PROG- buttons at the same time when selection is complete. Automatic return to program operation will occur after one minute.

9 Continuous (C)



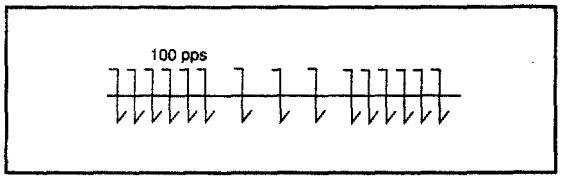
This setting produces a continuous stimulation at the set intensity and a rate of 100 pps.

10 Cycled Burst (B)



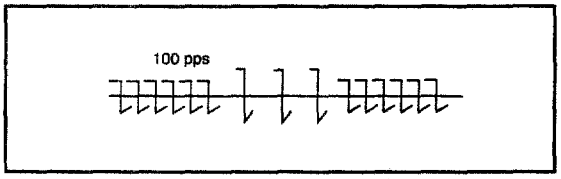
In the Cycled Burst program, stimulation is on for 2 seconds and off for 2 seconds.

11 Rate Modulation (R)



In the Modulated Rate program, for 0.5 second the rate is at 100 pps and for the next 0.5 second, it is at 50 pps. The cycle is then repeated. There is no off time. Both channels are used simultaneously.

12 Multi-modulation (M)



In the Multi-modulated program, for 0.5 second the rate is at 100 pps and the intensity is at 60% of set level and for the next 0.5 second, the rate is at 50 pps while the intensity is at 100% of set level. The cycle is then repeated. There is no off time. Both channels are used simultaneously.

Data Retrieval Controls

The Epix VT device stores usage and pain scale data. This feature is for clinician use only.

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General Operation

Just as pain is an individual sensation, so is pain relief. Pain relief regimens vary from person to person. Some patients may experience pain relief by using the device for only a few minutes a day. In some cases, continuous use of TENS may be required to control pain. Sometimes complete pain relief is not achieved immediately, but improves with time. Your clinician will help you determine the treatment regimen or program that is right for you. TENS should be used only under a clinician's directions.

Electrode Selection and Care

The Epix VT TENS device provides the best results when used with Empi electrodes and accessories. A variety of these products are available for your convenience. Your clinician or authorized Empi representative can help you select the appropriate products. To avoid skin irritation and ensure good contact with your skin, care for the electrodes as instructed on the electrode package. Care will vary with the type of electrode.

Initiating Treatment

STEP 1: Prepare the Skin

Before attaching the electrodes, identify those areas where your clinician has recommended electrode placement. Wash the area gently with mild soap and water, then rinse and dry the area thoroughly. (The use of rubbing alcohol is discouraged except where necessary to decrease excessive oils on the skin.) It may be necessary to trim excess body hair with scissors prior to applying the electrodes. Do not shave the area immediately before beginning treatment. Wait 24 hours after shaving an area before initiating treatment at that site. Failure to adequately prepare the skin may cause improper adhesion or skin irritation and provide less than ideal stimulation.

Note: Skin is not accustomed to exposure to the electrode gel and adhesives used with TENS. While Empi takes great care and tests all electrode materials to avoid problems, irritation may appear as redness, small pimple-like lesions, or blisters. If your skin develops any persistent redness or irritation, do not continue to apply the electrodes to the same area. Discuss this with your clinician or call your Empi representative.

STEP 2: Connect the Lead Wires to the Electrodes

Connect the lead wires to the electrodes before applying the electrodes to the skin. This will reduce the possibility of dislodging the electrodes.

STEP 3: Attach the Electrodes

Place the electrodes on the skin as recommended by your clinician. Generally, the electrodes should be at least two inches apart; however, your clinician will work with you to determine the most effective electrode placement. The electrodes should be comfortable to wear and should be placed exactly where you have been shown. The most common problems with TENS therapy are caused by failure to wear the electrodes as directed.

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Initiating Treatment *continued*

STEP 4: Turn On the Device

Turn on the Epix VT by depressing the button on the Pain Scale that best describes your current level of pain. Current control settings will be displayed on the Control Panel.

STEP 5: Select the Treatment Settings

Your clinician has recommended one of the program options explained in the Stimulator Controls and Features section of this manual. Set the device to the recommended setting if different from the one shown on the display.

Note: To avoid a startling effect, turn the TENS device off before adjusting the settings.

Note: Consult your clinician before changing the recommended settings.

STEP 6: Connect the Lead Wires to the Device

Caution: Always turn the TENS device off before connecting the lead wires to the device.

Push each lead wire connector into its corresponding Channel Output Jack located on the top of the device. The Channel Output Jack marked "1" is controlled by the Channel 1 Intensity Controls; the jack marked "2" is controlled by the Channel 2 Intensity Controls. If you only want to stimulate using one channel, you will need only one lead wire. Connect this single lead wire into either Channel Output Jack (Figure 5.)

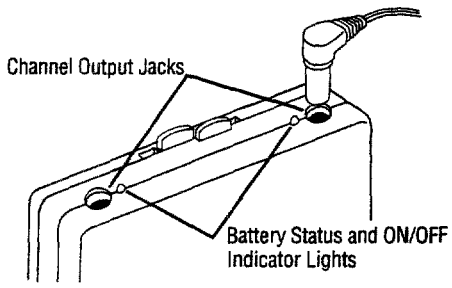


Figure 5. Connecting the Lead Wires

Note: Use care when you connect and disconnect the lead wires from the electrodes and the device. Pulling on the lead wire instead of its insulated connector may cause lead wire breakage.

STEP 7: Begin Treatment

Depress the Channel 1 and Channel 2 Intensity Controls until the stimulation is strong but tolerable. It is important that you can feel the stimulation.

The ON/OFF Indicator Lights should be on. If the ON/OFF Indicator Lights do not come on, or if they alternately turn on and off at a rapid pace, the battery needs to be changed. The display will also indicate low battery status.

Caution: Always turn the TENS device off when changing the battery.

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Initiating Treatment *continued*

The output of the device may decrease slightly during stimulation as the battery wears down. If this happens, you may need to increase the intensity slightly to maintain adequate stimulation.

STEP 8: Record Treatment

Before turning off the TENS device, you may want to record the location of the electrodes, the settings of all controls and any progress achieved. Good record keeping will help when resuming treatment or reviewing progress with your clinician. If after several treatments you do not achieve pain relief, consult your clinician for new electrode placement or stimulation program alternatives.

STEP 9: End Treatment

Enter your current pain level on the pain scale when treatment is complete. Then disconnect the lead wires, grasping them by the insulated connector, not the lead wire.

Remove the electrodes carefully from your skin, peeling them off gently in the direction that body hair lies. The electrodes may be left in place if treatment will be resumed shortly.

After the electrodes are removed, clean the skin thoroughly with mild soap and water. For electrode storage and care, refer to electrode packaging for instructions.

Changing the Battery

The TENS device is powered by a single battery. For best results, use Empi rechargeable or 9 Volt alkaline batteries. When replacing alkaline batteries, we recommend the use of Eveready Energizer model 522, or Varta brand model 4022. If your kit includes rechargeable batteries, see the Charging the Battery section of this manual for directions.

Change the battery when the low battery indicator light pattern occurs, or if the device will not turn on. See Battery Information in the Technical Section of this manual for the typical life of your alkaline or rechargeable battery. Actual battery life will depend upon the battery type, skin impedance, electrode type and device settings used.

Caution: Turn device off and disconnect the electrode lead wires before inserting a fresh battery.

1. Slide the battery compartment cover off the unit.

2. Remove the discharged battery from the unit by lifting the ribbon.

3. Place the new battery into the space provided (Figure 6). Be sure the terminals are in proper alignment. The "+" of the battery should be at the "+" terminal of the device and the "-" of the battery should be at the "-" terminal. Do not force the battery. If force is required, you may be putting the battery in backwards. Check the "+" and "-" markers.

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Changing the Battery *continued*

Caution: Inserting the battery incorrectly may cause the battery to rupture or generate intense heat if allowed to remain in the incorrect position. This may cause irreversible damage to the battery. If there are signs of this type of damage, discard or recycle the battery and order a replacement.

Ni-Cd

The proper disposal of rechargeable batteries may be regulated in your area. Contact your local waste management official for information regarding the environmentally sound collection, recycling and disposal of these batteries.

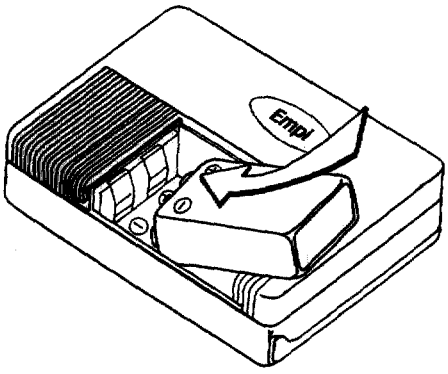


Figure 6. Battery Compartment

Charging the Battery

If you purchased a rechargeable battery system, you will typically charge one battery while using the other. If the Low Battery Indicator flashes, recharge the battery as soon as possible.

Caution: Do not attempt to charge alkaline batteries or any battery other than an Empi rechargeable battery.

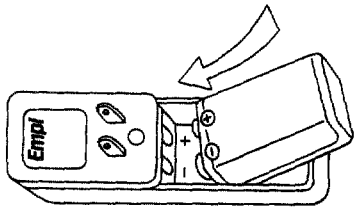


Figure 7. Battery Charger

1. Place the battery in the charger (Figure 7). The battery should slide in easily. If force is required, you may be putting the battery in backwards. Check the "+" and "-" markers.

Caution: The battery may overheat and rupture if it is inserted backwards.

2. Plug the charger into any standard 110V/60Hz outlet. The battery should be fully charged within 14 hours.

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Troubleshooting and Repair

Troubleshooting

If the TENS device does not function:

1. Make sure the battery is properly installed and the battery contacts are clean. Be sure to observe proper polarity markings when replacing the battery.

2. If the Status Lights are alternately flashing in a rapid on/off pattern or the battery status symbol shows on the display, replace the battery.

3. If the Indicator Lights are showing normal operation (not low battery status) and you feel no stimulation, check that the lead wires are properly connected and the electrodes are still in place. If the unit appears to be functioning, but there is no stimulation, the lead wires or electrodes may need to be replaced.

4. If the battery appears to be charged and the stimulator is not functioning, turn both Intensity Controls to zero. Then gradually increase the stimulation.

5. If the device does not seem to be saving data correctly, make sure that amplitude used was greater than 5mA.

6. If display is not visible, check that unit is turned on and battery is charged. See Repair Section if needed.

Repair

There are no user serviceable parts inside the stimulator. If the unit appears to be non-functional, call the Empi Service Center at 1-800-862-2343 for instructions.

In the case of repairs or returns outside of North America, notification and return shipment should be sent to an Empi Authorized Service Center. To locate the appropriate Service Center outside of North America, contact your Authorized Empi Distributor, or contact Empi directly at 1-651-415-9000.

Maintenance, Cleaning, Storage and Disposal

Maintenance

Check periodically for signs of wear or damage such as cracked insulation on lead wires, and replace these items as they wear out.

Under normal conditions, the stimulator does not require periodic maintenance or calibration; however, if it becomes necessary to perform periodic safety checks, all the necessary information is included in the Technical Information section of this manual. These checks should be performed by a qualified technician.

Cleaning

Cleaning the Stimulator: Use a cloth moistened with soap and water to clean the exterior of the device. Use of other cleaning solutions may damage the case. Never immerse the device in water or other liquids.

Cleaning the Battery Contacts: Gently clean the battery contacts using a cotton-tipped swab soaked in rubbing alcohol. Do not use sandpaper or other abrasive material.

Cleaning the Lead Wires: Periodically wipe the lead wires clean with a cloth dampened in a mild soap solution, then gently wipe them dry. Use of rubbing alcohol on the lead wires will damage the insulation and dramatically shorten their life.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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MAINTENANCE, CLEANING, STORAGE AND DISPOSAL *continued*

Storage

To properly store the stimulator for an extended period of time, i.e. 90 days or more, remove the battery from the stimulator and store the stimulator in a dry location.

Disposal

Ship the stimulator or rechargeable battery, postage prepaid, to the Empi Service Center for proper disposal or recycling of that item. Please enclose a note indicating that the item is being returned for disposal or recycling. Outside of North America, contact your Authorized Empi Distributor, or contact Empi directly at 1-651-415-9000.

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Physical Characteristics

Standard Measurement Conditions 23°C, 1kΩ Resistive load, 8.4V d.c. supply voltage

Waveform Balanced asymmetrical biphasic; nominally constant voltage positive phase and constant current negative phase over the AAMI load range of 200 to 1kΩ. 20% tolerance unless stated otherwise. See Figures B and C.

Standard Measurement

	Output	See Figure
Both Phases (Vpp)*	0 to 60V	A
1kΩ resistive (Ipp)*	0 to 60mA	A

*Vpp = Volts peak to peak *Ipp = mA peak to peak

Pulse width* Adjustable; 0 to 400 µs at 50% peak amplitude. See Figure A.

*Determined by the intensity setting.

Maximum Current

Absolute Average Value: 10 mA into 500Ω
Root Mean Square: 10 mA into 1kΩ
Electrode Surface Area 1.6 cm^2 minimum area recommended.

Program Options (PPR™)	Parameters
1 Extremely Low Frequency (ELF)	Rate = 0.5 pps, continuous output.
2 Dual Pulse (DP)	Rate = 20pps, 2 pulses, time between leading edges = 3.0 ms, burst mode, on time = 1s, off time = 1s.
3 High Frequency (HF)	Rate = 2.5 kHz, burst mode, on time = 0.25s, off time = 1.25s, Channel 2 on time to follow Channel 1 on time.
4 Bi-modal (BM)	Channel 1 rate = 100 pps, Channel 2 rate = 4 pps, burst mode, on time = 1s, off time = 1s.
5 Ramped Burst (RB)	Rate = 100 pps, ramp up time = 0.5 s, on time = 1s, ramp down time = 0.5s, off time = 3s. Ramp up starts from 0.
6 Alternating Ramped Burst (ARB)	Rate = 100 pps, ramp up time = 0.5s, on time = 5s, ramp down time = 0.5s, off time = 6s, Channel 2 follows Channel 1, Channel 2 ramp up starts at the end of Channel 1 ramp down. Ramp up starts from 0.
7 Amplitude Modulation (MA)	Amplitude modulation is done through pulse width modulation. Rate = 100 pps, modulation rate = 1.0 pps duty cycle = 50%, depth of modulation = -40%.

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Technical Information

Program Options (PPR™)	Parameters
8 Random Modulation (RM)	Rate is selected pseudo-randomly from 8 rates - 2, 10, 20, 40, 60, 80, 100, 150 pps; pulse width is selected pseudo-randomly from 7 values between 50% of set pulse duration and set pulse duration. Each combination to be on for 1s.
9 Continuous (C)	Preset rate = 100 pps, adjustable (2, 10, 20, 40, 60, 80, 100, 150 pps), continuous at set intensity.
10 Cycled Burst (B)	Preset rate = 100 pps, adjustable (2, 10, 20, 40, 60, 80, 100, 150 pps), on time = 2s, off time = 2s.
11 Rate Modulation (R)	Preset rate = 100 pps; adjustable (2, 10, 20, 40, 60, 80, 100, 150 pps), modulation rate = 1.0 pps. duty cycle = 50%, depth of modulation = -50%.
12 Multi-modulation (M)	Preset rate = 100 pps; adjustable (2, 10, 20, 40, 60, 80, 100, 150 pps), modulation rate = 1.0 pps, duty cycle = 50%, depth of modulation, Pulse duration = -40% when rate is not modulated, Rate = -50% when pulse duration is not modulated.

To Select Rate for Program Options 9, 10, 11, and 12

To Initiate	Press PROG+ and PROG- buttons together while device is on in the appropriate program option (9, 10, 11 or 12). Display will show the PPR letter (C, B, R, or M) and the current rate.
To change	Use PROG+ or PROG- button to go to the next or previous rate.
To Exit	Press PROG+ and PROG- buttons together. Automatic exit will happen after 1 minute and display will show the PPR number.

Data Retrieval

To Initiate	Press PROG+ and PROG- buttons together. Power up the device using any pain scale button. Display will show DATA along with the first data value.
To Advance	Use PROG+ or PROG- button to see the next or previous data.
To Exit	Shut the device off using any pain scale button.
To Clear Data	With PROG - button pressed, press PROG + button. Display will show "CL". Press PROG + button again (PROG - button is still pressed) to clear data or release both buttons to leave the data as is.

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Technical Information

Data Codes

P	Percentage of sessions with pain relief.
S	# of sessions (maximum 255). Only counts sessions where intensity is ≥ 5mA.
L	Average session length (hours and minutes; + or – 1 minute).
D	Most frequent degree of change in pain relief from 1 to 5 (e.g. a pain rating of high (4) when treatment is initiated and a pain rating of slight (1) when the treatment is terminated is scored as a 3 degree change in pain relief). This applies to sessions that recorded pain relief.
Ch1	Most frequently used intensity range for Ch1 (0-5mA, 6-20mA, 21-40mA, 41-60mA).
Ch2	Most frequently used intensity range for Ch2 (0-5mA, 6-20mA, 21-40mA, 41-60mA).

To Enable or Disable Audio

Power up the device using Descriptive Pain Scale button with both Channel 2 Intensity Control buttons pressed to toggle audio on or off. The mode is saved automatically.

Battery Information

Supply Voltage Range 7.0V d.c minimum to 10V d.c. maximum

Low Voltage Indicator Threshold 7.0V d.c.

Expected Battery Life

Nominal Settings:	PPR 1, both channels on at 50% of maximum intensity
Rechargeable Battery	(Ni-Cd) 37 hours
Rechargeable Battery	(Ni-MH 150mAhr) 40 hours
Alkaline Battery	105 hours

Recommended Batteries:

Rechargeable Use Empi rechargeable battery P/N 20008 (Ni-Cd) or P/N 200030 (Ni-MH) with Empi battery charger P/N 200022. IEC - 6F22 Use a 9 Volt battery brand such as Eveready Energizer No. 522 or Varta No. 4022 IEC - 6LR61



Type BF Applied Part. Internally powered only. Ordinary protection against entry of liquids. Continuous operation.

Physical Dimensions

Size (H x W x D)	9.5cm x 6.45cm x 2.38cm (3.7in. x 2.5in. x 0.94in.)
Approx. Weight (with Ni-Cd battery)	113 grams (4.0 oz.)

Environmental Conditions

Operating Temperature	0°C to +50°C, RH 30% to 75%, 50kPa to 106kPa
Transport and Storage Temperature	-40°C to +70°C, RH 10% to 90%, 50kPa to 106kPa

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Technical Information

Waveforms shown are typical:

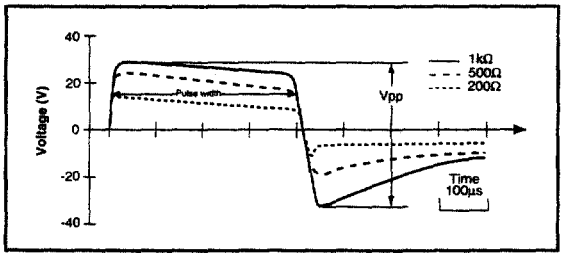


Figure A. Standard measurement output voltage across purely resistive loads at maximum High Output Intensity setting. Pulse width and Vpp measured as shown across a 1 KΩ load.

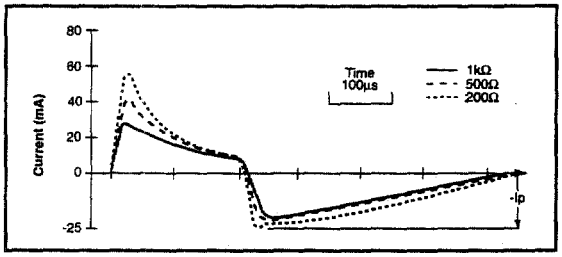


Figure C. Output current into AAMI loads at 50% of maximum High Output Intensity setting. Negative phase (undershoot) is nominally constant current.

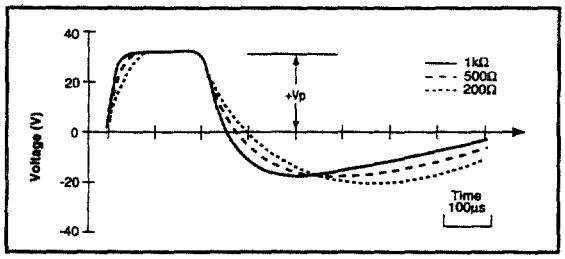


Figure B. Output voltage across AAMI loads at 50% of maximum High Output Intensity setting. Output is nominally constant voltage for intensity settings of 20 (80µs) or greater.

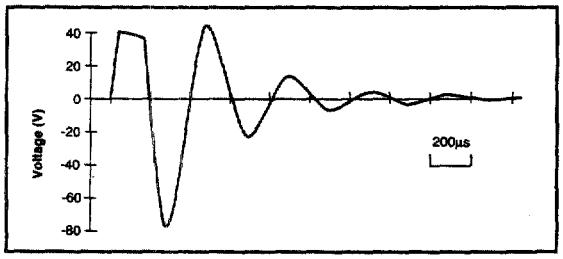


Figure D. Output voltage across a 1MΩ resistive load at 50% of maximum High Output Intensity setting.

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Declaration of Conformity

Empi, Inc., St. Paul, Minnesota, 55126 USA, declares under its sole responsibility, that the markings on your Epix VT TENS device are your assurance of its conformity to the highest applicable standards of medical equipment safety and electromagnetic compatibility. One or more of the following markings may appear on your device.

The Notified Body, TÜV Product Services, has granted Empi, Inc. EC Certificate #G1 96 04 17658 004. Decision according to Annex II, Clause 3 of Council Directive 93/42/EEC (Medical Device Directive).

CE 0123

CSA C22.2 No. 125-M1984
Electromedical equipment, Canadian Electrical Code.
Part II:Safety standards for Electrical Equipment. Risk Class 2.

c UL Listed

Transcutaneous Electrical Nerve Stimulator
Also classified by Underwriters Laboratories Inc. in accordance with ANSI/AAMI NS4-1985 American National Standard for TENS.

UL Listed 5P42

Issued by:

Joseph E. Laptewicz, Jr., President and CEO, Empi, Inc.

1 June, 1997
Date

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Limited Warranty and Disclaimer

I. Warning

While, in the opinion of Empi, Inc. ("Empi"), the use of the Epix VT Transcutaneous Electrical Nerve Stimulator (TENS) (the "Product") has met with some success in the treatment of pain, Empi makes no warranties to the purchaser as to the effectiveness of the product.

II. Warranty

A. Empi warrants to the Purchaser ("Purchaser") (and to no other person) that the Product (including any new or factory reconditioned Products, but excluding any accessories such as charger's, rechargeable batteries, electrodes, lead wires, tape adhesive patches and electrode cream) and the component parts thereof, distributed or manufactured by Empi, shall be free from defects in the workmanship and materials for the lifetime of the Purchaser (the "Warranty Period"). The warranty Period shall be shortened, however, in the following circumstances: (i) if the Product is sold outside of the United States, the Warranty Period shall be three (3) years, (ii) if the Product is classified as a used product by a third party payer for reimbursement purposes the warranty period shall be one (1) year and (iii) if the Product does not fit under any of the previous classifications, the Warranty Period shall be one (1) year. The applicable warranty period shall be measured from the date the Product is shipped to or delivered to purchaser.

B. Accessories including, but not limited to, charger's, rechargeable batteries, electrodes, lead wires, tape adhesive patches and electrode cream are excluded from the Warranty and are sold "AS IS" because their structure is such that they may be easily damaged before or during use.

III. Limitation of Liabilities and Disclaimer of Warranties

A. Empi's sole obligation in the case of any breach of its warranties set forth in Paragraph IIA above, shall be, at Empi's option, to repair or replace the Product with a new or factory reconditioned product without charge to Purchaser or to refund the purchase price of the Product. In order to recover under this Warranty, Purchaser must send Empi written notice of the defect (setting forth the problem in reasonable detail) prior to expiration of the Warranty Period, and within 30 days of discovery of the defect. Upon Empi's written request and authorization, Purchaser shall return the Product to Empi, freight and insurance prepaid, for inspection. Notice and return shipment shall be sent to Empi at Clear Lake Industrial Park, Clear Lake, South Dakota 57226. Purchaser may request shipment approval by calling Empi Warranty Repair Department on its toll free number 1-800-862-2343. In the case of repairs or returns outside of North America, notification and return shipment shall be sent to an Empi Authorized Service Center. To locate the appropriate service center outside of North America, contact your Authorized Empi Distributor, or contact Empi directly at 1-651-415-9000. Empi will not be responsible for damage due to improper packaging or shipment. If Empi determines in its sole reasonable discretion that the Product contains defective workmanship or materials, Empi

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will refund to the Purchaser the purchase price for the defective product, or return the repaired Product or a replacement thereof to Purchaser, freight and insurance billed to the Purchaser, as soon as reasonably possible following receipt of the Product by Empi. If Empi determines in its sole reasonable discretion that the Product does not contain defective workmanship or materials, Empi will return the Product to the Purchaser, freight and insurance billed to the Purchaser.

B. This Warranty is voided immediately as to any Product which has been repaired or modified by any person other than authorized employees or agents of Empi or which has been subjected to misuse, abuse, neglect, damage in transit, accident or negligence.

C. EXCEPT AS PROVIDED IN PARAGRAPH IIA, THE PRODUCT IS BEING SOLD ON AN "AS IS" BASIS, ALL ACCESSORIES ARE SOLD "AS IS", AND THE ENTIRE RISK AS TO THE QUALITY AND PERFORMANCE OF THE PRODUCT IS WITH PURCHASER. THE WARRANTY PROVIDED IN PARAGRAPH IIA IS INTENDED SOLELY FOR THE BENEFIT OF THE INITIAL PURCHASER AND EMPI DISCLAIMS ALL OTHER WARRANTIES, EXPRESS OR IMPLIED INCLUDING, BUT NOT LIMITED TO, ANY IMPLIED WARRANTIES OF MERCHANTABILITY AND FITNESS FOR A PARTICULAR PURPOSE; PROVIDED, HOWEVER, THAT NOTWITHSTANDING THE FOREGOING SENTENCE, IN THE EVENT AN IMPLIED WARRANTY IS DETERMINED TO EXIST, THE PERIOD FOR PERFORMANCE BY EMPI THEREUNDER SHALL BE LIMITED TO THE LIFETIME OF THE INITIAL PURCHASER. NO EMPLOYEE, REPRESENTATIVE OR AGENT OF EMPI HAS ANY AUTHORITY TO BIND EMPI TO ANY AFFIRMATION, REPRESENTATION OR WARRANTY EXCEPT AS STATED IN THIS WRITTEN WARRANTY POLICY.

(This Warranty gives Purchaser specific legal rights and Purchaser may also have other rights which vary from state to state. Some states do not allow limitations of how long an implied warranty lasts, so the above limitation may not apply to the Purchaser.)

D. EMPI SHALL NOT BE LIABLE TO ANY PERSON FOR ANY DIRECT, INDIRECT, SPECIAL, INCIDENTAL, OR CONSEQUENTIAL DAMAGES, LOST PROFITS OR MEDICAL EXPENSES CAUSED BY ANY DEFECT, FAILURE, MALFUNCTION OR OTHERWISE OF THE PRODUCT, REGARDLESS OF THE FORM IN WHICH ANY LEGAL OR EQUITABLE ACTION MAY BE BROUGHT AGAINST EMPI (E.G. CONTRACT, NEGLIGENCE OR OTHERWISE) THE REMEDY PROVIDED IN PARAGRAPH IIIA ABOVE SHALL CONSTITUTE PURCHASER'S SOLE REMEDY. IN NO EVENT SHALL EMPI'S LIABILITY UNDER ANY CAUSE OF ACTION RELATING TO THE PRODUCT EXCEED THE PURCHASE PRICE OF THE PRODUCT.

(This Warranty gives Purchaser specific legal rights and Purchaser may also have other rights which vary from state to state. Some states do not allow the exclusion or limitation of incidental or consequential damages, so the above limitation may not apply to the Purchaser.)

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Your authorized representative:

Empi®

Empi, Inc.
599 Cardigan Road
St. Paul, Minnesota 55126-4099 USA
1-651-415-9000; 1-800-328-2536

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OUR PRODUCTS

Electrotherapy for Rehabilitation



What is Electrotherapy?

Electrotherapy is the use of electrical stimulation of the peripheral nervous system to elicit muscle contractions or to override pain messages. Electrotherapy gives patients cost effective, non-addictive alternatives for treatment and rehabilitation. Empi is a leader in the research and development of electrotherapy devices.

TENS
- Epix XL®
- Epix VT®
- Eclipse+®
NMES
- Focus®



TENS

Transcutaneous Electrical Nerve Stimulation (TENS) is the application of an electrical stimulus for use in reducing pain. The device produces a low level electrical current.

TENS works by reducing pain message transmission. Consider what happens when you burn a finger. Placing your finger under cold water (a second stimulus) masks the pain from the burn. This is similar to the TENS effect. Additionally, if the stimulus is used at an intensity that causes mild muscle twitching, the body's own natural pain reliever, the endorphin neurohormone, is produced. This chemical interacts with receptors along the nerve pathway and blocks the perception of pain.[1] A similar effect occurs in runners.

TENS is indicated for the symptomatic relief and management of chronic, intractable pain and for post-surgical and post-trauma acute pain. TENS is a safe alternative to pharmacological approaches to pain control -- it is non-addictive and has no side effects except for the possibility of skin reaction to the electrodes. The use of TENS helps place control of the pain under the control of the patient.

Most commonly, TENS is used for low-back pain but can also be used for pain associated with many other conditions such as arthritis, chronic strains and sprains, neuralgia, RSD, shingles and degenerative joint disease.

TENS devices are restricted to sale by or on the order of a physician. The application of a TENS device requires medical knowledge and skill. Proper patient selection,

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electrode placement, parameters selection and patient education contribute to the successful use of TENS.

Empi's TENS devices are: Epix XL®, Epix VT® and Eclipse+®.

NMES

Neuromuscular Electrical Stimulation (NMES) is the application of an electrical stimulus for use in muscle rehabilitation. An electrical stimulus is passed from the device to an electrode that is placed on the skin over the motor point of a targeted muscle or muscle group. This stimulation results in a muscle contraction. By assisting patients to fully contract a muscle or muscle group, NMES can move a patient more quickly towards normal function and the resumption of their normal activities.

NMES is indicated for use in: 1) the retardation or prevention of disuse atrophy (wasting of the muscle due to lack of use); 2) muscle re-education, such as after surgery or trauma; 3) relaxation of a muscle spasm; 4) prevention of deep veneous thrombosis (blood clots due to inactivity) immediately after surgery; 5) maintaining or increasing range of motion; and 6) increasing local blood flow. A wide range of neurologic and orthopedic diagnoses will benefit from the use of NMES. Some of the most common uses include rehabilitation after knee surgery or traumatic injury, shoulder rehabilitation and CVA (stroke).

NMES devices are restricted to sale by or on the order of a physician. The application of a NMES device requires medical knowledge and skill. Proper patient selection, electrode placement, parameters selection and patient education contribute to the successful use of NMES.

Empi's NMES device is Focus®

Accessories

TENS and NMES devices require additional products to complete their electrotherapy system. These products are commonly referred to as accessories. The major components included in this category are electrodes, lead wires, batteries and skin care products. An electrode is an adhesive conductive pad that is applied to a patient's skin. Lead wires attach directly to the electrode, as well as the device. The electrical impulse is passed from the device, through the lead wire, to the electrode and patient.

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Batteries are used within the device to provide the necessary electrical output. Skin care products are also included in this category because of the role they play in maintaining healthy skin.

Empi provides a complete line of accessories that have been tested for performance and compatibility with Empi's medical devices.

[1] Guyton, A.C.: *Textbook of Medical Physiology.* Chapter 50. Somatic sensations: II W.B. Saunders Company. (1986).



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OUR PRODUCTS

Electrotherapy for Rehabilitation

Empi
CERVICAL TRACTION

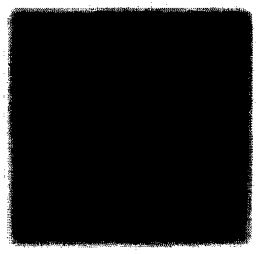
TENS
Epix XL®, Epix VT® and Eclipse+®

TENS
- Epix XL®
- Epix VT®
- Eclipse+®

NMES
- Focus®

INCONTINENCE THERAPIES
IONTOPHORETIC DRUG DELIVERY
THERAPEUTIC BRACING/ORTHOTICS

PRODUCT OVERVIEW



Epix XL® and Epix VT®

Empi's Epix XL (shown left) and Epix VT dual channel devices are the most advanced, yet simple-to-use, TENS devices available today for the treatment of pain. The features and uncompromising quality of the Epix devices contribute to its success. In support of this, an independent outcome study[1] of 506 long-term patients was conducted to document use, effectiveness and satisfaction with Empi's Epix XL. Patients reported high satisfaction with their use of the device; 74% were still using Epix XL for pain relief after six months (mean=12 months at time of survey), and of those who had stopped using TENS, 41% reported discontinuing use because their condition improved. Of those, 95% said they would use TENS again if they were re-injured. Additionally, results showed statistically significant change/improvement in the following: less pain interference with work and other activities; increased activity and pain management; decreased use of other therapies; and decreased use of narcotics, tranquilizers, muscle relaxants, NSAIDs and steroids.

[1] Fishbain, et al, Transcutaneous Electrical Nerve Stimulation (TENS) Treatment Outcome in Long-term Users. *The Clinical Journal of Pain*, 12:210-214.

Eclipse+®

The Eclipse+ is a lightweight, dual channel TENS device. With its long history of excellent performance, Eclipse+ is a quality alternative for the treatment of pain.

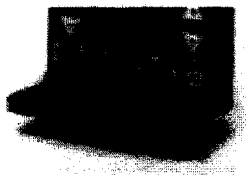
EMPI ADVANTAGES

Epix XL and Epix VT (shown right) feature a bisourced, biphasic



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waveform. The combined constant voltage, constant-current waveform provides a strong, yet comfortable stimulus that allows the clinician to prescribe a treatment program that can offer better potential for long term success. This unique waveform also provides an extra safety benefit for the patient in the event that an electrode pad accidentally pulls off. With the Epix devices, if an electrode is coming off, the smaller surface area making contact with the skin results in a drop off of stimulus, and the patient feels no discomfort. This important safety feature results in greater patient comfort and confidence with TENS. With improved patient compliance comes improved outcomes and less need for other pain-relieving products and services.

A number of treatment parameter options (12) are programmed into the devices; modifications can be made by the clinician if desired. A clinician can recommend the specific option(s) or may encourage the patient to select the program option(s) that the patients find most effective.

Empi's Epix devices meet or exceed the highest industry standards and fully comply to the ANSI/AAMI standard for TENS devices. These products are listed to applicable UL Standards and requirements by Underwriter Laboratories. The ANSI/AAMI standards were developed to ensure that devices meet important performance and safety requirements. Because patients use their TENS devices during many activities throughout the day, quality is very important. When dropped, even in water, Epix devices will continue to perform. The Epix devices stand up to the rigors of daily use over the long term and come with a lifetime warranty on parts and labor. Outside the U.S. and Canada, the warranty period is three years. (Note: limitations may apply.)

In addition to the features offered in the Epix XL, the Epix VT incorporates a patented, easy-to-use system for recording usage and effectiveness. A validated pain scale allows the patient to document pain levels before and after treatment. The clinician can assess the appropriateness of the TENS treatment program for any given patient. Data gathering and reporting are achieved easily. Epix VT is the perfect option for situations that demand measurable outcomes.

Epix VT also has a push-button control panel and a liquid crystal display. Its easy-to-use design benefits elderly

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patients who have difficulty reading dials or have limited hand functions. Safety connection lead wires are also standard on Epix VT.



The Eclipse+ (shown left) device has two channels for treatment of multiple sites or greater coverage over a general area. It offers a variety of modulation options (treatment programs) which vary the combinations of rate, pulse width and amplitude to deliver comfortable, gentle stimulation. A quality device, the Eclipse+ has a two year warranty on parts and labor and a limited lifetime warranty on parts. Outside the U.S. and Canada, the warranty period is two years. (Note: limitations may apply.)

For complete instructions for use, indications, contraindications, precautions and warnings see product instruction manual.

CAUTION: Federal law (USA) restricts this device to sale by or on order of a physician.



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Indications for Use

Empi

CERVICAL TRACTION

Pronex®
To provide traction to the cervical spine, thereby stretching the soft tissue structures.

ELECTROTHERAPY FOR REHABILITATION

Epix XL®, EpixVT® and **Eclipse+® TENS** devices are indicated for:

- Symptomatic relief and management of chronic, intractable pain
- Adjunctive treatment for post-surgical and post-trauma acute pain

Focus® NMES device is indicated for:

- Relaxation of muscle spasm
- Prevention or retardation of disuse atrophy
- Increasing local blood circulation
- Muscle re-education
- Prevention of venous thrombosis immediately after surgery
- Maintaining or increasing range of motion

INCONTINENCE THERAPIES

Minnova™, Innova® and **InnoSense™**
Pelvic Floor Stimulation (PFS) devices are indicated for acute and ongoing treatment of stress, urge or mixed urinary incontinence and where the following results may improve urinary control:

- Improvement of urethral sphincter closure (stress incontinence)
- Strengthening of pelvic floor muscles (stress incontinence)
- Inhibition of the detruser (bladder) muscle through reflexive mechanisms (urge incontinence)

Innosense is also indicated during incontinence treatment for assessing EMG activity of the pelvic floor and accessory muscles such as the abdominal or gluteal

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muscles.

IONTOPHORETIC DRUG DELIVERY

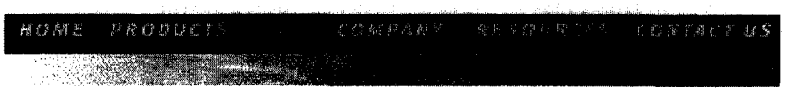
Dupel® and Relion™
Iontophoresis is an alternative to hypodermic injection for the administration of ionic drug solutions.

THERAPEUTIC BRACING/ORTHOTICS

Advance Dynamic ROM®
Used to increase joint range of motion and alleviate stiffness from contractures resulting from surgical procedures, prolonged immobilization and joint trauma.

Protonics®
Indicated for use with other forms of exercise to redevelop muscles, restore motion to joints, provide support, correct deformities and align body structures for functional improvement. It is an adjunctive component of patellofemoral pain syndrome rehabilitation exercise programs and Anterior Cruciate Ligament (ACL) reconstruction rehabilitation.

For complete instructions, indications, contraindications, warnings and precautions see instruction for use manual.



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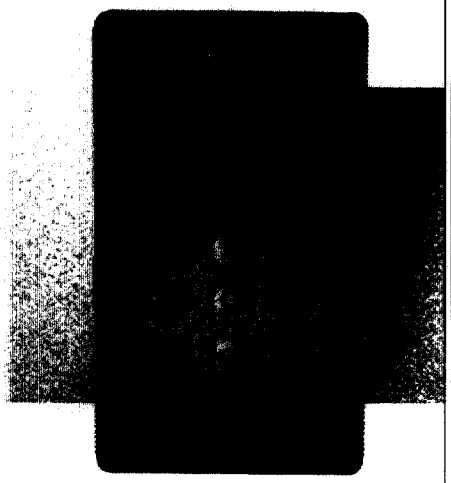
APPENDIX 17

REHABILICARE, INC.

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SMP-plus™ The Pain Relief Solution for Hard to Treat Patients



The SMP-plus is a state-of-the-art, easy to use TENS unit that effectively reduces pain in difficult to treat patients that have not responded to more traditional devices. Its unique SMP mode is especially beneficial for those suffering from chronic pain or pain syndromes similar to reflex sympathetic dystrophy. This device offers a variety of options to address each patient's specific pain problem.

SMP-PLUS OFFERS THESE OUTSTANDING BENEFITS

Choice of Modulations

The SMP-plus offers the clinician and patient the choice of traditional modes including constant and burst as well as modulated rates and widths in one easy to use device. This wide range of modulations ensures patients won't accommodate to the stimulation, resulting in more effective treatment.

Unique SMP Mode

The SMP mode offers unique modulation of rate and width specifically designed for effective treatment of sympathetic component-type pain disorders and many other chronic pain problems.

Precise Rate and Width Settings

A digital display allows for precise adjustment of the modulation's rate and width. The stimulator can be adjusted to accommodate changing pain patterns, improving pain relief and patient compliance. In addition, the SMP-plus "remembers" the last parameter settings each time the device is turned on, even when the batteries have been changed.

Easy to use keypad

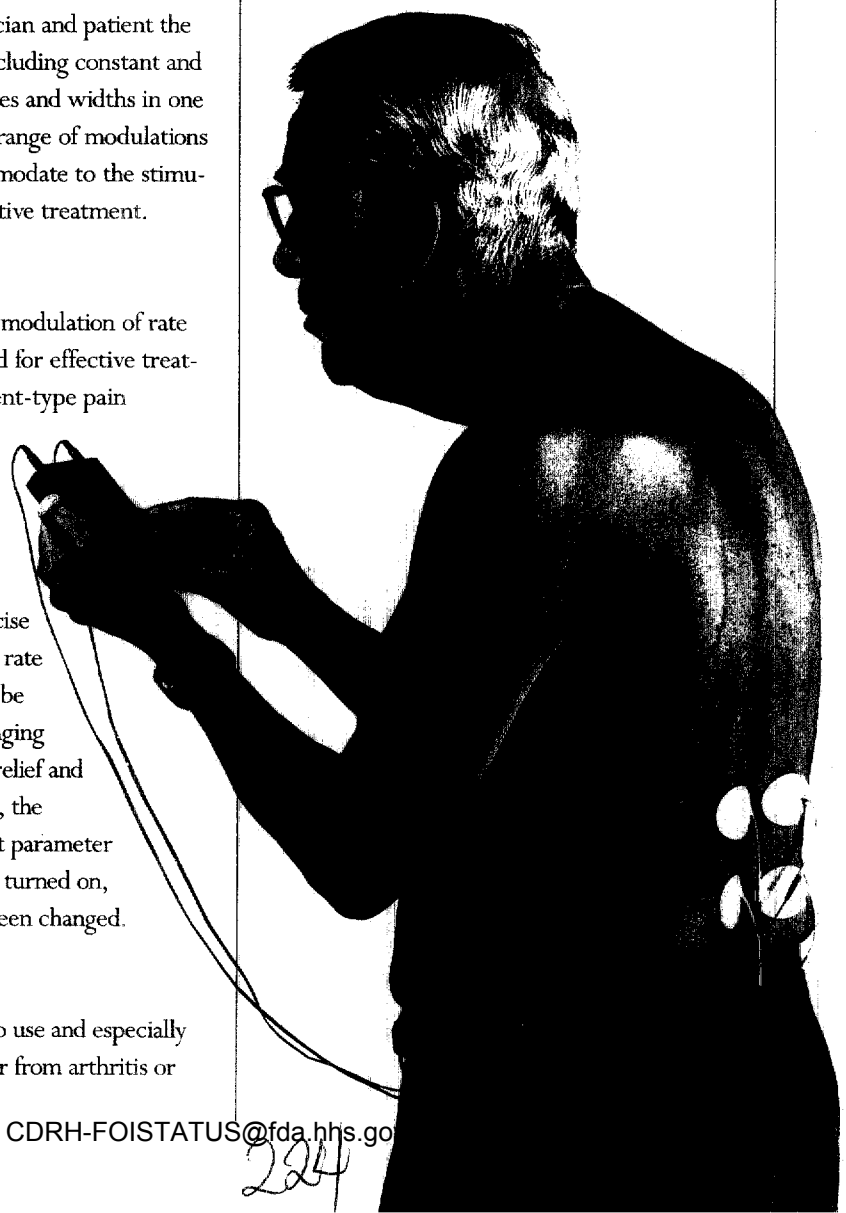
The keypad controls are easy to use and especially designed for patients who suffer from arthritis or have poor dexterity.

Safety Feature

If an electrode or lead wire disconnects during the treatment, the device immediately shuts off, preventing a startling "burst" of current that often occurs with other stimulators.

The SMP-plus is a fully featured pain control stimulator that interrupts the pain and inflammation cycle experienced by hard to treat chronic pain patients. Its ease of use makes it the ideal TENS choice for those needing versatility and simplicity.

SMP-plus™



Rehabilicare®

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov

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SMP-plus Product Data

About Rehabilicare

Rehabilicare is a leading designer, manufacturer and provider of electromedical pain management and rehabilitation products and services used for clinical, home health care, sports medicine and occupational medicine applications. Electromedical devices have broad application in rehabilitating injured or diseased muscle or other soft tissues. They are also proven to relieve acute and chronic pain.

Our product mix is one of the most comprehensive in the industry. Our devices facilitate faster recovery of muscle and soft tissue damage, reduce pain and swelling, increase blood circulation and range of motion, and help control muscle spasms. Health care professionals prescribe their use for a variety of circumstances including lower back pain, joint stiffness, muscle spasms, sports-related injuries and post-operative treatments.

Rehabilicare works with patients, clinicians and third party payors to provide cost-effective rehabilitation. Patient benefits from the use of portable electrotherapy are:

- *Continuity. Portable electrotherapy enables the patient to continue their therapy regime beyond the clinic setting.*
- *Effectiveness. Electrotherapy decreases rehabilitation time. Patients return to their normal functions quicker.*
- *Responsibility. Portable modalities reinforce patient responsibility and promote a more active role in their therapy.*

BASIC SPECIFICATIONS

■ **Output Current**	0-60 milliamps, adjustable
■ **Pulse Rate**	2-125 Hz, adjustable
SMP	20-125Hz. Rate modulates from set rate to a fixed rate of 2Hz. Pulse width modulates down 30% from set width and back in a 12 second cycle.
C (constant)	Provides continuous stimulation at set rate
B (burst)	8Hz per burst, 2 bursts per second
Modulated Rate	Rate alternates between set rate and 60% of set rate every 2.5 seconds
Modulated Width	Width alternates between set width and 60% of set width every 2.5 seconds
Multi-Modulated	Rate alternates between set rate and 60% of set rate every 2.5 seconds and width alternates between set width and 60% of set width every 2.5 seconds (alternates inversely with rate)
■ **Pulse Width**	40-300 microseconds, adjustable
■ **Waveform**	Biphasic, asymmetrical with zero net DC
■ **Maximum Charge per Pulse**	18 microcoulombs
■ **Power Source**	9 volt rechargeable or alkaline battery
■ **Dimensions**	3.75" x 2.5" x 1" 9.5cm x 6.4cm x 2.5cm
■ **Weight**	4.8 ounces/ 136.2 grams (including battery)
■ **Tolerances**	All electrical specifications are into real 500 (±10%) ohm load except as indicated

Rehabilicare®
1811 Old Highway 8
New Brighton, Minnesota 55112-3493 USA
Phone: (800)343-0488 or (813)623-1616
http://www.rehabilicare.com

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APPENDIX 17

CHATTANOOGA GROUP, INC.

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Volume 4

Intelect® *Legend Series*

Intelect® *Legend Stim* Clinical Reference Manual

Innovation starts here™

CHATTANOOGA GROUP, INC.

P.N. 78281C

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Intelect® Legend Stim

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Introduction

- ❑ Welcome to the Intelect® Legend Stim
- ❑ Features of the Intelect® Legend Stim
- ❑ Foreword
- ❑ Intelect® Legend Stim Product Matrix
- ❑ Liability Disclaimer
- ❑ Precautionary Instructions

Welcome to the Intelect® Legend Stim

The Intelect®Legend Stim designed and manufactured by Chattanooga Group, Inc., offers a new dimension in electrotherapy, combination and ultrasound treatments. This technology is made possible by advanced software design and digital signal processing. The result is a series of products with extraordinary versatility based on simplicity of operation.

Features of the Intelect® Legend Stim Include:

- **Multiwaveform Capability.**
  Interferential, Premod, Russian, and High-Volt currents are available to provide you the needed capability to manage pain and promote muscle strengthening all in one system.

- **Tactile Touch Control**
  Digital electronics and new user interface design give you simple tactile touch control of all system parameters.

- **Ergonomic Design and Function**
  The innovation of advanced tooling and injection mold technology yield a sleek and ergonomic case and interface that antiquates the traditional knob and metal box design. User interface design has also broken the traditions of hard to use, with a simple ***"1-2 Go"*** format.

- **Clear LCD Display**
  Clear, crisp LCD running ***1-2 Go software***. LCD control simplifies the display of treatment parameters and the navigation of optional settings.

- **Easy as One-Two-Go**
  In two steps you are ready to start therapy.

- **Programmable Start Up Presets**
  All power up presets can be individually customized to meet the clinic's needs.

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Foreword

This manual has been written for the owners and operators of the Intelect® Legend Stim. It contains general instructions for operation, precautionary instructions, and maintenance recommendations. In order to obtain maximum life and efficiency from your Intelect® Legend Stim and to assist in the proper operation of the unit, read and understand this manual thoroughly and become familiar with the controls on the panel as well as the various accessories that come with the unit before operating it.

This manual includes operator information and instructions for the Intelect® Legend Stim only. The specifications put forth in this manual were in effect at the time of publication. However, owing to Chattanooga Group's policy of continuous improvement, changes to these specifications may be made at any time without obligation on the part of Chattanooga Group, Inc.

Intelect®*Legend* Series from Chattanooga

Intelect® Legend Stim

- Dual Channel Operation
- Interferential Current
- Premodulated Current
- Russian Current
- Twin Peak High Volt
- Clear LCD display
- Tactile Touch Control Panel
- *1-2 Go Software*
- Programmable Presets

Intelect® Legend Ultrasound

- Dual Frequency Function
- Waterproof applicators
- Ergonomically formed applicators available in 2, 5 and 10 cm^2 sizes
- Head Warming
- Electronic Signature™
- Tactile Touch Control Panel
- *1-2 Go Software*
- Programmable Presets
- Simulation Input for Combination Therapy

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Liability Disclaimer

Before administering any treatment to a patient you should become acquainted with the operating procedures for each mode of treatment available, as well as the indications, contraindications, warnings, and precautions. Consult other resources for additional information regarding the application of electrotherapy.

Precautionary Instructions:

1. **CAUTION:** Read, understand and practice the precautionary and operating instructions. Know the limitations and hazards associated with using any electrical stimulation or ultrasound device. Observe the precautionary and operational decals placed on the unit.

2. **CAUTION:** Do not operate the Intelect Legend Stim when connected to any unit other than Chattanooga Group, Inc. devices. Do not operate the unit in an environment of short-wave diathermy use.

3. **WARNING:** Federal law restricts this device to sale by, or on the order of, a physician or licensed practitioner. This device should be used only under the continued supervision of a physician or licensed practitioner.

4. **CAUTION: DO NOT** use sharp objects such as a pencil point or ball point pen to operate the buttons on the control panel as damage may result.

5. **WARNING:** Explosion hazard if used in the presence of flammable anesthetics. The warning symbol for this hazard is prominently displayed on the cabinet.

6. **WARNING:** For continued protection against fire hazard, replace fuses only with ones of the same type and rating.

7. **WARNING:** Make certain that the unit is electrically grounded by connecting only to a grounded electrical service receptacle conforming to the applicable national and local electrical codes.

8. **WARNING:** This device should be kept out of the reach of children.

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Principles of Operation

- ❑ Initial Setup Instructions
- ❑ System Components
- ❑ Optional Accessories
- ❑ Warranty Registration
- ❑ System Operation
  - Operating Controls
  - General Setup Steps
  - Quick Start
  - Screen Layout

Initial Setup Instructions

Remove the Intelect® Legend Stim unit and any additional items ordered from the carton and inspect for damage that may have occurred during shipment. Check the voltage rating on the serial decal located on the bottom of the unit. Plug the system power supply in to a 100 Volt (Fig. 2.1) to 220/240 Volt (Fig 2.2) A.C. outlet, as required. **DO NOT** attempt to use Direct Current (DC). **DO NOT** attempt to use the unit if it is not properly grounded. Do not place unit in a location where the power cord could be tripped over or pulled out during treatment. Follow the procedures listed in the precautionary instructions located later in this section.

Figure 2.1
120 Volt
Hospital Grade

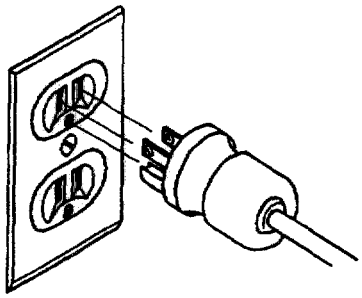
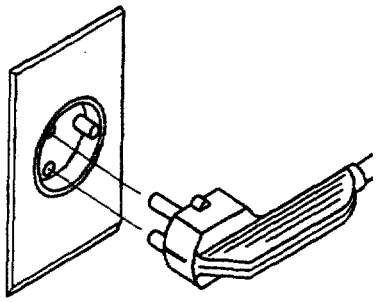


Figure 2.2
220/240 Volt



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System Components

The following accessories are included **(standard)** with your Intelect® Legend Stim.

76657	Lead, 120", Violet/Green
72853	Electrode Carbonflex, 3" Round, Red
72852	Electrode Carbonflex, 3" Round, Black
10648	Nylatex, 2-1/2" x 24", Sewn
78082	Intelect® Legend Stim Power Supply
78121	Intelect® Legend Stim Power Cord
78081	Operator's Manual

Optional Accessories

The following is a list of optional accessories available for the Intelect® Legend Stim

Item	Part #	Description
1	42004	Electrode, Self-Adhesive, 1.5 " x 3.5"
2	42006	Electrode, Self-Adhesive, 3" x 5"
3	71739	Sponge, 1-3/4" x 2-1/4" Package of 8
4	71737	Sponge, 3-1/4" x 5-1/4" Package of 8
5	74616	Sponge, 3-3/8" Round, Package of 6
6	10832	Strap, Nylatex, Long 2-1/2" X 48"
7	10648	Strap, Nylatex, Medium, 2-1/2" x 24"
8	10828	Strap, Nylatex, Short, 2-1/2" x 18"

DURA-STICK *SELF ADHESIVE ELECTRODES*

- 2" Round Electrode — Item Number: 42011
- 2" x 2" Square Electrode — Item Number: 42005
- 3" Round Electrode — Item Number: 42009
- 3" x 5" Electrode — Item Number: 42009
- 1.5" x 3.5" Electrode — Item Number: 42004

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Warranty Registration

Complete the warranty registration card and return it to Chattanooga within 10 days of purchase. The warranty registration card should be filled out complete with the system serial number and serial number of the included ultrasound applicator if applicable. Warranty registration will ensure that you will not be billed for services that are covered by the warranty policy.

CHATTANOOGA GROUP WARRANTY REGISTRATION CARD

Please return within one week of purchase.

Facility Name _____

Facility Owner/Director _____

Address _____

City _____

State _____ Zip _____ County _____

Telephone # _____ Fax # _____

PURCHASE INFORMATION

Purchase Date _____ Serial Number _____

Product Purchased _____ Catalog Number _____

Purchased From _____

How did you hear about this product? ☐ Journal ☐ Direct Mail Card ☐ Catalog

☐ Local Distributor ☐ Convention ☐ Other _____

FOR OFFICE USE ONLY: WARRANTY # _____

PN 15010E

Complete the entire card and return postage paid to the Chattanooga Group, Inc.

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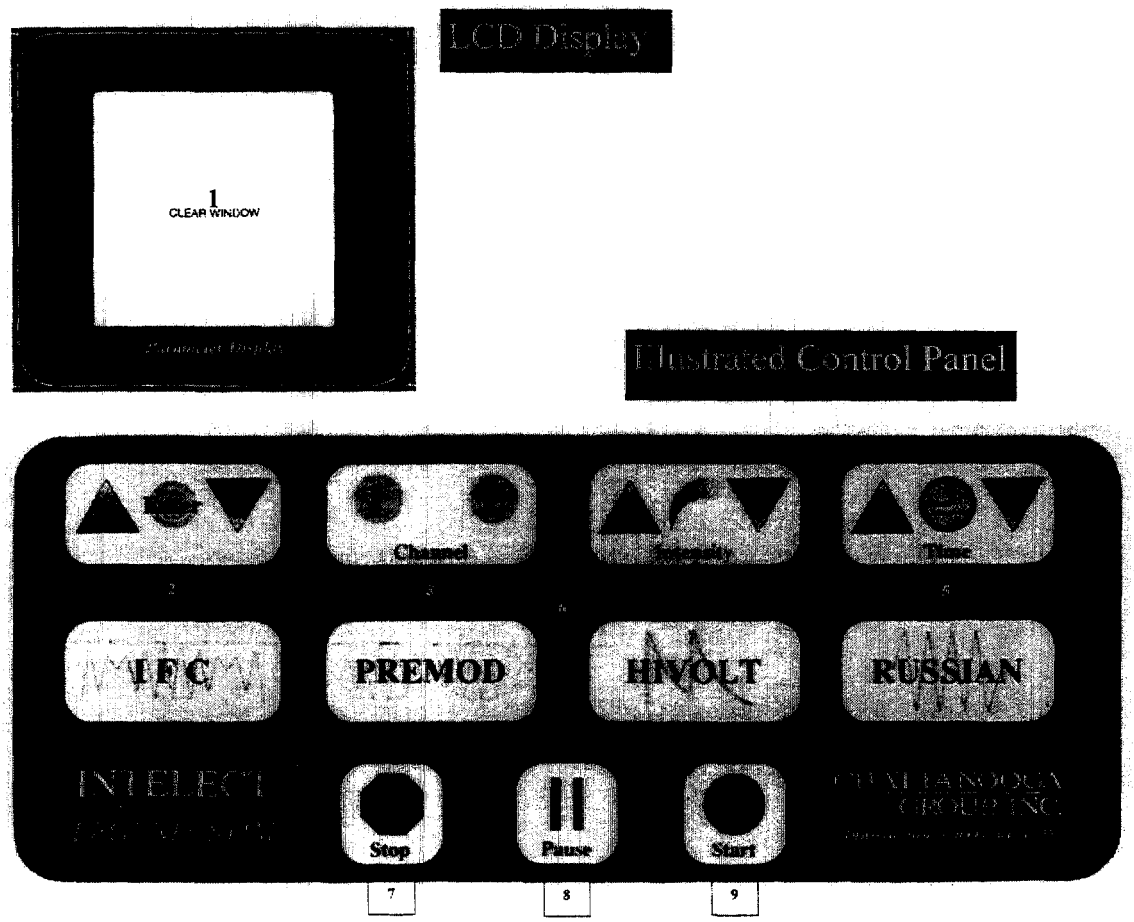
System Operation

Prior to operating the Intelect® Legend Stim become familiar with the following:

- ❑ Illustrated Control Panel
- ❑ LCD Display
- ❑ Modes of Treatment
  - Indications / Contraindications for treatment.
  - Specific instructions for performing each treatment.

Operator Interface

The operator interface consists of an illustrated control panel and a liquid crystal display (LCD). The operator is able to view parameter options on the LCD display and make selections by touching the designated area of the control panel. The displays will provide continual information during the treatments concerning amplitude and elapsed time. Waveform stimulation intensities are adjusted with control panel buttons. The stimulation output can be stopped by pressing the "PAUSE" or "STOP" buttons located at the bottom of the control panel.



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Operating Controls

1. LCD Screen Display
   - Provides visual display of parameters selected during all phases of treatment set up.
   - Channel display provides a constant update of channels as well as treatments and time remaining for channels in use.
   - There is less confusion because only the information directly related to the chosen mode of treatment is displayed.
2. ENTER - Parameter Selection Control
   - Select this prompt to change a treatment parameter to a value other than the default setting.
   - Use the up and down arrows adjacent the sides of the ENTER prompt to select a parameter for review.
3. Channel - Channel Selection Control
   - Select this prompt to display the parameters of channel selected or escape from a pop-up menu.
4. Intensity Control
   - Select this prompt to set or modify output intensity or amplitude.
5. Treatment Time Controls
   - Select this prompt to set or modify treatment time in minutes.
6. Waveform Option Buttons
   - **IFC - Interferential Stimulation:** This mode of therapy is delivered with two channels and four electrodes. Choose the high frequency range, the low frequency range, or both, along with Sweep to deliver current to a more general area.
   - **PREMOD - Premodulated Stimulation:** Excellent for treating small areas or where the placement of four electrodes is not practical. This mode is quite versatile as it offers a premodulated interferential current using one channel and two electrodes. You may choose to set up two separate premodulated treatments at the same time using two channels.
   - **HIVOLT - High Volt Stimulation:** Twin-Peak High Volt current is designed to deliver very short duration pulses which are very low in charge or power output. Treatment can be administered using either pads or probes.
   - **RUSSIAN - Russian Stimulation:** Through this mode, you can deliver muscle stimulation treatments choosing from a list of options including Single, Reciprocal, and Co-Contraction. Choose from various cycle times and ramp times, or customized the burst frequency.
7. Output Stop Control
   - Select this prompt to stop a treatment session.
8. Output Pause Control
   - Select this prompt to pause a treatment session.
9. Output Start Control
   - Select this prompt to begin a treatment session.

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General Setup Steps

The design of the illustrated control panel allows you to setup a treatment faster than ever. Careful grouping of treatment options allows you to easily identify and select from the appropriate options a specific mode of treatment. Two simple steps are all that is needed prior to pressing START and initiating treatment.

Quick Start

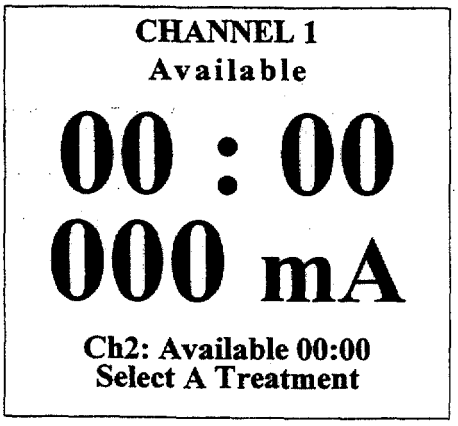
The following is a general quick step by step procedure for using the Intelect® Legend Stim. Before proceeding refer to the cautions related to the mode of use selected. See pages 13-17 for stated cautions.

PROCEDURE	COMMENTS
Turn power on	The unit will power up to the channel available screen.
Clean area to be treated	Follow steps in preparation for treatment.
Position electrodes	Secure electrodes in the area to be treated.
Select Mode of use	Select stimulation
Set "Intensity"	Set intensity of the channel(s) selected.
Select "Start"	To begin treatment.
End treatment	Remove electrodes and inspect treatment area.

Screen Layout

There are three types of screen displays: Channel Available, Active Parameter Display, and Parameter Change screens. Each of these screens are formatted for easy navigation.

1. Channel Available Screen

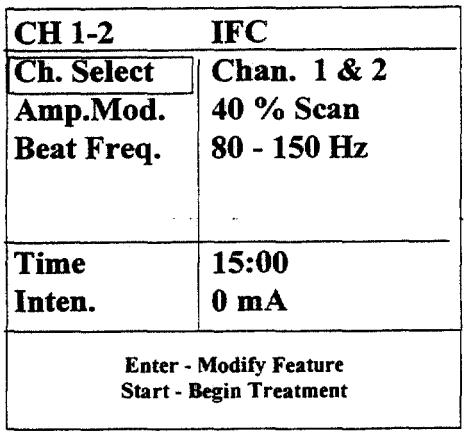


The Channel Available screen serves as the opening screen when the unit is first powered up. It will display default available channel as well as basic text help at the bottom of the screen to prompt you to action. The Channel Available screen will reappear after you have initiated a treatment providing a status of the waveforms selected, intensity level and elapsed treatment time.

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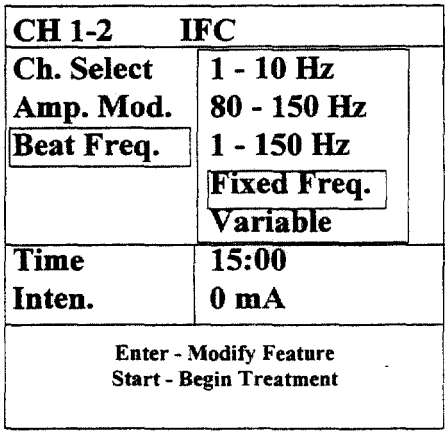
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2. Active Parameter Display Screen.



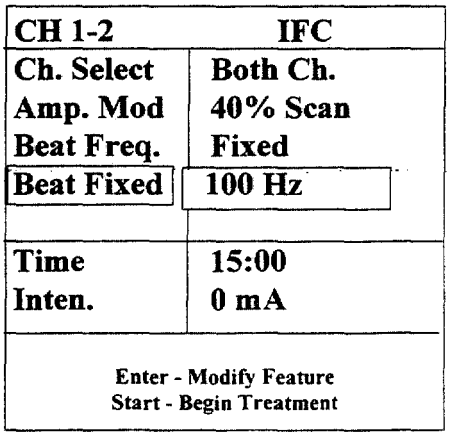
Active Parameter Display Screen: When a waveform is selected for use, that waveforms preset parameters will be displayed on the LCD. Basic text help is displayed at the bottom to prompt the user to action.

3. Parameter Change Screen.



Parameter Change Screen: In this example, moving the highlight bar to Beat Frequency and pressing ENTER will display the available Beat Frequency parameter options. Moving the highlight bar to Fixed Frequency and pressing ENTER will display the Fixed Frequency change box.

Parameter Change Box and Display of Inactive Parameters.



The once Inactive Beat Fixed option is active highlighted with a change box surrounding its preset value of 100 Hz. At this point the user can modify this value using the up or down arrow keys. After making a modification you must press ENTER to validate the change.

NOTE:
This same sequence of active and inactive parameter options and change sequences is repeated for all waveforms.

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Parameter Adjustment

Parameter adjustment ranges for pain modulation modes of stimulation.
Each mode of treatment offers preset treatment parameters for quick set up. Refer to individual sections for descriptions of preset treatment parameters. You can change any of the waveforms presets to match your own most common treatment protocols.

Parameter adjustment ranges for modes of stimulation

	Interferential	Premodulated	Russian	High Volt
Function	Electrodes	Electrodes	Electrodes	Electrodes, Probes
Mode	NA	NA	Single, Reciprocal, Co-Contraction	NA
Carrier Frequency	5000 Hz	5000 Hz	2500 Hz	NA
Beat Frequency	0-200 Hz	0-200 Hz	20-100 Hz	1-120 Hz
Pulse Frequency	NA	NA	NA	0-220 pps
Burst Frequency	NA	NA	20-100 Hz	NA
Scan Mode	On / Off	N/A	N/A	NA
Scan Time	15 sec	N/A		N/A
Sweep Time	15 sec	15 sec	N/A	N/A
Duty Cycle	N/A	N/A	10 - 50%	NA
Ramp Up / Ramp Down	N/A	N/A	.5, 1, 2, 5 sec	.5, 1, 2, 5 sec
Cycle Time	15 sec	N/A	5/5, 10/10, 10/20, 4/12, 10/30, 10/50,Continuous	5/5, 10/10, 10/20, 4/12, 10/30, 10/50, Continuous
Alternating Time in Polarity	N/A	N/A	N/A	Pos.(+), Neg.(-)
Polarity	N/A	N/A	0-100 mA Peak into 500 ohm load	0-500 Volts
Amplitude	0-50 mA RMS	0-50 mA RMS	200 Volts Peak to Peak	0-500 Volts
Voltage (max.)	200 Volts	200 Volts	N/A	0-2500 mA Peak
Treatment Time	1 to 60 min	1 to 60 min	1 to 60 min	1 to 99 min

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Indications / Contraindications / Adverse Effects for Electrical Stimulation

- ❑ Interferential / Premodulated
  - Indications / Contraindications
  - Warnings / Precautions
- ❑ Preventing Adverse Effects
- ❑ Russian, High Volt
  - Indications / Contraindications
  - Warnings / Precautions

Interferential Current

Indications

- ❑ Symptomatic relief of chronic, intractable pain.
- ❑ Management of pain associated with post-traumatic or postoperative conditions.

Contraindications

- ❑ This device should not be used for symptomatic pain relief unless etiology is established or unless a pain syndrome has been diagnosed.
- ❑ This device should not be used on patients with demand type cardiac pacemakers.
- ❑ This device should not be used over cancerous lesions.
- ❑ Electrode placements must be avoided that apply current to the carotid sinus region (anterior neck) or transcereberally (through the head).

Warnings

- ❑ The long term effects of chronic electrical stimulation are unknown.
- ❑ Safety has not been established for the use of therapeutic electrical stimulation during pregnancy.
- ❑ Adequate precautions should be taken when treating individuals with suspected or diagnosed heart problems, or epilepsy.
- ❑ Benefits of Interferential stimulation have not been established for pain of central origin.
- ❑ This device is to be used as a symptomatic treatment for pain and has no curative value. Patients should be cautioned and their activities regulated if pain is suppressed that would otherwise serve as a protective mechanism.
- ❑ Electronic monitoring equipment (such as ECG monitors and ECG alarms) may not operate properly when electrical stimulation is being utilized.

Precautions

- ❑ Isolated cases of skin rash may occur at the site of electrode placement following long-term applications. The irritation may be reduced by use of an alternate conductive medium or an alternative electrode placement.
- ❑ Effectiveness of this treatment is dependent upon patient selection.

Adverse Effects

- ❑ Skin irritation and burns beneath the electrodes have been reported with the use of therapeutic electrical stimulation.

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Premodulated Current

Indications

- Symptomatic relief of chronic, intractable pain..
- Management of pain associated with post-traumatic or postoperative conditions.

Contraindications

- This device should not be used for symptomatic pain relief unless etiology is established or unless a pain syndrome has been diagnosed.
- This device should not be used on patients with demand type cardiac pacemakers.
- This device should not be used over cancerous lesions.
- Electrode placements must be avoided that apply current to the carotid sinus region (anterior neck) or transcereberally (through the head).

Warnings

- Long-term effects of chronic electrical stimulation are unknown.
- Safety has not been established for the use of therapeutic electrical stimulation during pregnancy.
- Adequate precautions should be taken when treating individuals with suspected or diagnosed heart problems, or epilepsy.
- Benefits of Premodulated stimulation have not been established for pain of central origin.
- This device is to be used as a symptomatic treatment for pain and has no curative value. Patients should be cautioned and their activities regulated if pain is suppressed that would otherwise serve as a protective mechanism.
- Electronic monitoring equipment (such as ECG monitors and ECG alarms) may not operate properly when electrical stimulation is being utilized.

Precautions

- Isolated cases of skin rash may occur at the site of electrode placement following long-term applications. The irritation can usually be reduced by use of an alternate conductive medium or an alternative electrode placement.
- Effectiveness of this treatment is dependent upon patient selection.

Adverse Effects

- Skin irritation and burns beneath the electrodes have been reported with the use of therapeutic electrical stimulation.

Russian, High Volt

Indications

- Relaxation of muscle spasms.
- Prevention or retardation of disuse atrophy.
- Increasing local blood flow.
- Muscle re-education.

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IFC - Interferential Current (Sine Wave)

- ❑ Introduction to Interferential
- ❑ Quick Start
- ❑ Setup Procedure
- ❑ Preparation for Treatment
- ❑ Treatment Procedures
  - Treatment Parameters
  - To Modify Treatment Parameters
- ❑ Terminating Treatment
- ❑ Technical Specifications

Introduction to Interferential

Interferential current consists of two channels with two sinusoidal waveforms: one of fixed frequency and one of variable frequency. When the four electrodes are positioned so the two channels cross each other, the waveforms mix within the tissues to produce a train of pulses whose frequency and amplitude are dependent on the sweep mode, beat frequency and amplitude settings, respectively.

Quick Start

The following is a quick step by step procedure for using interferential stimulation. Before proceeding refer to treatment cautions on page 23.

PROCEDURE	COMMENTS
Turn power on	The unit will power up to the channel available screen.
Clean area to be treated	Follow steps in preparation for treatment.
Position electrodes	Secure electrodes around area to be treated.
Select "IFC"	To select interferential stimulation.
Set "Intensity"	Set intensity level for both channels.
Select "Start"	To begin treatment.
End treatment	Remove electrodes and inspect treatment area.

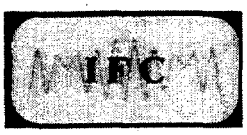
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Setup Procedure: INTERFERENTIAL (IFC)

The following sequence of events are followed to begin an Interferential treatment:

Step 1. Press IFC and set intensity.



CH 1-2	IFC
Ch. Select	Chan. 1 & 2
Amp.Mod.	40 % Scan
Beat Freq.	80 - 150 Hz
Time	15:00
Inten.	30 mA

Enter - Modify Feature
Start - Begin Treatment



Note: You have the option to set the intensity of both channels simultaneously or independently.

Step 2. Press START to begin treatment.



CHANNEL 1
IFC

15 : 00
30 mA

Ch2: IFC 15 : 00
Enter - View Settings

Channel Display Screen will update with waveform, intensity level and elapsed time.

Modifying Power Up Preset Parameters

With the exception of output intensity all power up preset parameters can be modified using the following sequence of steps:

1. Select and change desired parameter setting, next press ENTER.
2. Next simultaneously press and hold the PAUSE and the ENTER button.

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Preparation for Treatment

- ❑ Refer to section three to become familiar with the following:
  - Indications and contraindications for interferential current.
  - Warnings of adverse effects of therapeutic electrical stimulation.

- ❑ Refer to section four to become familiar with the following:
  - Securing electrodes in place.
  - Removal and storage of electrodes.
  - When to replace electrodes.
  - Care and cleaning of electrodes.

- ❑ Before applying electrodes to the area to be treated:
  - Clean the areas of the skin where electrodes will be applied with soap and water or an alcohol wipe and allow the area to dry completely.
  - Excessive hair may be trimmed, but shaving an area is not recommended immediately prior to electrode placement.

- ❑ Choose size of electrodes suitable for the area to be treated:
  - Remember current density (use as large an electrode as possible).
  - Make sure electrodes are intact, clean and securely plugged into lead wires.
  - Position electrodes, avoiding areas of scars, moles, discoloration, broken skin surface, skin folds/creases, or areas of impaired sensation, unless low amplitudes are used and the skin is examined carefully.

Detailed Treatment Procedures

Remember most patients are unfamiliar with electrical stimulation and may be anxious or apprehensive during the initial sensation of current. If the patient is extremely apprehensive, either discontinue the treatment or set the "Output Intensity" at a level where the patient just feels the current. Allow the individual to become accustomed to the current before increasing the intensity.

Treatment Cautions:

- Never turn the power on or off while the unit is connected to the individual.
- Stop the treatment before removing or attaching electrodes or leads. Leads and electrodes should be applied to the patient before a treatment is initiated.
- Never use leads or electrodes that are damaged or worn, this may result in injury to the patient.
- Consult published sources for electrode placements, settings, and treatment duration.
- Make sure all electrodes make full contact with the patient's skin.

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1. **Place the power switch in the "ON" position.**
   The display screen will indicate the machine is going through its power up procedures and system checks. When completed, the Channel Display screen will appear.

2. **Connect electrodes to lead wires and plug into jacks for channels selected.**

3. **Adhere electrodes to the location to be treated.**
   Secure electrodes in the area to be treated. Refer to guidelines under preparation for treatment earlier in this section.

4. **Select "IFC" for Interferential current.**

5. **View and verify the preset parameters for interferential current.**

Preset parameters for interferential current; Beat Frequency: 80-150 Hz, Amplitude Modulation: 40% Scan, Treatment Time: 15 minutes.

6. **To modify treatment parameters prior to starting treatment:**
   - Use the up and down arrows located next to the ENTER button to navigate through the parameters available for interferential current. Time and output intensity are modified by touching their respective up or down control buttons.
   - Once you have highlighted a desired parameter select ENTER to display a pop-up menu of options available for this mode of treatment.
   - Use the up and down arrows to highlight the desired option, then select ENTER.

7. **Set "Intensity" using the controls located on the control panel.**
   Set the output intensity for both channels using the arrow keys located on the INTENSITY button. The amplitude is first displayed on the Parameter Display screen, then amplified on the Channel Display screen after start is pressed.

8. **Press "Start" to initiate the treatment.**
   The stimulation will ramp up to the set values and the Channel Display screen will reappear, displaying the channels and waveforms in use as well as the treatment time remaining for each channel.

9. **To modify settings during treatment: It is recommended that you Pause the treatment session prior to implementing a parameter change.**
   - Select the channel to modify using the Channel 1 / 2 button located on the control panel.
   - Touch ENTER to display parameters of that channel on the LCD display.
   - Once you have highlighted a desired parameter, select ENTER to display a list of options available for this mode of treatment.
   - Use the arrows once again to highlight a desired option and then select ENTER to accept.
   - Use the Treatment Time Control to alter treatment time.
   - Select START to resume treatment.

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10. Terminating Treatment

When treatment ends, a tone will sound and the intensity will ramp to 0. Remove electrodes from patient and inspect area of skin treated.

Modifying Treatment Parameters

Treatment parameters can be modified prior to or during a treatment session. To modify interferential or any session parameters, the session parameters must be displayed on the LCD.

Modify Beat Frequencies: Beat Freq.

CH 1-2	IFC
Ch. Select	Chan. 1 & 2
Amp.Mod.	40 % Scan
Beat Freq.	80 - 150 Hz
Time	15:00
Inten.	30 mA
Enter - Modify Feature Start - Begin Treatment	

Using UP / DN keys place highlight around Beat Freq. and touch ENTER

CH 1-2	IFC
Ch. Select	1 - 10 Hz
Amp. Mod.	80 - 150 Hz
Beat Freq.	1 - 150 Hz
	Fixed Freq.
	Variable
Time	15:00
Inten.	30 mA
Enter - Modify Feature Start - Begin Treatment	

Next a pop-up box appears displaying all Beat Freq. options. Use the UP / DN arrows to select new Beat Freq. Then press ENTER to validate change.

Technical Tip

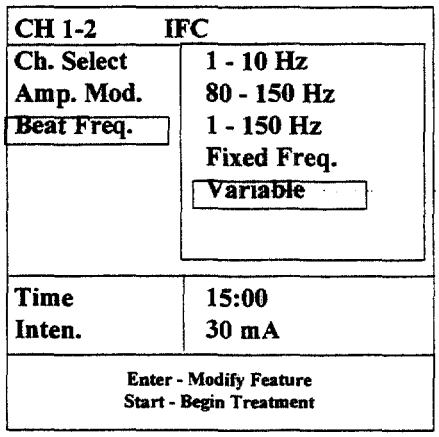
Beat Frequency: The number of times per second that the current rises in intensity to its maximum and falls to its minimum value. The Beat Frequency is the difference between the two medium frequencies. When the machine automatically changes the Beat Frequency within a preselected range, this is termed Sweep.

Suggestion: Some patients may not tolerate parameter changes during a session unless the PAUSE key is used to ramp stimulation down prior to making a change.

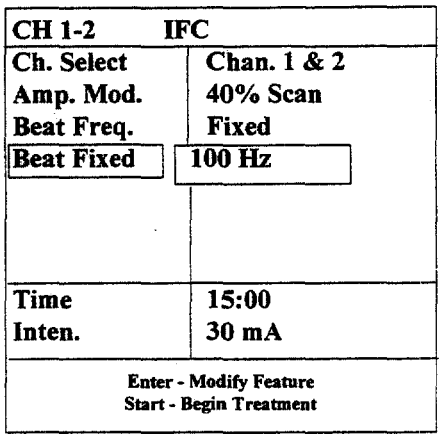
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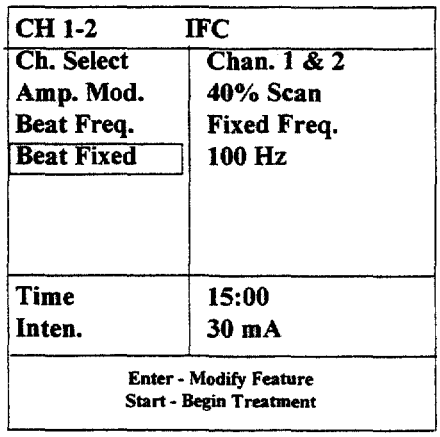
Changing to Fixed Frequency



Select Fixed Freq. and press ENTER.



Fixed Freq. preset to 100 Hz you can change preset value using the UP / DN keys.

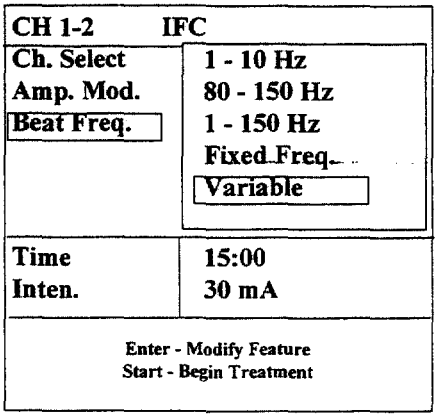


Press ENTER to validate and save change.

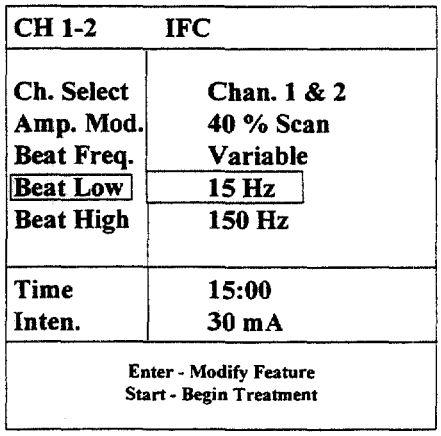
Technical Tip

Fixed Beat Frequency - Single beat frequency selected by the operator between 1 - 150 Hz. In other words, a constant or fixed difference between the two medium frequencies.

Changing to Variable Frequency



Select Variable and press ENTER.



Use UP / DN keys to set Beat Low value and then press ENTER.

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Modifying Beat Frequencies continued.

CH 1-2	IFC
Ch. Select	Chan. 1 & 2
Amp.Mod.	40% Scan
Beat Freq.	Variable
Beat Low	15 Hz
Beat High	125 Hz
Time	15:00
Inten.	30 mA

Enter - Modify Feature
Start - Begin Treatment

Use UP / DN keys to set Beat High value and press ENTER to validate change.

Technical Tip

Variable Beat Frequency - The machine automatically changes the beat frequency within the preselected Low and High range as set by the user.

Amplitude Modulation: Amp. Mod.

Amplitude modulation can be modified in the following ways:

Technical Tip

Amplitude modulation: Is a method of alternating the Interferential current output amplitude.

CH 1-2	IFC
Ch. Select	Chan. 1 & 2
Amp.Mod.	40% Scan
Beat Freq.	80 - 150 Hz
Time	15:00
Inten.	30 mA

Enter - Modify Feature
Start - Begin Treatment

Using arrow keys place highlight around Amp. Mod. amplitude modulation.

CH 1-2	IFC
Ch. Select	Chan. 1 & 2
Amp. Mod.	100 % Scan
Beat Freq.	80 - 150 Hz
Time	15:00
Inten.	30 mA

Enter - Modify Feature
Start - Begin Treatment

CH 1-2	IFC
Ch. Select	
Amp. Mod.	40 % Scan
Beat Freq.	100 % Scan
	Static
Time	15:00
Inten.	30 mA

Enter - Modify Feature
Start - Begin Treatment

Press ENTER to display options.

Technical Tip

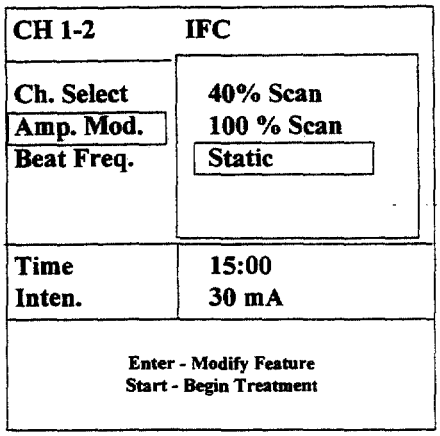
Scan - Rotating of the static interferential field from 100% amplitude to 60% or 0% depending on the selection. This movement or "Scanning" effect is produced by rhythmically varying the current intensity of each channel.

Use UP / DN keys to select 40% or 100% Scan.
Press ENTER to validate change.

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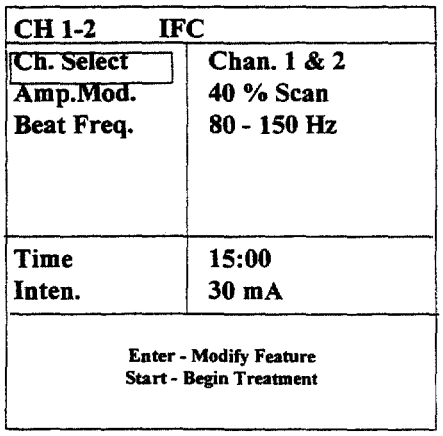


Use UP / DN keys to select Static. Press ENTER to validate change.

Technical Tip

Static - Static interferential field is the "clover-leaf pattern" and is used to describe the area of interference effect.

Setting Channel Output



Technical Tip

Output intensity is preset to deliver set stimulation levels from both channels simultaneously. This can be modified so stimulation can be set one channel at a time if so desired. To make this selection follow these commands. With the highlight bar positioned over the Ch. Select command, press Enter. This will change output intensity settings to Channel 1. At this point raise the intensity of channel 1 using the Intensity keys. When at desired levels, press Enter to set channel 2. The intensity level of channel 1 will remain on as channel 2 intensity level is being set.

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Setting Output Intensity

CH 1-2	IFC
Ch. Select	Chan. 1 & 2
Amp.Mod.	40 % Scan
Beat Freq.	80 - 150 Hz
Time	15:00
Inten.	30 mA
Enter - Modify Feature Start - Begin Treatment	

Output intensity is set using the intensity up or down control arrow buttons located on the illustrated control panel. After your intensity threshold is set press the START button. At this point intensity will ramp down momentarily then slowly ramp up to set levels.

Changing Treatment Time

CH 1-2	IFC
Ch. Select	Chan. 1 & 2
Amp.Mod.	40 % Scan
Beat Freq.	80 - 150 Hz
Time	15:00
Inten.	30 mA
Enter - Modify Feature Start - Begin Treatment	

Treatment time can be changed by using the up or down arrow buttons located on the illustrated control panel. Treatment time is displayed numerically on the parameter display screen. When the START button is touched treatment time is amplified and displayed on the Channel Display screen.

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Technical Specifications For Interferential Current

Output Channels: 1- 2

Amplitude: 0-50 mA RMS into a 500 ohm load

Current Limit: 50 mA RMS

Voltage (max.): 200 Volts Peak to Peak

Carrier Frequency: 5000 Hz

Beat Frequencies: 0-200 Hz

Maximum RMS Current Density:

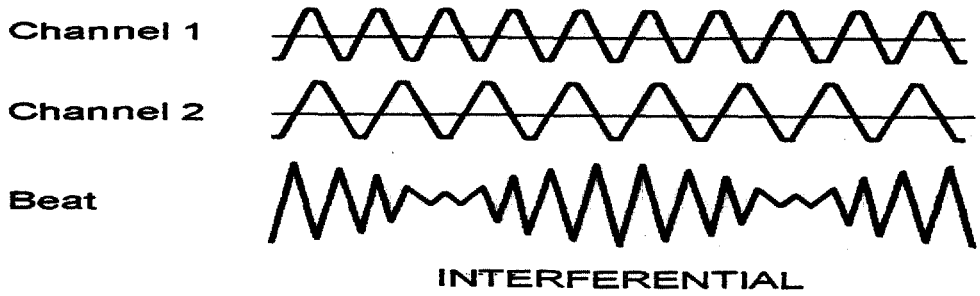
- 3" x 5" Electrode: 5.2 μA/mm²
- 2" Diameter Electrode: 24.7 μA/mm²

Maximum Power Density:

- 3" x 5" Electrode: .365 mw/mm²
- 2" Diameter Electrode: 1.74 mw/mm²

Area of Conductive Surface:

- 3" x 5" Electrode: 15 in² (9,677 mm²)
- 1 5/8"x 2" Electrode: 3.25 in² (2,0972)
- 2" Diameter Electrode: 3.14 in² (2,027 mm²)



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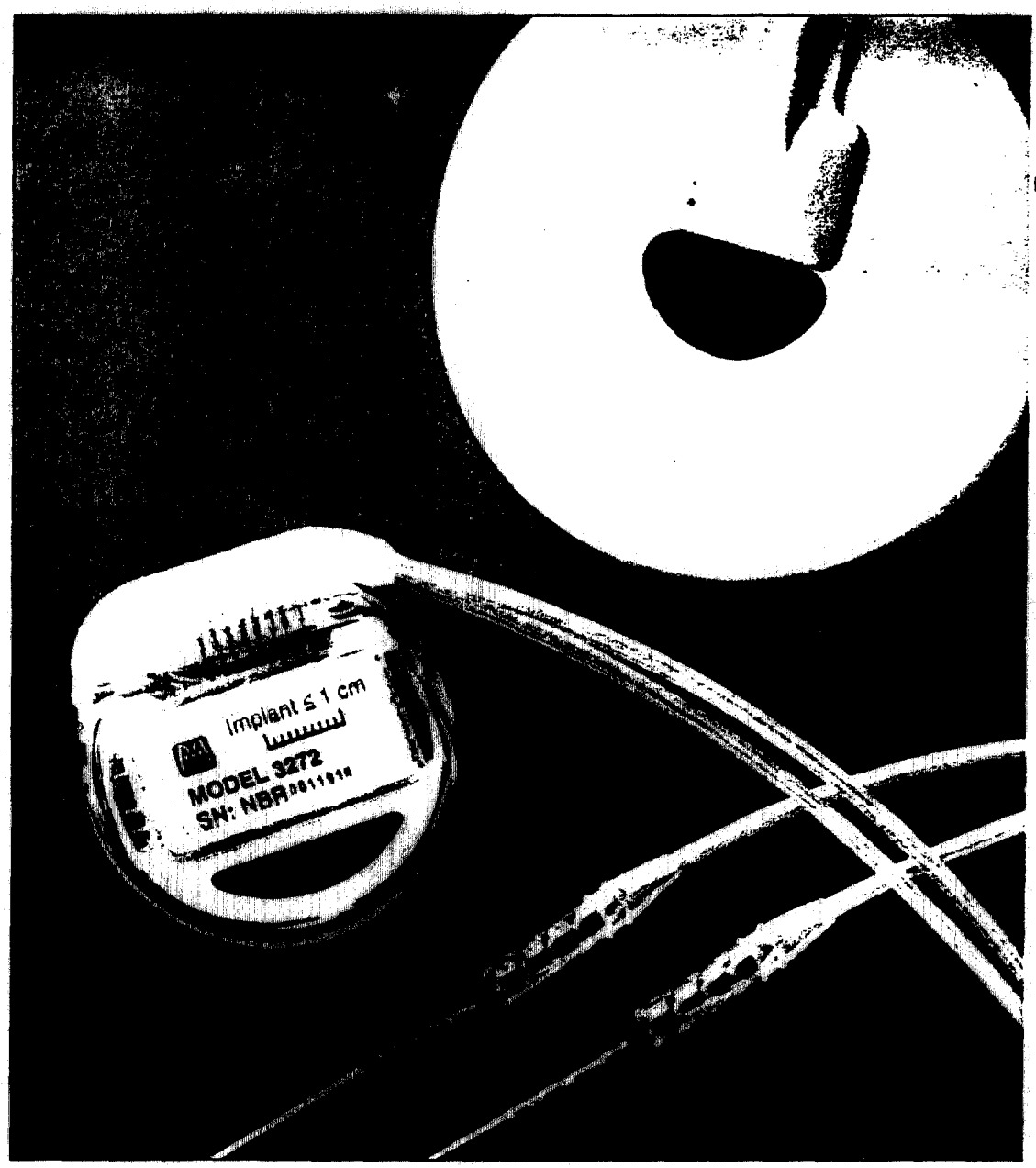
APPENDIX 17

MEDTRONIC, INC.

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mattrix® System Reference Guide

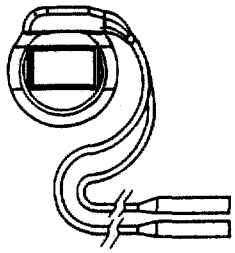
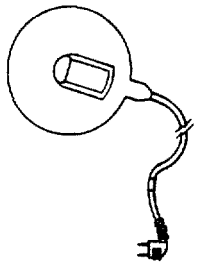
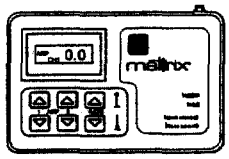
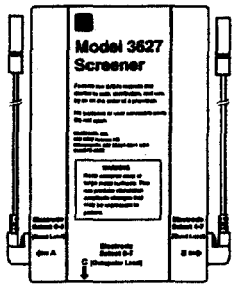


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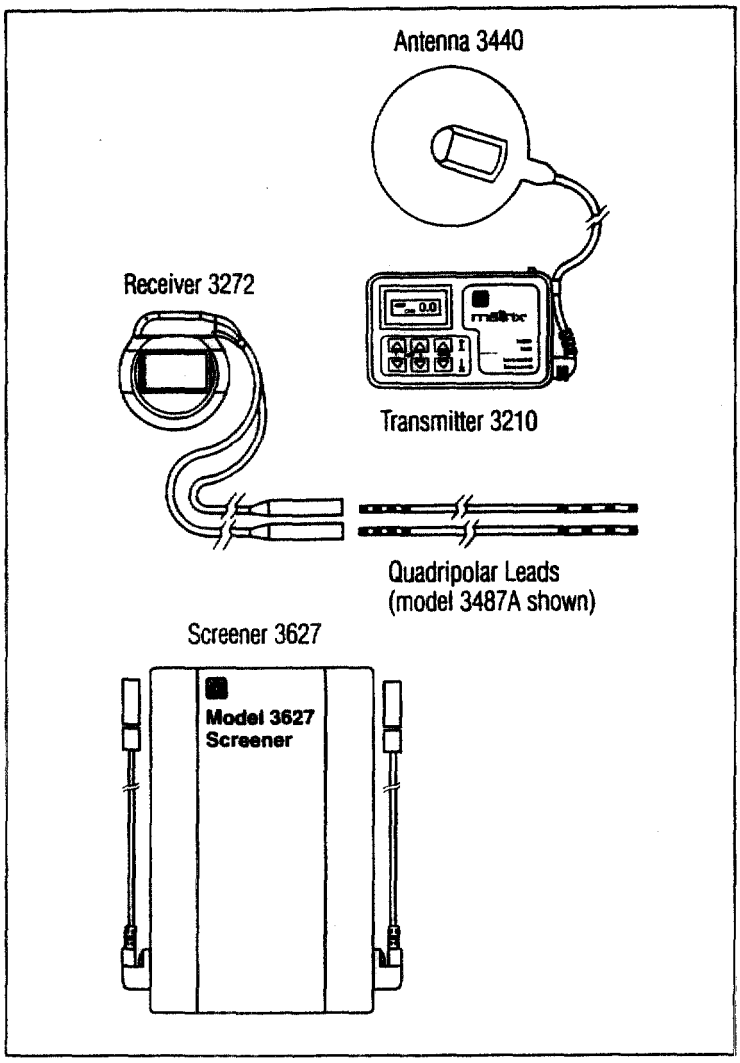
Table 1. Mattrix System Components		
Model 3272 Receiver	Implanted device that receives signals from the Model 3210 Transmitter. It has no battery and derives its power from the transmitter.	
In-line quadripolar leads	Two implanted quadripolar leads that deliver electrical stimulation.	 Model 3487A PISCES-Quad® Lead  Model 3888 PISCES-Quad Plus® Lead  Model 3587A Resume II® Lead
Model 3440 Antenna	The antenna provides the link between the receiver and transmitter. It connects to the transmitter. Tape patches or adhesive discs attach the antenna to the skin over the receiver.	
Model 3210 Transmitter	External component that contains the electronics for programming and powering the implanted receiver.	
Model 3627 Screener	Temporary external programming and power source used for stimulation testing.	

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Figure 1. Configuration of Mattrix Components.



Stimulation Modes

The Mattrix system has two stimulation modes:

- Single Stim™ mode
- Dual Stim™ mode

In the Single Stim mode, the two Mattrix leads can be programmed to the same amplitude, pulse width, and rate. In the Dual Stim mode, the amplitude and pulse width *can be programmed independently* for each lead. The programmed rate is the same for both leads.

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2

Indications

The Medtronic Mattrix system is indicated for spinal cord stimulation (SCS). A Mattrix system with the model 3272 receiver is also indicated for peripheral nerve stimulation (PNS). The system is indicated as an aid in the management of chronic, intractable pain of the trunk or limbs.

Contraindications

Patients are contraindicated for internalization if they are unsuccessful in receiving pain relief during trial stimulation, or if they are unable to properly operate the transmitter.

Implantation of an SCS or PNS system is contraindicated for patients with a cardiac demand pacemaker, implantable cardiac cardioverter/defibrillator, or for those patients who will be exposed to magnetic resonance imaging (MRI).

Patient Selection

The most likely candidates for the Mattrix system have neuropathic pain and any one of these characteristics (Figure 2):

- Pain covering more than one vertebral segment
- Bilateral pain pattern that cannot be adequately treated with one lead
- Pain patterns requiring multisite stimulation
  - -Cervical and thoracic
  - -Multiple PNS applications

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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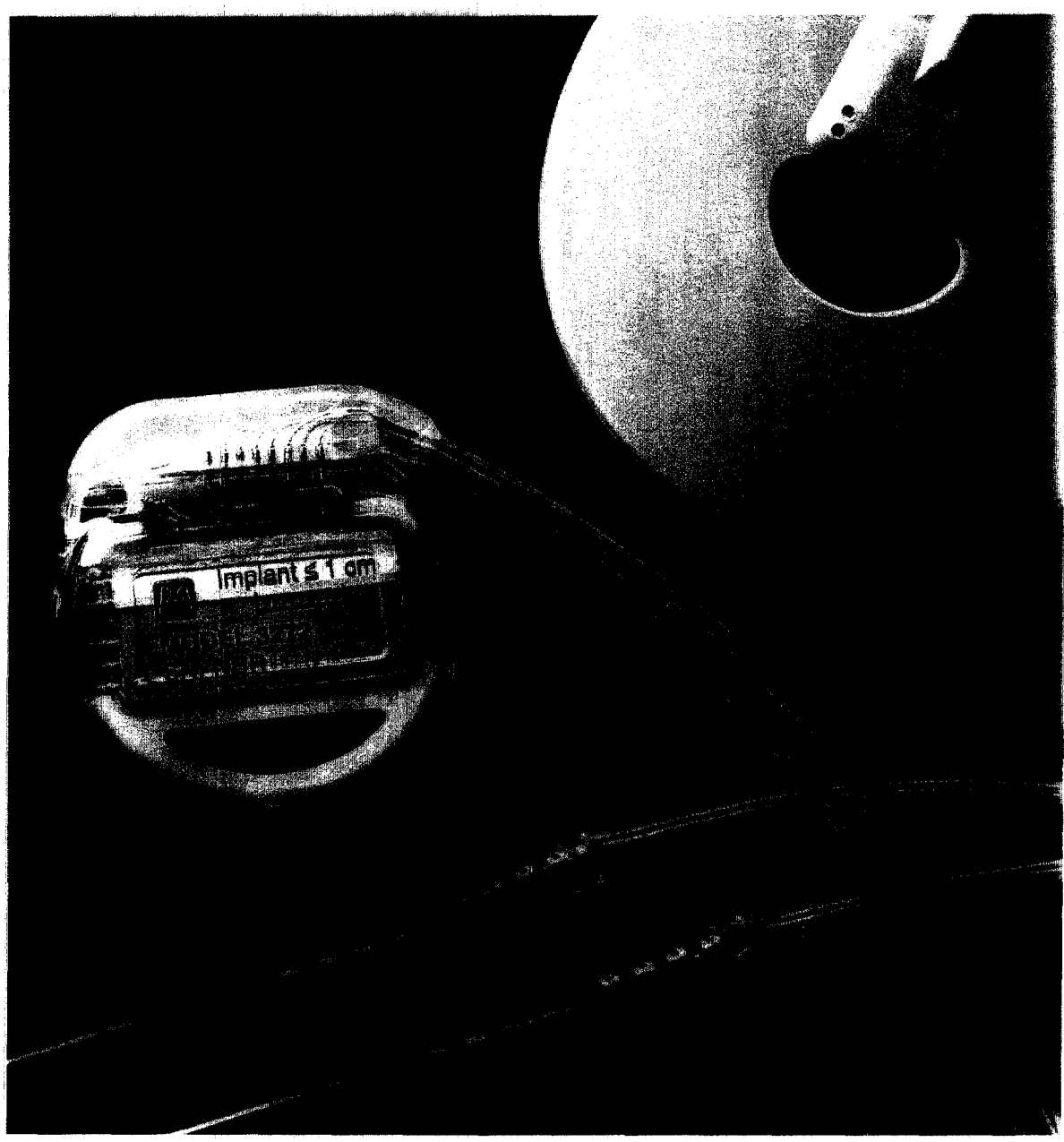
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mattrix® NEUROSTIMULATION SYSTEM



THE ONE WAY TO GET TWO STIMULATION MODES

Medtronic

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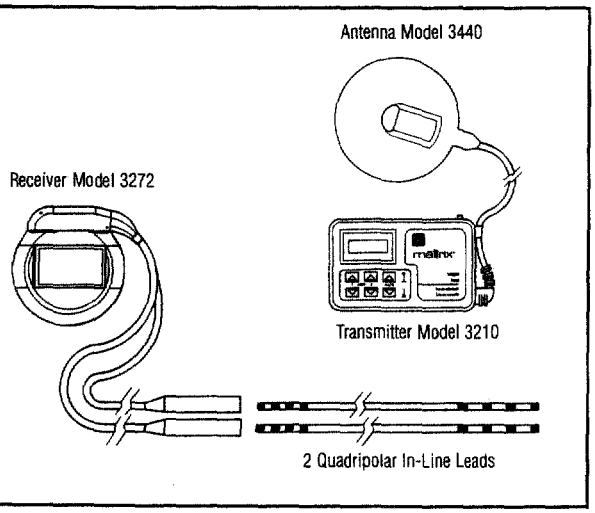
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Patient Screening Helps Ensure Therapy Success

When it has been determined that spinal cord stimulation (SCS) might be an appropriate therapy for a patient, screening will help determine easily and efficiently:

- Whether a one-lead system or a two-leads system should be implanted, thereby saving implant costs and time
- Whether Single Stim mode or Dual Stim mode is the most appropriate for the patient's pain pattern.

Mattrix System Components



Electrical Parameters*

Parameter	Receiver Model 3272
Stimulation Modes	Single Stim or Dual Stim
Output Configuration	2x4
Amplitude	
2x4	
Lead 1	0-12 V in 0.1 V steps
Lead 2	0-12 V in 0.1 V steps
Rate	
Single or Dual Stim Mode	5-240 pps in 1 pps steps
Pulse Width	
Single or Dual Stim Mode	50-500 microsec in 10 microsec steps
Battery Type	9 V alkaline or nickel-cadmium

* Specifications are approximate.

Indications

The Medtronic Mattrix® Neurostimulation system is indicated for treatment of chronic, intractable pain of the trunk or limbs. The Mattrix Receiver Model 3272 system is also indicated for peripheral nerve stimulation.

Contraindications

Unsuccessful pain relief during trial stimulation of the spinal cord, or inability of patients to properly operate the system. The Mattrix system also is contraindicated for patients with an implantable cardiac pacemaker or cardioverter/defibrillator, or for those patients who will be exposed to magnetic resonance imaging (MRI).

Warnings/Precautions/Adverse Events

Safety has not been established for pregnancy or pediatric use. Patients should not drive or use dangerous equipment during stimulation. Systems may be affected by or adversely affect cardiac pacemakers, cardioverter/defibrillators, external defibrillators, MRI, diathermy, ultrasonic equipment, electrocautery, radiation therapy, theft detectors, security systems, and aircraft communications systems. Adverse events may include: undesirable change in stimulation described by some patients as uncomfortable, jolting or shocking; hematoma, epidural hemorrhage, paralysis, seroma, CSF leakage, infection, erosion, allergic response, hardware malfunction or migration, pain at implant site, loss of pain relief, chest wall stimulation, and surgical risks. Patient selection criteria include physiological origin for the pain, appropriate surgical candidate, detoxification from narcotics, and availability of long-term post-surgical management.

CAUTION: U.S. federal law restricts this device to sale, distribution, and use by or on the order of a physician.

Refer to the product manual for additional information and instructions for use.

Medtronic

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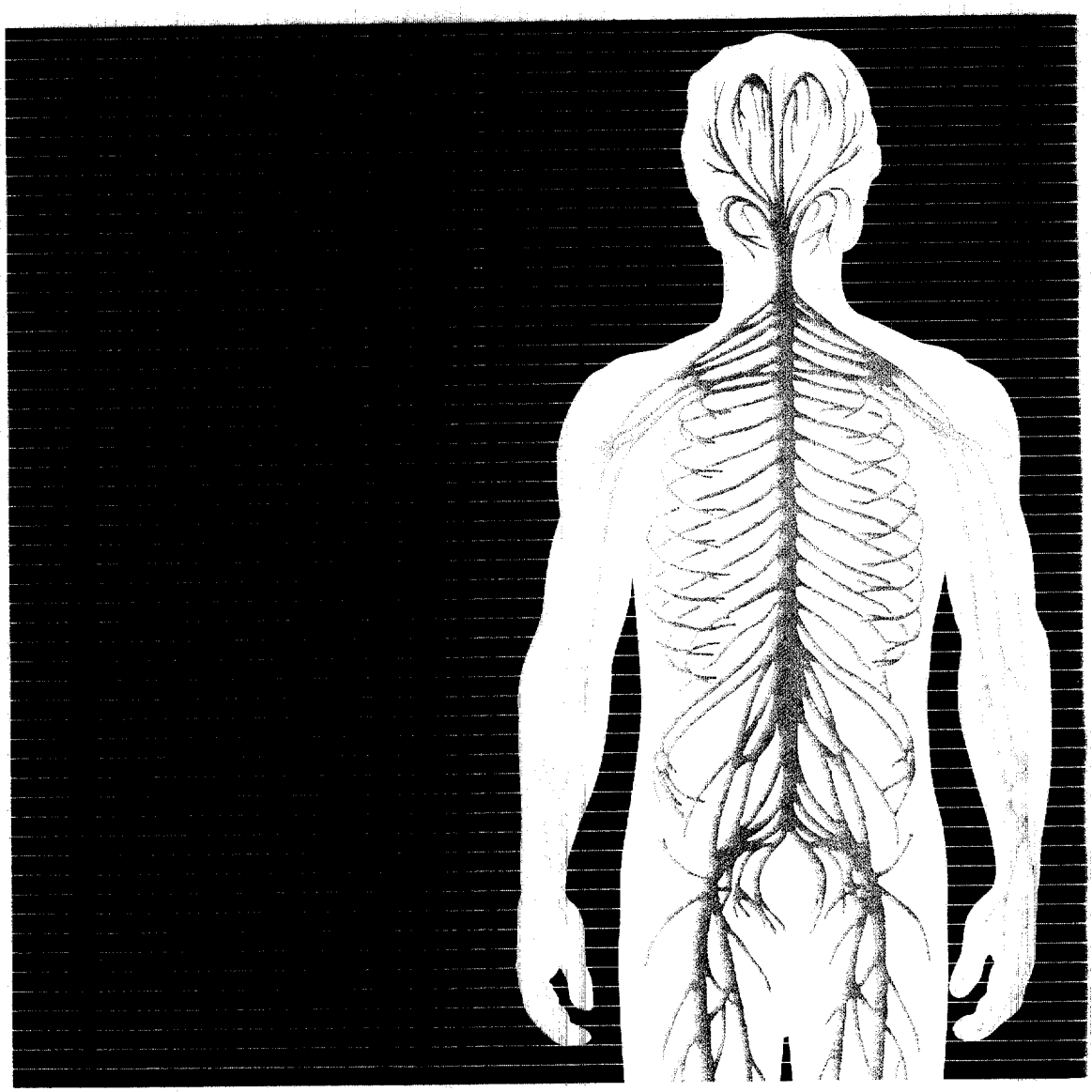
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Medtronic

PERIPHERAL NERVE STIMULATION



Lead Implantation Guide for Treatment of Chronic Pain

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Caution

US Federal law restricts this device to sale by or on the order of a physician.

Refer to the product manual for additional information and instructions for use.

Indications

The Medtronic X-Trel® system and the Mattrix® system with the Model 3272 Receiver are indicated for peripheral nerve stimulation (PNS), either as the sole mitigating agent, or as an adjunct to other modes of therapy used in a multidisciplinary approach to chronic pain alleviation. Peripheral nerve stimulators are used to stimulate, electrically, a peripheral nerve in patients to relieve severe, intractable pain. The X-Trel system and the Mattrix system are also used for spinal cord stimulation (SCS) and are indicated in the management of chronic pain of the trunk and limbs.

Contraindications

The recommended patient selection method includes a period of direct stimulation of the dorsal column, or targeted peripheral nerve, to evaluate the patient's tolerance for the sensation of stimulation, the patient's ability to operate devices, and the efficacy of the system. An unsuccessful trial should result in discontinuation of this mode of therapy.

Implantation of a PNS or SCS system is contraindicated for patients with a cardiac demand pacemaker or for those patients who will be exposed to magnetic resonance imaging (MRI).

⚠ **Warnings**

⚠ **Pregnancy** — Safety for use during pregnancy or delivery has not been established.

⚠ **Pediatric Use** — Safety and effectiveness of this system have not been established for pediatric use.

⚠ **Cardiac Pacemakers** — Under certain conditions, neurostimulation systems may adversely affect the operation of cardiac demand pacemakers.

⚠ **Cardioverter Defibrillators** — Under certain conditions, neurostimulation systems may affect the therapies programmed into cardioverter defibrillators.

⚠ **External Defibrillators** — Safety for use of external defibrillatory discharges on patients with neurostimulation systems has not been established.

⚠ **Magnetic Resonance Imaging** — Use of Magnetic Resonance Imaging (MRI) may result in dislodgement or heating of the neurostimulator and/or lead. The voltage induced through the lead and neurostimulator may cause uncomfortable "jolting" or "shocking" levels of stimulation. Patients should not be exposed to the electromagnetic fields produced by MRI.

⚠ **Components** — The use of non-Medtronic components with this system may result in damage to Medtronic components, less than adequate stimulation, or increased risks to the patient.

⚠ **Diathermy** — The effects of diathermy on patients with an implanted neurostimulation system are unknown. Since internal components may be damaged, using diathermy over an implanted lead or neurostimulator is not recommended.

⚠ **Equipment Operation** — When using stimulation, patients should not operate potentially dangerous equipment such as power tools or automobiles.

⚠ **Postural Changes** — Postural changes or abrupt movements may cause an increase or decrease in the perceived level of stimulation. Higher levels of stimulation have been described by some patients as uncomfortable, "jolting" or "shocking".

⚠ **Theft Detectors and Screening Devices** — Theft detectors found in public libraries, department stores, etc., and airport/security screening devices may cause the stimulation power source for an implantable neurostimulation system to switch ON or OFF. It is also possible that sensitive patients, or those with low stimulation thresholds, may experience a momentary increase in their perceived stimulation. Higher levels have been described by some patients as uncomfortable, "jolting" or "shocking" as they pass through these devices. For a system with a Model 3272 Receiver, the leads and extensions must be routed adjacent to one another. If a patient has a system with non-adjacent implanted leads, some theft detectors may affect their stimulation.

⚠ **Screener Use** — Do not use two Model 3625 Screeners simultaneously with dual lead systems. The screener interaction may cause incorrect screening results.

⚠ **Antenna Use** — Do not place the transmitter directly over or adjacent to the antenna during stimulation as this may reduce the stimulating amplitude or affect other stimulation characteristics. Warn the patient to wear the transmitter several inches away from the implanted receiver to avoid this type of interference.

⚠ **Transmitter Push Buttons** — Accidental bumping of the transmitter buttons when in the SET position could cause a change in stimulation, which could result in unpleasant or less effective stimulation. Warn the patient to leave the OFF/SET/LOCK switch in the LOCK position at all times except when adjusting the controls.

⚠ **Precautions**

⚠ **Infection** — As with all surgical procedures, the risk of infection is present with the implantation of this system. Avoid unduly prolonged trial screening. If using the RF system prior to wound healing, use a sterile barrier between the transmitter antenna and receiver implant wound. Use antibacterial soap to clean skin, and supplied hypoallergenic adhesive disc to attach antenna. Clean skin and replace disc as needed.

⚠ **Handling Components** — The implanted components of this system were designed to perform in the extremely hostile environment of the human body. However, these components may be damaged by excessive traction or sharp instruments. Any component showing signs of damage should not be used.

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The following practices will help ensure the component's life:

- Do not bend or kink the lead.
- Do not tie a suture directly to the lead. Use one of the anchors (where applicable) supplied in the lead kit.
- Do not pull the lead taut when implanted. Leave it as loose as possible to avoid unnecessary tension on the lead.
- When handling the lead with forceps, use only a rubber-tipped bayonet forceps.
- Be extremely careful when using sharp instruments around the lead to avoid damaging the lead.
- For PNS applications, be extremely careful to avoid excessive manipulation and irritation of the peripheral nerve.

⚠ **Connections** — Wipe off any body fluids from the lead contacts or connector before connecting. Contamination of connections can affect neurostimulation.

⚠ **Component Failures** — The physician should be aware that all neurostimulation systems may unexpectedly cease to function. A system may fail at any time due to random failures of the system components. These events, which can include electrical shorts or opens and insulation breaches, cannot be predicted.

⚠ **High Output Ultrasonics** — It is not recommended to use high output ultrasonic devices, such as an electrohydraulic lithotriptor on patients with an implanted neurostimulator. While there is no danger to the patient, exposure to high output ultrasonic frequencies may result in damage to the neurostimulator circuitry.

⚠ **Ultrasonic Scanning** — Ultrasonic scanning equipment may cause mechanical damage to an implanted neurostimulator if used directly over the neurostimulator implant site.

⚠ **Electrocautery** — RF from electrocautery can damage a receiver. No electrosurgical tip should ever be used in the vicinity of an implanted neurostimulator-lead system.

⚠ **Defibrillators** — Use of defibrillatory discharges in the vicinity of an neurostimulator or lead can cause permanent damage to the neurostimulator.

⚠ **Radiation Therapy** — Radiation therapy can cause damage to electronic components of a receiver. It is not recommended to use radiation therapy directly over a receiver.

⚠ **Patient Selection** — Patients should be carefully selected to assure that their pain is of physiologic origin. Also, patients must be appropriate candidates for surgery.

⚠ **Patient Detoxification** — It is recommended that patients undergo detoxification from narcotics prior to implant.

⚠ **Patient Management** — To help ensure maximum benefits from the neurostimulation system, long-term, postsurgical management of patients is recommended.

⚠ **Internal Switches**—Reduce amplitude to zero (0) volts before making any changes in the internal physician switch settings. In addition, patients should be warned not to adjust the internal physician switches (RF System). While failure to abide by this warning may not be dangerous, per se, it could lead to less effective or unpleasant stimulation.

⚠ **Cross Talk** — Low amplitude cross talk from the radiofrequency (RF) signal that programs the electrodes, typically 0.75 volts or less, may be perceived by some patients. Patients should be tested prior to internalization at zero (0) volts amplitude to determine sensitivity to this signal.

⚠ **Aircraft** — Do not use the transmitter while flying in an aircraft. Airlines recommend that electronic devices, especially those generating radio frequency signals, not be used while in flight to assure no interference occurs to aircraft communication systems.

⚠ **Other Transmitters** — Instruct your patients not to use the transmitter of another patient or loan their transmitter to another patient. Explain that the therapy programmed into a patient's transmitter is a prescription only for that patient.

⚠ **Implanting Two Neurostimulators** — If there is a need to implant two neurostimulators in a patient, they must be implanted at least 12 inches (RF-receivers) apart from each other to minimize interference.

Adverse Events

As with all surgical procedures, the implantation of a Peripheral Nerve Stimulation (PNS) system involves some risks. In addition to those normally associated with surgery, implantation and/or use of a PNS system carries the following risks:

- Undesirable change in stimulation, possibly related to cellular changes around the electrode(s), shifts in electrode position, loose electrical connections, or lead/extension fractures, which at high stimulation levels has been described by some patients as uncomfortable, "jolting," or "shocking."
- Patients on anticoagulation therapies may be at greater risk for postoperative complications, such as hematomas, that can result in paralysis.
- Receiver migration
- Persistent pain at the receiver site
- Seroma at the receiver site
- Lead migration
- Allergic or immune system response to the implanted materials
- Infection
- Loss of pain relief may return patient to his or her underlying pain condition
- Nerve damage or degeneration

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5. LEAD IMPLANTATION OVERVIEW

The first stage of a Peripheral Nerve Stimulation (PNS) procedure is the implantation of a stimulating lead.

When the ulnar, median, radial, common peroneal, or tibial nerves are stimulated, either the On-Point® or Resume® II quadripolar lead are recommended. Use of these surgical leads requires creation of a graft or fascial flap to separate the electrode from direct contact with the nerve. Surgical lead implantation is usually performed under general anesthesia, with local anesthesia used when appropriate to enable patient feedback during test stimulation.

One key to the technical success of a PNS procedure is the accurate placement of the stimulating lead, which results in paresthesia that covers the patient's painful area. Therefore, lead placement is determined by patient feedback during intraoperative testing. Performing lead implantation under local anesthetic, or an appropriate general anesthetic, allows for this feedback. Therefore, consideration should be given to the patient being awake and alert during the test stimulation period.

Implantation accessories required for each stage of the system implant procedures are included in the respective product kits (lead, extension, and neurostimulator). Lead implantation accessories packaged in the lead kit include:

- Introducer accessories
- Tunneling tools
- Anchors, insulation boots, and hex wrenches
- Percutaneous extension (for test stimulation)
- Screening cable

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6. SURGICAL LEAD IMPLANTATION

This chapter is divided into sections that address individual nerve sites. It describes the ulnar and median nerve lead implantation in detail. Subsequent nerve implant descriptions outline only those procedures that differ from the ulnar and median nerve instructions.

For Peripheral Nerve Stimulation (PNS) using the surgical lead, it is recommended that you create a graft or a fascial flap to help prevent direct contact between the lead paddle electrode surface areas and the nerve. Both implant techniques are described in this chapter. The focus, however, is on the graft implant technique.

The On-Point® Lead has a web mesh feature that helps facilitate the implantation procedure. It also has a flat connector. The Resume® II Lead, which can also be used for PNS therapy, does not have the web mesh and has an in-line connector. The implant techniques for both types of connectors are discussed on the following pages.

The selection of the desired implant technique and lead should be based on your clinical judgement regarding the most appropriate therapy for your patient.

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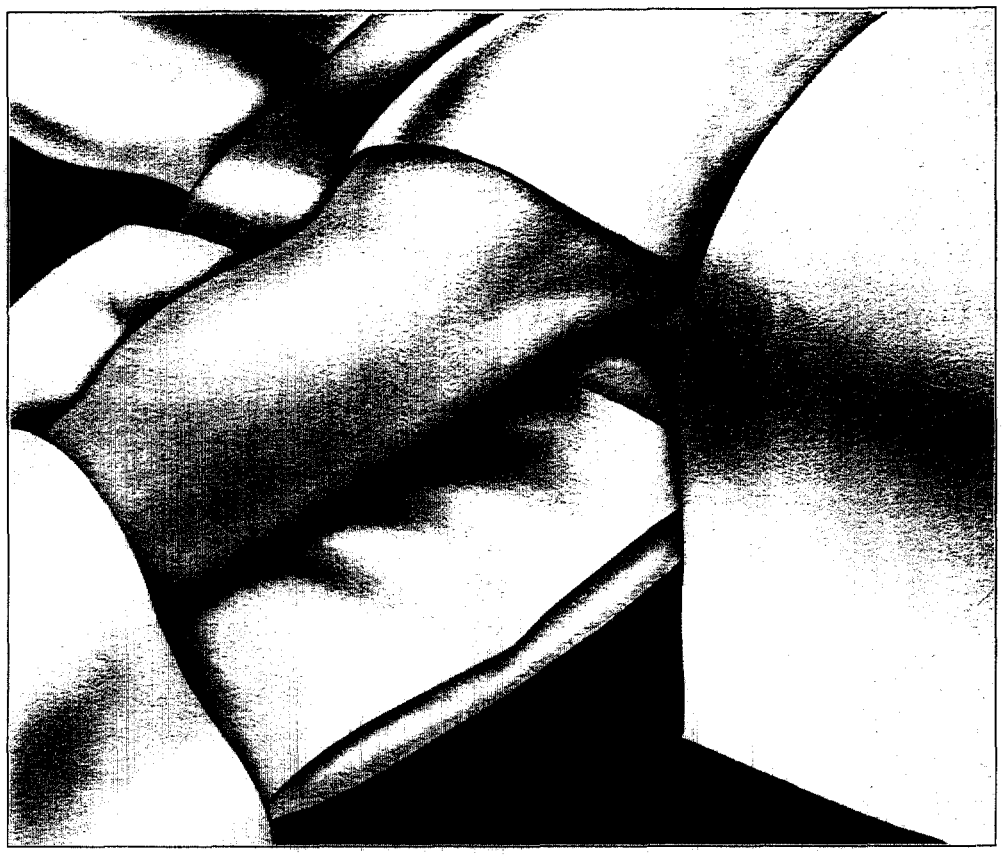


Figure 1: Prepare and drape the patient

ULNAR AND MEDIAN NERVES

Prepare and drape the patient. The procedure is generally performed under general anesthesia with the entire arm and shoulder draped. If intraoperative test stimulation is planned, consideration should be given to ensure that the patient can be awake during that part of the procedure. If the procedure is performed under local anesthesia, refer to the appropriate lead technical manual for instructions on intraoperative test stimulation. No tourniquet is used (Figure 1). The use of a tourniquet is quite difficult and considerable bleeding may occur. It may be possible, however, to use a small Esmarch tourniquet that constricts the arm near the axilla to allow hemostasis for better visualization during the dissection of the nerve.

Prophylactic antibiotics can be administered intravenously for protection from postoperative infection.

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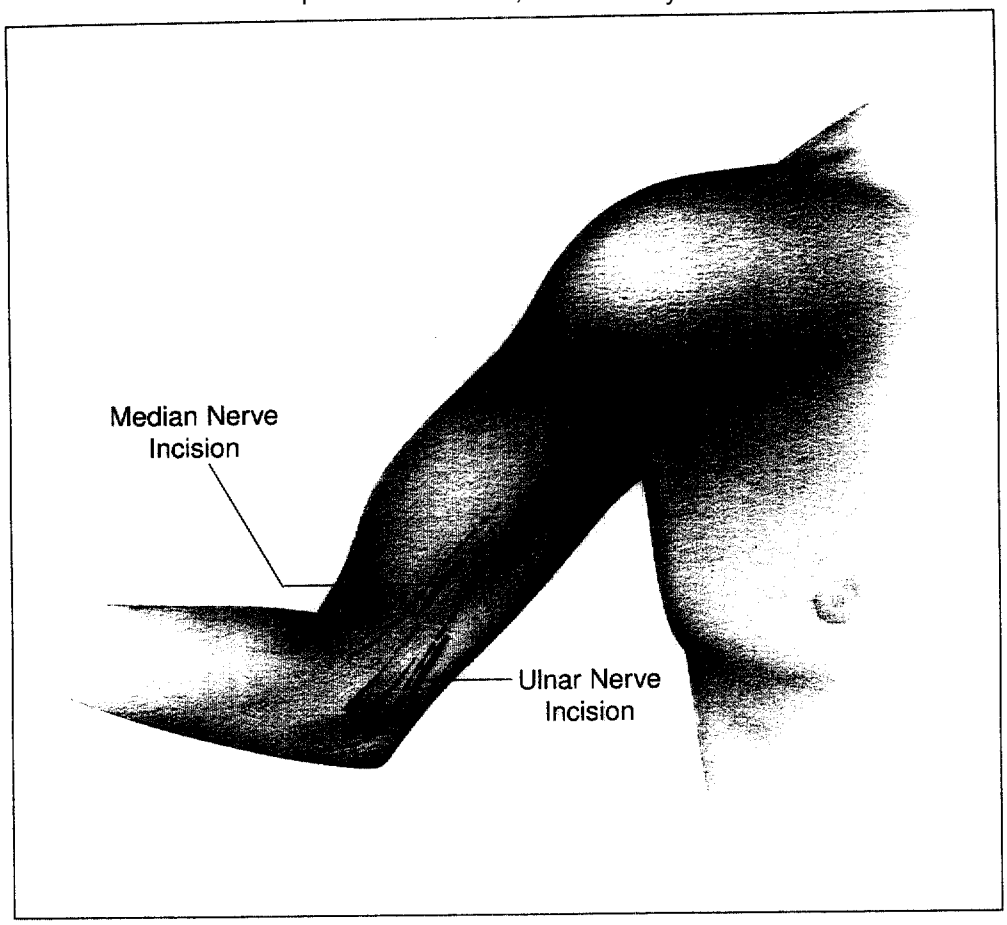


Figure 2: Make incision for ulnar nerve

Make the incision for the **ulnar nerve** approximately 3 cm proximal to the medial epicondyle (Figure 2). Extend the incision diagonally across the course of the ulnar nerve for a total distance of approximately 12 cm.

NOTE: The median nerve is discussed later.

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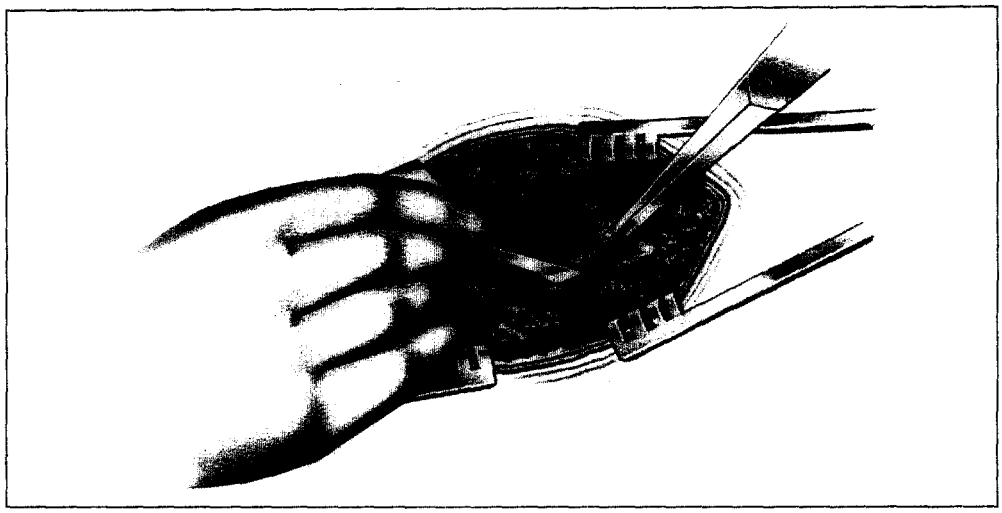


Figure 3a: Harvest fascia as free graft

Clean and mark an area approximately 1 cm by 5 cm. Carefully dissect down to the fascia (Figure 3a).

Harvest this section of fascia as a free graft that will be applied to the lead paddle.

NOTE: It is usually easier to harvest this graft prior to incising the fascia because the proper size can be ascertained.

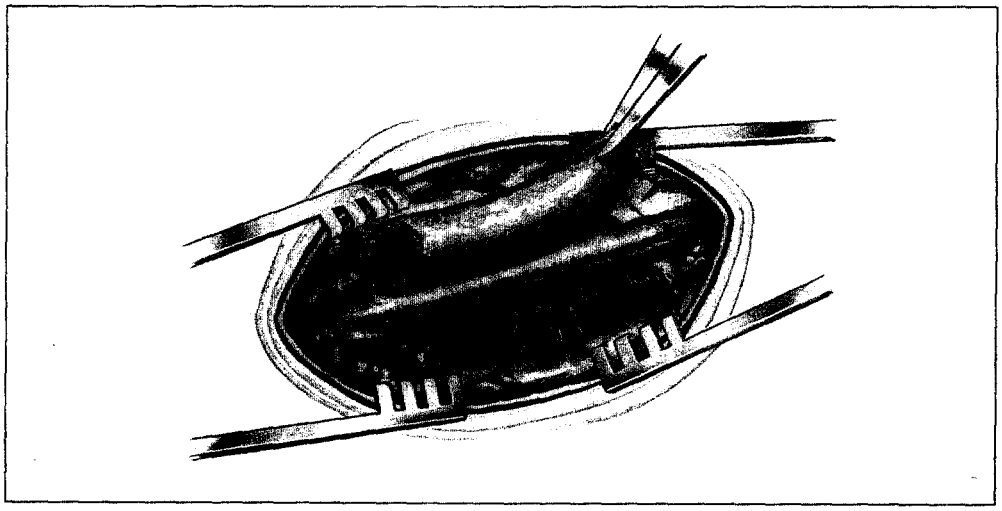


Figure 3b: Create fascial flap (optional technique)

For the optional fascial flap technique, create a soft-tissue flap to shield the electrodes from direct contact with the nerve (Figure 3b).

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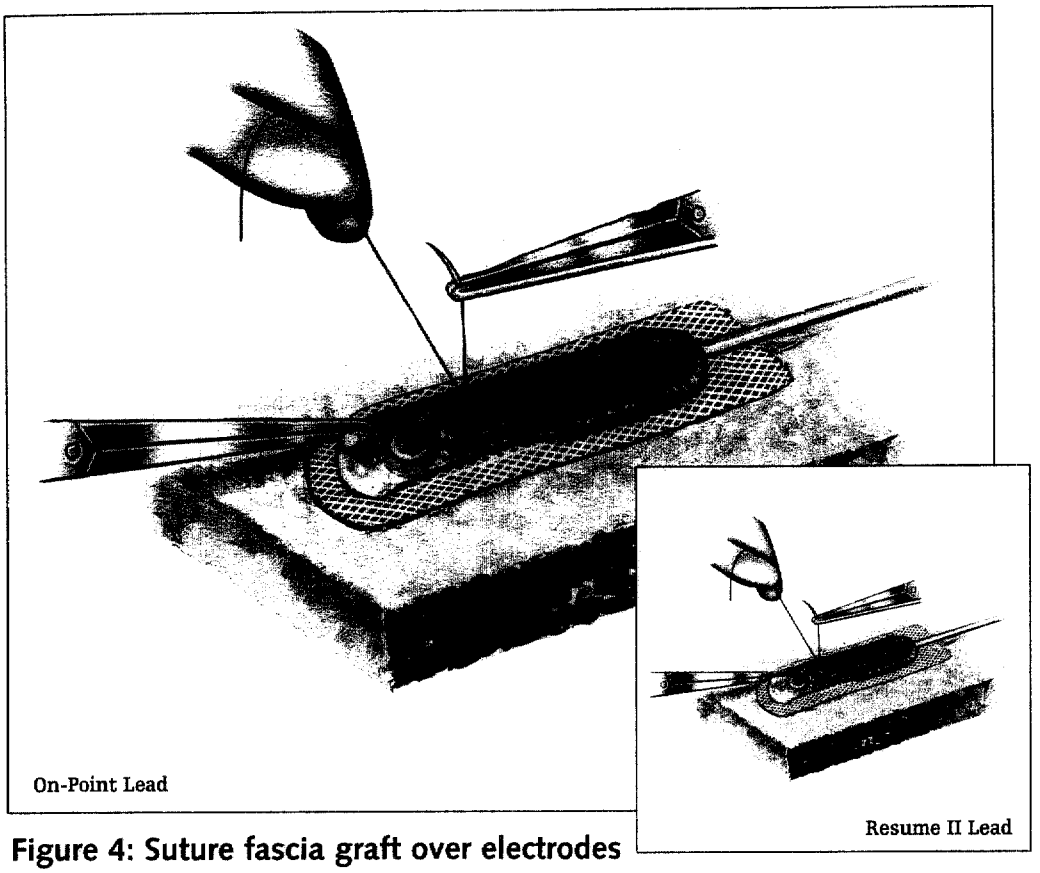


Figure 4: Suture fascia graft over electrodes

After harvesting the graft, place it on a damp sponge. For the **On-Point Lead**, trim the mesh surrounding the electrode paddle to the desired distance from the paddle. Use sharp scissors to ensure that the edges do not fray. The fascial graft should be stretched slightly so that it fits without wrinkles, but it should not be placed so tightly as to pull loose around the sides.

Suture the graft over the electrode side "face" of the paddle to the mesh surrounding the paddle. Use multiple peripheral interrupted sutures with 5-0 nylon on a very small, sharp needle. Sew clear of the electrodes and conducting wires (Figure 4). For the **Resume II Lead**, suture the graft over the "face" of the paddle using multiple peripheral interrupted sutures with 5-0 nylon on a very small, sharp needle (Figure 4 insert). This graft procedure is done to prevent direct contact between the electrode surface area and the nerve.

⚠ **CAUTION**

Use care when trimming the **On-Point Lead** mesh to avoid cutting the lead body or electrode paddle.

⚠ **CAUTION**

Care must be taken not to damage the electrodes or conducting wires while suturing. Suture on the periphery of the lead paddle supporting matrix, clear of electrodes and their wires.

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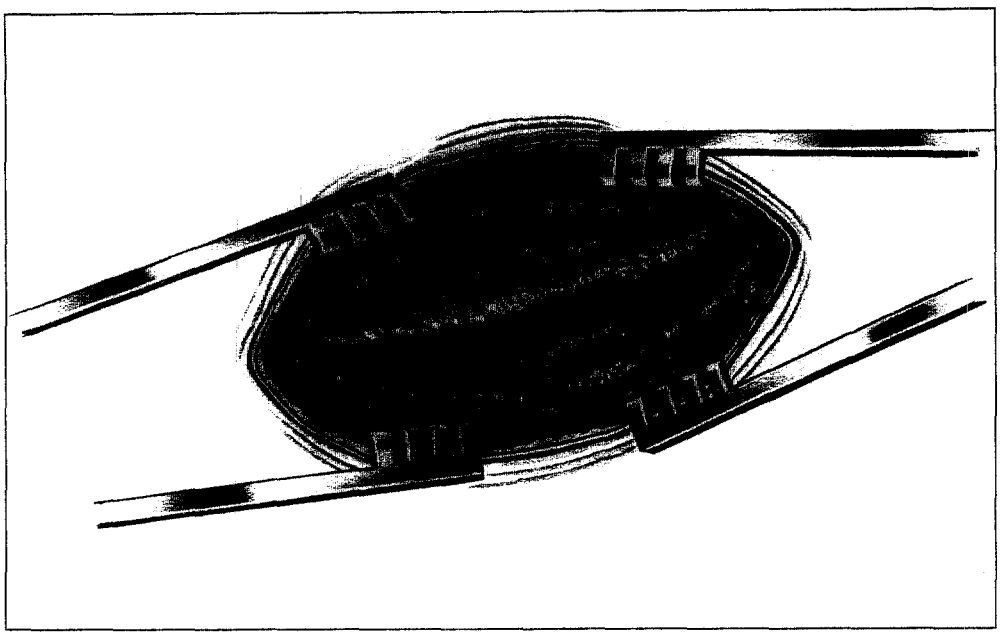


Figure 5: Expose the nerve

To expose the **ulnar nerve**, enlarge the window from where the graft was removed by incising the fascia proximally and distally to expose the ulnar nerve (Figure 5).

> ⚠ **WARNING**
>
> The antebrachial cutaneous nerve also runs in this general area. Exercise care and verify that you have correctly identified the ulnar nerve, which is larger than the antebrachial nerve.

To expose the **median nerve,** make the incision somewhat more anterior and slightly proximal to the ulnar nerve (See Figure 2 on page 9). The primary difference in this dissection is that the median nerve lies with the brachial artery and vein. Otherwise, the procedure is essentially the same.

> ⚠ **WARNING**
>
> The brachial artery and vein must be protected and retracted when the median nerve is dissected out because the median nerve lies within their proximity.

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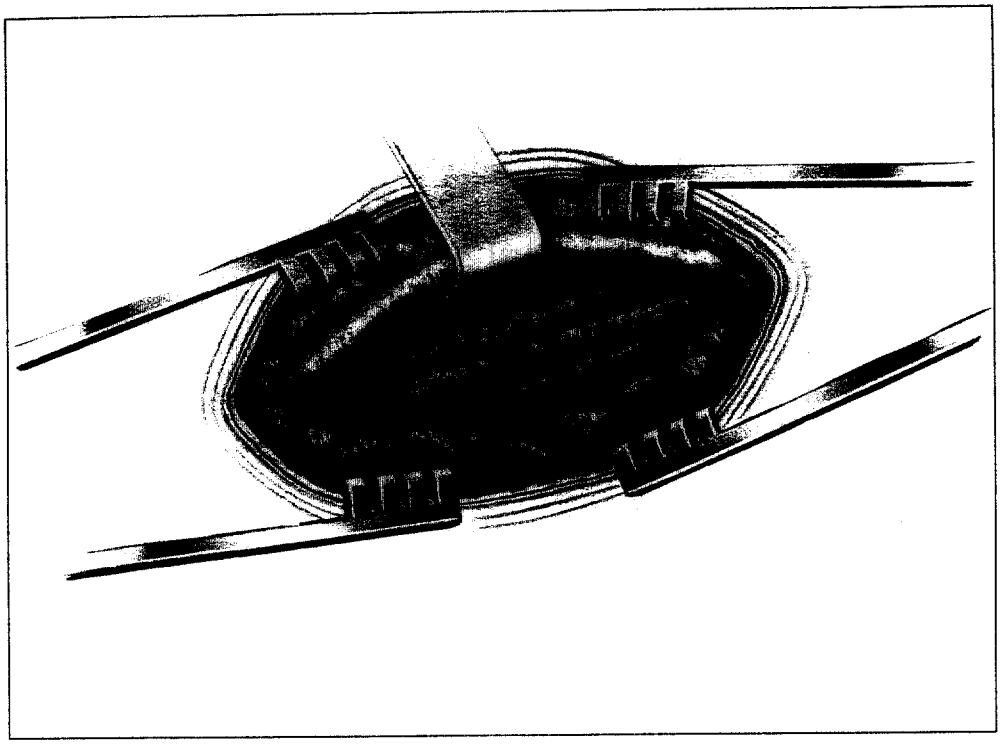


Figure 6: Carefully retract the nerve

After the nerve has been dissected free and has been immobilized for a distance of approximately 5 or 6 cm, carefully retract the nerve so that the electrode paddle can be placed underneath it (Figure 6).

It is recommended that you use a 1/4 inch Penrose drain passed around the nerve to retract it. This makes it easy to handle the nerve, and helps to reduce any potential to damage it.

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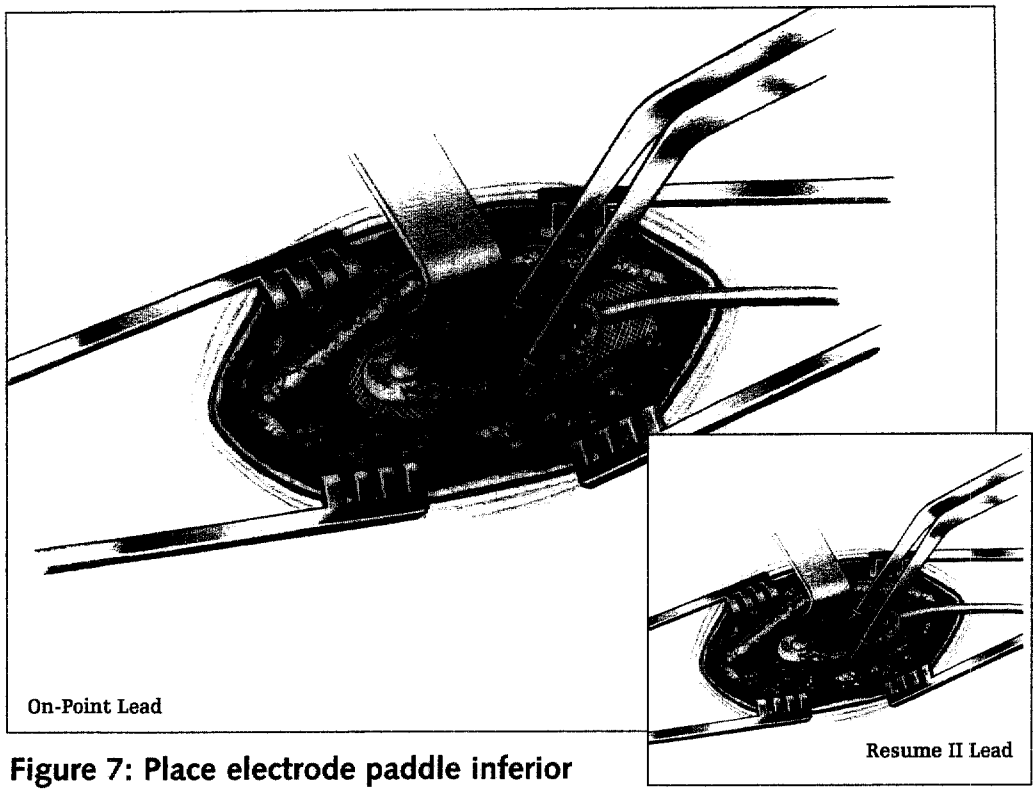


Figure 7: Place electrode paddle inferior to nerve

Place the electrode paddle inferior to the nerve in the enlarged window of the incision where the graft was taken (Figure 7). Some physicians also place the electrode paddle superior to the nerve with the soft tissue barrier in between the electrodes and the nerve.

NOTE: To test stimulate or to confirm proper lead position, an intraoperative stimulation test may be conducted before anchoring the electrode paddle. Refer to the applicable lead implant manual for intraoperative test stimulation instructions.

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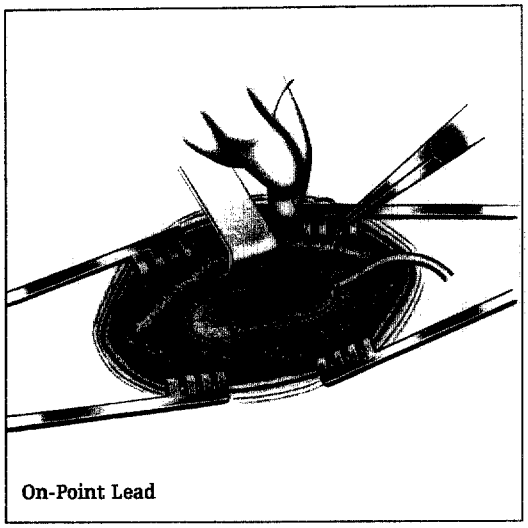


Figure 8: Suture electrode paddle in place (On-Point Lead)

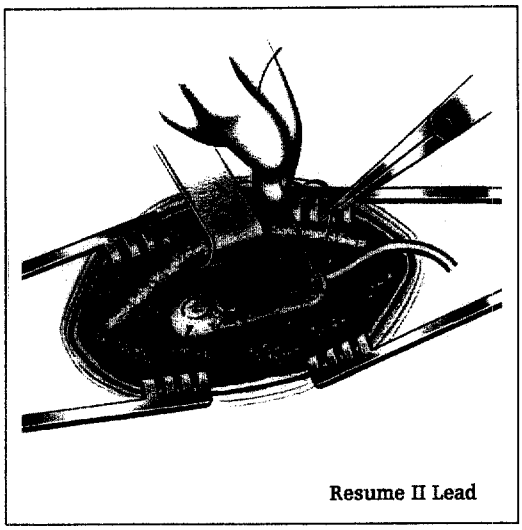


Figure 9: Suture electrode paddle in place (Resume II Lead)

ELECTRODE PADDLE ANCHORING

For the **On-Point Lead**, suture the mesh on the electrode paddle into the surrounding tissue with multiple small sutures of 5-0 nylon (or equivalent) on a very sharp, small needle. This will anchor the electrode paddle into place and help minimize its migration (Figure 8).

⚠ **CAUTION**

Suture on the periphery of the **On-Point Lead** supporting mesh or **Resume II** lead paddle supporting matrix, clear of the electrodes and their wires. For the **On-Point Lead**, do not place the sutures in the mesh above the paddle/lead junction.

⚠ **CAUTION**

Use care to ensure that the lead body does not rub against the nerve as it progresses toward the extension.

For the **Resume II Lead**, suture the electrode paddle to the surrounding tissue. Use multiple small sutures of 5-0 nylon (or equivalent) on a very sharp, small needle (Figure 9).

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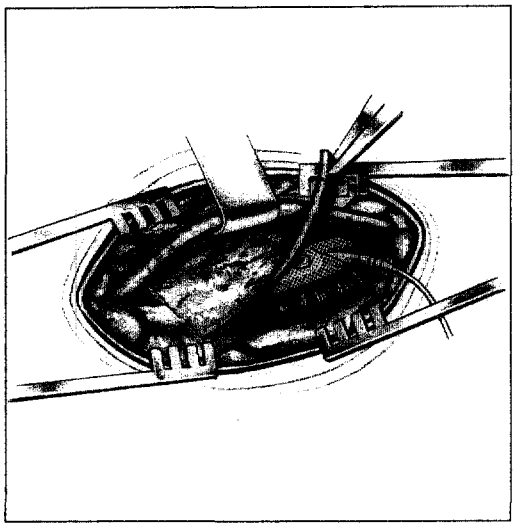


Figure 10: Secure lead body with anchor

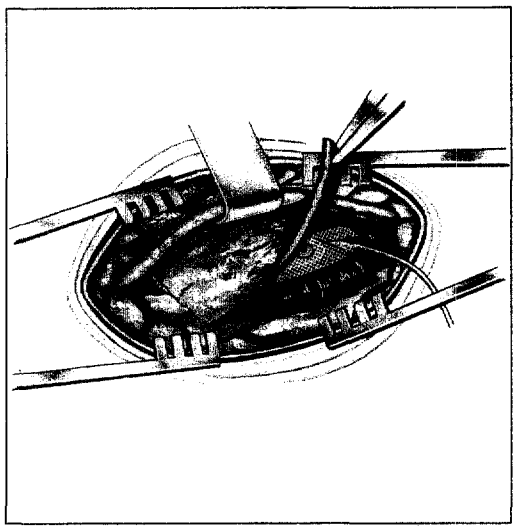


Figure 11: Secure lead body with mesh

LEAD BODY ANCHORING

Before proceeding with the implantation, the lead body should also be anchored (Figures 10 and 11). Proper anchoring of the lead body helps to minimize its movement after surgery. A two-wing anchor is packaged with the **On-Point** and the **Resume II** leads. When using the **On-Point Lead**, an alternate anchoring method using the lead mesh may be chosen. Both techniques are described in this section.

NOTE: The **Resume II** Lead kit also has a three-winged anchor and a twist-lock anchor. Refer to the lead technical manual for instructions on the use of these anchors. Some adaptation of the instructions given in the technical manual is required.

For the **On-Point Lead**, lubricate the anchor with sterile saline or an antibiotic solution to make it easier to slide it onto the lead. Carefully place the anchor onto the lead body. Position the anchor so that the lead body orientation is away from the nerve. Suture the anchor to the lead body with 2-0 silk, non-absorbable (or equivalent) suture. An assistant should hold the anchor steady by clasping the anchor wings as you tie sutures around the lead in the three anchor grooves.

⚠ **CAUTION**

Do not use polypropylene sutures because they can damage the anchor.

Route the lead body away from the nerve's path. Suture the anchor to the underlying tissue with 2-0 silk non-absorbable (or equivalent) sutures (Figure 10).

When using the **On-Point Lead**, you can also create a lead body anchor by carefully cutting the mesh in line with the lead body.

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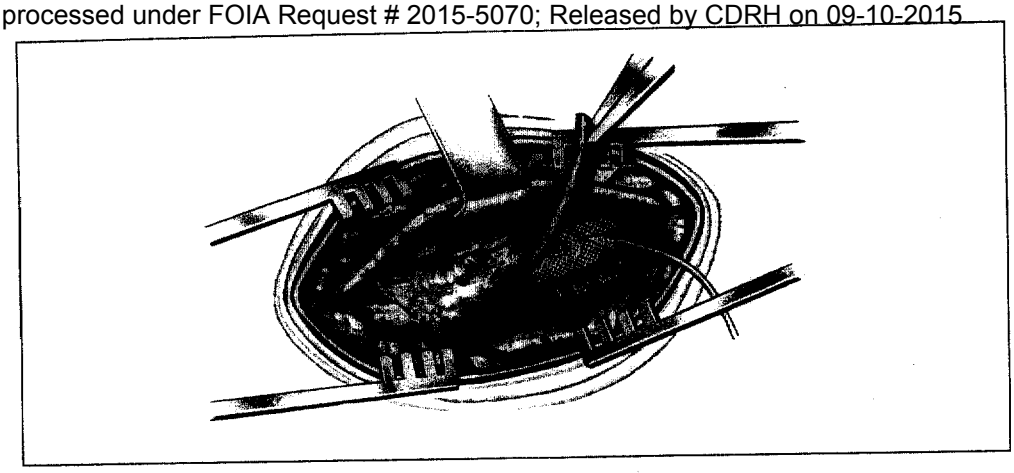


Figure 12: Fascial flap option lead positioning

Exercise care to avoid cutting into the lead body or electrode paddle. Fold the mesh over and secure it to the lead body away from the nerve using 2-0 silk, non-absorbable (or equivalent) suture. Suture the mesh to the underlying tissue (Figure 11).

⚠ **CAUTION**

Use care not to cut the lead body or electrode paddle.

For the **Resume II Lead**, lubricate the anchor with sterile saline or an antibiotic solution to make it easier to slide it onto the lead. Carefully place the anchor onto the lead body. Position the anchor so that the lead body orientation is away from the nerve. Suture the anchor to the lead body with 2-0 silk, non-absorbable (or equivalent) suture. An assistant should hold the anchor steady by clasping the anchor wings as you tie sutures around the lead in the two anchor grooves.

⚠ **CAUTION**

Do not use polypropylene sutures because they can damage the anchor.

Route the lead body away from the nerve's path. Suture the anchor to the underlying tissue within 2-0 silk, non-absorbable (or equivalent).

If using a soft-tissue flap instead of a graft, place the lead inferior to the isolated section of the targeted nerve with the nerve centered lengthwise over the lead electrodes. Anchor the lead to the underlying tissue in place and pull the flap of fascial tissue between the lead and nerve to create a protective layer (Figure 12).

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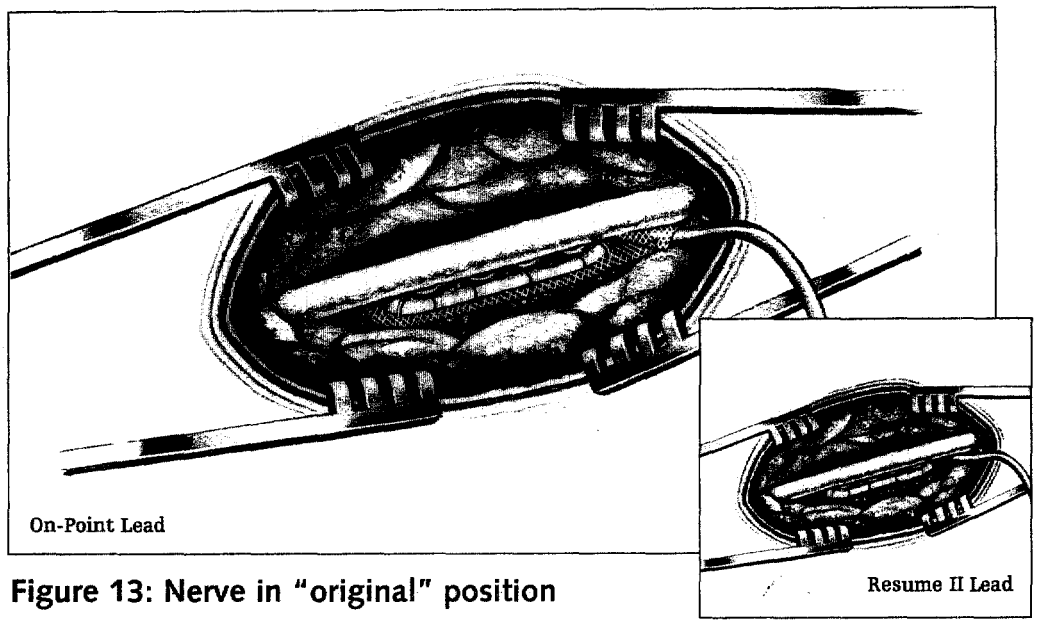


Figure 13: Nerve in "original" position

Allow the exposed nerve to return to its original position. This should center the nerve over the top of the four electrodes on the electrode paddle (Figure 13). Once the paddle has been attached and the nerve has returned, allow the soft tissues to fall over it. Inspect the paddle-nerve interface to ensure that good apposition is maintained. The surrounding soft tissues hold the position of both the electrode paddle and the nerve. Flex and extend the patient's elbow several times to ensure that no undue stretch on the electrode paddle occurs.

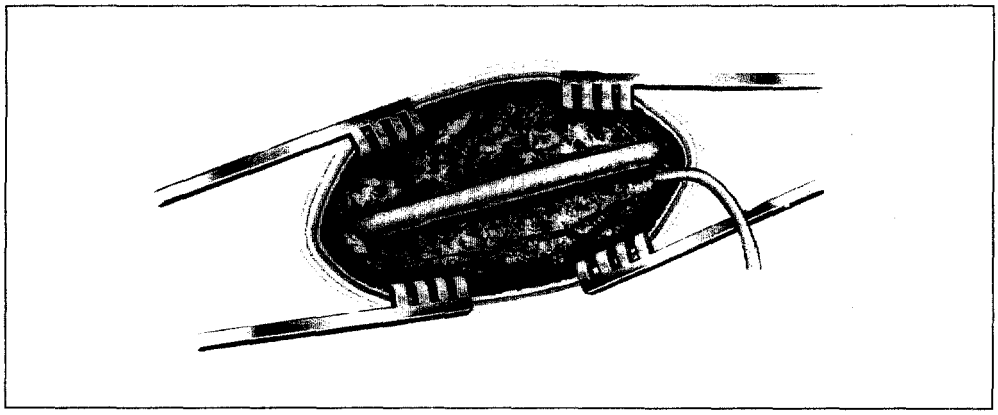


Figure 14: Nerve in "original" position (optional flap technique)

Fascial Flap

If a flap is used, allow the nerve to return to its original position as shown in Figure 14 and suture the flap to the adjacent fascia.

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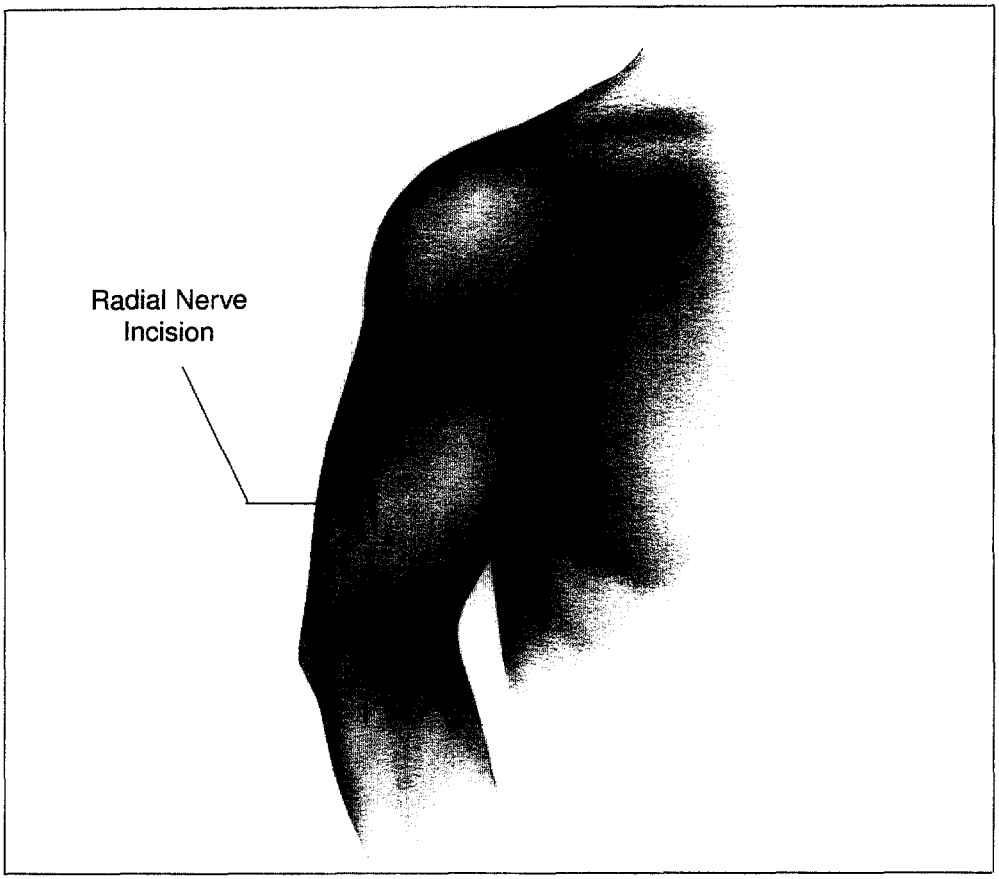


Figure 15: Radial nerve incision

RADIAL NERVE

The implant procedure for **radial nerve** poses some surgical challenges that differ from that for the ulnar and median nerves. This is primarily because of the radial nerve's location and its relative inaccessibility as it passes through the muscle. The primary challenge stems from the need to select a relatively short portion of the nerve for implantation of the electrode paddle. It is necessary to develop this interval between the emergence of the radial nerve from the musculospiral groove in the posterior aspect of the mid-portion of the humerus proximally, and its entrance into the proximal forearm distally (Figure 15).

Remember that the nerve divides soon after its entrance into the forearm. Therefore, particularly in short patients, the length of the segment that is suitable for implantation of the electrode paddle is a relatively short distance. As previously mentioned, the dissection of the radial nerve is somewhat more difficult because the nerve passes through muscle tissue. Because the entire arm and the shoulder are draped out, as described previously for the ulnar and median nerves, the use of a tourniquet is quite difficult and considerable bleeding may occur. It may be possible, however, to use a small Esmarch tourniquet that constricts the arm near the axilla to allow hemostasis for better visualization during the dissection of the nerve.

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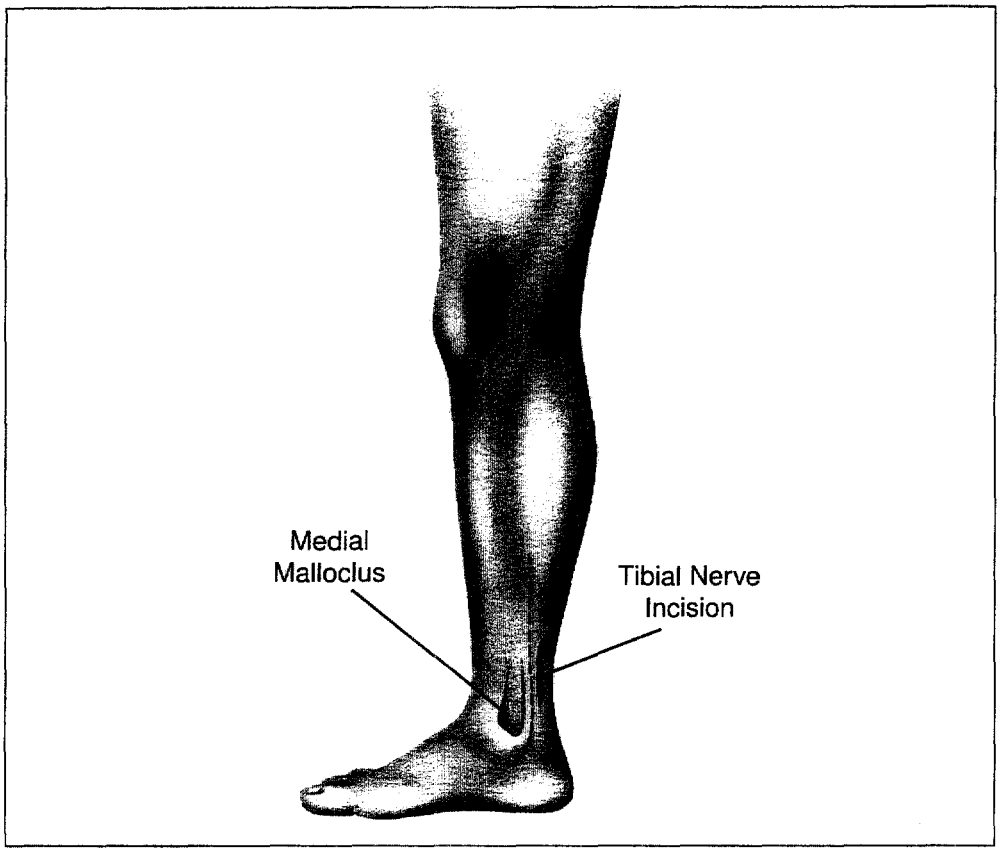


Figure 16: Tibial nerve incision

TIBIAL NERVE

The **tibial nerve** lies closely associated with the posterior tibial artery and vein. The main trunk of the nerve is easily visualized. However, sometimes a small branch of the nerve exits from the main body of the nerve somewhat proximal. If such a branch exists, it is important to dissect it out and include it with the main trunk of the nerve. Failure to stimulate this small nerve will sometimes cause failure to cover all of the pain in the heel.

Make the point of incision for the tibial nerve on the medial side of the ankle from a point approximately 5 cm proximal to the medial malleolus. It should lie directly posterior to the posterior surface of the tibia (Figure 16).

Extend the incision in this location down through the fatty tissue to the fascia where you can harvest the free fascial graft. Then, open the fascia and approach the nerve.

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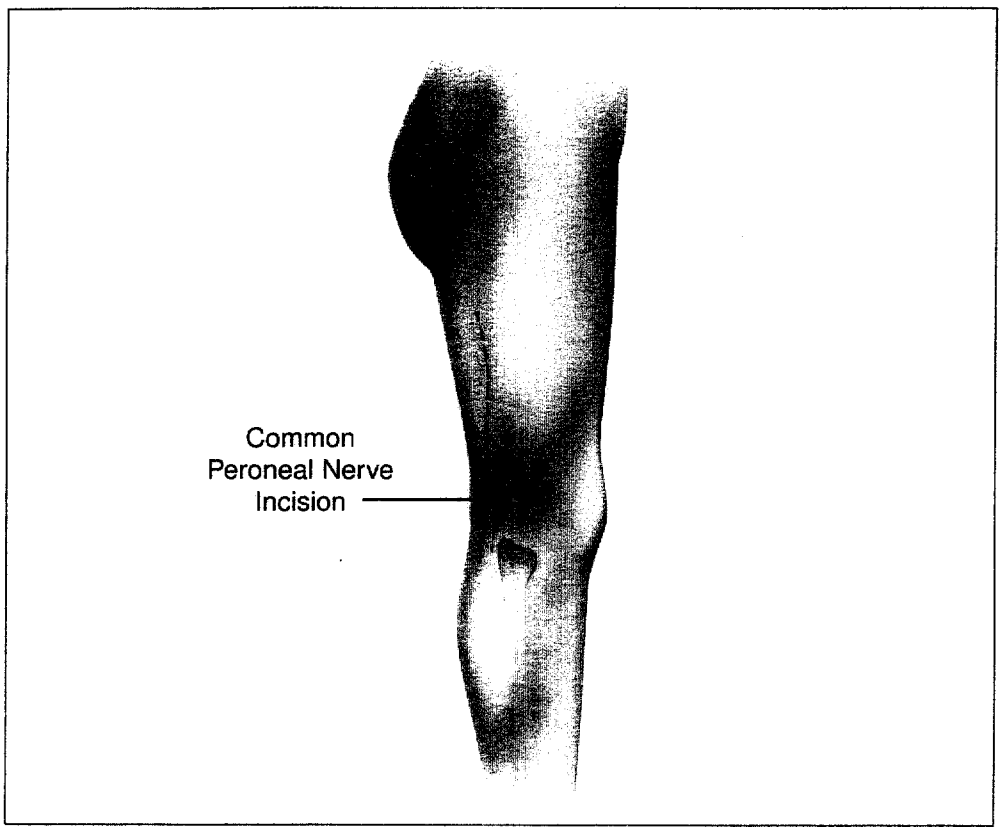


Figure 17: Common peroneal nerve incision

COMMON PERONEAL NERVE

It is recommended you conduct the common **peroneal nerve** exploration with the patient tilted on the appropriate support so the leg is just less than lateral. The angle will make the exposure much easier. The procedure is also much easier if done under tourniquet control. This is possible only if the tourniquet can be placed high up in the groin so that a majority of the thigh can be prepped and draped.

Make the incision at a point opposite the head of the fibula. Extend the incision up for a distance of 10-12 cm, just anterior to the tendon of the biceps femoris (Figure 17). Dissect and identify the nerve.

Trace the nerve down to the point where it curves around the neck of the fibula. It is not necessary to free up the nerve beyond approximately 4 cm proximal to the beginning of the curve. A small accessory nerve branch may also be found in this region.

Isolate the accessory nerve and pull it over the major nerve so that both will be included in the area of stimulation.

Create a free fascial graft from the region of the iliotibial band. Skive the band to remove approximately one-half of the thickness.

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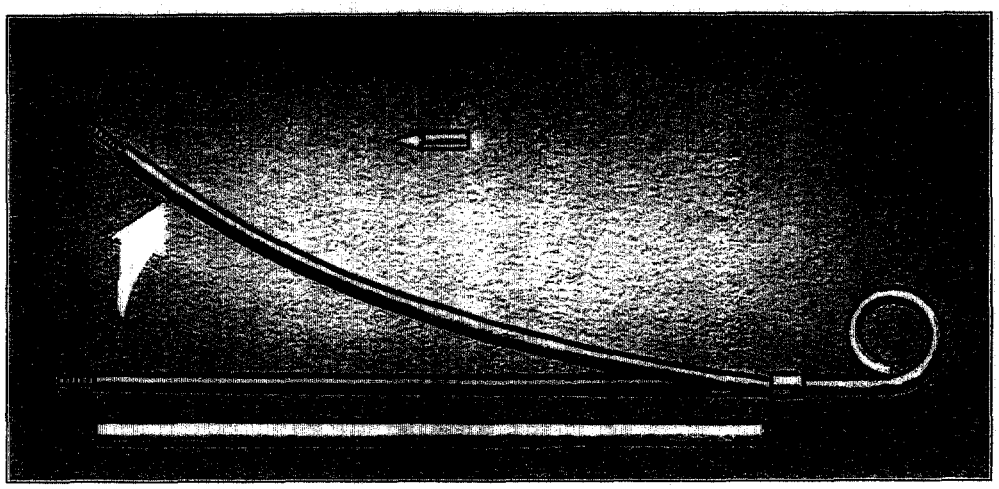


Figure 18: Assemble tunneling tool and gently curve as needed

TUNNEL PERCUTANEOUS EXTENSION

There are two options typically considered at this point in the procedure. The neurostimulator can be internalized immediately, or the percutaneous testing wires of the lead can be externalized for the trial screening period of three to five days. The latter method is recommended, because it allows you to further evaluate the patient's response to stimulation prior to implantation of the neurostimulator.

Once you achieve appropriate positioning of the lead, you can externalize the percutaneous testing wires for test stimulation. Place the passing straw, packaged in the lead kit, over the shaft of the tunneling tool. Then, screw the metal tip onto the tool (Figure 18). The shaft of the tunneling tool is malleable and may be gently curved to fit the contours of the patient's anatomy.

Tunneling the percutaneous extension is performed in two steps. First, tunnel from the electrode paddle site to the lead/extension connector site. Second, tunnel from the lead/extension connector site to the percutaneous wire exit site. The following describes the first step of tunneling to the lead/extension connector site. The second step is procedurally identical.

NOTE: The **On-Point Lead** has an attached percutaneous extension. The **Resume II Lead** has a separate percutaneous extension that you must attach.

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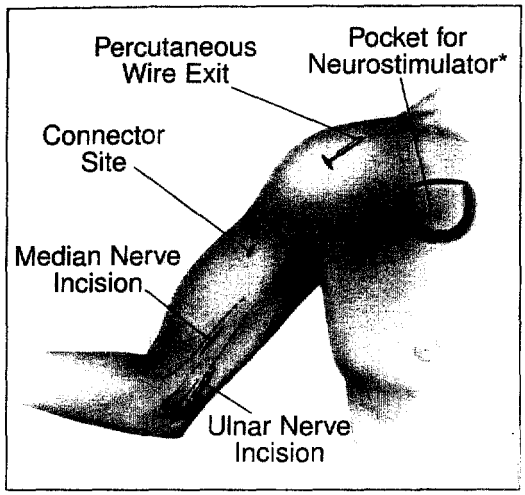


Figure 19a: Ulnar or Median nerve tunneling

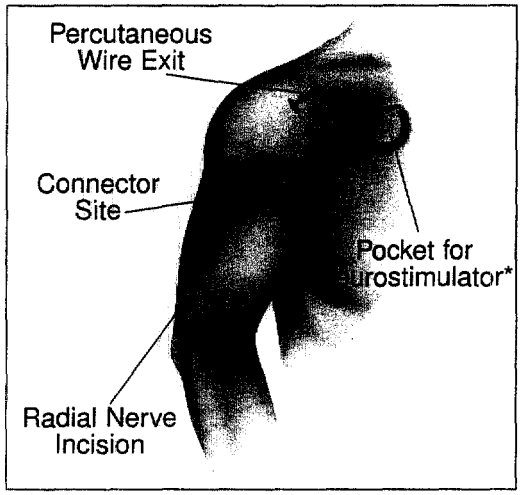


Figure 19b: Radial nerve tunneling

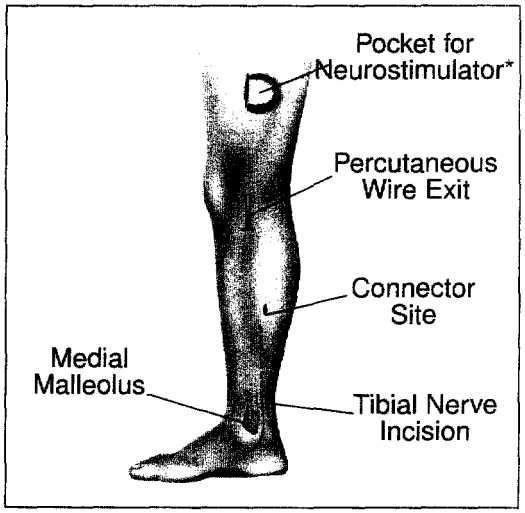


Figure 19c: Tibial nerve tunneling

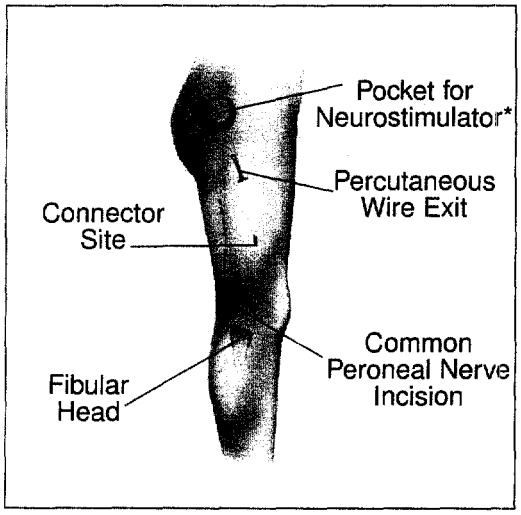


Figure 19d: Common peroneal nerve tunneling

*Shown for later reference.

Make a 0.5-1.0 cm lead/extension connector site incision about 6 cm from the original lead paddle incision. If desired, you may, in advance of implantation, lay the lead out on the patient to estimate where the connector site will be. The incision should be made in the same plane and roughly parallel to the original lead paddle incision (Figures 19a, 19b, 19c, and 19d). Take care not to move the electrode paddle during any of the tunneling procedures.

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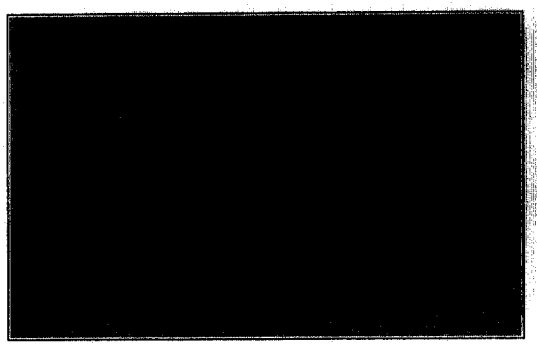


Figure 20a: Install boot and connect lead to extension

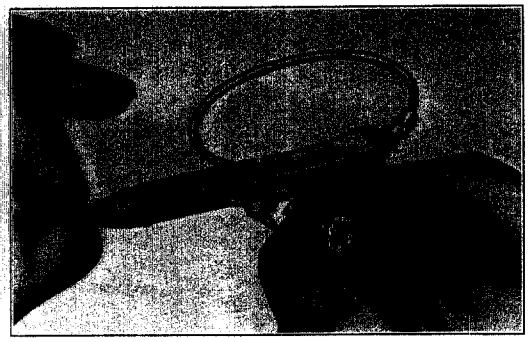


Figure 20b: Tighten setscrews



Figure 20c: Suture wide end of boot

If using the **Resume II Lead**, complete the following procedure before tunneling.

For the **Resume II Lead**, you must connect the percutaneous extension to the lead's in-line connector. Remove the silicone insulation boot from the lead kit and irrigate it with sterile saline or antibiotic solution. Then, slip it onto the connector end of the lead body with the open end facing out. Pass the boot down the lead body, exposing the four metal bands on the end of the lead (Figure 20a).

Slip the connector end of the lead into the percutaneous connector. Carefully align the lead's four metal bands under the four setscrews in the extension connector. Check that these metal bands are centered under the setscrews. Tighten all four setscrews using the hex wrench (Figure 20b). Exercise caution and do not overtighten the setscrews. Gently pull on the connection to ensure that it is secure.

⚠ **CAUTION**

Wipe off any body fluids from the lead contacts or connector before connecting.

⚠ **CAUTION**

Do not overtighten setscrews.

Push the silicone boot over the extension connector and tie one suture around the wide end of the boot for stabilization (Figure 20c). Sterile water may be used to lubricate the boot. As noted earlier, a separate boot is not used with the **On-Point Lead** during testing because it has a pre-attached percutaneous extension.

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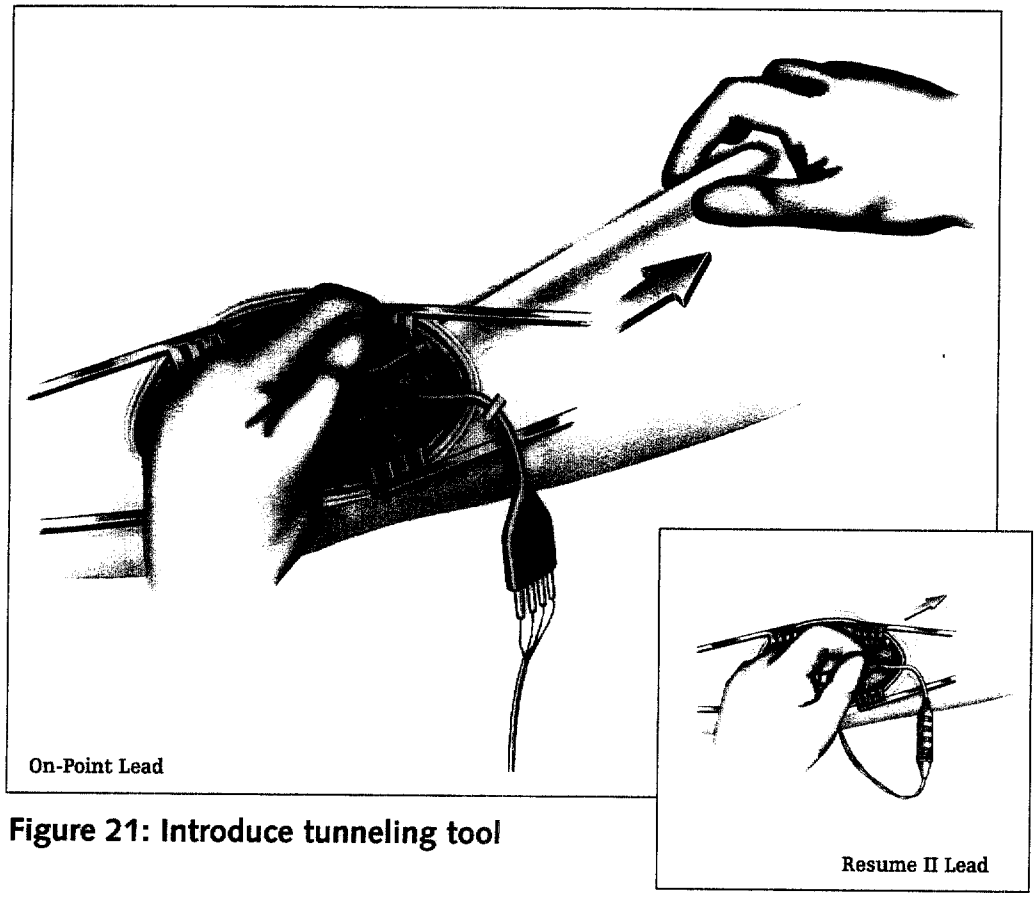


Figure 21: Introduce tunneling tool

Introduce the tunneling tool, with the passing straw in place, into the electrode paddle implant site. The shaft of the tool is malleable and may be gently curved to fit the contours of the patient's body. Advance the tool subcutaneously. Push the skin over the advancing tip (Figure 21) to help control direction. Continue until the tip exits the lead/extension connector site. The tip of the tunneling tool should come far enough out of the connector site exit incision so that the passing straw on the shaft of the tool is clearly exposed.

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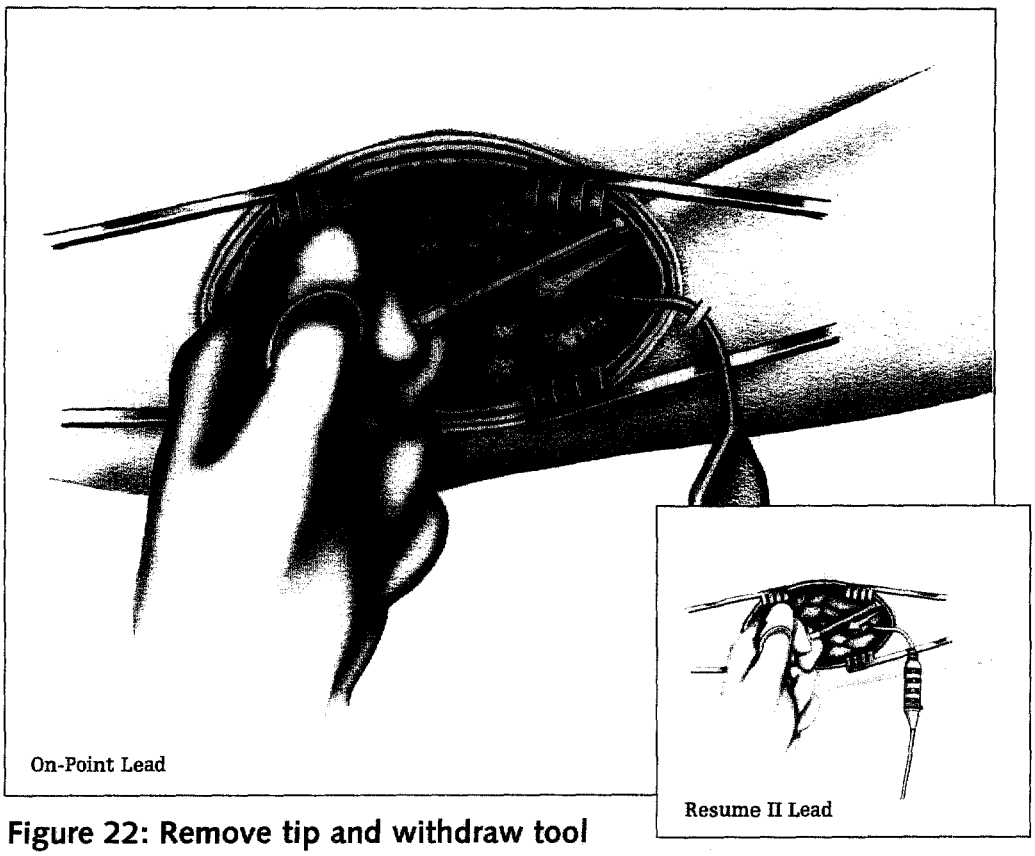


Figure 22: Remove tip and withdraw tool

Remove the metal tip from the tunneling tool. Next, remove the tunneling tool by pulling it out of the passing straw at the electrode paddle site. Temporarily, leave the passing straw in place (Figure 22); you will remove it after the next step.

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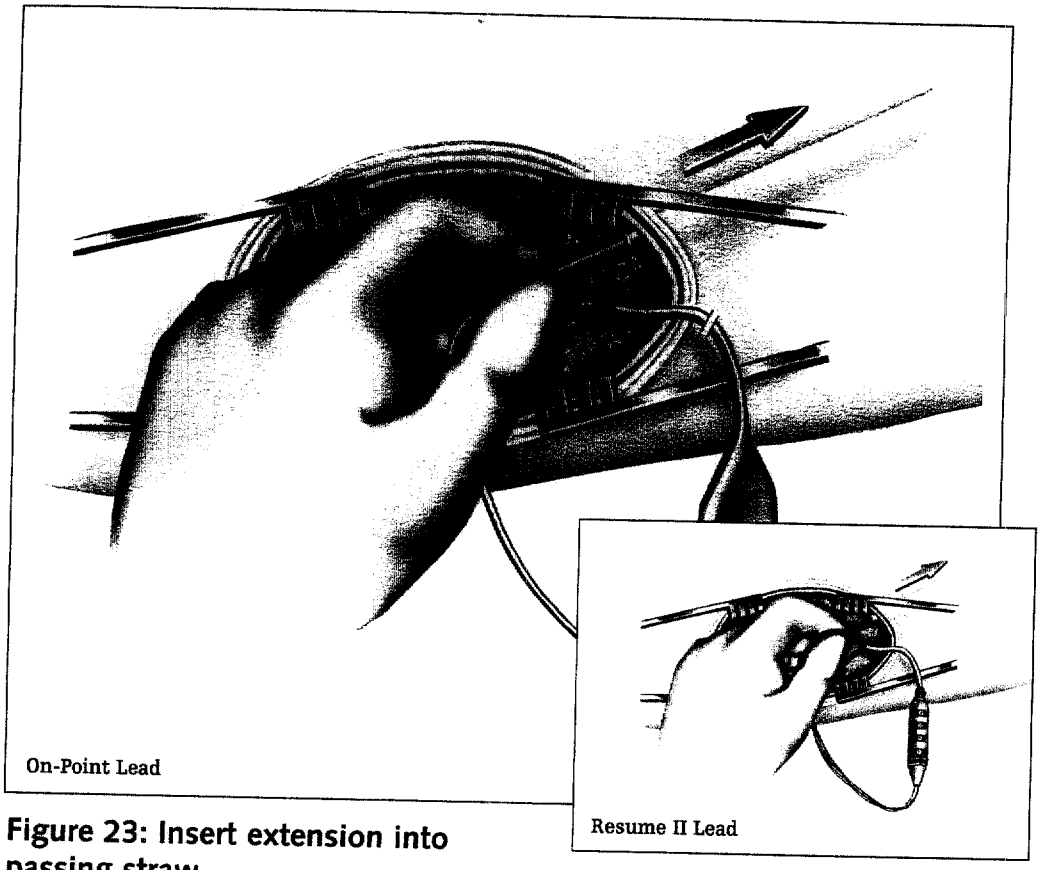


Figure 23: Insert extension into passing straw

For the **On-Point Lead** with it's pre-attached extension, insert the percutaneous extension into the passing straw. Feed it through the straw (Figure 23) and out the connector site incision.

If you are using the **Resume II Lead**, its separate percutaneous extension must be attached as previously described. Insert its percutaneous extension into the passing straw (Figure 23 inset) and out the connector site incision.

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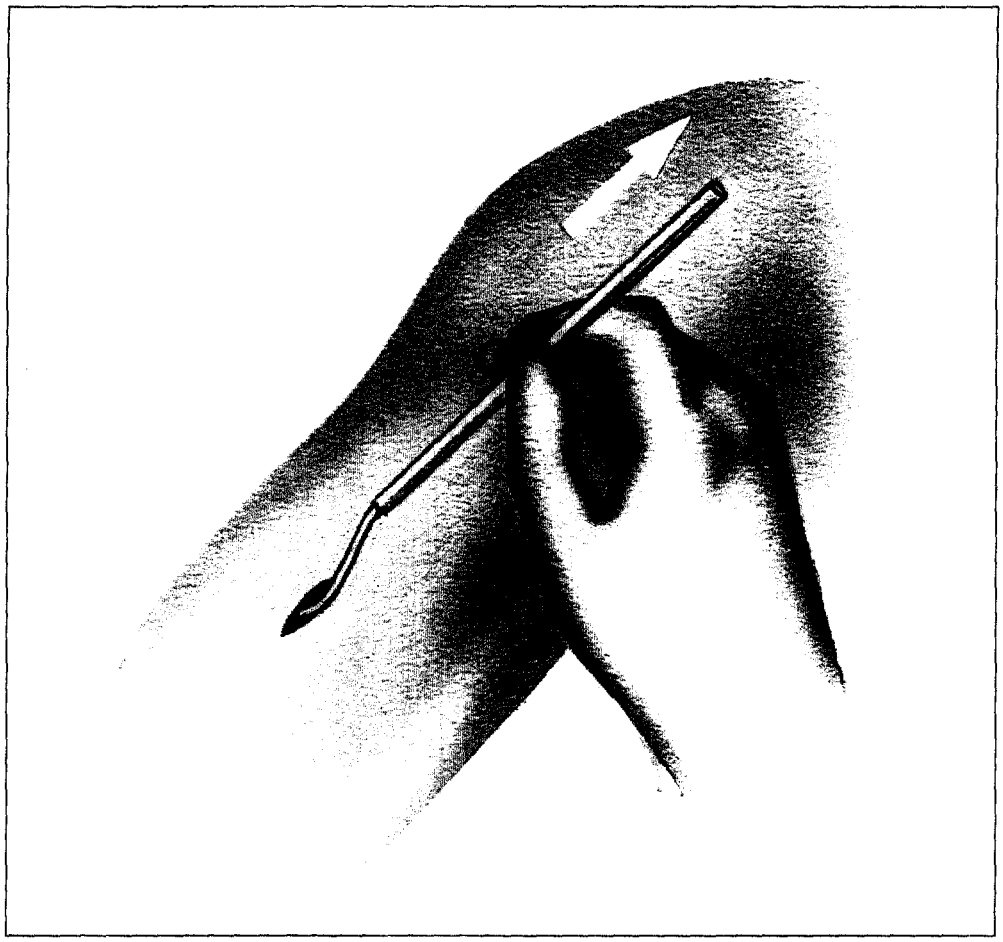


Figure 24: Remove the passing straw

Remove the passing straw by pulling it out of the connector site incision, leaving the percutaneous extension in place (Figure 24). Make a small stab wound at the final percutaneous wire exit site. Repeat the tunneling process from the lead/extension connector site to the percutaneous wire exit site wound.

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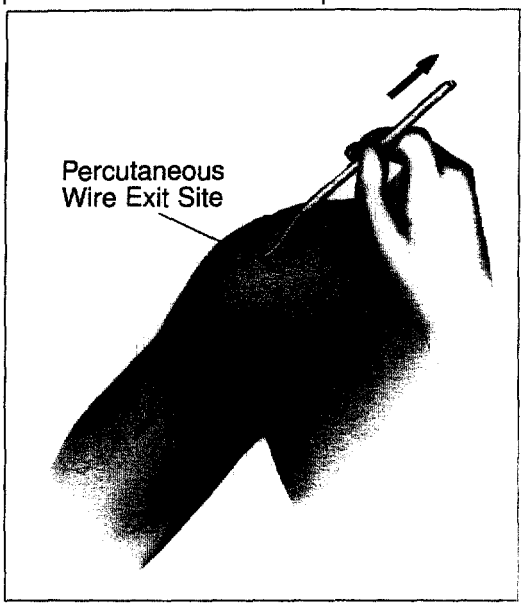


Figure 25a: Remove passing straw

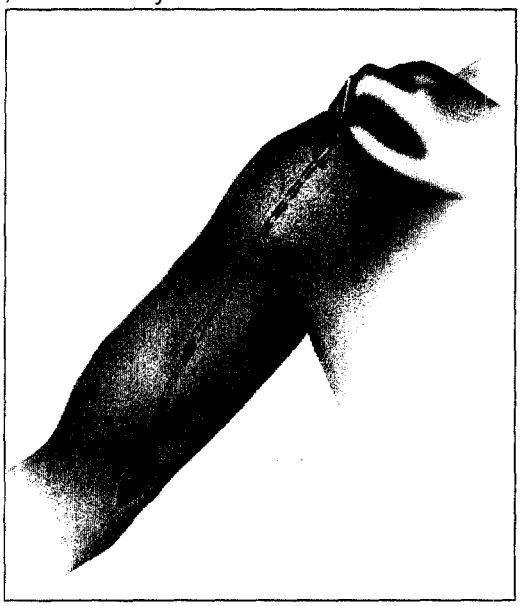


Figure 25b: Gently pull extension

Feed the percutaneous extension through the passing straw and out the exit wound. Remove the passing straw (Figure 25a). Gently pull the percutaneous extension pin connector to ensure access to the percutaneous extension pin connector (Figure 25b).

NOTE: For the flat connector used on the **On-Point Lead**, it may be necessary to use blunt dissection to allow it an adequate path.

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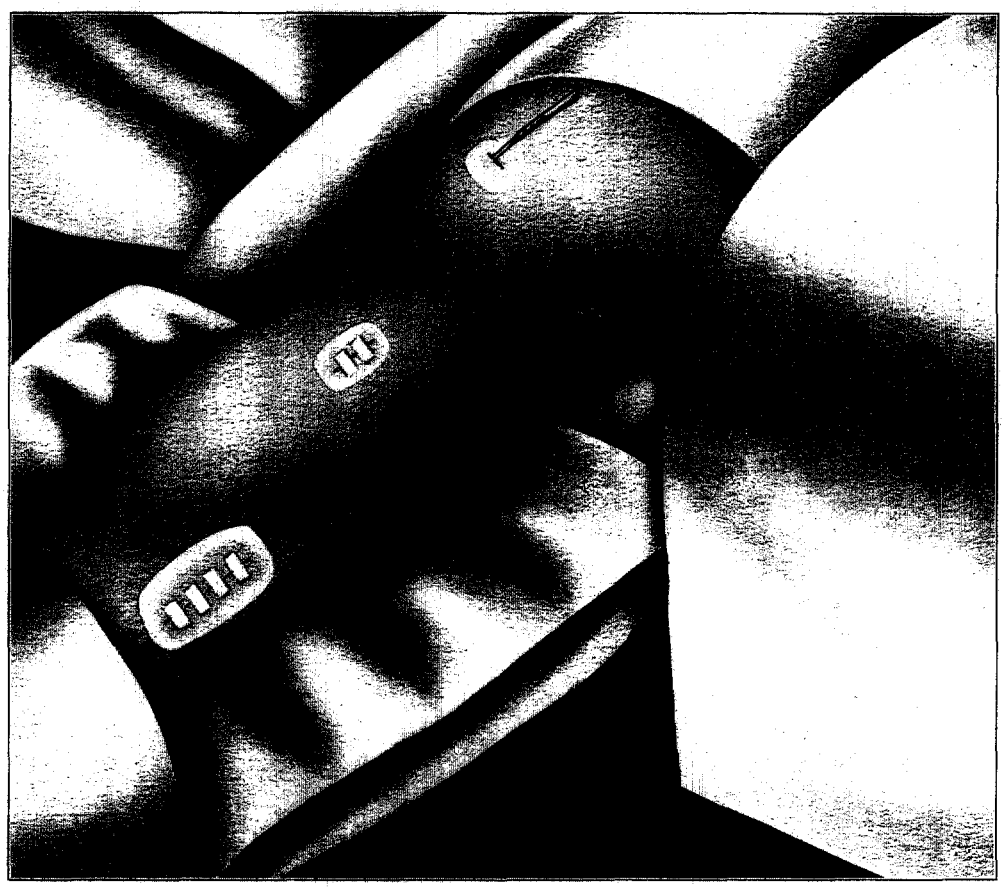


Figure 26: Close and dress wounds

Close the incisions per normal techniques with subcutaneous and subcuticular sutures and skin tapes. Cover the wounds with thin, sterile, bio-occlusive dressings (Figure 26). This will allow the wound to be inspected visually postoperatively. The percutaneous wires, which emerge from the small stab wound in the anterior shoulder (shown here), should likewise be covered with a sterile, bio-occlusive dressing (Figure 26) to help keep the first 2-3 cm of the extension sterile.

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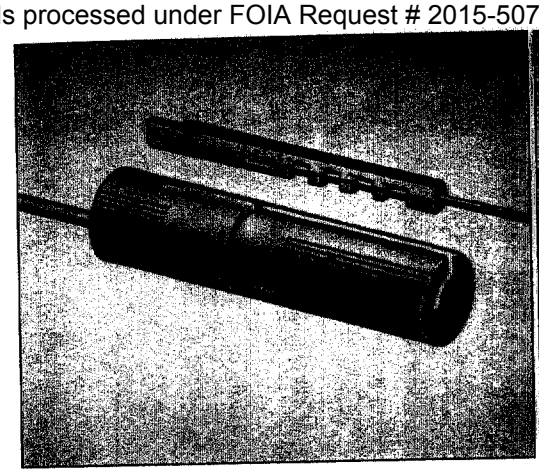


Figure 27a: Position pin connector and twist-lock connector

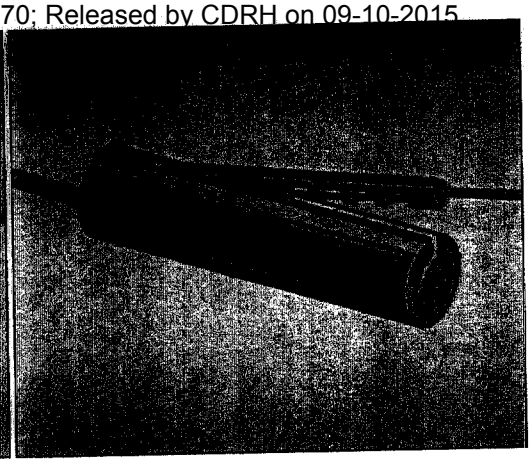


Figure 27b: Secure pin connector's end in groove

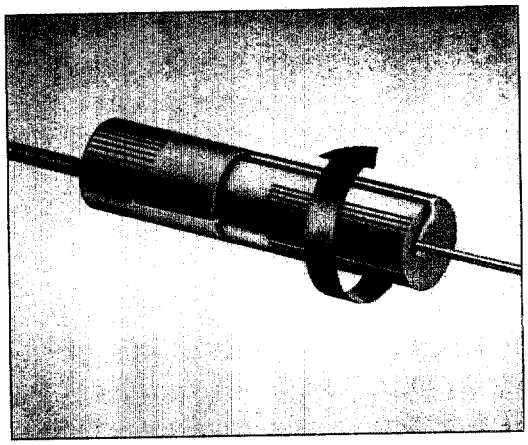


Figure 27c: Lock the twist-lock connector

TRIAL SCREENING

Once the patient has returned to his/her room, the trial screening period can begin by connecting the screening cable to the percutaneous extension. The screening cable, which is packaged with the lead kit, has a cylindrical twist-lock connector into which the lead's percutaneous extension pin connector fits (Figure 27a).

Join the two connectors by inserting the pin connector into the groove of the twist-lock connector at a slight angle (Figure 27b). Check that pin connector is completely inserted and level in the twist connector before closing it.

Once the connector is fully seated, lock it in place by turning the twist connector clockwise (Figure 27c).

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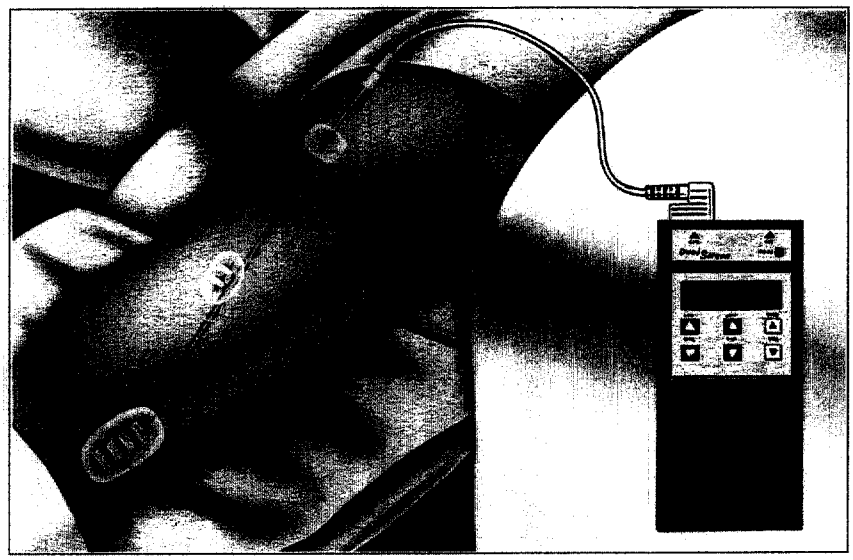


Figure 28: Screener connected to lead

Set the screener settings in the physician mode in accordance with the Model 3628 Screener technical manual. For a single-lead system, use Channel 1 in SingleStim™ mode with Channel 2 OFF. For a dual-lead system, use the DualStim™ mode after making adjustments for the first lead. Explain the screener use to the patient in accordance with the screener technical manual. Check that the Model 3628 Screener is OFF. Then, connect the screening cable to the screener (Figure 28).

NOTE: Trial screening can be conducted for three to five days with the goal of finding optimal stimulation and paresthesia coverage to determine whether satisfactory pain relief can be achieved.

When the trial screening period is complete, discuss the results with the patient and decide whether to proceed with the permanent system.

If the trial screening period results in a decision to proceed, schedule surgery to internalize the PNS system. Common criteria for proceeding are:

- The patient has received at least 50% pain relief,
- The patient demonstrates a strong desire to proceed.

⚠ WARNINGS

To help prevent possible uncomfortable patient stimulation:

- Turn the screener OFF before connecting or disconnecting the screening cable(s).
- Do not operate the screener with the CH 1 or CH 2 contacts exposed.
- Set the amplitude, pulse width, and rate to match the patient's stimulation tolerance level.
- Set the amplitude to zero before changing the electrode polarity.

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Appendix 18
Electrode Comparison Chart

Company	**Vertis Neuroscience Seattle, WA**	**TECA Corporation Pleasantville, NY**	**Medtronic, Inc Minneapolis, MN**	**Medtronic, Inc Minneapolis, MN**
Product	**Vertis PNT Kit**	**TECA Disposable Monopolar Needles**	**DMN™ Disposable Monopolar Needle Electrodes**	**Resume II Lead/Electrode**
Model/Catalog No(s)	SG XXX (used with PNT Control Unit)	902-DMFxx-TP and 902-DMGxx-TP series (xx = needle length)	DMFxx and DMNxx series (xx = needle length)	Model 3587a (used with Mattrix Neurostimulation System)
510(k) Reference	NA – this submission	K973442	K950314	K915540
Indications for Use	Intended to electrically stimulate peripheral nerves.	Intended to electrically stimulate peripheral nerves or record electrical signals (in electromyography).	Intended to electrically stimulate peripheral nerves or record electrical signals (in electromyography).	Indicated for spinal cord stimulation and for peripheral nerve stimulation. Indicated for treatment of chronic, intractable pain of the trunk or limbs.
Intended User	clinician use	clinician use	clinician use	clinician use
Specifications				
electrode material	stainless steel	stainless steel	stainless steel	platinum/iridium
electrode [invasive] length	5 – 30mm (0.5 - 3.0cm)	25 – 75mm (2.5 – 7.5cm)	25 – 75mm (2.5 - 7.5cm)	30, 60cm (electrode + lead) 2.4cm (electrode array)
electrode diameter	0.25mm	0.36 – 0.46mm	0.33mm – 0.40mm	1.37mm
electrode - sharps protected	protected	unprotected	unprotected	unprotected
How Used				
implanted	no	no	no	yes
introduction method	percutaneous	percutaneous	percutaneous	percutaneous
insertion depth	up to 30mm (3cm)	up to 75mm (7.5cm)	up to 75mm (7.5cm)	up to 60cm (to peripheral nerves or spinal cord)
insertion/treatment duration	30 - 45 minutes	45-60 minutes	45-60 minutes	days/years – temporary or permanent implant
tissue contact	skin/tissue	skin/tissue	skin/tissue	skin/tissue

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Company	**Vertis Neuroscience Seattle, WA**	**TECA Corporation Pleasantville, NY**	**Medtronics, Inc Minneapolis, MN**	**Medtronics, Inc Minneapolis, MN**
Product	**Vertis PNT Kit**	**TECA Disposable Monopolar Needles**	**DMN™ Disposable Monopolar Needle Electrodes**	**Resume II Lead**
How Provided				
sterile	yes	yes	yes	yes
reusable	no	no	no	no
packaging	blister tray/lid	blister pouch	blister pouch	blister tray/lid

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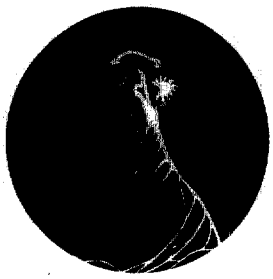
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APPENDIX 19

TECA CORPORATION

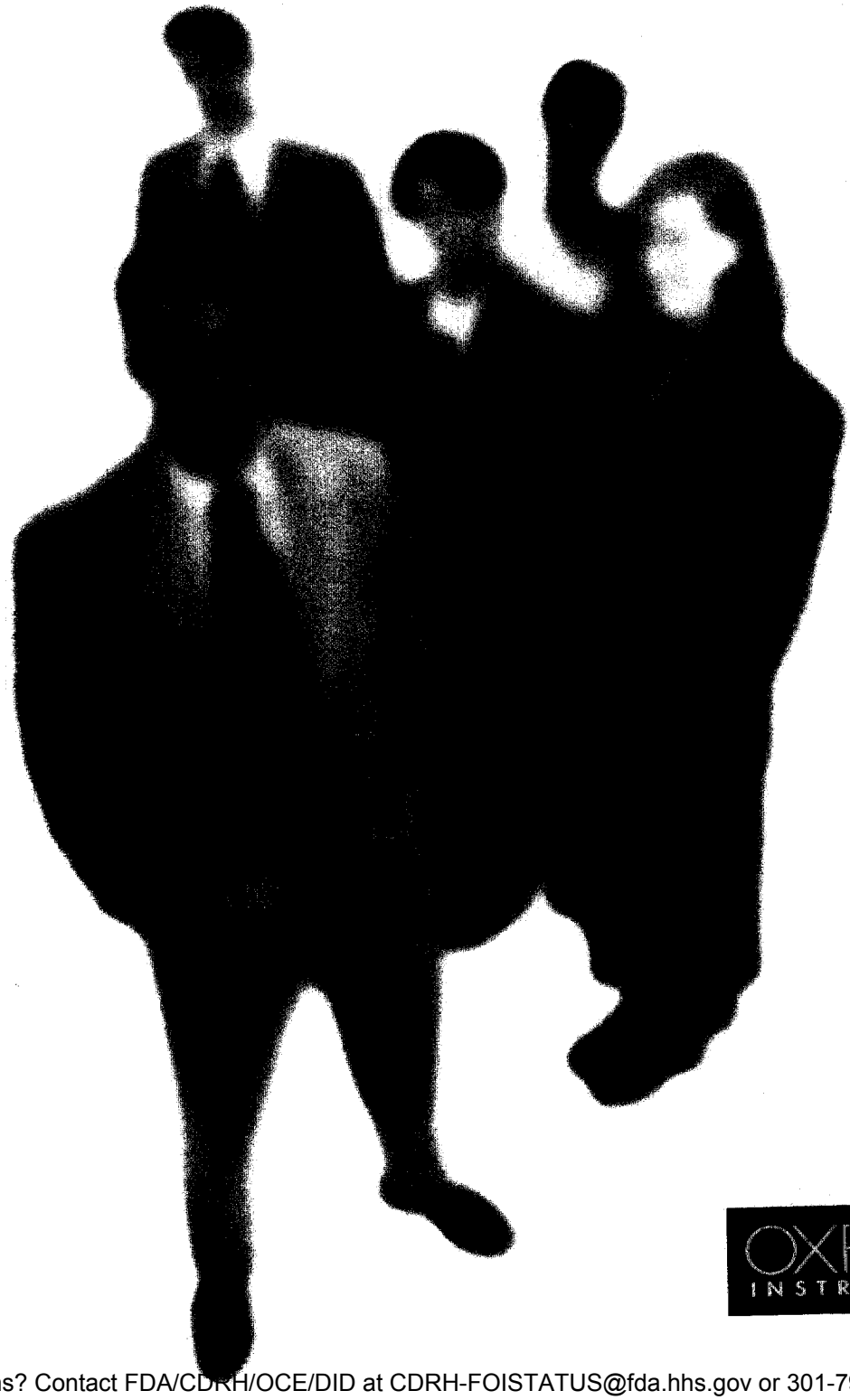
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OXFORD INSTRUMENTS

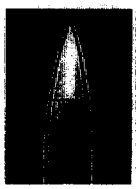
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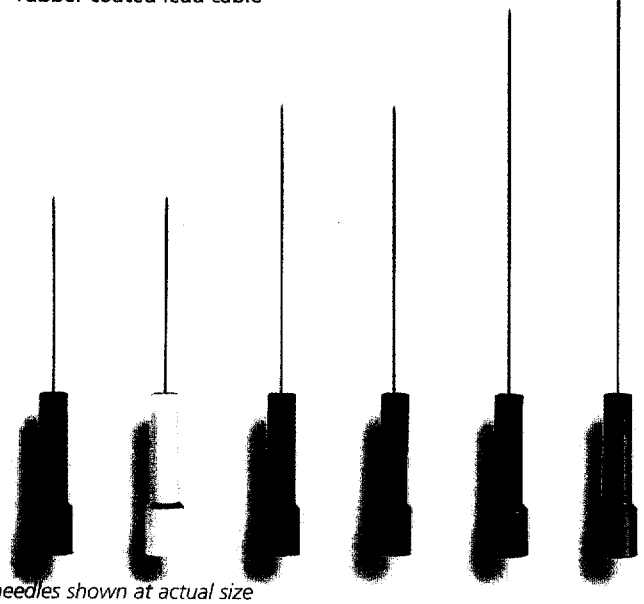
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TECA Disposable Monopolar Needles



The TECA Disposable Monopolar needles offer the following benefits:

- Stainless steel needle, ground to a consistently sharp point
- Coated with a low friction insulator for ease of insertion
- Color coded by needle size for easy identification
- Consistently low impedance levels for accurate recordings
- Plug into a reusable, ultra-flexible rubber coated lead cable



needles shown at actual size

Length	Needle diameter (mm)	Hub color	Recording area (mm²)	Catalog Number	Price
1"(25mm)	0.36 (28G)	Red	0.28	**902-DMF25-TP**	**$166.00**
1"(25mm)	0.46 (26G)	Yellow	0.34	**902-DMG25-TP**	**$166.00**
1.5"(37mm)	0.36 (28G)	Orange	0.28	**902-DMF37-TP**	**$166.00**
1.5"(37mm)	0.46 (26G)	Green	0.34	**902-DMG37-TP**	**$166.00**
2"(50mm)	0.46 (26G)	Blue	0.34	**902-DMG50-TP**	**$166.00**
3"(75mm)*	0.46 (26G)	Violet	0.34	**902-DMG75-TP**	**$97.00**

48 per box. *Note: Catalog # **902-DMG75-TP** in boxes of 24 electrodes.

For 2mm plug version, remove TP from end of catalog number

Product Information

Demountable disposable monopolar needle electrodes made of stainless steel, coated with an insulator. **FOR SINGLE USE ONLY.** Individually sealed, sterilized by gamma irradiation. Requires reusable lead cable Catalog # **902-RLC(-TP)**.

Reusable Lead Cable (Non-shielded)

To connect to the TECA Disposable Monopolar Needle [illegible] ultra-flexible insulated lead wire with moulded connec[illegible] Terminating in a touchproof plug to connect to most E[illegible] instruments. 6 per pack.

Touchproof Catalog # **902-RLC-TP** _____ **$26.00**
2mm Catalog # **902-RLC** _____ **$26.00**

Shielded Reusable Lead Cable for Disposable Monopolar Needle Electrodes

24" (61cm) shielded lead wire with integrally molded monopolar needle connector and 5 pin DIN connector. Compatible with most EMG instruments. 1 per package.



Catalog # **902-SLC** _____ **$26.00**

Monopolar Needle Sample Pack

Contains 12 Disposable Monopolar needle electrodes, three of each size shown below and one reusable lead cable. Best selection for evaluating the range of TECA Disposable Monopolar Needles.

Length	Needle diameter (mm)	Hub color	Recording area (mm²)
1"(25mm)	0.36 (28G)	Red	0.28
1.5"(37mm)	0.36 (28G)	Orange	0.28
1.5"(37mm)	0.46 (26G)	Green	0.34
2"(50mm)	0.46 (26G)	Blue	0.34

Touchproof Catalog # **902-INTROPAK-TP** _____ **$46.00**
2mm Catalog # **902-INTROPAK** _____ **$46.00**

Shuttle cable

Shielded connection cable, 24" (61cm) long, with 3 x 2mm or 3 x Touchproof sockets terminating in a 5 pin DIN plug.

Touchproof Catalog # **2002-TP** _____ **$24.00**
2mm Catalog # **2002** _____ **$24.00**

Extension Cable for Monopolar Needles

24" (61cm) lead terminating in 2mm or Touchproof plug and socket. Package of 6 (3 red, 3 black).

Touchproof Catalog # **902-EX-TP** _____ **$36.00**
2mm Catalog # **902-EX** _____ **$36.00**

When ordering, refer to Catalog # in bold print

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APPENDIX 19

MEDTRONIC, INC.
DMN ELECTRODES

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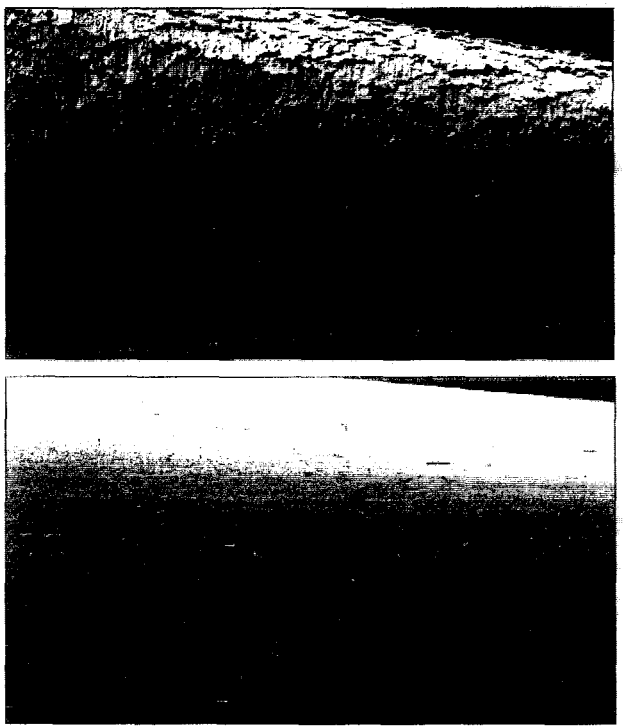
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(Unretouched, actual scanning electron microscope images)



Company Profile

Medtronic Functional Diagnostics, formerly Dantec/Synectics, is a world leader in electrodiagnostic instruments and accessories.

Medtronic
When Life Depends on Medical Technology

Medtronic Functional Diagnostics
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Shoreview, MN 55126-2978
USA
Telephone: (612) 514-1700
FAX: (612) 514-1710
Toll-free: (800) 227-3191
www.medtronic.com

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Medtronic

DMN™★

Disposable Monopolar Needle Electrodes



Sharp and Smooth
for Patient Comfort

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Design

DMN™ ★ design takes into account all those issues important to the physician:

- Color coding — for easy identification
- Ergonomic shape — for physician comfort
- Fitted connection — for easy needle/cable interface and quiet recordings, unshielded and shielded.

Quality

Medtronic Functional Diagnostics' new improved processes result in:

- Uniformly sharp electrodes — consistently
- Reduced friction between needle and tissue
- High quality recording characteristics

This new DMN™ ★ processing provides your patients greater comfort while providing you with high quality electrodes that are easy to use and affordable.

Trial Kit

Try the new Medtronic DMN™ ★ and prove to yourself that this needle electrode is designed to perform for you and your patients.

The DMN™ ★ Kit contains 5 electrodes in a variety of sizes: (1) DMF25, (2) DMN37, (1) DMF37 and (1) DMN50. This way you can select which of the DMN™ ★ electrodes fit your requirements.

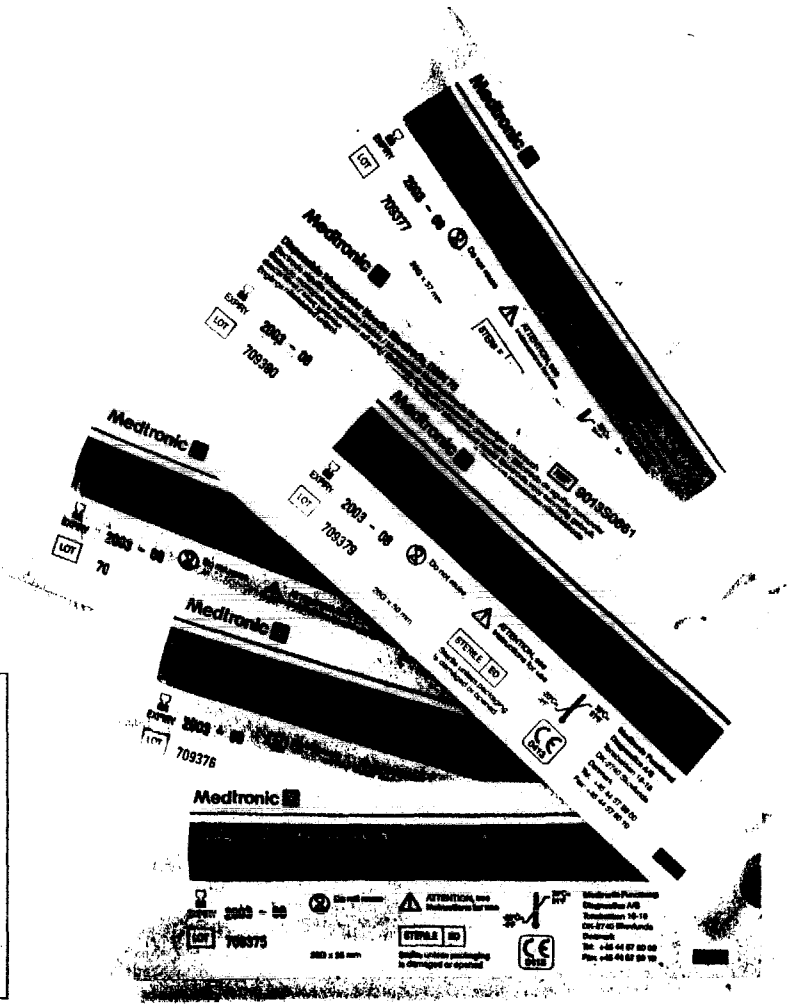
Variety of DMN™ ★ Electrodes

Model	Length	Diameter	DMN Kit Contents Quantity
DMF25	25 mm	0.33 mm	1
DMN25	25 mm	0.40 mm	0
DMF37	37 mm	0.33 mm	1
DMN37	37 mm	0.40 mm	2
DMN50	50 mm	0.40 mm	1
DMN75	75 mm	0.40 mm	0

How can I order the DMN™ ★ Electrodes?

It's simple. All you have to do is fill in the reply card and mail or fax it to us. Or you can contact us directly if you want to know more about our needle range and our *Freedom Standing Order Discount Program* which ensures that you receive needed quantities on a regular basis at a cost savings.

For more information, call 1-800-227-3191 or fax 1-612-514-1709



Contact:

Medtronic Functional Diagnostics, Inc.
tel: 1-800-227-3191 fax: 1-612-514-1709

✔ Yes, I would like to:

- ❒ order my DMN™ ★ Kit including a cable, US $11 (Order #9013S0111)
  (appropriate taxes and handling charges will be applied)
- ❒ be contacted and know more about the *Freedom Standing Order Discount Program*
- ❒ receive a free Accessory Catalog
- ❒ receive more information about Medtronic Functional Diagnostics' instruments

Please ship to:

Title: _____

Name: _____

Dept.: _____

Address: _____

City: _____

State: _____ Zip: _____

Telephone: _____

Fax: _____

E-mail: _____

PO # _____

Date/Signature: _____

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APPENDIX 19

MEDTRONIC, INC.
RESUME II

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mattrix® System Reference Guide

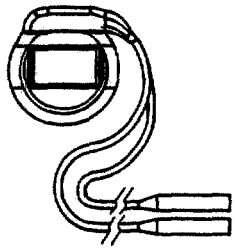
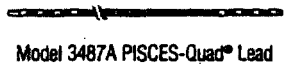
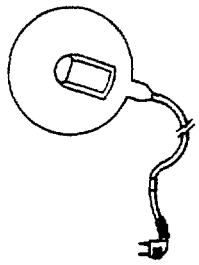
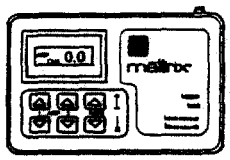
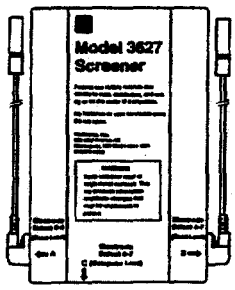


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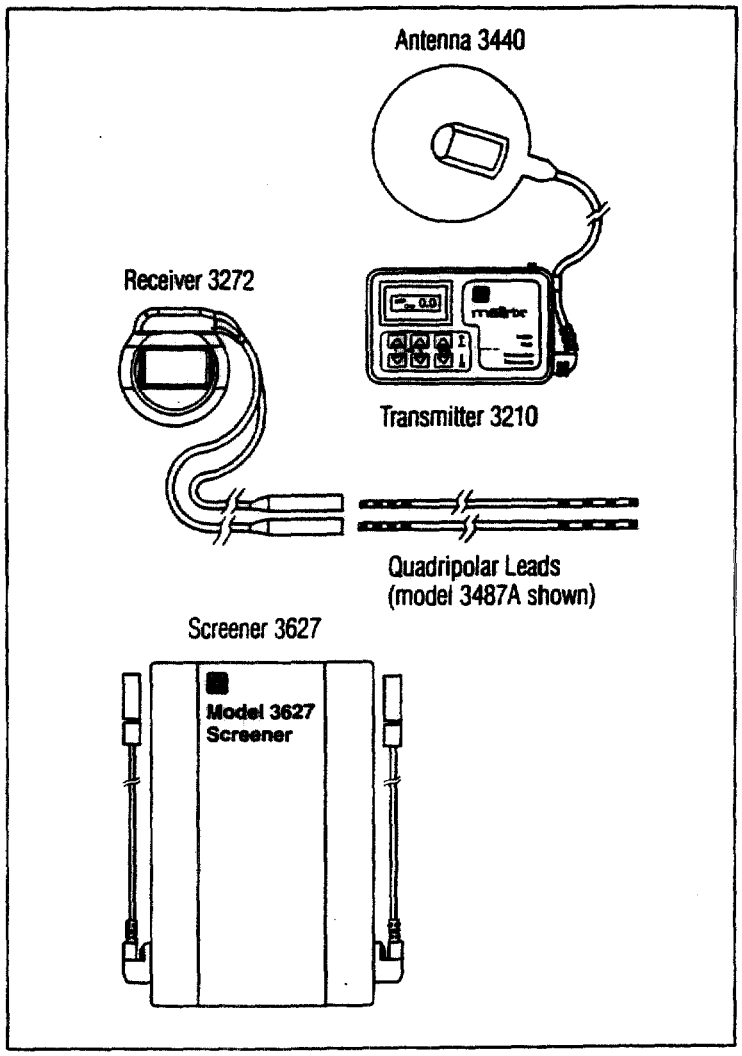
Table 1. Mattrix System Components		
Model 3272 Receiver	Implanted device that receives signals from the Model 3210 Transmitter. It has no battery and derives its power from the transmitter.	
In-line quadripolar leads	Two implanted quadripolar leads that deliver electrical stimulation.	 Model 3487A PISCES-Quad® Lead  Model 3888 PISCES-Quad Plus® Lead  Model 3587A Resume II® Lead
Model 3440 Antenna	The antenna provides the link between the receiver and transmitter. It connects to the transmitter. Tape patches or adhesive discs attach the antenna to the skin over the receiver.	
Model 3210 Transmitter	External component that contains the electronics for programming and powering the implanted receiver.	
Model 3627 Screener	Temporary external programming and power source used for stimulation testing.	

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Figure 1. Configuration of Mattrix Components.



Stimulation Modes

The Mattrix system has two stimulation modes:

- Single Stim™ mode
- Dual Stim™ mode

In the Single Stim mode, the two Mattrix leads can be programmed to the same amplitude, pulse width, and rate. In the Dual Stim mode, the amplitude and pulse width *can be programmed independently* for each lead. The programmed rate is the same for both leads.

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Indications

The Medtronic Mattrix system is indicated for spinal cord stimulation (SCS). A Mattrix system with the model 3272 receiver is also indicated for peripheral nerve stimulation (PNS). The system is indicated as an aid in the management of chronic, intractable pain of the trunk or limbs.

Contraindications

Patients are contraindicated for internalization if they are unsuccessful in receiving pain relief during trial stimulation, or if they are unable to properly operate the transmitter.

Implantation of an SCS or PNS system is contraindicated for patients with a cardiac demand pacemaker, implantable cardiac cardioverter/defibrillator, or for those patients who will be exposed to magnetic resonance imaging (MRI).

Patient Selection

The most likely candidates for the Mattrix system have neuropathic pain and any one of these characteristics (Figure 2):

- Pain covering more than one vertebral segment
- Bilateral pain pattern that cannot be adequately treated with one lead
- Pain patterns requiring multisite stimulation
  - -Cervical and thoracic
  - -Multiple PNS applications

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Neurostimulation Systems



Expanding the Array of Pain Control Solutions

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PERCUTANEOUS LEADS

...al steerability with Medtronic's coiled wire design
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Pisces-Quad® Compact Lead
- For a more precise, focused field
- Lead electrodes 3 mm long, 4 mm spacing
- Electrode span 24 mm

Pisces-Quad® Lead
- Lead electrodes 3 mm long, 6 mm spacing
- Electrode span 30 mm

Pisces-Quad Plus® Lead
- Lead electrodes 6 mm long, 12 mm spacing
- Electrode span 60 mm

...RGICAL LEADS

...atients who can benefit from increased
...ability.

...® Lead
...ost requested surgical lead on the market
...ddle 8 mm wide, 2 mm thick

... Lead
...er epidural spaces
...le 6.6 mm wide, 1.4 mm thick

...S Lead
...ve-distribution pain
...h skirt surrounding paddle
...mm wide, 1.4 mm thick

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... wide, 1.8 mm thick
...h Synergy and ... Systems

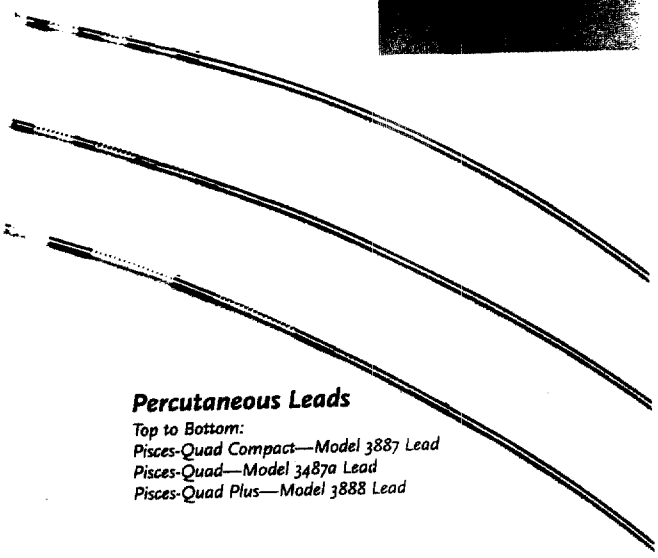
...COVERAGE

...systems ... allow broader

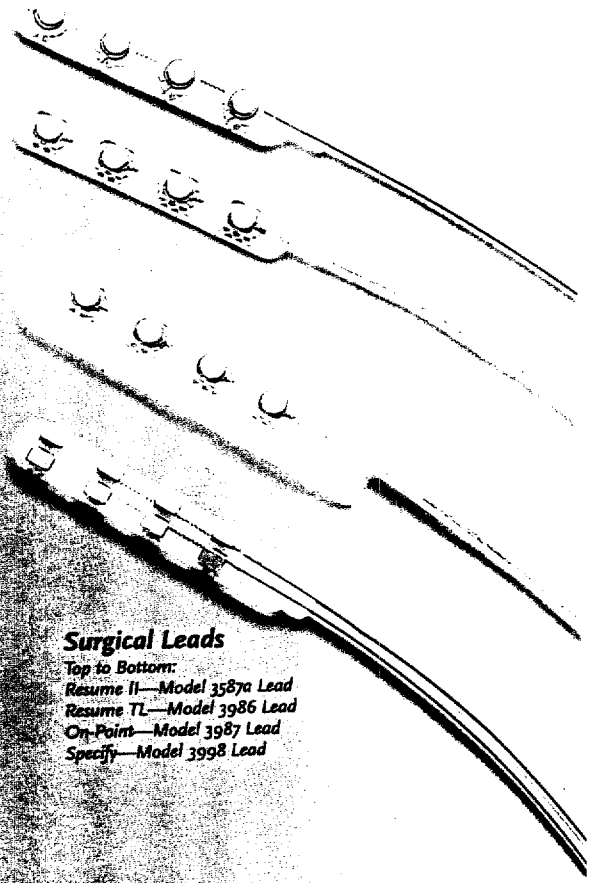
...of Medtronic ... in-line leads



Dual4 E...
Specify ...
Two Pis... ...3887 Leads



Percutaneous Leads
Top to Bottom:
Pisces-Quad Compact—Model 3887 Lead
Pisces-Quad—Model 3487a Lead
Pisces-Quad Plus—Model 3888 Lead



Surgical Leads
Top to Bottom:
Resume II—Model 3587a Lead
Resume TL—Model 3986 Lead
On-Point—Model 3987 Lead
Specify—Model 3998 Lead

Note: Not all leads/extensions are compatible with all systems. Consult the system components sheet for a list of compatible components.

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Appendix 20
Substantial Equivalence Discussion and Rationale
Vertis PNT System (PNT Control Unit and Accessories)

The following information is provided in accordance to the "Premarket Notification 510(k)" Manual (HHS Publication FDA 95-4158) released by the Food and Drug Administration. The 510(k) "Substantial Equivalence " Decision Making Process - decision tree enclosed in this Appendix is reproduced from the above noted Manual (derived originally from ODE Bluebook Memorandum No. K86-3, June 30, 1986 - "Premarket Review Notification Program").

Substantial Equivalence Decision Tree

Vertis Neuroscience, Inc. believes the Vertis PNT System (PNT Control Unit and accessories) to be substantially equivalent to legally marketed devices in commercial distribution prior to May 28, 1976. The decision process/path we used to arrive at this conclusion is shadowed in the decision tree (Attachment A) in this Appendix. A discussion of this path follows.

Substantial Equivalence Discussion and Rationale

Per the sequence in the decision tree:

New device comparison to Marketed Devices

In this Notification, the Vertis PNT System has been compared to the Empi Inc., Rehabilicare, Inc., Chattanooga Group, Inc. and Medtronic, Inc. nerve stimulators and TECA Corporation and Medtronic, Inc. nerve stimulation electrodes. These devices are currently legally marketed devices that have been previously determined to be substantially equivalent to devices in commercial distribution prior to May 28, 1976.

Indications/Intended Use

The Vertis PNT System is intended for use for the symptomatic relief and management of chronic, intractable pain and/or as an adjunctive treatment in the management of post-surgical and post-trauma acute pain.

Nerve Stimulator - PNT Control Unit: The intended use of the Empi Inc., Rehabilicare, Inc., Chattanooga Group, Inc. and Medtronic, Inc. nerve stimulators are identical or substantially the same as for the Vertis PNT Control Unit nerve stimulator.

Thus, there is *no* difference in the indications for use of the Vertis PNT Control Unit in comparison to the intended use of the substantially equivalent nerve stimulators. Thus, the devices have the same intended use.

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Nerve Stimulation Electrodes - Safeguide Electrodes: The intended uses of the TECA Corporation and Medtronic, Inc. nerve stimulation electrodes are identical to the Vertis Safeguide electrodes. These electrodes are all intended for use for conduction of electrical stimulation from a nerve stimulator to a patient. Furthermore, they are intended for stimulation of peripheral nerves.

Furthermore, the Vertis Safeguide electrodes and the substantially equivalent devices are all electrodes that are placed percutaneously - through and below the surface of the skin - and are used in conjunction with nerve stimulators in delivering electrical stimulation in a percutaneous manner and for stimulation of peripheral nerves.

Thus, there is *no* difference in the indications for use of the Vertis electrodes in comparison to the intended use of the substantially equivalent electrodes. Thus, the devices have the same intended use.

Technological Characteristics

The features and characteristics of the Vertis PNT System (Control Unit nerve stimulator and electrodes) in comparison to substantially equivalent devices were itemized in detail in the comparison charts in Appendix 16 and Appendix 18.

In review of this information, it is apparent that the Vertis PNT Control Unit and electrodes have very similar and in many instances, identical technological characteristics to substantially equivalent devices. The following obvious similarities are noted for reference.

Similarities:

- device system use conditions:
    - o indications for use
    - o intended user
    - o portability

- nerve stimulator characteristics and features:
    - o accessories available (e.g., electrodes, cables)
    - o therapy (e.g., waveform, phase duration, output amplitude, frequency range, output charge)
    - o therapy conditions (e.g., multiple output channels)
    - o device controls (e.g., on/off and therapy intensity controls, LCD text prompts, data recording capabilities)
    - o electrical safety (e.g., output protection, patient isolation)
    - o technical standard compliance

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- electrode characteristics and features:
  - o medical grade (biocompatible) materials
  - o varying configurations available (e.g., sizes, lengths)
  - o electrode placement method (percutaneous)
  - o skin/tissue contact
  - o sterile
  - o single use (non reusable)
  - o packaging

Differences - New Characteristics Effect on Safety or Effectiveness

The Vertis PNT System (Control Unit nerve stimulator and electrodes), however has some different technological characteristics in comparison to the substantially equivalent devices. In accordance to the substantial equivalence decision tree, these characteristics could affect safety or effectiveness and accordingly, are discussed as follows:

Method of therapy delivery – percutaneous electrodes

To provide reference information, a historical discussion of percutaneous electrical stimulation is provided in Attachment B to this Appendix. This discussion includes a discussion of historical regulatory classifications.

Conclusion: This discussion indicates that there is historical and regulatory precedence for the manner in which Vertis percutaneous neuromodulation therapy (PNT) is delivered - peripheral nerve stimulation accomplished in a percutaneous manner. Please refer to Attachment B for all details of this discussion.

To assess the percutaneous therapy aspects of the Vertis PNT System in comparison to substantially equivalent devices, an in-depth discussion is provided in Attachment C to this Appendix. This includes a discussion and cross-reference to several other Appendices that contain extensive bench, animal and clinical studies.

Conclusion: The conclusions from these studies are summarized as follows:

Potential Safety and Effectiveness Issue	Study/data available from Vertis	Discussion/ Location of data	Conclusion
Risk of Thermal Injury/Burn	Current Density Analysis	Appendix 21	Vertis observed no tissue damage as a result of thermal effects from PNT electrical stimulation.
Risk of Electrode Corrosion - Toxicity	Current Density Analysis and Animal Study	Appendix 21 Appendix 22	Vertis observed no electrode corrosion that would be clinically significant or cause tissue damage.

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Risk of Tissue Disruption/Injury	Animal study	Appendix 22	Vertis observed no significant physiological impact to tissue when exposed to worst-case Vertis PNT electrical stimulation parameters.
Risk of Ineffective or Unsafe Use (e.g., infection) in a Clinical Application for Pain Management – Published Studies	Summary of recent published percutaneous electrical stimulation clinical studies	Appendix 23	Studies demonstrated the safety and effectiveness of percutaneous electrical stimulation.
Risk of Ineffective or Unsafe Use (e.g., infection) in a Clinical Application for Pain Management – Vertis Clinical Study	Vertis clinical trial	Appendix 24	Studies demonstrated the safety and effectiveness of Vertis percutaneous neuromodulation therapy (PNT).

Physical characteristics and Clinic vs. Patient Use

The PNT Control Unit is designed to be used by a physician/clinician in a clinic environment. It is not intended to be used by a patient in a home environment. Accordingly, in terms of physical characteristics (size and weight – recorded in Appendix 16), the Vertis PNT Control Unit is nearly identical to the Chattanooga nerve stimulator, which is a nerve stimulator designed to be used in the clinic and not for patient portable use.

Conversely, per the comparison chart in Appendix 16, the Vertis PNT Control Unit is noted to be larger dimensionally and by weight, than the substantially equivalent EMPI, Inc., Rehabilicare, Inc., or Medtronic, Inc. nerve stimulators, which are designed to be highly portable devices, that patients can easily carry externally or internally (via implantation) and use themselves at home.

Power supply

Per the comparison chart in Appendix 16, the power source of the Vertis PNT Control Unit is AC power (plugs into the wall). This is identical to the Chattanooga nerve stimulator, which is also AC powered. This characteristic is consistent with the above use description that both the Vertis and Chattanooga devices are intended to be used by clinicians only (not patients) in a clinic. This is in contrast to the EMPI Inc., Rehabilicare Inc., and Medtronic, Inc. devices, which are designed to be lighter weight, more portable, out-of-clinic use devices and accordingly, are battery powered for maximum portability.

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Based on the discussion above and in supporting appendices of the characteristics of the Vertis PNT System that differ from the substantially equivalent devices, Vertis answers the substantially equivalent decision tree (Attachment A in this Appendix) questions in the following manner:

Do the new characteristics of the Vertis PNT System raise new types of safety or effectiveness questions?

No. *New* questions are *not* raised. There are no new questions that are unique to the Vertis PNT System. The types of questions that are raised are the *same* questions that would be asked regarding any current nerve stimulator that is delivering electrical stimulation and for percutaneous stimulation of peripheral nerves. Refer to the discussion that follows.

Do accepted scientific, methods exist for assessing effects of the new characteristics? Are performance data available to assess effects of new characteristics? Performance data demonstrates equivalence?

Yes. Valid scientific methods exist to assess the new characteristics of the Vertis PNT System. A summary follows:

Method of therapy delivery – percutaneous electrodes

Valid scientific methods were used in the conduct of the bench, animal and human clinical studies. These studies were designed to ask and answer potential questions regarding the safety and effectiveness of percutaneous electrical stimulation.

Conclusion: The discussion in Attachment C of this Appendix and supporting data presented in Appendices 21-24 demonstrated that any new characteristics associated with the Vertis PNT System do NOT raise new questions of safety or effectiveness.

Physical characteristics and Clinic vs. Patient Use

Valid methods used to assess Vertis PNT Control unit physical aspects, in comparison to the substantially equivalent devices, are obvious weight and dimensional measurements.

Performance data is available – please refer to the device comparison charts in Appendix 16. Vertis believes the physical characteristics of the PNT Control Unit are appropriate for an in-clinic device system and have been shown to be substantially equivalent to other devices used in a clinic situation (e.g., the Chattanooga substantially equivalent device noted in Appendix 16).

Thus, the physical characteristics of the PNT Control Unit raises NO new questions regarding safety and effectiveness

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Power supply

Valid methods exist to assess the PNT Control Unit power supply (wall power). These test methods and acceptance criteria are in accordance with IEC60601-1:1993 (UL 2601) Medical Electrical Equipment, Part 1: General Requirements for Safety and Amendments A1:1991, A2:1995.

Performance data is available to demonstrate the acceptability of the PNT Control Unit power supply and is discussed in Appendix 9 in conjunction with other safety standard adherence and performance testing.

The PNT Control Unit power supply meets the appropriate FDA-recognized consensus standard requirements. Thus, the power supply characteristic raises NO new questions regarding safety and effectiveness.

Decision (per Decision tree)

"Substantially Equivalent" Determination

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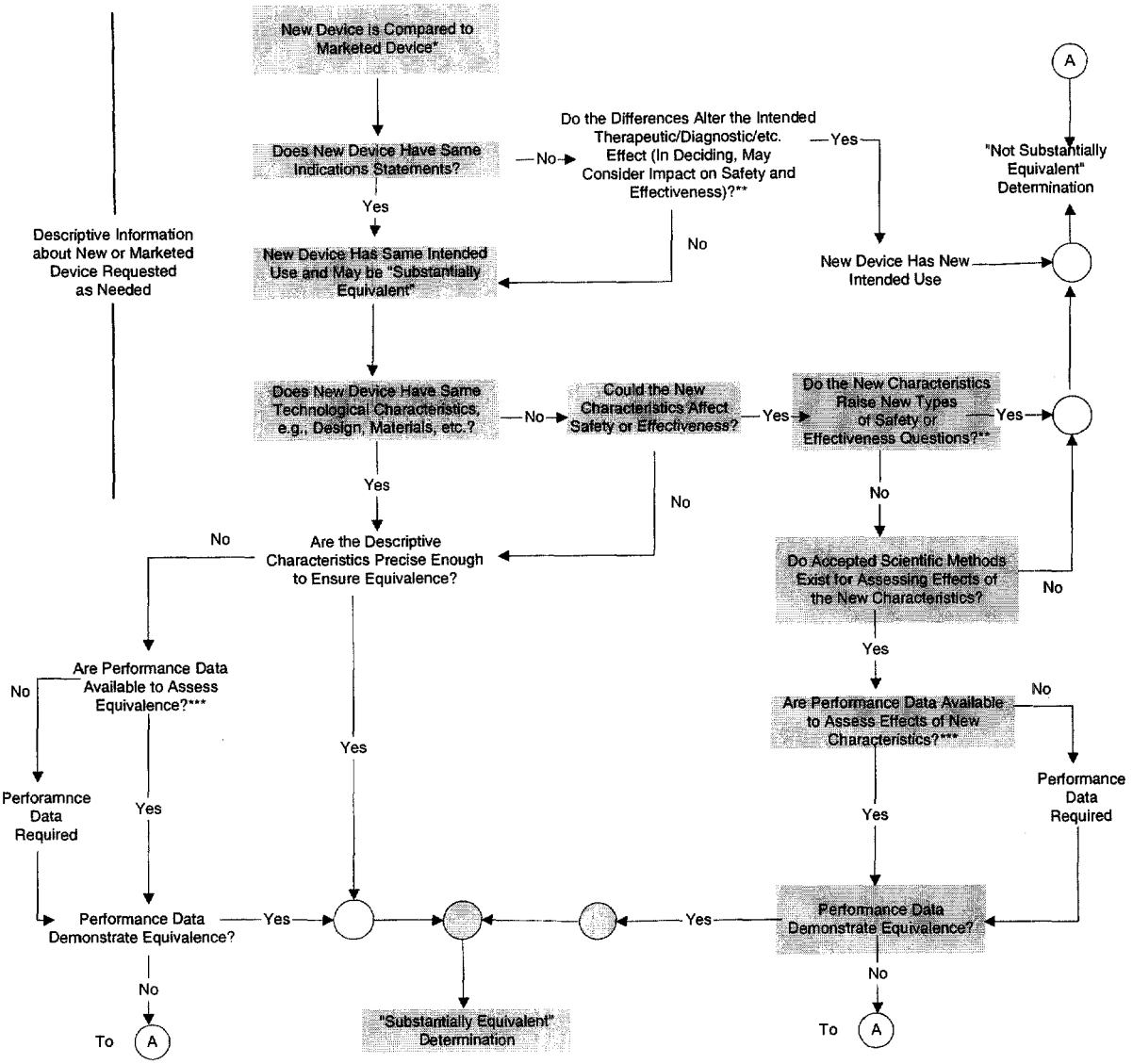
APPENDIX 20

ATTACHMENT A

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Appendix 20 – Attachment A
510(k) "Substantial Equivalence" Decision-Making Process (Detailed)



* 510(k) submissions compare new devices to marketed devices. FDA requests additional information if the relationship between marketed and "predicate" (pre-Amendments or reclassified post-Amendments) devices is unclear.

** This decision is normally based on descriptive information alone, but limited testing information is sometimes required.

*** Data may be in the 510(k), other 510(k)s, the Center's classification files, or the literature.

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APPENDIX 20

ATTACHMENT B

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Appendix 20 – Attachment B
Substantial Equivalence Discussion –
Historical and Regulatory Discussion – Percutaneous Electrical Stimulation

Note: Scientific/technical literature referenced in the following discussions are detailed in the bibliography in Appendix 28. For convenience, copies of selected references are also included in Appendix 28.

The following summarizes historical information regarding percutaneous electrical stimulation for pain management. This discussion also includes a discussion of historical regulatory classifications of percutaneous electrical stimulation. Relevance of this information to Vertis percutaneous neuromodulation therapy (PNT) is also noted. Contents of this section are as follows:

Topic	pages in this Appendix
Historical Discussion - Peripheral nerve stimulation	2 –3
• Overview	
• History	
• Mechanism	
Regulatory History	3 –9
• FDA definitions - Pain management devices	
• Review of FDA Classification Information/References	
• Percutaneous electrode historical use	
• Percutaneous electrode historical description	
• Relevance to Vertis PNT therapy	
• Conformance to AAMI NS-15	

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Historical Discussion - Peripheral nerve stimulation

Overview: Use of electrodes to stimulate peripheral nerves is not a new concept. Literature supports the presence and successful clinical use of peripheral nerve stimulation for pain relief as early as the 1960s.

Over the years, peripheral nerve stimulation has been used in a variety of pain management applications. In 1979, FDA classified several pain management devices (transcutaneous nerve stimulators, peripheral nerve stimulators and spinal column stimulators). These classification documents (19, 20) and the scientific references used in support of the FDA classification decisions, report on the use of peripheral nerve stimulation for pain management in chronic low back pain, phantom limb pain, osteoarthritis pain, pain associated with trauma or injury to peripheral nerves, etc.

Overall, the advantage of peripheral nerve stimulation is that it offers the clinician an alternative to more invasive and risky procedures involving the nervous system (e.g., fully implanted spinal column stimulators, implanted analgesic medication infusion pumps, etc.) or pharmacological regimes.

History: The ANSI/AAMI NS4 -TENS, NS14 - Spinal cord stimulators- and NS15 - Peripheral nerve stimulators (21, 22, 23) technical standards provide a brief, but comprehensive, historical overview of peripheral nerve stimulation. Some of that information is provided here for general reference. ANSI/AAMI NS15 (23, page 5) notes:

- "The idea that electrical stimulation of body organs can serve as a therapeutic modality for the modification of abnormal physiology in humans has been applied in several fields, most notably cardiology. The use of electrical stimulation of peripheral nerve fibers in the management of chronic, intractable pain began in the 1960s."

- "Interest in this field was sparked by the publication of the "Gate Control Theory" (Melzack & Wall, 1965 [24]). According to this theory, sensory mechanisms for the perception of pain are controlled by a negative feedback or gating mechanism located in the spinal cord. Activated by impulse activity in large-diameter, myelinated, peripheral, cutaneous nerve fibers or their collaterals in the dorsal columns of the spinal cord, this "gate" closes to inhibit the transmission of nerve impulses from the smaller fibers associated with nociception. Although such impulse activity could be achieved by mechanical stimulation of peripheral mechanoreceptors, electrical stimulation is easier to apply." The "Gate Control Theory" has served as the rationale for the clinical use of electrical stimulation of the nervous system as a therapeutic modality in the management of pain.

- "The initial clinical application of current to nerves for the relief of pain involved the stimulation of myelinated afferent nerve fibers in peripheral nerve pathways. Shelden (1966 [25]) proposed that the pain relief observed upon stimulation of the trigeminal nerve was due to depolarization and the reduction of afferent impulses. Wall & Sweet (1967 [26]) reported that stimulation of peripheral nerves caused

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temporary pain relief that outlasted the period of application of current, occasionally by several hours. Sweet & Wepsic (1967 [27]) reported that peripheral nerve stimulation produced continued satisfactory pain relief in a small group of patients".

***Mechanism*:** Various theories have been postulated regarding the mechanism of electrical stimulation of the nervous system as a therapeutic modality in the management of pain. For reference purposes, AAMI NS15 (23, page 6) summarizes the proposed mechanisms as follows "peripheral nerve stimulation may reduce the perception of pain by:

- interfering with action potential conduction, particularly at branch points of primary afferents (frequency related conduction block);
- local "gate" mechanisms in the dorsal horn, where pain signals may be blocked;
- producing affects higher in the central nervous system, possibly by the competitive "jamming" of pain signals;
- initiating an ascending-descending pain control loop that terminates in the spinal 'gate';
- influencing release of endogenous factors that act on pain perception or nociception centrally or peripherally, (e.g., sympathetic neurotransmitters)."

Summary: Use of electrodes to stimulate peripheral nerves for pain mitigation is not a new concept - it has been used by the medical community in excess of 30 years. Scientific literature supports the presence and successful clinical use of peripheral nerve stimulation for pain relief as early as the 1960s.

It is important to note that peripheral nerve stimulation can occur through a variety of electrical stimulation methods, such as transcutaneous stimulation, percutaneous stimulation or stimulation via percutaneous or fully implanted electrodes. The difference among these various methods is simply how the electrical stimulation is delivered to the peripheral nerves.

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Regulatory History

FDA definitions – Pain management devices:
In 1979, FDA established the following regulatory classifications for pain management devices:

- Transcutaneous electrical nerve stimulators for pain relief are Class II devices and are defined by 21 CFR 882.5890 as "a device used to apply an electrical current to electrodes on a patient's skin to treat pain".

- Implanted peripheral nerve stimulators for pain relief are Class II devices and are defined by 21 CFR 882.5870 as "a device that is used to stimulate electrically a peripheral nerve in a patient to relieve severe intractable pain. The stimulator consists of an implanted receiver with electrodes that are placed around a peripheral nerve and an external transmitter for transmitting the stimulating pulses across the patient's skin to the implanted receiver".

- Implanted spinal cord stimulators for pain relief are Class II devices and are defined by 21 CFR 882.5880 as "a device that is used to stimulate electrically a patient's spinal cord to relieve severe intractable pain. The stimulator consists of an implanted receiver with electrodes that are placed on the patient's spinal cord and an external transmitter for transmitting the stimulating pulses across the patient's skin to the implanted receiver".

Review of FDA Classification Information/References – Percutaneous electrode historical use:

Transcutaneous: As per the FDA definitions above, transcutaneous electrical stimulators employ cutaneously placed electrodes to achieve peripheral nerve stimulation. There is no invasive component to these devices.

- The FDA Neurological devices panel report (28), which was the scientific reference used in FDA's 1979 classification of TENS devices in 21 CFR 882.5890, noted that TENS devices were used initially "as a non-invasive means of testing the patient's response to electrical stimulation to determine the suitability of implanting a stimulator for the relief of pain in that particular patient".

  TENS devices are still often used in this manner – to assess a patient's response and/or potential suitability for a more invasive procedure. And of course, TENS devices are also now used as stand-alone pain management devices.

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Percutaneous: As per the FDA definitions above, Class II implanted peripheral nerve stimulator systems have an antenna affixed to the patient's skin overlying an *implanted* receiver. For these devices, electrical impulses are transmitted from an *external* transmitter across the skin – via *implanted*, insulated lead wires with bare electrode surfaces - to specific peripheral nerves. Similar to the peripheral nerve stimulators, Class II spinal column stimulators employ an implanted receiver but the implanted electrodes are placed on the patient's spinal cord.

- In FDA's 1979 classification of spinal column stimulators (29), one of the scientific references used by FDA to support the 21 CFR 882.5880 classification decision was by Long and Erickson (30). The authors noted the value of using either transcutaneous or *percutaneous* peripheral nerve stimulation as a means of screening patients for spinal column stimulation. Specifically, the authors noted the following:

  > "Externally applied electrical currents and peripheral nerve stimulators have been shown to be of significant value in pain treatment".
  >
  > "Dorsal column stimulation should be applied to patients only after careful screening for psychoneurotic traits and comprehensive management. If feasible, peripheral nerve stimulators are preferable to spinal cord stimulators. Pain relief by external or *percutaneous* peripheral nerve or spinal cord stimulation is necessary before implantation of a dorsal column stimulator except in rare instances" (emphasis added).

- It is clear from the scientific literature used as references and cited as part of the 1979 FDA classification activities (19, 20, 28, 29, 30), that the medical community had evolved to not only using transcutaneous electrodes, but also percutaneous electrodes were being routinely used to assess or treat patients for pain relief.

  This practice of using *percutaneous* electrical stimulation to treat patients for pain mitigation (e.g., prior to subsequent full implantation of a peripheral nerve stimulator or a spinal column stimulator system), continues to this day with many clinicians.

  - For an example, please refer to the Medtronic instruction manual "Peripheral Nerve Stimulation" (copy provided in Appendix 17). As noted in the manual indications (page i), this labeling is for the Medtronic Mattrix system. The Mattrix was cleared by the FDA as a Class II (per 21 CFR 882.5870) peripheral nerve stimulator used for pain management. Refer to Appendix 16 for information regarding this device.

    Pages 7-31 of the Medtronic manual discuss in detail the placement of electrodes that will be used for electrical stimulation.

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Specifically, electrodes are placed and a portion of the electrode terminates percutaneously (through the skin) to attach to an external stimulator. In this configuration, the patient undergoes a screening process (pages 31-32 of manual) to evaluate if they are achieving adequate pain management. As noted in the manual (page 32), "Trial screening can be conducted for three to five *days*". (emphasis added).

- Summarily, regarding the use of electrodes placed percutaneously for pain management, North, et al of John Hopkins University reported in 1993 on a 2 decade experience (31) and noted the following:

  "All patients were screened with a temporary electrode to establish satisfactory relief of pain before implantation of a permanent device".

  "We continue to use temporary percutaneous electrodes as a screening technique to demonstrate satisfactory pain relief before a permanent system is implanted".

  "The criteria for proceeding from a temporary to a permanent implant have varied widely; some authors have required a minimum of 70% reported pain relief and some have required a test phase as long as *2 months*" (emphasis added).

Summary: From these references, it is important to note that both historically and in current medical practice, nerve stimulation electrodes are being routinely placed in a percutaneous manner to achieve the intended use of pain management. These electrodes extend through the skin (percutaneous) and are left in this position for many days.

Furthermore, the practice of placing nerve stimulation electrodes in a percutaneous manner and using them for electrical stimulation to relieve pain has historical precedence back to the early 1970s. Scientific references describing this percutaneous use were part of FDA's original review, and were cited as references by the FDA, in the pain management device classification activities in 1979.

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Review of FDA Classification Information/References – Percutaneous electrode historical description:

The review of FDA's original regulatory classification documents (19, 20, 28, 29, 30) for pain management medical devices yields an additional important piece of information, summarized as follows:

- In FDA's 1979 classification of peripheral nerve stimulators (20), one of the scientific references used by FDA to support the 21 CFR 882.5870 classification decision was by Erickson and Chou in 1974 (32). The authors noted the following:

  > "Implantable dorsal column stimulators and peripheral nerve stimulators have been used for the relief of chronic pain at the University of Minnesota Hospitals for the past four years". The authors described the spinal column stimulators they used and then went on to describe the peripheral nerve stimulators in use. "The second type of device is a peripheral nerve stimulator (PNS) comprised of an electrode placed around a peripheral nerve and similarly attached to a lead wire and receiving device. When activated, the patient perceives a tingling or vibratory sense in the distribution of this nerve which is capable of relieving pain located in this area".
  >
  > In describing the electrical stimulating techniques: "These techniques relate specifically to the implantation of pain relieving devices and will be described in detail. We have available, small flexible electrodes which can be inserted through a 17 gauge needle into the spinal column adjacent to the spinal cord or into an extremity adjacent to a major peripheral nerve". "Once the nerve has been located, the electrode is inserted through the [17 gauge] needle adjacent to the nerve and *taped to the skin*. The electrode is then connected to a stimulating device and *left in place for one or two days*. The patient has control of the stimulating device and is able to determine whether or not he can adequately control his pain by electrical stimulation" (emphasis added).

Summary: Among the considerable scientific literature available and reviewed by the FDA during the pain management device classification activities, this reference (32) was considered important enough by the FDA to be specifically cited (as reference #3) in FDA's 1979 final rule (20) to classify peripheral nerve stimulators.

As noted on page 4 of this Attachment, the final CFR description for peripheral nerve stimulators uses the words "implanted" receiver with electrodes" in conjunction with an external stimulus generator. Clearly however, as this reference describes, during classification, FDA was aware that electrodes were also routinely placed percutaneously (not necessarily always "implanted") for pain management. These percutaneous electrodes extended through the skin and were used for several days in combination with the external stimulus generator.

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Review of FDA Classification Information/References – Relevance to Vertis PNT therapy:

Based on the previous discussions (pages 2-7), the following points are made with respect to the relevance of this information to Vertis therapy.

- Vertis percutaneous neuromodulation therapy (PNT) is peripheral nerve stimulation accomplished in a percutaneous manner.

- Vertis electrical stimulation therapy is delivered by placing the nerve stimulation electrodes in a percutaneous manner. This percutaneous placement of electrodes for pain management is not new – it is consistent with the 30+ years of historical medical use of electrodes in this manner.

- Vertis percutaneous electrodes are placed by a clinician for therapy delivery (e.g., of 30 minute duration) and then immediately removed. Historical and current use of percutaneous electrodes for pain management shows that the electrodes are often left in the patient for many days. Vertis believes that the short duration of the Vertis therapy/electrode use raises less concern regarding device safety (e.g., reduced risk of infection).

- A review of original 1979 FDA classification documents and the scientific literature used in support of the classification decisions indicates that percutaneous electrode/electrical stimulation for pain management was used in the medical community in the 1960 - early 1970s and FDA naturally, was aware of this usage.

- The Vertis PNT system is consistent with the 1960-70s device configuration/descriptions for peripheral nerve stimulation therapy. Fundamentally, Vertis nerve stimulation therapy is delivered through percutaneous electrodes (the Safeguide electrodes) connected to an external stimulus generator (the PNT Control Unit).

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Conformance to AAMI

Lastly, in addition to the historical and regulatory review regarding peripheral nerve stimulation. Vertis also assessed the Vertis PNT therapy for compliance to current standards – the AAMI NS-15 peripheral nerve stimulator standard (23).

Results are summarized below:

Stimulation parameters	**Recommended by AAMI NS-15, section 3.2.2**	**Delivered by Vertis PNT System**	**Vertis PNT complies with AAMI?**
Pulse frequency	1 to 1,500 pulses per second (pps)	4 to 50 pulses per second (pps)	Yes
Pulse width	1 to 2,000 microseconds (μsec)	200 μSec, (or 400 μSec for a complete biphasic pulse).	Yes
Output voltage/current	0 to 15 volts (V) through a 500-ohm load (0 to 30 mA)	Maximum of 7.5 V through a 500-ohm load (15mA) - calculated at worst-case voltage/ current at 4 pps (4Hz).	Yes

Summary: Vertis therapy complies with current technical standards for peripheral nerve stimulation.

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APPENDIX 20

ATTACHMENT C

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Appendix 20 – Attachment C
Substantial Equivalence Discussion –
Percutaneous Electrical Stimulation

As discussed in Appendix 20 - Attachment B, percutaneous electrical stimulation of peripheral nerves for pain mitigation is not a new concept; it has been used by the medical community in excess of 30 years.

The Vertis PNT System (Control Unit nerve stimulator and electrodes) stimulates peripheral nerves and achieves pain mitigation by delivering electrical stimulation using percutaneous electrodes. Accordingly, it is important to evaluate the safety and effectiveness of the percutaneous electrical stimulation.

This Appendix discusses the *potential* safety and effectiveness questions of percutaneous electrical stimulation in comparison to the substantially equivalent devices.

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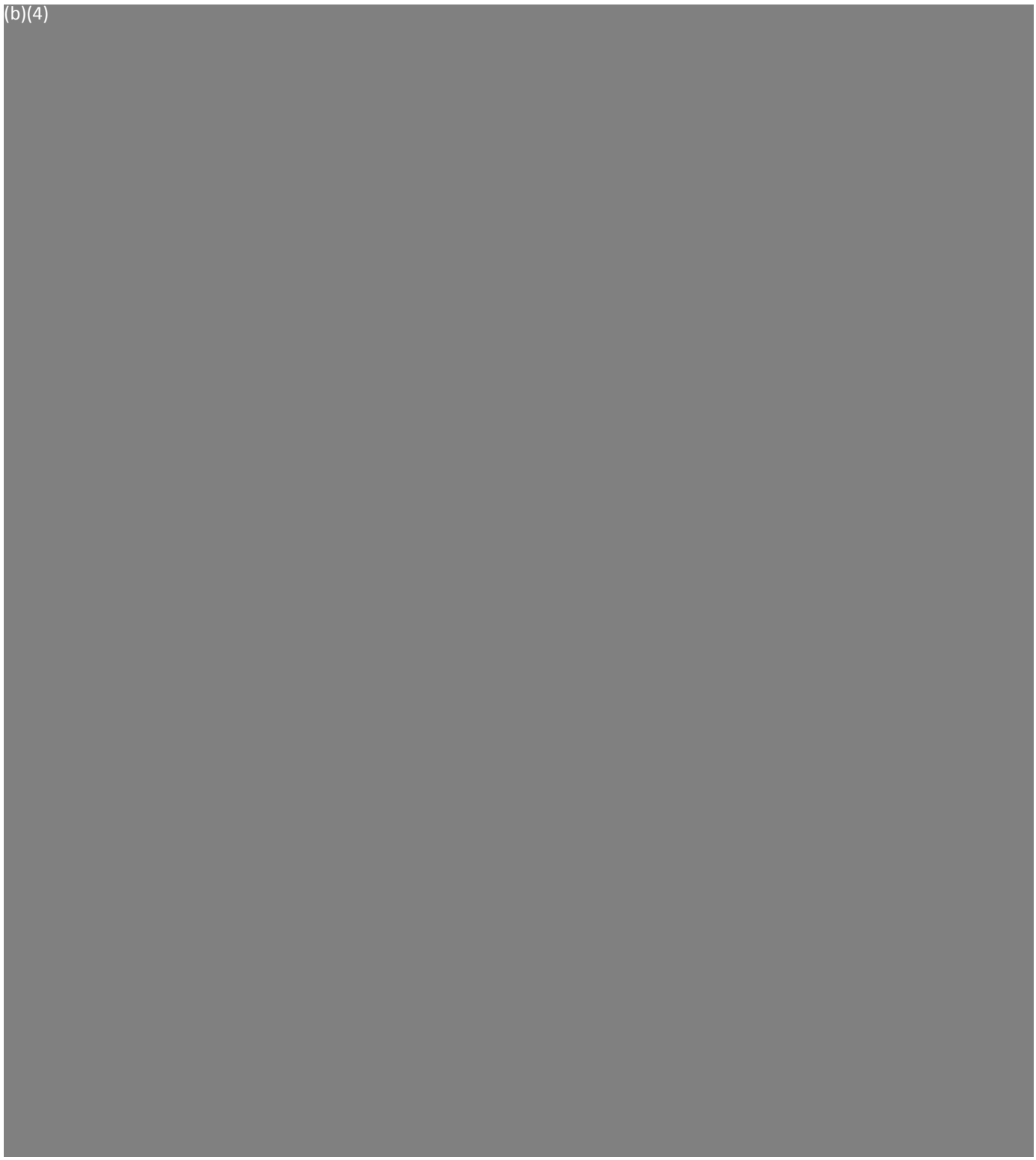
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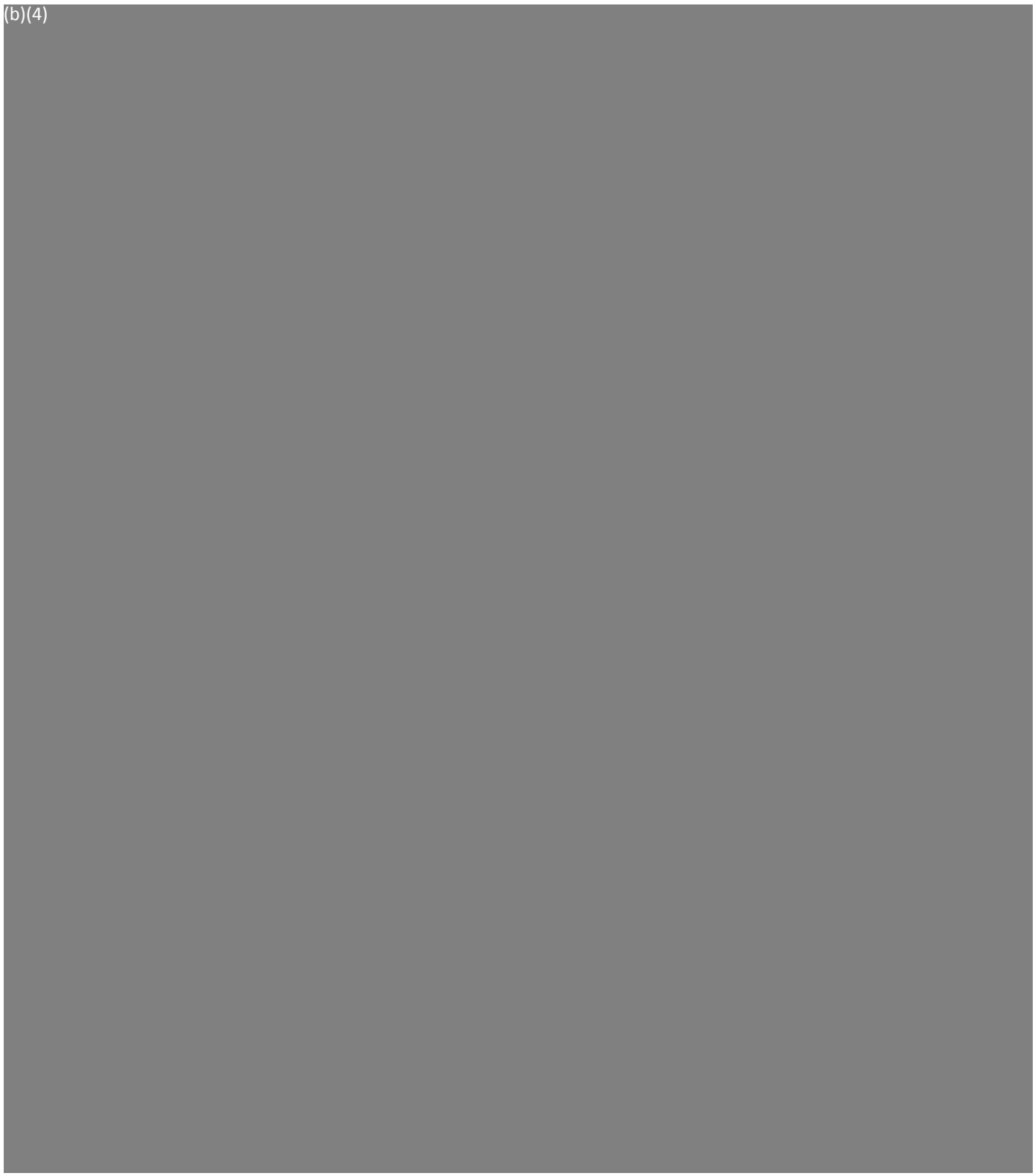
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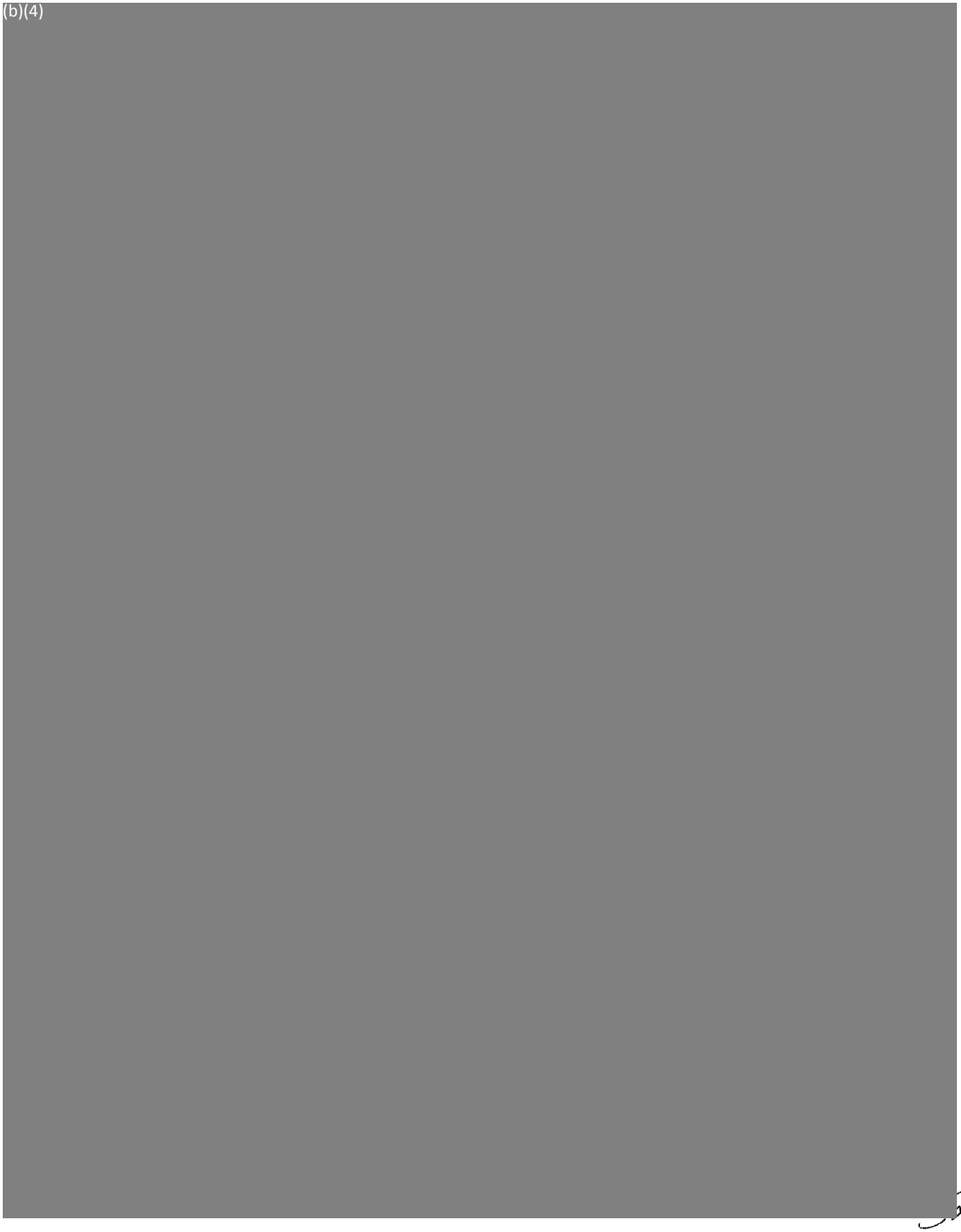
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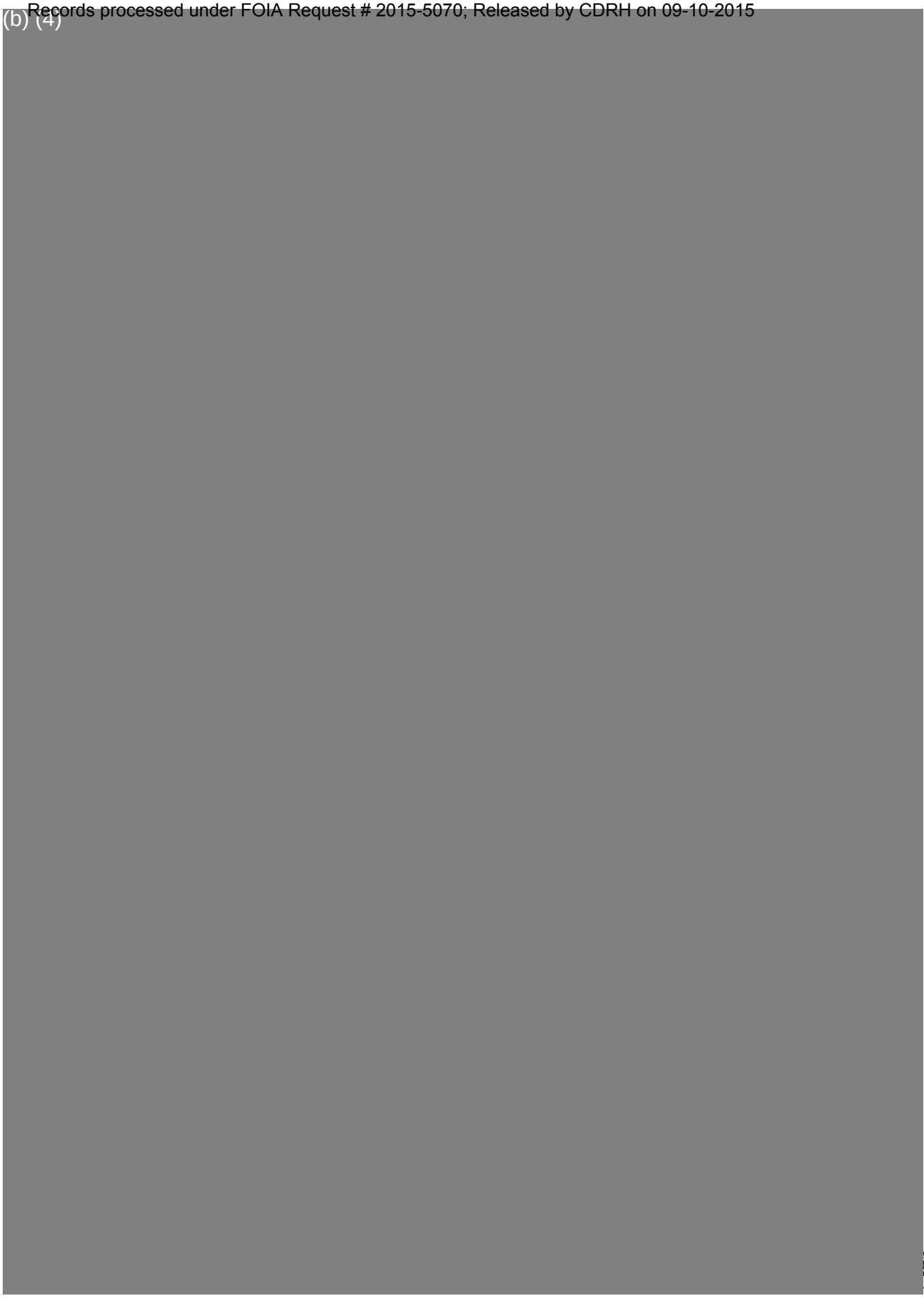
Appendix 21
Current Density Analysis

(b) (4)

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Finite Element Analysis (b)(4)

submitted to

Vertis Neuroscience
2102 Fourth Avenue, Suite 200
Seattle WA 98121-2329

submitted by

(b)(4)

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APPENDIX 21

REFERENCES

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References – Current Density

The following literature was cited in Dr. Grill's report. Copies of these are enclosed in this Appendix for convenience.

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INTRAMUSCULAR ELECTRICAL STIMULATION: TISSUE DAMAGE

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Coiled wire electrodes have been evaluated for intramuscular electrical stimulation. Monophasic cathodal stimulation at average current densities not exceeding 10 μamp/mm² (0.2 μC/mm²/stimulus pulse at 50 Hz) shows no increased tissue trauma over that incurred by passive implant. At average current densities greater than 50 μamp/mm² (1.0 μC/mm²/stimulus pulse at 50 Hz), extensive tissue damage occurs. The muscle tissue damage appears to be secondary to blood vessel damage. With balanced charge biphasic stimulation, greater charge densities could be used without the effect of increased tissue damage. However, to avoid electrode corrosion, the maximum charge injection during the cathodic phase should be less than 0.4 μC/mm² at 50 Hz. Balanced charge biphasic stimulation is considered safer than monophasic stimulation, and is recommended for chronic use.

INTRODUCTION

Coiled stainless steel wire electrodes, of the type described by Caldwell and Reswick (4), are used for controlled electrical activation of skeletal muscle (8, 9). Stainless steel has been used in these applications because of its practical availability and high strength compared to platinum and its commonly available alloys (3). The coiled wire electrodes have been evaluated and found to be safe under passive conditions (4), but studies under stimulating conditions have not been previously reported.

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Tissue damage can be expected to be related to the chemical and mechanical properties of the electrode. In the active region of the electrode, where the metal is in direct contact with the tissue medium, tissue damage may result from changes in local chemistry. These are the result of electrochemical reactions occurring on the surface of the electrode during stimulation (1, 2, 5).

This paper presents the results of studies on the tissue reaction occurring with coiled wire electrodes in the inactive region of the electrode where the metal is coated with an insulator and the active region where bare metal is exposed to the tissue medium.

METHODS AND MATERIALS

Nineteen adult cats weighing between 2.0 and 3.5 kg were used. The animals were anesthetized with IV-administered sodium pentobarbitol, titrated to effect a relatively light level of anesthesia. Test electrodes were implanted, parallel to the muscle fibers under aseptic conditions, in the following muscles of both sides: *tibialis anterior, medial gastrocnemius,* and *triceps brachii.* Subsequent to electrode insertion, the animals were intubated and placed on a respirator; curare was administered IV to minimize animal motion due to motor nerve excitation at the higher stimulus levels. The electrodes were formed from polyurethane insulated wire, 28 μm in diameter (304 stainless steel because 316 was unavailable in this wire diameter), and 45 μm in diameter (316 stainless steel). The overall diameter of the coiled electrode ranged from 160 to 200 μm. The effective bare wire or stimulating surface area was approximately 10 mm^2 (except where otherwise noted). The electrode construction and insertion techniques were identical to those described by Caldwell and Reswick (4); however the silicone rubber filler was omitted.

Electrical stimulation was applied to each of the six coiled wire electrodes in each animal. Indifferent electrodes, formed of saline-soaked pads, surrounded all four limbs of each animal and shared a common connection. Each muscle was stimulated for six hours at a rate of 50 Hz. The length of stimulation was chosen as a reasonable period to maintain the animal under anesthesia and a period sufficiently long to reach steady-state electrode conditions (supported by data reported later and shown in Fig. 6). The test frequency, 50 Hz, was chosen because it is an upper limit for most practical applications. Two types of stimulating waveforms—both regulated current—were studied: one rectangular monophasic; the other, balanced charge biphasic. The balanced charge biphasic waveform, and the method of generating the waveform are illustrated in Fig. 1. In all cases, the cathodic phase was rectangular and applied first (in time) to the intramuscular (IM) electrode. Pulse amplitudes of the rectangular phase were, in all cases, 20 mA; durations of 50, 100, 500, and 1000 μsec were used. The electrodes and stimulus parameters were identical in all six muscles of an individual animal. After the six hour stimulation period, the external portion of the

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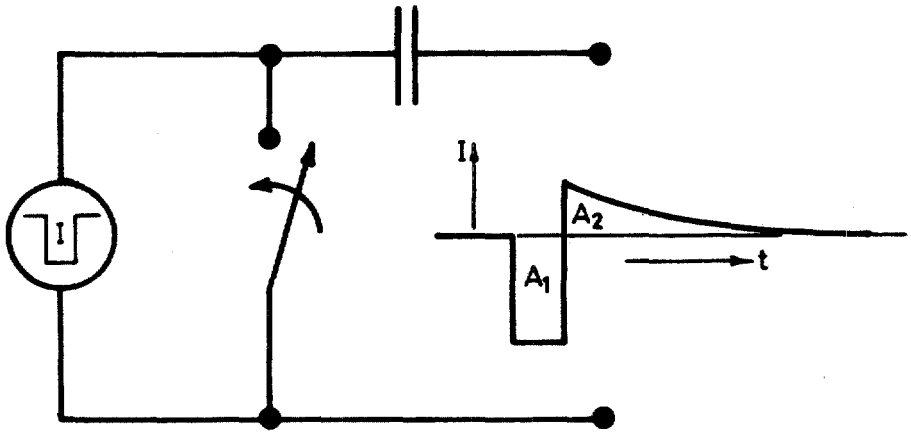


FIGURE 1. Schematic diagram of the biphasic stimulator used in these experiments. The cathodic phase is generated by the regulated current pulse generator, operating into the series combination of the load (tissue), and the capacitor. The shunting switch is open during the cathodic phase, but is closed at all other times. Therefore, all charge flowing during the cathodic phase must flow in the reverse direction in the interpulse interval. The net result is that $A_1 = A_2$ and, therefore, the net charge flow is balanced (=0).

electrode was cut at the skin surface, and the animals were allowed to recover from the anesthesia. Five to six days after the six-hour stimulation period, the experimental muscles were excised. Serial cross-sections (2–3 mm thick) were cut from each muscle, and frozen in liquid nitrogen. The sections removed are shown schematically in Fig. 2. Section I was taken close to the electrode tip, but did not include the electrode track. Sections II and III were located in the region of the active portion of the electrode. Section IV was drawn from the insulated region of the electrode as far as possible from the active region (usually greater than 10 mm). Frozen sections, 16 μm thick, were stained with hematoxylin and eosin. Areas of the muscle showing necrotic or degenerating fibers, cellular infiltrates, increased connective tissue, or regenerating fibers were defined as evidence of damage. The extent of the damaged area was measured from the projected microscopic image (X68) with a planimeter.

Measurements of pH change (or rate of change) were made by placing

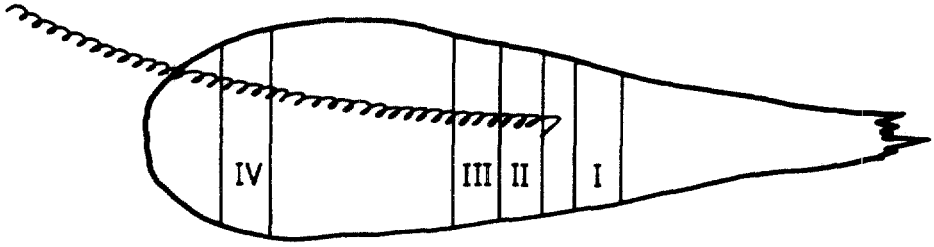


FIGURE 2. Schematic representation of test muscle showing the relationship between the electrode, and tissue samples removed. Sections II and III are in the region of the deinsulated tip of the electrode. Section IV is in the insulated region of the electrode.

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pH-sensitive paper (range 2 to 12) at right angles to the long axis of the electrode coil. The electrode coil and pH sensitive paper were then placed in an insulated tray, and covered with approximately 5 mm of 0.9% normal saline. A pair of large platinum reference electrodes were placed on either side of the coiled electrode at a distance of approximately 60 mm.

Electrode potential measurements were made at 37 °C, in 0.9% normal saline, and referenced to a standard saturated calomel electrode. The ohmic portion of the potential, that part not associated with the electrochemical reactions (5, 6), has been subtracted from all values given. The corrosion potential was defined as the anodic potential at which the current–voltage relationship first exhibited a nonlinear relationship and large increases in current were observed for small increases in voltage.

RESULTS AND DISCUSSIONS

Active Implants

Microscopic observation of the muscle sections indicates that the largest area of tissue damage occurred in the vicinity of the deinsulated or active portion of the electrode (Sections II and III). Damaged areas in Section I were always much smaller or nonexistent. Areas showing damage in the insulated region of the electrode (Section IV) exhibited very little variability in general appearance. This region was characterized by a number of small basophilic fibers with large nuclei and nucleoli indicating recovery from physical trauma (Fig. 3). Occasionally a few (4 to 10) necrotic fibers were

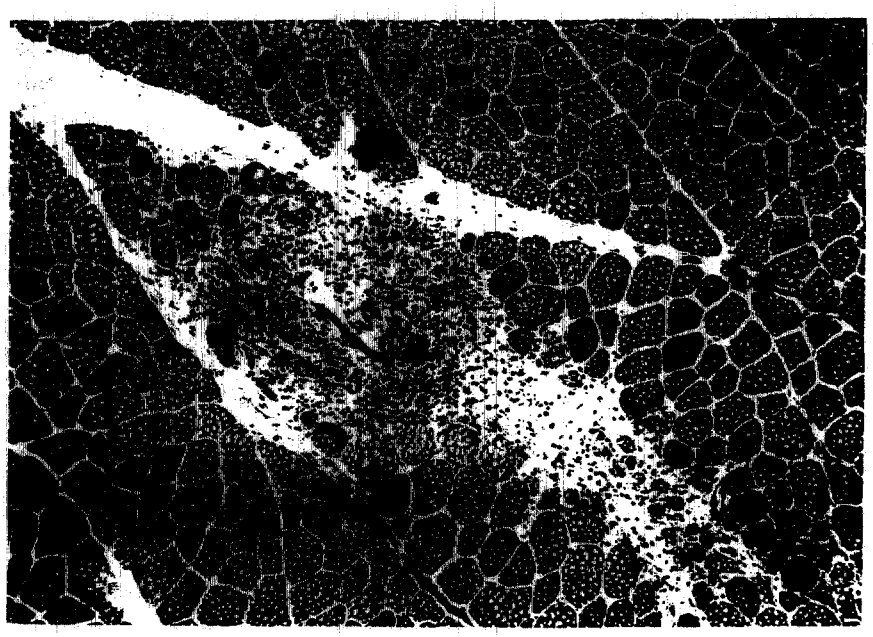


FIGURE 3. Photomicrograph from active implant study. Tissue shown is taken from Section IV, in the region of the insulated portion of the electrode. Section stained with hematoxylin and eosin. The bar shown in the photograph is 100 μm in length.

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seen in this segment, but this appeared to be a random phenomenon. The average of the area measurements in Section IV, for the electrode constructed from 28 μm wire, was 0.53 mm^2 (s = 0.19, n = 7) and for the electrode constructed from 45 μm wire was 0.51 mm^2 (s = 0.13, n = 5). These values are not significantly different, and were averaged to yield a value of 0.52 mm^2 (s = 0.16, n = 12). The significance of this damage can be assessed by estimating the force loss incurred by a muscle losing a similar amount of contractile tissue. Assuming a muscle force production of 2 kg/cm^2, a force loss of approximately 10 gm would occur. A force loss of this value would not be detected for most muscles.

The averaged results, obtained by combining the measurements taken from Sections II and III for both the 28 μm wire and the 45 μm wire, are graphically presented in Fig. 4. Damaged area measurements taken for experiments performed at 0.1 and 0.2 μC/mm^2 (50 and 100 μsec pulse durations), were not statistically different from the control results. Microscopically, the results were indistinguishable. At charge densities of 1 and 2 μC/mm^2 (500 to 1000 μsec), the results from muscles stimulated with biphasic pulses (net charge per pulse = 0) were not statistically different from the control. It was however, noted that during the biphasic experiments (only at the 1 to 2 μC/mm^2 level) an electrode would occasionally fail (appearing to open circuit) before the end of the six-hour stimulation period. Failed electrodes, at the time of removal from the muscle, all appeared both corroded and broken at the junction between the insulated region and the 10 mm deinsulated tip.

The results obtained with monophasic stimulation in the 1 to 2 μC/mm^2 range showed substantial increase in areas showing damage. In addition to a large increase in the average area, there was also a marked increase in the standard deviation. Microscopic observation indicated a large number of necrotic fibers in the area of the electrode track. These areas were irregular in shape, and the electrode track was not necessarily centered in the damaged region. In those muscles in which the track ran close to an artery, the vessels almost always appeared involved. The vessels revealed pronounced proliferation of the muscular component and intimal fibrosis, as well as occasional complete occlusion of the lumen (Fig. 5). Vascular damage was only seen in sections stimulated with monophasic pulses in the range 1 to 2 μC/mm^2. We conclude that the large area of muscle fiber damage in those experiments is secondary to blood vessel damage.

Factor Causing Damage

The results suggest that, compared to biphasic stimulation, monophasic stimulation, particularly at higher charge densities, results in larger areas of damage. Electrochemical reactions at the electrodes are most likely to be involved in the damage process. Assuming that electrochemical reactions were perfectly reversible for biphasic stimulation, the difference between the two waveforms, manifest in the region of the electrode is likely to be

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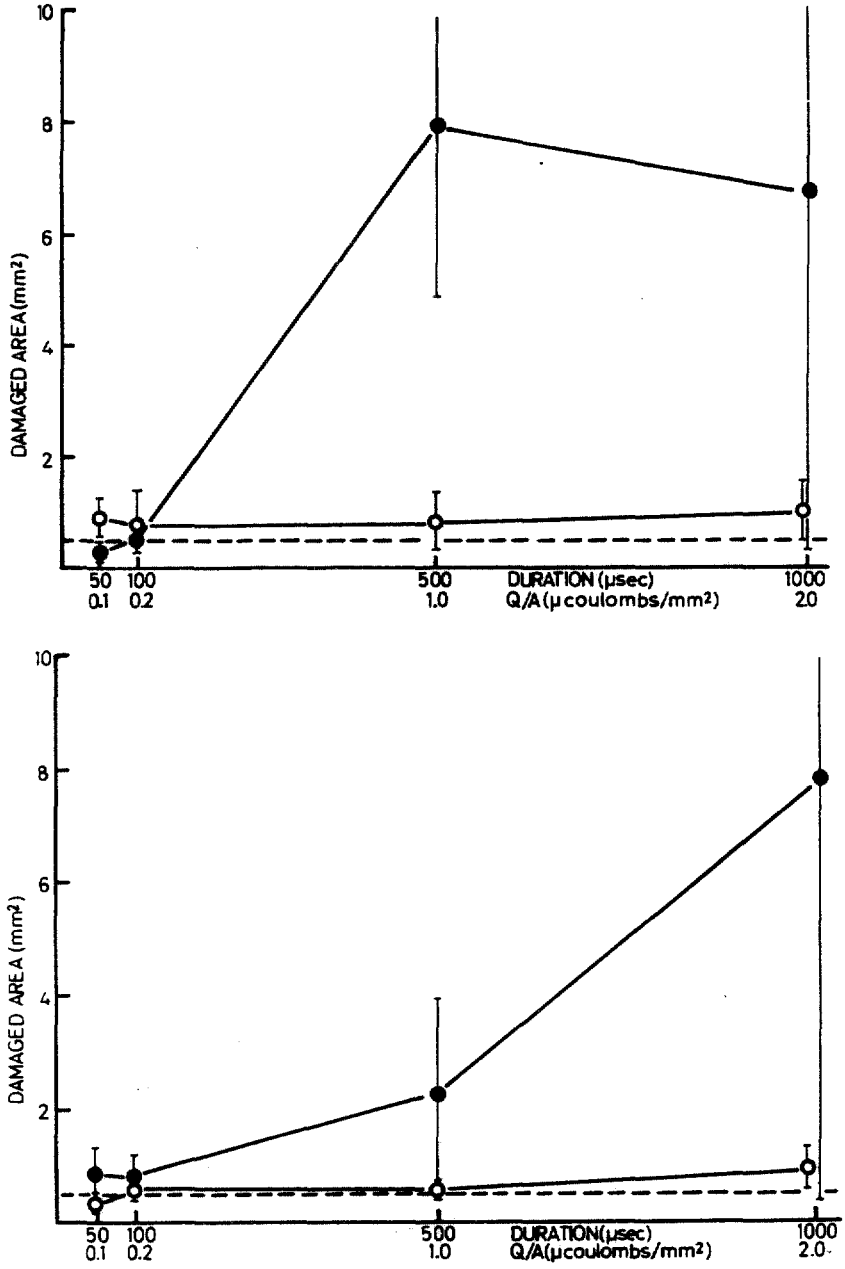


FIGURE 4. Graph of averaged results obtained from active implants. The average area occupied by abnormally staining tissue is shown on the vertical axis, as a function of pulse duration and charge density during the cathodic phase of the stimulus pulse. The average area measured in the insulated portion of the electrode track (control) is shown as a dashed horizontal line. Filled circles are results from animals stimulated with monophasic current pulses: open circles are results from studies involving balanced charge biphasic stimulation. Standard deviations for each datum point are shown as vertical lines. Data presented in (a) were obtained from studies employing 28 μm, 304 stainless steel wire, in the fabrication of the electrode. Data presented in (b) involved electrodes fabricated from 45 μm, 316 stainless steel wire.

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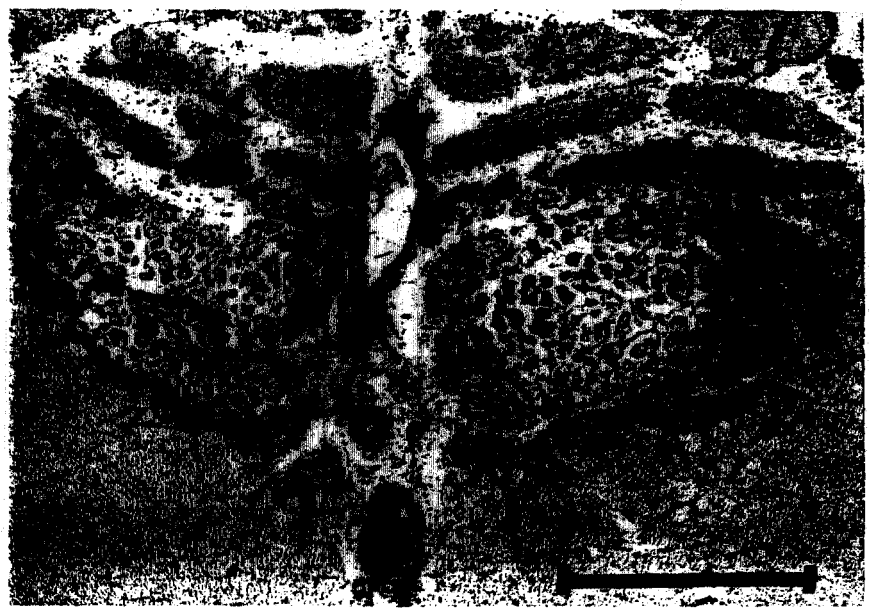


FIGURE 5. Photomicrograph from active implant study. Tissue taken from Section III (deinsulated region). Muscle stimulated with monophasic stimulation at a per pulse charge density of 1 $\mu C/mm^2$. Electrode fabricated from 45 μm wire. The section was stained with hematoxylin and eosin. The bar shown in the photogaph is 1 mm in length.

H_2 evolution (7) with monophasic stimulation. The H_2 evolution results in increased local OH^- concentration and higher local pH. Gas is not expected to cause mechanical damage because our *in vitro* studies show gas bubbles forming slowly around the electrode. Thus, it seems reasonable that the gas can be absorbed by the circulatory system.

Testing the rate of pH change *in vitro* for all waveforms evaluated in the *in vivo* studies yields the results shown in Fig. 6. A significant pH change occurs for all waveforms except biphasic stimulation in the 0.1 to 0.2 $\mu C/mm^2$ (rectangular phase) region. The rate at which the pH changes increases with increasing charge injection. However, the rate of pH change resulting from monophasic stimulation at the lower charge density was greater than that occurring with biphasic stimulation at higher charge densities.

The results of the *in vitro* pH study show that the pH changes for monophasic stimulation. Therefore, tissue damage must be related to the rate of pH change, rather than to the pH change itself. The results shown in Fig. 6 indicate that muscle tissue can tolerate (or buffer) pH changes occurring at rates corresponding to the 0.2 $\mu C/mm^2$ level (minimal tissue damage); but not at rates corresponding to the 1.0 $\mu C/mm^2$ level, where extensive damage was found to occur. The pH change, or H^+ concentration change, is related to charge density. The rate at which the H^+ concentration changes is equal to the time rate of charge injection, or to current density. Therefore,

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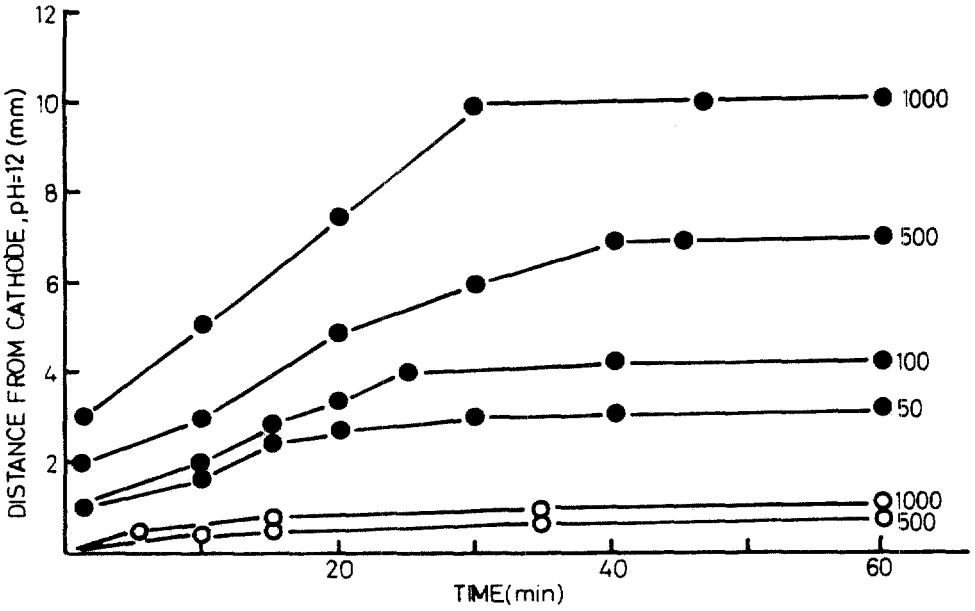


FIGURE 6. Results of *in vitro* pH measurements. The vertical axis indicates the distance from the cathode for which the pH reaches or exceeds 12 as a function of time (horizontal axis). Filled data points were obtained with monophasic stimulation, open data points with balanced charge biphasic stimulation. Pulse duration for each curve is given on the right hand side. The electrode area in each case was approximately 10 mm^2. Frequency of 50 Hz and amplitude of 20 mamp were applied in each case.

the results suggest that damage will not occur at average current densities less than or equal to 10 μamp/mm^2 (50 Hz, 0.2 μC/mm^2) but will occur at or above average current densities of 50 μamp/mm^2.

This hypothesis was tested in additional experiments conducted on three animals. In the first animal a constant 100 μamp cathodal current was applied for six hours to each of the six IM electrodes, each with 10 mm^2 of surface area. The resulting current density was then 10 μamp/mm^2. In the second six-hour study, the stimulus was monophasic, 20 mamp, 1000 μsec rectangular pulses at 5 Hz, rather than 50 Hz. The surface area of the electrodes was 10 mm^2. The average current density was then 10 μamp/mm^2. In the third experiment, monophasic, 20 mamp, 100 μsec pulses were applied at 50 Hz to electrodes with 2 mm^2 of surface area, rather than 10 mm^2. The reduced surface area resulted in an average current density of 50 μamp/mm^2 over the six-hour stimulation period.

The results of these tests, shown as closed circles in Fig. 7, indicate that average current densities of 10 μamp/mm^2 cause no increase in tissue damage over the control or passive implant; while average current densities of 50 μamp/mm^2 cause damage significantly greater than the control. The open circles and the control line in this figure are the averaged values taken from Fig. 4a and b.

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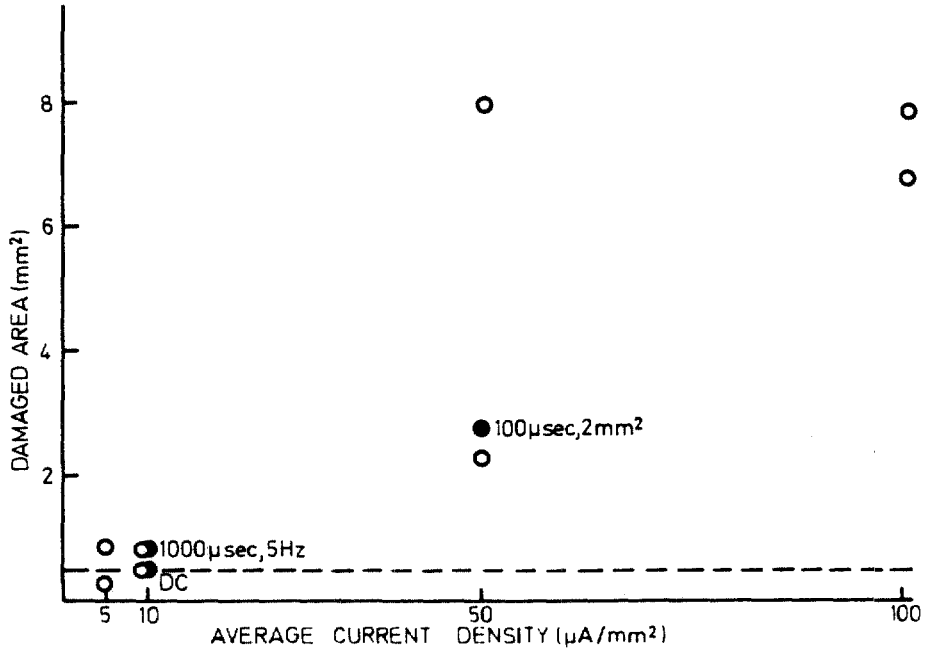


FIGURE 7. Tissue damage as a function of average current density. Open circles are the results obtained with monophasic stimulation, taken from Fig. 4a and b. Closed data points were obtained by altering the electrode area or frequency from the previous experiments, in order to adjust the average current density to a "safe" or "unsafe" value. The damage incurred in the insulated (control) region is shown as a dashed line.

Based on the results of these experiments, we conclude that continual stimulation at average current densities less than or equal to 10 μamp/mm^2 result in minimal damage to skeletal muscle. Short bursts at greater average current densities may be tolerated but cannot be recommended on the basis of these data. In most large muscles the loss of muscle tissue would not be considered significant. Further, damage to muscle fibers appears to be secondary to vascular damage and results when the OH^- generation rate exceeds the buffering rate of the body. One may logically assume more extensive damage when the stimulating electrode is adjacent to a relatively large arterial branch. A random spatial relationship between the electrode and local blood supply would explain the large standard deviation observed in the means for the higher areas of damaged tissue.

Electrode Corrosion

The tissue damage results obtained for biphasic stimulation strongly advocate the use of a biphasic waveform. However, the loss of the electrode through corrosion must also be avoided. Although most electrodes used in the biphasic studies showed no obvious signs of corrosion a few failed, demonstrating the presence of corrosion. Referenced to a saturated calomel

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electrode, voltage measurements of the electrode potential at the point of corrosion yield the following results:

Electrode	Corrosion Potential	Voltage Ramp Rate
1	+ 0.41 V	0.1 V/min
2	+ 0.39 V	0.5 V/min
3	+ 0.39 V	0.05 V/min

In observing the electrode potential (*in vitro*) of a series of 16 coiled wire electrodes, it was found that, for a fixed amplitude of 20 mamp, frequency of 50 Hz, and area of 10 mm^2, the average duration at which the anodic potential reached 0.40 V was 244 μsec (n = 16, s = 28, range from 200 to 320 μsec).

The "critical" pulse duration was evaluated by long-term *in vitro* tests at 200 and 500 μsec pulse durations; other parameters were the same as previously stated. These tests showed no evidence of corrosion occurring in six electrodes subjected to the 200 μsec pulse after seven days of 24 h, continuous stimulation (50 Hz, 20 mamp, 10 mm^2 area). However, all six electrodes studied at 500 μsec failed within 24 h, the earliest failure occurring after three hours.

The observation that the corrosion potential of stainless steel was achieved in these experiments at pulse durations between 200 and 500 μsec explains why the change in pH was observed to occur in the 500 and 1000 μsec range, but not at the 50 and 100 μsec *in vitro* studies. Irreversible reactions occurring during the cathodic phase (H_2 evolution and OH^- formation) are balanced by the irreversible reactions which occur during the anodic phase (corrosion).

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electric field vector always lies in a plane parallel to the coil plane. Since the slices where the field is computed are all parallel to the coil plane, the field shown is the total electric field; there is no out-of-plane component. This figure illustrates that the current (which is everywhere parallel to the electric field) flows in circular loops that are strongest near the top of the sphere (closest to where the coil is located) and flow in a direction opposite that of the coil current. The scale is computed from the assumption that the coil is excited from a 500-μF capacitor charged to 500 V, coupled through a 5:1 lossless transformer. The peak di/dt in the one-turn is 5.5×10^8 A/s, and goes to zero in abaut 74 μs. The field shown is computed at the point in time when di/dt is maximal. The maximum electric field strength inside the sphere is 760 V/m directly beneath the coil winding at the sphere boundary.

Figure 9.23 shows the induced electric field from a different coil. This figure has the same 11-cm-diameter sphere, but has a double square-shaped coil 5 cm on an edge located 1.5 cm above the conducting sphere. The currents in the coil flow in the directions indicated by the arrows on the coil. The center conductor is made of two wires, each carrying a current equal to that of the outer conductors. For this arrangement, the boundary conditions significantly affect the total field. Unlike the previous example, the electric field is not always parallel to the coil plane. The field shown in Fig. 9.23 is computed assuming the same driving circuit as the previous example. The peak di/dt in the coil is 2.3×10^8 A/s, and goes to zero in about 115 μs. The electric field in the sphere is strongest (665 V/m) at the top boundary of the sphere directly beneath the center of the coil where the two squares adjoin. The return path for the current in the center region is complicated. The current divides in three main directions: to the right, to the left, and down. Because of this dispersion of the return path, the central current is much stronger than the current in other regions, producing a more focal stimulus. The strong central current magnitude decays rapidly with depth, much more so than with the circular coil. The current near the boundary away from the strong central current does not decay as rapidly with depth, because it is the return current path for both the central current at the given depth as well as currents above it.

10

High-Voltage and High-Current Injuries

MICHAEL A. CHILBERT

10.1 Introduction

Several modes of injury can result from electrical accidents, including tissue destruction, cellular excitation, and trauma secondary to the passage of current. Thermal injuries in the extremities can lead to amputation because of the deep nature of the burn. Cell lysis can also destroy tissue if there is a sufficient electric potential across the cell membrane. The effects of lysis are sometimes delayed. Cellular excitation of muscle and nerve can lead to fibrillation or transient neural dysfunction. The leading cause of death from electricity is attributed to fibrillation. Secondary injuries result from flash burns, falling, or gross contraction of the voluntary muscles.

Electrical accidents result in nearly 1100 deaths per year in the United States, 10% of which are caused by lightning. One-third of these deaths are caused by voltages below 1000 V occurring in the home and workplace. Low voltages account for more than half of the industrial deaths (Dalziel, 1978), High-voltage deaths are typically from industrial accidents. About 2% of low-voltage accidents and 10% of high-voltage accidents are fatal.

The number of accidents resulting in survivable injury are not consistently documented, because victims are not admitted to the same critical-care areas within a given facility and those not surviving at the scene are not admitted. Victims of severe burns are, of course, admitted to burn-care units, while those afflicted only with cardiac maladies are not. Typical injury reports include only the burn victims. One reason for this is that the management of electric burns is complicated and the evaluation of the burn's extent is very difficult and may require multiple procedures.

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Electric burn injuries account for 4–6% of all admissions to burn-care facilities (Hammond and Ward, 1988; Hunt et al., 1980; Rosenberg and Nelson, 1988). These burns cover an average of 12% of the body surface area (BSA) but result in limb amputation for 50–70% of the cases. The average BSA resulting in subsequent death is only 34%, compared to a much higher BSA percentage for thermal burns.

This chapter emphasizes electrical burn injury and its theoretical basis. The physical parameters affecting the character of injury and including impedance considerations and current distribution throughout the body are also included. Discussions of thermal and nonthermal trauma follow. Lightning injuries often have unique characteristics and traumatic sequelae; these are to be discussed as well. Important to the pathophysiology of electric trauma are the clinical observations and treatment of the accident victim.

10.2 Modes of Injury

The following sections provide background for the forms of trauma seen clinically. Thermal trauma has the greatest consequence to survivors of electric accidents; loss of limb is often the result. Nonthermal trauma has the form of lesions in neural and connective tissues. Lightning injuries often involve lesions exclusive of burns. Other trauma affects the heart rhythm and can result in fibrillation.

Thermal Injury

Thermal injury is caused by heating of tissue from the passage of current. The amount of heat generated in the tissue depends on spatial and temporal patterns of current density and tissue resistivity. The current density and resistivity are, in turn, affected by the heat generated in the tissue. Consequently, the process of thermal injury involves a feedback process.

The calculation of the heat generated in the tissue is given in terms of energy density:

$$Q_j = J^2 \rho t \tag{10.1}$$

where Q_j is the thermal energy density (J/cm^3), J is current density (A/cm^2), ρ is the resistivity (Ω/cm), and t is the duration of application(s). From this equation the temperature increase in the tissue can be determined. In its simplest form the thermal energy density can be related to the change in temperature in the following manner:

$$Q_j = pc\Delta T \tag{10.2}$$

where p is the tissue density (g/cm^3), c is the specific heat of tissue (J/g °C), and ΔT is the temperature change (°C). Equation (10.2) assumes that there

are no thermal losses by conduction to adjacent media, by convection into nonstationary media, or by convection or radiation into air. In other words, all boundaries of the specific volume are adiabatic, and there are no internal heat sinks or sources in the volume. By solving for the change in temperature using Eqs. (10.1) and (10.2),

$$\Delta T = \frac{Q_j}{pc} = \frac{J^2 \rho t}{pc} \tag{10.3}$$

the result gives a greatly simplified equation for the temperature change in tissue. Equation (10.3) illustrates the primary relationship among the current density, resistivity, the duration of current, and the resulting change of temperature. Thermal injury depends on the duration of exposure and the temperature (Henriques, 1947; Henriquez and Moritz, 1947). The temperature threshold for cutaneous thermal damage is about 44°C, indicating that thermal injury will not occur below this temperature. Cutaneous burns occur when the temperature is elevated for a sufficient length of time: 45°C requires more than 3 h, 51°C requires less than 4 min, and 70°C requires less than 1 s for injury (Henriques, 1947; Henriques and Moritz, 1947). Temperature levels that cause injury in other tissues are similar, as is the injury rate for a given temperature. Electrically induced thermal injury of muscle begins at 43°C with a 1-A current in the limb for 15 min, and at 46°C the tissue damage is much greater (Chilbert et al., 1985b). Electrically induced thermal damage to peripheral nerve has been noted to occur at 48°C after several seconds.

One important aspect of electrical burning is the rate at which heat is deposited and removed. The deposition of heat is dependent on the current density and resistivity. Resistivity decreases temperature, causing further increases in current density and temperature. This aspect of resistivity change is rarely considered in burn models because of the resulting nonlinear equations. Heat is removed from the tissue by conduction into adjacent tissue, by convection and radiation into the air at the surface, and by blood flow. To account for conduction and blood flow effects, one can expand Eq. (10.2) into:

$$pc\frac{\partial^2 T}{\partial t^2} = k\frac{\partial^2 T}{\partial x^2} + k\frac{\partial^2 T}{\partial y^2} + k\frac{\partial^2 T}{\partial z^2} + wp_b c_b(T_b - T) + q_m + q_j \tag{10.4}$$

where T is the tissue temperature, k is the thermal conductivity of tissue, w is the blood perfusion rate, p_b is the blood density, c_b is the specific heat of blood, T_b is the initial temperature of blood, q_m is the volumetric rate of metabolic heat generation, and q_j is the volumetric rate of electrical heating. Note that the first three terms of the equation describe the tissue conduction and the fourth term describes the effects of vascular convection. Equation (10.4) is termed the *bioheat equation*, which was

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Table 10.1. *Thermal conductivity values (k) for skin, fat, and muscle*

Tissue or medium	Conductivity, $k \times 10^3$ (W/cm °C)
Amorphous	2.09
Skin	3.40
Fat	3.23
Muscle	5.00
Water (40°C)	6.32

Source: Data from Pennes (1948), Olsen et al. (1985), Song et al. (1988).

expressed in its initial form by Pennes (1948) and has been modified extensively for various applications (Song et al., 1988). Table 10.1 lists measured values of thermal conductivity for skin, fat, and muscle of human and hog tissues. These values have been used in thermal models as well. Values for the thermal conductivity of water are included for comparison. The thermal conductivity of blood used by Song et al. (1988) was 5.0×10^3 W/cm °C. Other parameter values used were $p_b = 1.05\ g/cm^3$ and $c_b = 3.8$ J/g °C. The value for w is 2–12 (ml blood)/(ml tissue)/s for dermal perfusion.

Lee and Kolodney (1987b) developed a unidimensional, axisymmetric model for the heating resulting from a high-voltage electrical contact in the upper limb. The limb was modeled as a coaxial cylinder having a 10-cm diameter and included layers to represent bone, muscle, fat, and skin of 1.0-, 3.5-, 0.3-, and 0.2-cm thicknesses, respectively. The bioheat equation used for this model included the term for electrical heating while neglecting metabolic heat. Lee and Kolodney show that tissue perfusion is critical for the removal of heat in the tissue, but does not significantly modify the heating process during the application of current.

Thermal injury due to the passage of current is dependent on the current path, which is determined by the contact points on the body (sometimes termed entry and exit sites). Once the current is inside the body, its distribution is determined by tissue resistivity. Early perceptions of current in the body stated that it would flow equally through all tissues or that it would flow along the path of least resistance (in the vessels and nerves). Both are wrong, but are still referred to in clinical reports. Experimental evaluation of the current path through the body has shown that the resistivity of each tissue in a given cross section determines the current distribution through the cross section (Chilbert et al., 1983, 1985b, 1988, 1989; Sances et al., 1981a, 1983).

Tissue resistivity is typically anisotropic; that is, the resistivity varies with current direction. For example, muscle has a lower resistivity along its fibers than across them, and skin has a high resistivity across its layers and a lower resistivity along its layers. Some tissues can be considered isotropic when no directional differences exist in the tissue. The implications of anisotropic resistivity in thermal burns is that the direction of current through a given tissue may explain selective tissue trauma seen away from the contact site. This selective tissue destruction is well documented in the clinical literature and is seen in muscle tissue near the bone (Artz, 1974, 1979; Hammond and Ward, 1988; Luce et al., 1978; Moncrief and Pruitt, 1971; Ponten et al., 1970; Rosenberg and Nelson, 1988; Sances et al., 1979; Wang et al., 1984, 1985, 1987; Zelt et al., 1988).

Selective thermal trauma can also be related to tissue resistivity changes with temperature and events at the contact site. As the tissue temperature increases, the resistivity decreases, altering the current distribution and subsequent temperature changes in the tissue. Contact site events that change the current distribution are desiccation and arcing. Desiccation of skin at the contact will cause the total current to decrease rapidly. This limits the contact time at voltages below 1000 V and the trauma is usually limited to the contact region. With higher voltages, arcing can occur over the desiccated tissue and alter the current path.

Electroporation

When the electric field strength across the cell membrane is sufficiently large, the cell membrane will rupture and cause cell lysis (Lee and Kolodney, 1987a). The process that causes cellular rupture is called *electroporation*, which is an increase in membrane permeability due to development of aqueous pores in the membrane (Lee et al., 1988). Electroporation of the cell membrane leads to rupture when the pore size becomes large enough or when fusion of several pores occurs. Calculation of the membrane potential uses cable theory, which is discussed in Chapter 4, and depends on the cell length, cell diameter, the internal fluid conductivity, the membrane conductivity, and the thickness of the cell membrane.

The membrane potential causes the pore size to increase proportionately until an irreversible state is reached. This state occurs when the pore size reaches a diameter of one-half the thickness of the membrane. The membrane potential causing ruture is in the range of 800 to 1000 mV. Reversible electroporation has been noted to occur below a 200-mV membrane potential. The incidence of pores has been evidenced by experimentally observed increases in membrane permeability, but the exact

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mechanism of electrical membrane failure has not been determined (Lee and Kolodney, 1987a). Theoretical analysis of the membrane potential uses cable theory, which is discussed in Chapter 4, and has been derived for electrical injury situations by Gaylor et al. (1988).

The role of electroporation in electrical injury is related to the electric field strength in the biological medium. Studies of muscle cells in culture by Lee et al. (1988) have shown that an electric field strength between 50 and 300 V/cm will disrupt cells of 1 mm. This is consistent with values of the membrane potential of his earlier study (Lee and Kolodney, 1987a). For smaller cells, such as fibroblasts of 10-μm diameter, the electric field strength that causes rupture exceeds 1000 V/cm. The relation of this data to accident victims is given in Sec. 10.5. The membrane potential is dependent on the cell length, cell diameter, and membrane thickness until the cell is electrically long, after which the membrane potential depends on the length constant and the electrical field strength (see Chapter 4). Muscle cells greater than 1 cm in length can be considered electrically long. For small cells the membrane potential depends mostly on length, while for longer cells it depends on the diameter and for medium-length cells the dependence is on both (Gaylor et al., 1988). The electric field needed for electroporation decreases as temperature increases. Consequently, the tissue trauma caused in a region of elevated temperature is related to both electroporation and temperature.

Fibrillation

The effects of electricity on the heart have been thoroughly discussed in Chapter 6. This chapter will focus on short-duration, high-voltage, and high-current applications. Power-line accidents typically result in severe burns, whereas household voltages result in fibrillation (Sances et al., 1979). Most deaths at power-line voltages are attributed to burns or to secondary trauma such as falling. Severe burns or complications arising from them are the causes of death in the hospital. Rarely is instantaneous death attributed to fibrillation at high voltages, yet several case reports of latent cardiac anomalies have been published (Ahrenholz et al., 1988; Dixon, 1983; Guinard et al., 1987; Hammond and Ward, 1988; Rouse and Dimick, 1978; Wilson et al., 1988). The minimum fibrillation level, as discussed in Chapter 6, is well documented; several equations to approximate its character with application time have been published. Similarly, nonfibrillating and defibrillating levels have been documented. However, fibrillation can occur at high current levels with very short application times, suggesting that these levels are not constant and may vary in a similar fashion to the minimum fibrillation level.

Reports on the experimental evaluation of fibrillation began before the beginning of this century. Ferris et al. (1936) published a comprehensive study on fibrillation from currents up to 17 A for a duration of 0.3 s. Until recently, most studies of fibrillation have used current levels below 10 A to delineate minimum electrical thresholds for the cardiovascular system. Kouwenhoven (1964) reported that fibrillation does not occur above 7.5 A when the contact lasts longer than 1 s. Since 1980 this author and co-workers have been involved with the study of electrical injuries and current pathways associated with high voltages and currents (Chilbert et al., 1983, 1985a, 1985b, 1988; Prieto et al., 1985; Sances et al., 1979, 1981a, 1981b, 1981c, 1983). It was noted that fibrillation often occurred at current levels greater than 10 A, and one study investigated high-current fibrillation in hogs (Chilbert et al., 1989).

In the high-current fibrillation studies of the authors and co-workers, the current delivery system supplied 1.5 to 200 cycles of 60-Hz currents between 1 and 51 A at voltages between 500 and 6000 V. The current was applied during the preselected cardiac cycle through a triggering circuit synchronized with the cardiac waveform (Chilbert et al., 1988). Nineteen fibrillations occurred in 67 runs performed on 20 animals. Two fibrillations were induced with currents starting in the QRS interval, lasting 25.5 cycles, and occurring in animals that had been previously defibrillated. One fibrillation associated with the P wave lasted for 200 cycles at a current of 3 A. The fibrillation associated with the T–P interval was at 51 A, six cycles long, and was a first fibrillation; however, its point of initiation was at the end of the T wave (Fig. 10.1); the actual occurrence of the T wave could only be approximated by temporal extrapolation. Results show that 18 out of 32 short-duration runs involving the T wave caused fibrillation; 9 fibrillations out of 14 runs occurred below 10 A and 9 out of 18 occurred above 10 A. As the current increases, the likelihood of defibrillation increases (see Chapter 6). This also indicates that the likelihood of fibrillation decreases with current amplitude and has been noted by others (Dalziel, 1968, 1972; Geddes et al., 1986). The short-duration applications used here were always less than one complete cardiac cycle (excluding the run of 200 cycles).

The work of Ferris et al. (1936) has shown that, for current durations of 30 ms (about 2 cycles at 60 Hz) during the sensitive intervals, fibrillation can be induced by 15-A, 60-Hz currents in sheep. They also noted that the high-voltage, short-duration shocks do not show a cumulative effect (i.e., increase fibrillation's rate of occurrence), and that normal cardiac rhythm returned within 5 min in the nonfibrillating runs. Of 913 runs in 132 sheep, only 100 resulted in fibrillation. They recorded 11 fibrillations

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out of 16 runs at 4 A, 6 fibrillations out of 17 runs at 12 A, and one fibrillation out of 51 runs at 24 A. This shows a decrease in the likelihood of fibrillation as the current level increases; the occurrence at 25 A is about 10 times less than that at 5 A. This is consistent with the hog data above. For currents of 4 to 14 A applied for 30 ms during the other intervals of the cardiac cycle, no fibrillations were recorded; however, 4-A currents applied for 150 ms to 260 ms did cause occasional fibrillations.

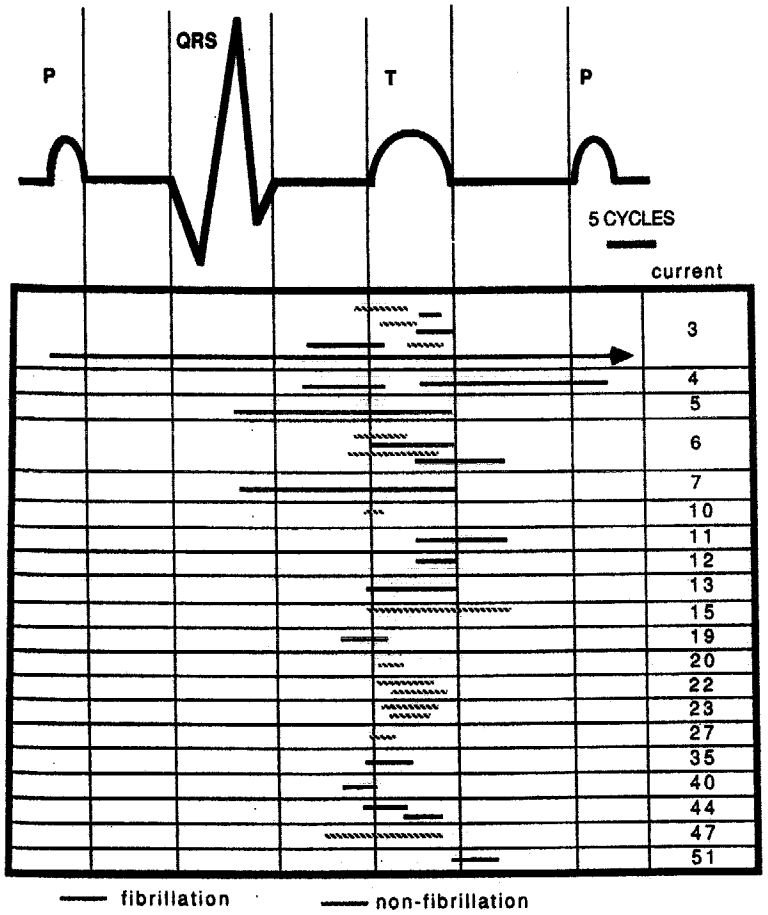


Figure 10.1 Occurrence of fibrillation during specific periods of the cardiac cycle. Current applications causing fibrillation all are associated with the T-wave period. Fibrillation occurs less frequently at higher current levels. All currents involve the cardiac cycle shown if normal cardiac rhythm is extrapolated past the onset of current. (From Chilbert et al., © 1989 IEEE.)

Table 10.2. *Heart/body ratio of animals and humans*

Species	N	Average weight: Heart (g)	Average weight: Body (kg)	Ratio (%) heart/body
Human	*	280	70	0.40
Hog	9	300	79	0.38
Dog	10	170	22	0.77
Sheep	25	270	56	0.48
Calf	10	420	70	0.60

Source: Data from Ferris et al. (1936), Chilbert et al. (1989).

The Ferris study tabulated body weight and heart size of sheep, hogs, dogs, and calves. One important aspect of body weight and heart size is the ratio between the two (Table 10.2). This ratio suggests that, for similar body weights, the hog heart is closest in size to the human heart, since the body weight and the ratio are very similar. The thoracic circumference of hogs and humans is also comparable for specimens of the same weight, although the cross-sectional arrangement of organs and other tissues is different. The similarities of ratio and circumference suggest that the hog is an excellent model for fibrillation in humans. Also, the results of Ferris et al. (1936) show that hogs tend to fibrillate at lower-than-average current levels, thus making the hog a conservative model for ventricular fibrillation.

The statistical inference of the current is useful for development of safe circuitry, but the occurrence of fibrillation is more accurately based on the current density in the heart. However, voltage is usually the only known electrical parameter in the accident situation, and the total current can only be estimated. Consequently, the current density in the heart is entirely unknown. If one could estimate the current density in the heart, the probability of fibrillation could be predicted more accurately.

10.3 Impedance Considerations and Current Distribution in the Body

The ensuing sections will present first the total body impedance and the effects of current and voltage on it. The total body impedance will then be analyzed in terms of the contact impedance and segmental body impedances. The segmental body impedance can be further analyzed in cross section, and the current density levels in various tissues and organs will be presented.

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Total Body Impedance

The current that flows through the body in high-voltage and high-current injuries is determined by the total body impedance and its change with time. The voltage is typically constant in electrical injuries and fluctuates only when the maximum power of the source is reached (Sances et al., 1981b). The minimum total impedance typically assumed for low-voltage electrical accident analysis is 500 Ω (Dalziel, 1978; Taylor, 1985), and variations to this value are discussed in Chapter 2. At high voltages the total impedance of the body is less in short-duration contacts, while for longer durations the values increase with time.

Figure 10.2 depicts the current-time relationship for electrical contact at three low-voltage levels. The current amplitude can be separated into three phases determined by its rate of change with time. The initial phase occurs as the contact is established (the contact impedance is rapidly reduced), sometimes termed the breakdown of the electrode–skin interface. The middle phase is the phase of maximal current flow. Increases during the middle phase can be attributed to heating of the tissue near the electrode contact and in cross sections where large current densities occur. The final phase occurs when the tissue under the electrode becomes highly resistive

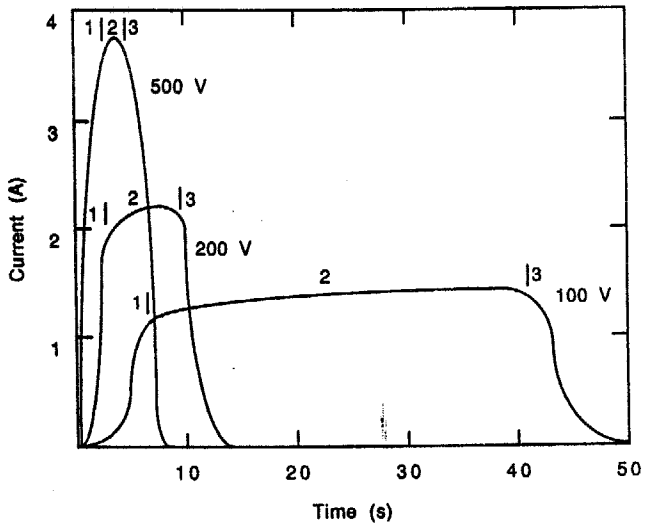


Figure 10.2 Relationship of current to time for a 5-cm disk in contact with the skin of a hog at different voltages. Note that an increasing voltage results in a decrease in the effective application time. Each trace shows the triphasic characteristics for current, which are the initial phase (1), middle phase (2), and final phase (3), as described in the text.

Table 10.3. *Measured changes with voltage in the hog*

Volts	*n*	Effective application time (s)	Maximum applied current (mA)	Minimum total resistance (Ω)	Total energy (J)
75	13	205	721	104	8773
100	14	92	806	124	6008
150	15	21	1087	138	2789
200	13	11	1227	163	2208
250	11	5.6	1471	170	1734

Note: Values for a 2.5-cm-diameter disk applied to the hindlimb with a large plate electrode on the other hindlimb.

and stops passing current, caused by desiccation or charring of the skin. The rate at which these three phases occur decreases as the voltage increases (Fig. 10.2). The three phases are present over a range of application times (Carter and Morely, 1969a, 1969b; Prieto et al., 1985; Sances et al., 1981a, 1981b). Application times for five voltage levels are listed in Table 10.3 and show the decrease in time with increasing voltage. Also note that the minimum total impedance increases with applied voltage. Similarly, the total energy decreases with increasing voltage. The changes in impedance and energy are caused by the rate of charring at the electrode site. The contact phenomenon of Fig. 10.2 is applicable for low voltages that do not support arcing.

High voltages and high currents are usually associated with arcing at the electrode site (Sances et al., 1979, 1981c). The initial and middle phases of the current-time plot can occur within milliseconds; the onset of arcing is the final phase. Voltages above 1000 V are sufficient to arc through air and desiccated skin. Once arcing is established, the arc length and internal impedance limit the current. Figure 10.3 shows that current falls with time when an arc is established, indicating that the arc length increases as tissue is burned away. The arcing appeared to occur over regions of uncharred tissue, taking the path of minimum resistance (Sances et al., 1981c). The tissue removal by the arc continues until the circuit is interrupted or the limb is transected. At 7200 V (Fig. 10.3), soft tissue was removed from the limb within 5 s; the remaining 11 s were required to transect the bone. At 14,400 V, limb transection time is about 3 s. Circuit interruption can occur when the nonconduction path length exceeds the voltage's ability to

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maintain an arc or by the standard means of a ground-fault interrupter, circuit breaker, or fuse (see Chapter 11).

Experimental studies of electrical burn injury have been performed in the hog, since this animal approximates the human in skin, anatomy, weight, and cross-sectional dimensions better than other species. The total impedance of the hog at high voltages for different electrode types and locations is given in Fig. 10.4. This figure shows that a large contact (plate electrode) on the hindlimb decreases the total impedance and that forelimb-to-hindlimb impedance is greater that hindlimb-to-hindlimb impedance. This is further exemplified in Table 10.4, which shows a decreasing impedance with increasing contact area and perimeter. As the location of the band electrodes is moved up the limbs, the impedance decreases, which is consistent with observations made previously (Prieto et al., 1985; Sances et al., 1981b). The impedance also changes with the applied voltage level.

Impedance depends on both applied voltage and duration of application (see Fig. 10.10). At low voltages applied for long time periods (those that exceed the second phase), the impedance increases with voltage while the total energy decreases (Fig. 10.5a). The decrease in total energy with increasing voltage indicates less tissue heating at higher voltages (Table 10.3). For short periods of time ($t < 1$ s), the impedance is dependent on the initial phase of the current waveform (Fig. 10.2). The short-duration impedance at low voltages will therefore decrease as the voltage increases, which is evident in Fig. 10.5b. High-voltage impedance changes are similar to those of low-voltage changes. Short-duration contacts occurring in the

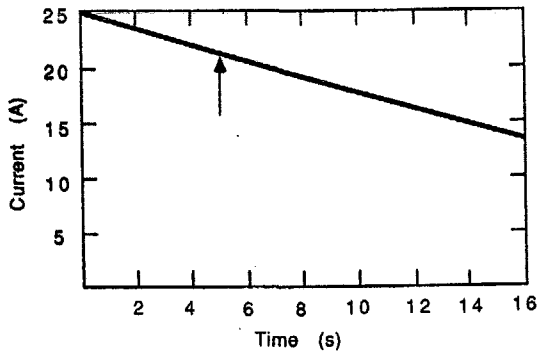


Figure 10.3 Current versus time of application for limb transection at 7.2 kV. Arrow indicates point of soft tissue removal; remaining time is needed to transect the bone. The initial value of current was 25 A and the final value was 14.8 A. The contact was between a wire contact on the hindlimb and a large plate under the other hindlimb. [From Sances et al. (1981b), © 1981 IEEE.]

first phase are typically less than 100 ms, and long-duration contacts would be denoted by the onset of arcing.

Body impedance varies with voltage, time of application, and contact parameters. Increasing the voltage increases the current and decreases the total impedance for short application times. The longer application times increased the peak current at lower voltages, since the tissue resistivity decreases with increasing temperature near the electrode sites. The electrode contact site on the limbs determined the contact area and the perimeter for the band electrodes (Table 10.4), and this affects the total current flow as well. In general, increasing the area and perimeter increases the current for a given voltage; consequently, the largest parts of the limbs had a greater contact area and perimeter and allowed greater current passage with the band electrodes. Also, the location of the contact on the body will affect the total abody impedance, since different current paths in the body have different impedances.

Contact Impedance and Segmental Body Impedance

Contact impedance will limit the level of current in the body, its duration, and its path, and the probable extent of trauma. The remaining portion of the total impedance can be divided into individual impedances for the various segments of the body. These segmental body impedances can be modified to account for tissue heating away from the contact points. Tissue heating decreases impedance, thereby increasing current. By

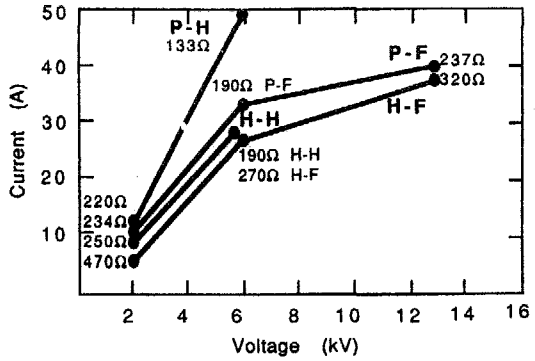
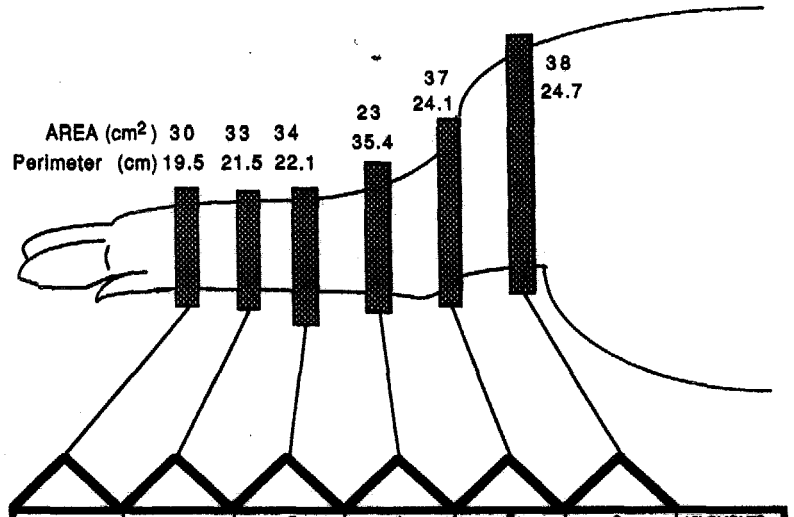


Figure 10.4 Current versus voltage for first contact in the hog. P-H is large plate electrode-to-hindlimb wire configuration, P-F is large plate electrode-to-forelimb wire, H-H is hindlimb-to-hindlimb wire contacts, and H-F is hindlimb-to-forelimb wire contacts. The plate was located under the hindlimb opposite the wire contacts. Total body impedances are shown for each measurement point and were determined from the average current for each run. [From Sances et al. (1981b), © 1981 IEEE.]

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Table 10.4. *Total body resistance (Ω) for band electrodes located on the hindlimb and analogously on the forelimb (8-cm disk electrode values d included for comparison)*



1	2	3	4	5	6	KILOVOLTS
				880 (d)		0.5
	490	444	366	268	235	1.5
	724	500		543 (d)		
558	485	429	300	230		3.0
492	450	379	297	200	166	4.5
	475	408	321	258		
			292	274		6.0

Source: Adapted from Chilbert et al., 1989.

combining information from the contact impedance and the segmental body impedances, one can better model the effects of electrical trauma.

Experimental evaluation shows that, for circular and elliptical contacts, the contact impedance is related to contact area and perimeter (Prieto et al., 1985). Figure 10.6 shows the relationship of total body impedance to the contact area and contact perimeter and gives their proportional relationships. Furthermore, the total impedance of the body can be described by the sum of the internal impedance and the contact impedance,

where the contact impedance can be expressed as

$$R_c = K(A)^{-1/4}(P)^{-1/2} \quad (10.5)$$

where R_c is the contact resistance, K is a constant of resistivity, A is the electrode contact area, and P is the electrode contact perimeter. For a circular electrode $R_c = 0.3K/r$, where r is the electrode radius. The constant of resistivity depends on the applied voltage, temperature, and skin condition (wet, dry, abraded, etc.). For electrode contact studies at 100 V and with a dry contact, Prieto et al. (1985) derived a value for K of 264 for areas between 0.3 cm^2 and 20.3 cm^2 and perimeters between 2 and

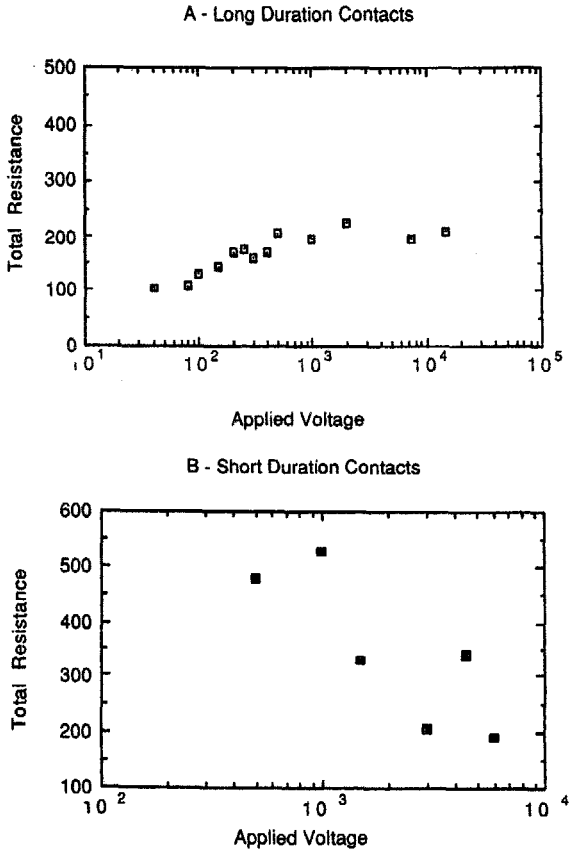


Figure 10.5 Minimum total body resistances for voltages applied between the hindlimb and a large plate on the opposite hindquarter. (a) Voltages were applied for long time periods (through the third phase of the current-time waveform). (b) Voltages were applied for short time periods (the frist phase of the current-time waveform).

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28 cm. The result of a least-squares linear regression fit of this equation to the experimental data gives a correlation coefficient of 0.94. As the electrode size increases in this model, the contact resistance approaches zero, leaving only the internal impedance to limit the flow of current.

Further analysis of the contact has been performed by using finite-element analysis on an axisymmetric model in two dimensions. Figure 10.7 shows the boundary and arrangement for the analysis of a circular disk containing the skin and includes tissue layers for skin, fat, and muscle. The model is based on a 5-cm-diameter disk with a potential of 100 V contacting the tissue, which is a nonhomogeneous, anisotropic, semi-infinite medium. Model parameters are listed in Table 10.5. The model includes analysis of surface and volume heat transfer effects and temperature-dependent resistivities. The tissue layers are each homogeneous, and the skin and fat layers have isotropic resistivities. The muscle resistivity is anisotropic (Fig. 10.1), with its transverse resistivity defined in the z direction and its longitudinal resistivity defined in the r direction. The thermal properties are isotropic in all tissues.

The model determines the current density and temperature distribution in the tissue. Plots of the thermal isoclines resulting after 5 s of contact are shown in Fig. 10.8a and after 9 s in Fig.10.8b. The thermal gradient emanates from the edge of the disk and proceeds somewhat concentrically

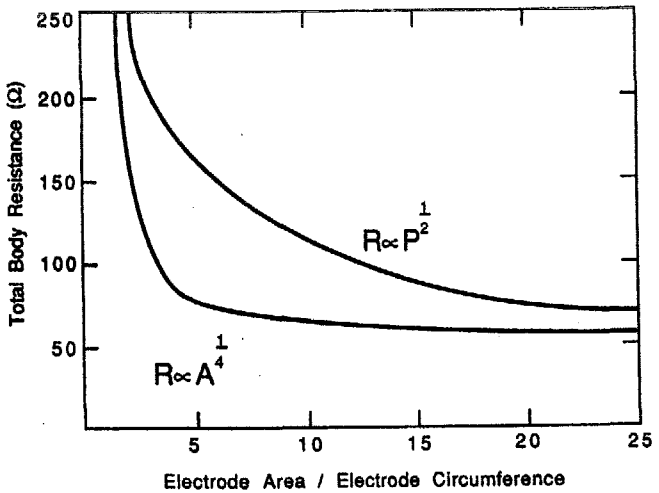


Figure 10.6 Total body resistance compared to electrode contact area and electrode contact circumference for circular and elliptical contacts. The proportional relationships indicate the best-curve fit of experimental data to the curves using a least-squares linear regression algorithm.

deeper into the tissue. Surface temperatures indicate a peak value at the edge of the disk (Fig. 10.9), showing the effect at the edge. The electrode edge effect of increased temperature has been shown experimentally by Sances et al. (1981) in saline and in the hog using a thermographic camera. The total current entering the tissue through the disk electrode is shown in Fig. 10.10. The model compensates for changes in skin that exceed 100°C by rapidly increasing the resistivity, resulting in a drop in the current after 9 s. This simulates desiccation of the skin comparable to experimental observations of Prieto et al. (1985). The analysis shows that the greatest temperature increase occurs under the edge of the disk and indicates that the current density is greatest at this region of the contact. Therefore, the majority of current entering the tissue does so near the edge of the electrode. More than 50% of the current entering the tissue enters in the outer 15% of the disk radius or in the outer 28% of the total area. These results indicate the importance of the circumference to the level of current that will flow into the body. Disk electrodes at high voltages of similar size to those used previously at household voltage levels show similar changes

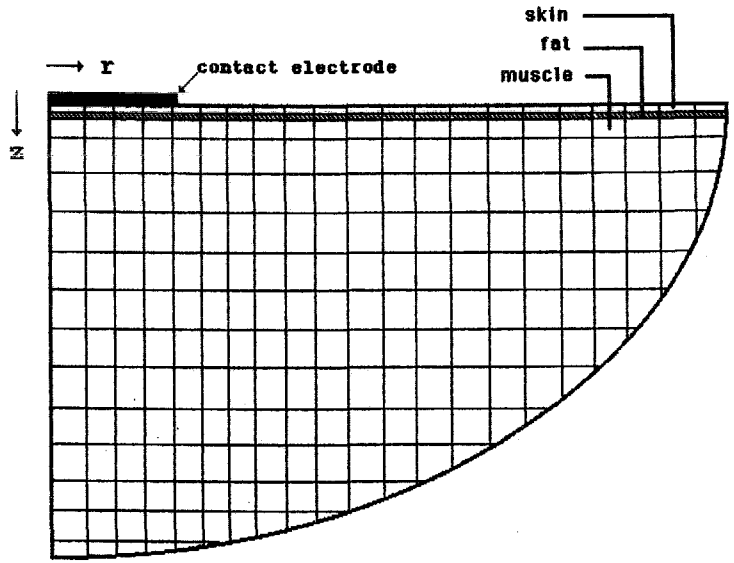


Figure 10.7 Geometric arrangement for an axisymmetric finite-element analysis of a disk on a three-layered, semi-infinite medium. The model contains three homogeneous layers for skin, fat, and muscle. The skin and fat layers have isotropic resistivity, while the muscle layer has anisotropic resistivity. The model includes surface and volume heat transfer effects and temperature-dependent resistivities. Thermal properties are isotropic in all tissues.

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Table 10.5. *Finite-element analysis parameters for a disk electrode in contact with a nonhomogeneous, anisotropic, semi-infinite medium used to model electric burn injury at the contact site*

Dimensions (cm)	
Disk radius	2.5
Skin thickness	0.15
Fat thickness	0.35
Dirichlet boundary conditions	
Ambient air temperature (°C)	25
Initial tissue temperature (°C)	37
Disk potential (V)	100
Reference potential (V)	0
Material properties	
Electrical resistivity (Ω cm)	
Skin	280
Fat	375
Transverse muscle	650
Longitudinal muscle	290
Thermal conductivity ($W\,cm^{-1}\,°C^{-1}$)	
Skin	0.037
Fat	0.020
Muscle	0.042
Density ($g\,cm^{-3}$)	
Skin	1.00
Fat	0.85
Muscle	1.05
Specific heat ($J\,g^{-1}\,°C^{-1}$)	
Skin	3.2
Fat	2.3
Muscle	3.8
Heat transfer coefficient: $13.45 \times 10^{-6}\,W\,cm^{-2}\,°C^{-1}$	

due to contact area and edge length, indicating that the results of the finite-element analysis are valid at high voltages as well (Chilbert et al., 1989; Prieto et al., 1985). Theoretical studies by Caruso and colleagues (1979) showed that current is concentrated at the edge of an electrode to a degree that depends on the conductivity layers beneath the electrode (see Fig. 2.9).

The internal impedance can be represented by segmental resistances of the body, making the total impedance determination independent of contact location. Each body segment can be modeled by either a constant resistance or a temperature-varying resistance. Figure 10.11 shows segmental resistance percentages for the human body based on the internal hand-to-hand values being 100%. The calculation of segmental impedance

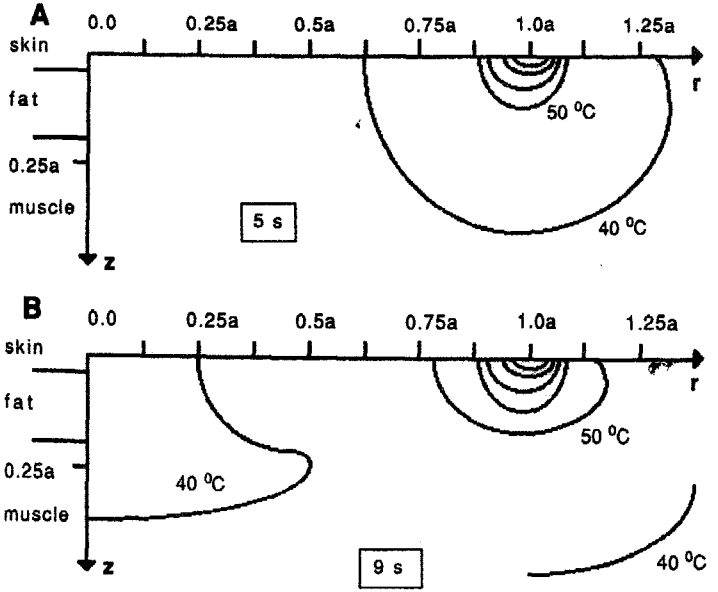


Figure 10.8 Results of the finite-element analysis showing thermal isoclines at (a) 5 s and (b) 9 s. isocline increment is 10°C per contour. The disk potential was 100 V, and the model continued until tissue temperatures exceeded 100°C. Current density levels under the disk are very similar to the thermal isoclines.

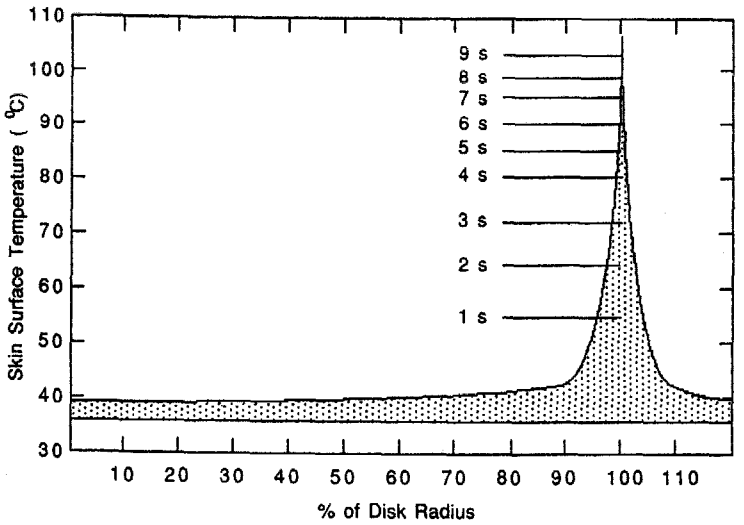


Figure 10.9 Temperature along the surface of the skin during the first 10 s of current flow. The graph approximates the transient temperature distribution for an isopotential disk of 100 V contacting a nonhomogeneous, semi-infinite medium. The peak temperature at the disk's edge is given for each second of contact.

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is then

$$R_s = R_{hh}\left(\frac{S}{100}\right) \tag{10.6}$$

where R_s is the segmental resistance, R_{hh} is the internal hand-to-hand resistance, and S is the segmental percentage in Fig. 10.11 for the desired

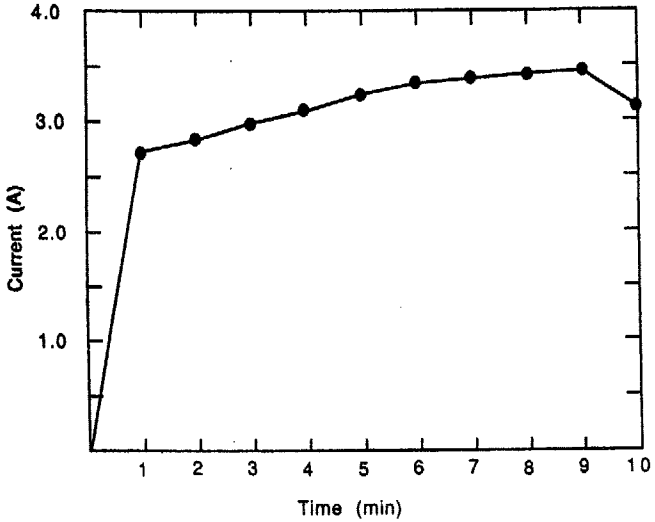


Figure 10.10 Total current flowing into the tissue from the 2.5-cm disk at 100 V for a 10-s contact. The current falls off after 9 s due to the skin temperature exceeding 100°C, when tissue desiccation would occur.

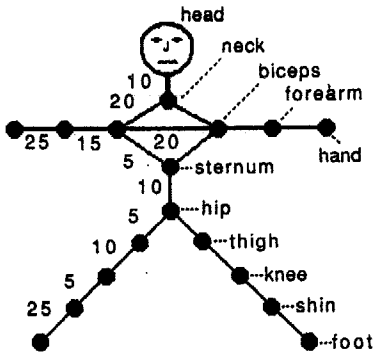


Figure 10.11 Segmental body resistances for the human body. Numbers indicate the percentage of the total internal hand-to-hand resistance between each of the designated parts of the body. Figure derived from Figs. 2.38 and 2.39 and from Biegelmeier (1985).

body segment. Chapter 2 gives some values for internal resistance in humans, but the evaluation of the contact impedance is usually quite different in those studies. The hand-to-hand resistance is used as a reference because most accidents involve a hand-to-hand contact. Experimental studies in the hog have shown that the total internal resistance is 370 Ω, the forelimb is 150 Ω, the hindlimb is 170 Ω, and the body impedance is 45 Ω. These measurements were made at voltages around 10 V and at a constant 60-Hz current of 7 mA.

Tissue resistivity is inversely related to temperature. The slow rise in current during phase 2 (Fig. 10.2) is likely the result of decreasing resistivity with increasing temperature. Body segments in contact with the electrodes, or otherwise subject to temperature change, can be modeled with a variable resistance value that is temperature-dependent. Each segmental body resistance can be modified to change with temperature using the following equation:

$$R_{ts} = R_s(1 - 0.025\,\Delta T) \tag{10.7}$$

where R_{ts} is the resistance modified by the temperature change ΔT. Experiment shows that increasing temperature decreases resistivity at a rate of 2.5% per °C, which is about 5 Ω cm/°C for muscle tissue (Chilbert et al., 1983, 1985b). At low voltages, heating occurs in the vicinity of the contacts, if at all. High-voltage tissue heating occurs around limb joints, at the contact sites, and in regions of small cross-sectional area. Changes in the overall resistance will increase the total current flowing through the body and likewise increase the tissue current density. Since tissues in a given cross section have different resistivities, there will be different current densities in the different tissues; thus, specific heating in the tissues will also be different. This leads to nonuniform heating and tissue trauma.

Tissue Current Densities and Current Distribution

The extent of thermal trauma and the likelihood of fibrillation depend on the current density in tissue and current distribution in the body. Current densities have been measured in the tissues of the limbs in hogs using a constant-current source (Chilbert et al., 1985a, 1985b, 1989; Sances et al., 1981a, 1983). Figure 10.12 gives the limb current densities for given applied currents between the hindlimbs measured in the region of the hindlimb shown in Fig. 10.13. Table 10.6 lists values of current density and resistivity at specific applied current levels between the hindlimbs. The listed voltage values are initial values, since the voltage drops with time when the current is held constant. Table 10.7 gives tissue resistance, resistivity, current, current density, and energy density for

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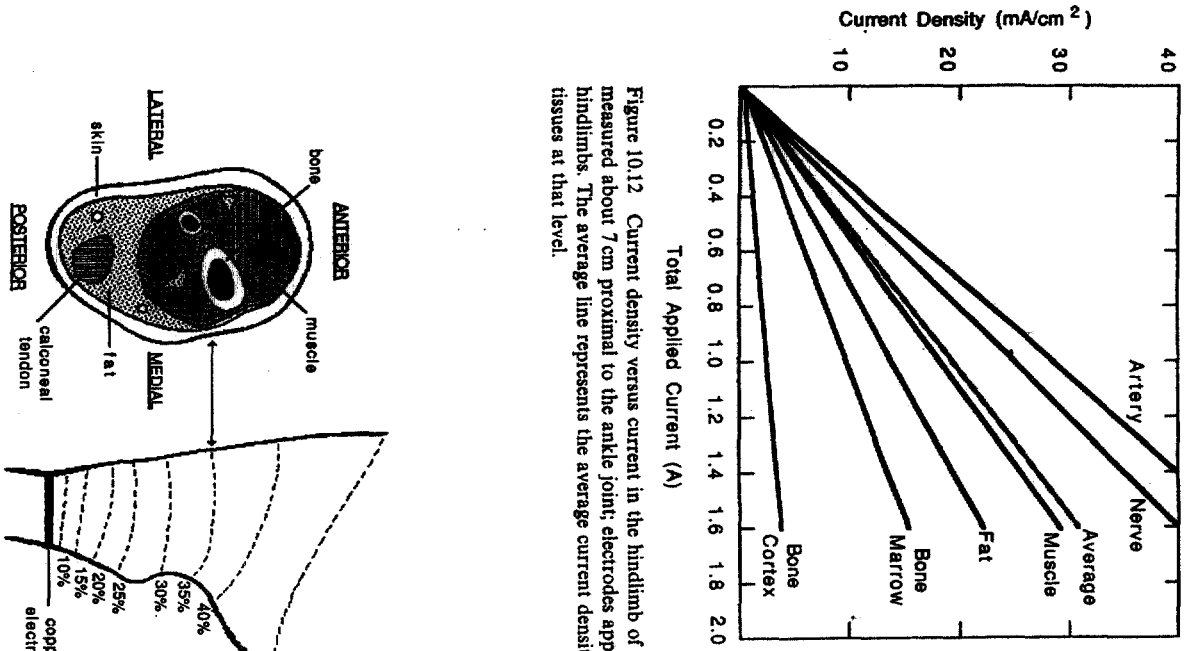


Figure 10.12 Current density versus current in the hindlimb of the hog measured about 7 cm proximal to the ankle joint; electrodes applied across the hindlimbs. The average line represents the average current density in all the tissues at that level.

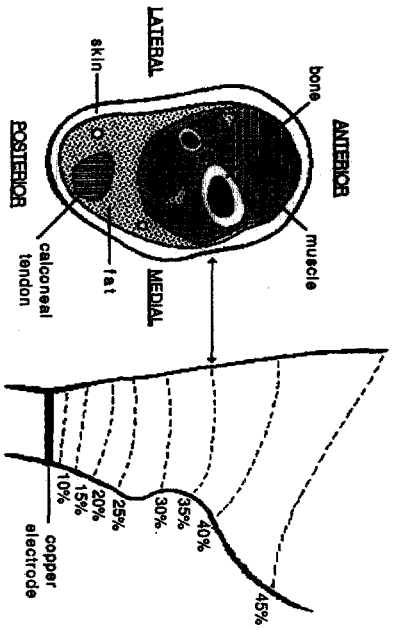


Figure 10.13 (a) Cross section of the hog hindlimb where current densities were measured. (b) Hindlimb location of measurement region shown with isopotential percentage lines of the applied voltage for electrodes placed on the hindlimbs.

Table 10.6. *Tissue current density and resistivity in the limb versus applied current from hindlimb to hindlimb in the hog*

Constant applied current (mA)	Initial applied voltage (V)	Artery		Nerve		Muscle			Fat		Bone marrow		Bone cortex	
		J	ρ	J	ρ	J_L	ρ_L	ρ_T	J	ρ	J	ρ	J	ρ
10	6	0.32	147	0.26	201	0.18	296	512	0.12	375	0.10	550	0.03	1828
30	15	1.18	145	0.86	209	0.50	282	525	0.43	360	0.27	531	0.09	1880
100	45	3.4	152	3.0	191	2.0	295	483	1.5	352	1.0	535	0.30	1832
300	135	9.8	140	8.7	197	7.0	287	501	4.9	377	3.1	547	0.85	1859
600	260	21.0	150	15.2	196	12.0	292	492	9.3	366	5.3	542	2.0	1876
1000	415	35.9	155	27.1	200	19.5	290	650	13.4	386	8.1	525	2.8	1836

Note: J in mA/cm^2, ρ in Ω cm, J_L = longitudinal current density, ρ_L = longitudinal resistivity, ρ_T = transverse resistivity of muscle.
Source: From Sances et al., 1983.

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Table 10.7. *Typical values measured in the hindlimb cross section of the hog*

Tissue	Tissue resistivity (Ω cm)	Tissue resistance (Ω)	Current density (mA/cm²)	Tissue current (mA)	Tissue area (cm²)	Energy density (J/cm³)
Vessel	155	911.76	51.61	8.77	0.17	412.90
Nerve	200	1666.67	40.00	4.80	0.12	320.00
Muscle (L)	290	19.24	27.59	415.72	15.07	220.69
(T)	650	—				
Fat	380	31.77	21.05	251.79	11.96	168.42
Bone marrow	550	495.50	14.55	16.15	1.11	116.36
Bone cortex	1850	898.06	4.32	8.91	2.06	34.59
Tendon	398	196.19	20.09	40.78	2.03	160.70
Dermal layers	432	50.94	18.52	157.04	8.48	148.15
Average/ total	363	8.85	22.05	903.95	41.00	176.3

Note: Applied voltage = 400 V between the hindlimbs, current = 0.9 A. Electric field strength = 8 V/cm. Resistivity and current density were measured experimentally. Cross-sectional tissue resistance = (resistivity)(tissue area)/(length = 1 cm), tissue current = (current density)(tissue area), tissue energy = (current density)(current density)(resistivity)(time = 1 s). Cross-sectional areas were determined by digitization of a limb section taken through the measurement region. Averaged values are resistivity, current density, and energy density. Total values are resistance, current, and area.

one current application of 0.9 A with an initial voltage of 400 V. This table shows how the current is distributed through the cross section of Fig. 10.13 before tissue trauma and heating alters the current path. Current density in the limbs is more likely to change at high current levels than in the body because significant heating occurs almost exclusively in the limbs and at the contacts.

Current density measured in the body structures is given in Table 10.8, along with the corresponding resistivities. Linear extrapolation of current densities (as in Fig. 10.12) in the body for higher levels of current is accurate, since the tissue temperature in the body changes minimally. The largest current densities are found in the back region. The back muscle at the level of the upper lumbar region has a current density of 0.223 mA/cm², and the spinal cord current density is approximately 0.280 mA/cm² for the same region when a current of 100 mA is applied from the forelimb to the opposite hindlimb. Various current density levels in the spinal cord are reported in Table 10.9 for three different

Table 10.8. *Current density and resistivity in the hog for 100 mA applied from left forelimb to right hindlimb*

	n	J (mA/cm²)	S.D.		ρ (Ω cm)	S.D.
Ventral intestine	4	0.071	0.077		511	43.1
Dorsal intestine	4	0.077	0.049		610	96.9
Back muscle:						
Neck	1	0.021	—		—	—
Upper thoracic	1	0.061	—		—	—
Middle thoracic	1	0.141	—	Longitudinal:	270	—
Upper lumbar	4	0.223	0.079	Transverse:	1006	58.6
Lumbosacral	1	0.055	—			
Kidney	4	0.097	—		447	61.2
Liver	4	0.065	—		570	37.5
Lung	4	0.058	0.033		1605	42.8
Heart (transverse to axis)	4	0.073	0.044		800	—
Abdomen, midline (skin, fat, muscle layers)	4	0.065	0.032		547	28.6
Abdomen, side (skin, fat, muscle layers)	4	0.076	0.028		560	42.0

Note: Current density in back muscle as measured in the longitudinal direction.
Source: From Sances et al., 1983.

Table 10.9. *Spinal cord current density for 100 mA applied across the limbs*

	Transverse J (mA/cm²)	Longitudinal J (mA/cm²)
Forelimb–forelimb		
Cervical	0.0155	0.0247
Thoracic	0.0022	0.0058
Lumbar	—	0.0011
Forelimb–hindlimb		
Cervical	0.0075	0.0708
Thoracic	0.0100	0.299
Lumbar	0.0080	0.257
Hindlimb–hindlimb		
Cervical	—	—
Thoracic	0.0008	0.0020
Lumbar	0.0057	0.0040

Note: Transverse spinal cord resistivity = 1970 Ω cm, longitudinal resistivity = 214 Ω cm.
Source: From Sances et al., 1983.

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contact orientations. High current levels in the spinal cord can lead to latent neural dysfunction (Sances et al., 1979). At a level of 10 A applied for 30 s, the spinal-cord temperature was elevated only 1.5°C, showing that temperature in the cord is not an important factor in its trauma (Sances et al., 1983). The cross-sectional area of the spinal cord is 0.07% of the body cross section, but the cord carries 0.12–0.15% of the total current.

Current distribution in the limb changes with time and temperature and is shown by the change in tissue current densities given in Table 10.10. Initial values of resistivity and current density are also shown in Table 10.7 for all tissues. Current shifts from artery, nerve, tendon, and dermal layers to muscle and fat. The increase of current in muscle and fat is due to increased temperature and tissue degradation. The decrease of current in the other tissues is due to an increase in resistivity or a slower decrease in resistivity. Nerve and vessel resistivities increase with temperature once tissue damage occurs, whereas muscle resistivity decreases with tissue damage. The ultimate distribution of tissue trauma is related to the peak temperature in the tissue. The peak temperature is determined from the energy density, which is affected by the resistivity and current distribution. However, the resistivity changes with temperature, thus altering the rate of temperature change. For muscle, where the resistivity decreases with temperature, the tissue damage occurs more selectively, as different parts of the muscle become damaged at different rates and enhance the current flow through the damaged regions. This phenomenon is the likely cause for selective muscle groups that are completely burned being next to groups having only minor trauma.

10.4 Thermal Trauma

Thermal burn injury is the most common trauma that occurs at high current and high voltage levels, although electroporation may also cause tissue damage. In this section the resultant electrical trauma will be referred to in terms of thermal burns. This section will discuss the anatomical and physiological aspects of electrical burns, which occur at the contact site, in the deeper tissues, around the joints, and in the spinal cord. Thermal trauma depends on the current density in the tissue more than the resistivity, as indicated by Eq. (10.1).

Heating at the Contact Site

Most burns are at or near the point of contact. When the injury current is high, then trauma can also be seen farther away from the con-

Table 10.10. *Simultaneous current density and temperatures 7 cm proximal to distal tibia versus time with 1-A current applied from hindlimb to hindlimb*

Time (min)	Applied voltage (V)	Artery		Nerve		Muscle		Fat		Bone marrow		Bone cortex	
		J	T (°C)	J	T (°C)	J	T (°C)	J	T (°C)	J	T (°C)	J	T (°C)
0	355	30.0	39.0	24.3	38.5	13.3	39.0	9.5	38.5	3.0	39.0	1.8	39.0
2	293	28.7	41.0	22.8	41.5	12.5	40.5	10.5	42.0	3.1	40.0	1.9	40.0
4	265	27.1	43.0	21.9	44.5	12.5	42.5	12.8	45.5	3.1	42.5	2.0	42.5
6	253	26.5	46.0	21.0	47.5	12.2	44.5	14.4	49.0	3.2	44.0	2.0	44.0
8	235	25.5	47.0	20.5	49.5	12.2	46.5	14.8	52.0	3.1	46.0	1.9	46.0
10	220	25.0	48.5	20.0	52.0	12.2	47.5	15.0	54.0	3.1	47.0	1.9	47.0

Source: From Sances et al., 1983.

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tact site. The discussion here will relate the transient temperature to the severity of burn and the effects of blood flow on the extent of injury. The superficial burn is characterized by three regions of tissue destruction and charring at the electrode contact edge (Fig. 10.14). The first region of tissue destruction, which is adjacent to the electrode contact, contains desiccated and denatured tissue, indicated by erupted blisters, shrinkage of the tissue, and charring at the edge of the contact. The second region is the ischemic region, where the tissue is devoid of blood flow but retains its fluid content. The outermost region, represented by a darkened ring caused by hemorrhage and thrombosis of the microvasculature, appears several minutes after current is stopped. These burn regions extend into the deeper layers of the dermis as well (Fig. 10.15). The burns result in a full-thickness burn and will extend into underlying muscle tissue when the current is sufficiently high. Desiccation is deeper at the electrode edge than in the center. Histological evaluation of the dermis shows that the trauma from electrical burns is very similar in character to nonelectrical thermal damage. The extent of trauma can be determined by the transient temperature response of the tissue.

Henriques (1947) and Henriques and Moritz (1947) have investigated the thermal tissue response in terms of the time-temperature relationship. The general results indicate that as the peak temperature increases, the

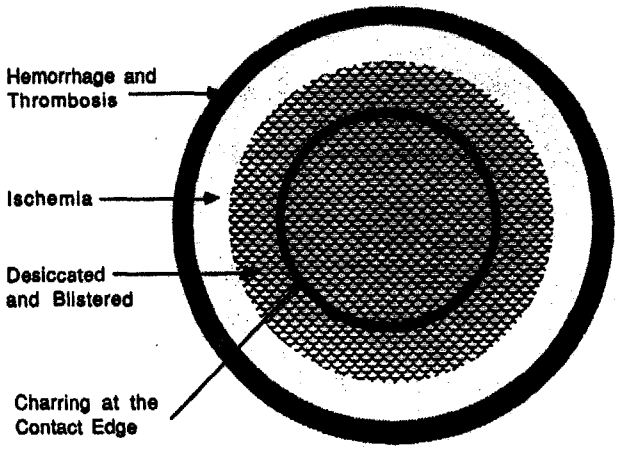


Figure 10.14 Superficial burn resulting from a circular contact at 100 V. There are three distinct regions of trauma: a desiccated region adjacent to the electrode having erupted blisters, an ischemic region that maintains its fluid content, and a hemorrhagic region darkened by thrombosis. Also shown is a ring of charring that occurs at the electrode edge.

time necessary for trauma decreases exponentially. Skin will burn at 45°C after several minutes, but at 60°C only a few seconds is required. Experimentally measured temperatures are given in Fig. 10.16 for a circular electrode of 5-cm diameter having a 100-V potential and applied through the third phase of the current-time waveform (Fig. 10.2). The measured temperatures corresponds well with the finite-element model results of Fig. 10.8. In general, the peak temperature delay from the time of peak current increased primarily with distance from the edge of the electrode (Fig. 10.17). A secondary effect increasing the time delay of peak temperature is the depth from the skin surface, and regions without blood flow (ischemic regions of Figs. 10.14 and 10.15) also had longer delays. The secondary effects are due to heat radiation and convection at the surface and to slower heat conduction in ischemic tissue.

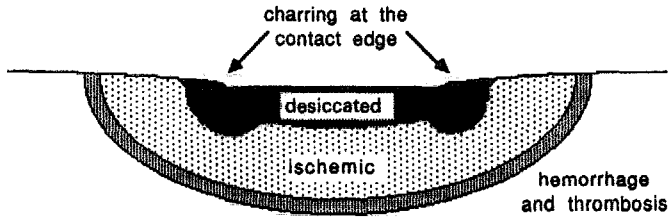


Figure 10.15 Dermal cross section beneath a circular contact at 100 V. The resultant injury is a full-thickness dermal burn. The three regions of Fig. 10.14 are present. Desiccated tissue extends deeper into the tissue at the electrode edge than at the center.

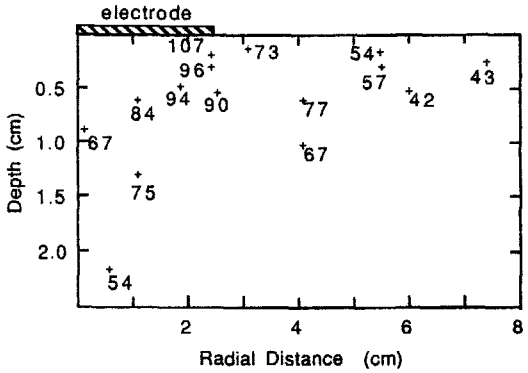


Figure 10.16 Peak tissue temperatures measured experimentally beneath a 5-cm-diameter circular contact at 100 V in five hogs. The voltage was applied until the current ceased from desiccation of the contact site (phase 3 of the current-time waveform). (Adapted from data of Prieto et al., 1985.)

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Tissue perfusion by blood is an important factor in the generation of electrical burns. Comparing the above in-vitro studies to studies in situ, the results show significant variations in the total applied energy, contact time, and rate of tissue cooling. The parameters of voltage, electrode size, average power, and minimum total resistance were the same. The total energy applied was 24% less in situ than in vivo, the contact time was 21% less in situ that in vivo, and the rate of tissue cooling was 50 to 75% less in situ than in vivo. This factor is important to the evolution of electrical burn trauma, since the data indicate that blood flow helps lessen the severity of the trauma in short-duration contacts.

Heating of the Tissues

When currents are high and/or application times are long, trauma extends beyond the contact site, requiring surgical intervention and possibly amputation. The trauma affects primarily the limbs and is typically located in muscle tissue. Peripheral nerves and blood vessels are also affected, because they are usually adjacent to affected muscle. Bone is usually the least affected, but adjacent muscle is affected more than distant muscle. Deep tissue injury depends critically on the current pathway. As noted by Eq. (10.3), the distribution of current is based on the electric field

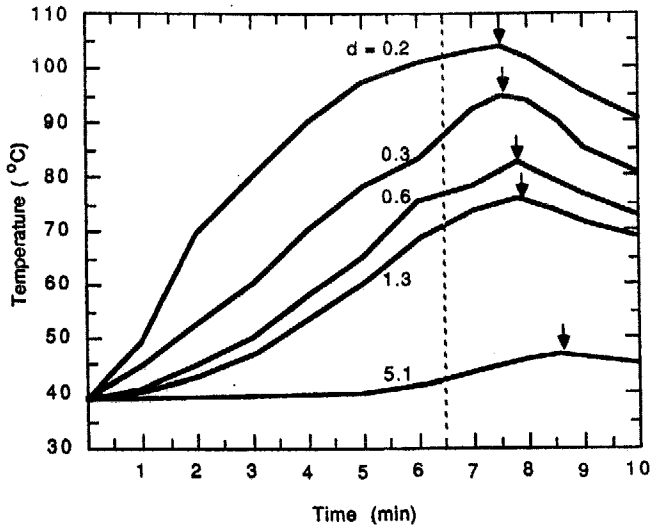


Figure 10.17 Plots of tissue temperatures beneath the electrode at different depths (cm) with time, 100 V contact. Peak temperatures do not occur simultaneously, but at times related to depth below the electrode edge following the current falloff of phase 3, as indicated by arrows. Broken line indicates current cessation.

strength of a given cross section and the tissue resistivity. Once the current distribution is established, the heating can be evaluated.

Heating of tissue and subsequent resistivity changes have been investigated in hogs and dogs (Sances et al., 1983; Chilbert et al., 1985b). Table 10.9 shows that current density in fat decreases with temperature but increases in artery, muscle, and nerve. Tendon and dermal current density decreases with temperature. The current path will shift due to changes in the resistivity. This change is due to a direct temperature dependence of resistivity and to tissue degradation. Tissue degradation causes increased resistivity in nerves and vessels while decreasing muscle resistivity. Neural tissue increases 80–100% in resistivity when thermally injured, while muscle decreases as much as 80%. The changes in muscle resistivity become more important when one considers that a large change in impedance could be indicative of burn severity.

Studies performed by the author (Chilbert et al., 1985a 1985b) indicate that tissue temperature, resistivity, and the severity of trauma can be correlated in muscle tissue. Figure 10.18 shows the measurement sites in the dog gracilis muscle for temperature and resistivity. Electric burn trauma was induced by passing 1-A currents at 60 Hz until the distal measurement site reached a temperature of 60°C. Peak temperatures along the muscle decreased proximally as the limb cross section increased

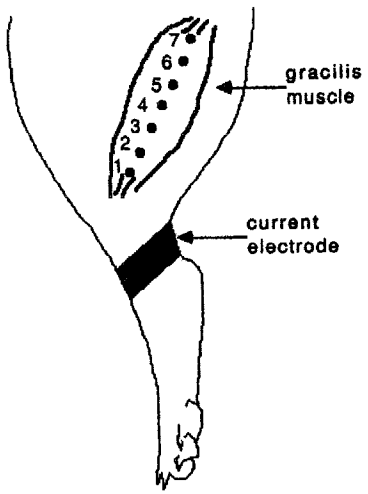


Figure 10.18 Measurement sites in the gracilis muscle of the hindlimb of a dog. Temperature and resistivity were measured at each site. Site 1 is the most distal and site 7 is the most proximal.

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(Fig. 10.19). Regions 1 and 2 exceeded 50°C, while the remaining regions remained below 47°C. Severe trauma was noted in regions 1 and 2, while regions 6 and 7 had edema with minimal structural changes. Regions 3, 4, and 5 were in a transition zone between viable and nonviable tissue. The resistivity increased proximally, but all values were less than control values (Fig. 10.20). The initial resistivities at the onset of the 1-A current increased 35% because of muscular contraction; they then declined with increasing temperature. The resistivities continued to decline even as the tissue cooled, indicating further progression of tissue injury.

Thermal trauma to peripheral nerves is also related to the maximum temperature reached. The temperature in a nerve is most likely dependent on the temperature of the surrounding tissue. The peak temperature of nerve in Table 10.10 shows that it is only 2°C less than the tissue in which it was measured (i.e., fat). Neural activity (indicated by averaged evoked response) decreases with temperature as neurons are damaged. Degradation of the peripheral nerve response with a thermal injury (not electrically induced), caused by slowly increasing the temperature, shows the development of trauma (Fig. 10.21). Important features of the evoked response indicate that certain neurons are more sensitive to increased temperature, noted by a larger decrease at 45°C and at 50°C. Which neurons are affected

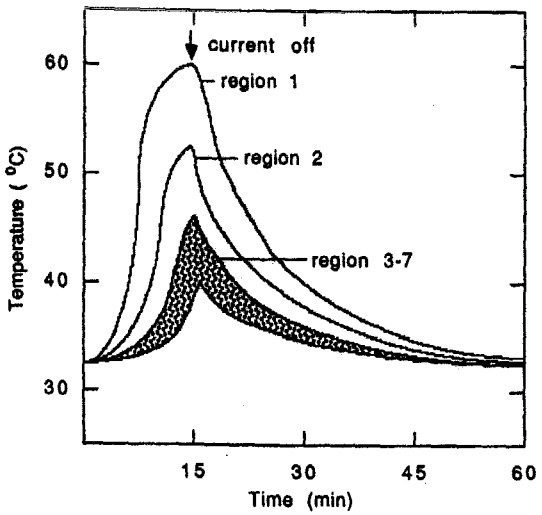


Figure 10.19 Temperature increase caused by the flow of a 1-A current with time. Current was applied for 15 min. Temperatures at regions 1 and 2 were elevated above 50°C, while the other regions were between 40 and 46°C and are grouped together.

at these temperature levels in not presently known. For rapid heating of the nerve the temperature of trauma is above 50°C, where recovery of the evoked response is usually rapid once the temperature reaches that of the body. However, heating of the nerve with electric current causes permanent damage at lower temperatures. The evoked response is always immediately affected by current, at levels above 3.5 mA/cm^2 along the nerve, causing blocking of the response from 5 to 20 min. Once temperatures exceed 45°C, permanent reductions in the evoked response are observed, and above 50°C the response nerve returns. This suggests that the current may affect neurons directly exclusive of temperature, possibly by electroporation. Limited studies in the spinal cord are consistent with peripheral nerve information, but the temperature threshold for electrically induced trauma is lower.

Thermal trauma to bone is seldom seen except at very high voltages (Sances et al., 1981b). The high resistivity of cortical bone prevents significant direct heating and protects the marrow as well. Table 10.10 shows that bone has the lowest temperature in cross section. Muscle tissue near the bone is often burned, while muscle tissue away from the bone is not

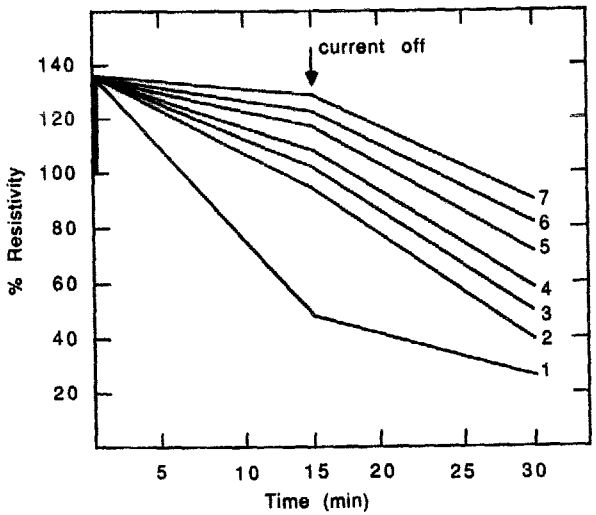


Figure 10.20 Changes in resistivity measured during and following the application of a 1-A current. Resistivities of muscle were measured in the transverse direction and perpendicular to the direction of current flow and are given in percent of control values. Initial increase of resistivity is due to the contraction of the muscle by stimulation from the current. Initial resistivity is for contracted muscle at time = 0 min. Muscle resistivity continues to decrease with decreasing temperature after current is turned off at $t = 15$ min in region 1.

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affected. Some clinicians have erroneously attributed this phenomenon to heating of the bone. The cause is due to higher current densities in the muscle near the bone (Sances et al., 1983). The result is that muscle near the bone heats faster, which decreases the resistivity and increases the current density, thus propagating the injury. The reason for this is that the energy in the tissue is related to the square of the current and the resistance; consequently, the energy is more dependent on current changes than changes in resistance.

Joint regions in the limbs are more susceptible to trauma than in tissue around the longbones. In cross section the joints have a large quantity of bone compared to other more conductive tissues. This creates very high current densities in the more conductive tissue, consequently causing severe trauma at the joint while leaving tissues by the long bones viable (Sances et al., 1983; Zelt et al., 1988). Also, the joint capsules have been known to disrupt explosively from the buildup of steam (Sances et al.,

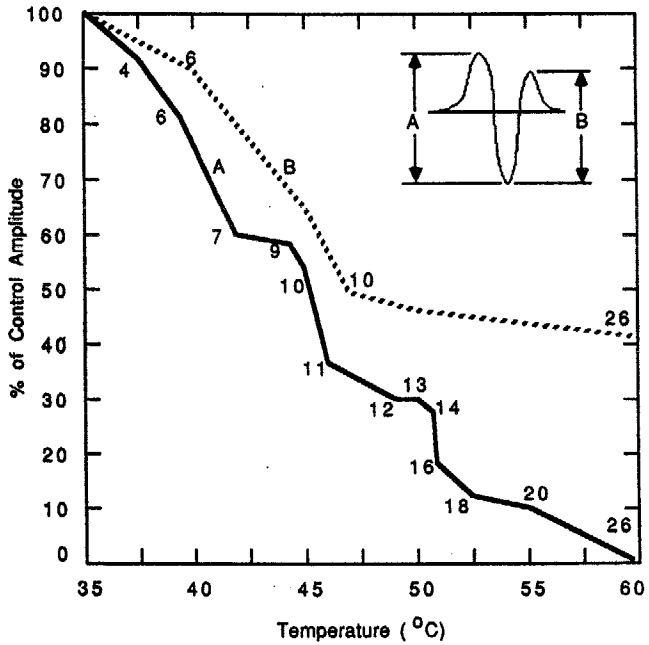


Figure 10.21 Changes in the evoked response of the tibial nerve in the hog with temperature. The reductions in the peak amplitudes were permanent. The first component of the evoked response is denoted by A, and the second is denoted by B. Numbers on curves indicate time in minutes after the temperature increase was started. Amplitude is given in percent of normal evoked response amplitude.

1981b, 1983). However, if the victim has the ability to flex the joint, the current will have an alternate path through the skin surfaces above and below the joint, thus preserving the joint. This has been noted clinically around the elbow, where burn marks appear on the skin proximally and distally.

10.5 Nonthermal Trauma

Lesions in tissue not caused thermally are likely caused by electroporation (Lee et al., 1988). Typically, the electric field strength needed to rupture muscle cells must exceed 100 V/cm. Similar levels are probably necessary for neural cell damage as well. Also, it has been noted that temperature increases the likelihood of electroporation occurrence at a given temperature. Studies in the peripheral nerve of hogs show that no significant alterations in the evoked response occur at current densities up to 167 mA/cm^2. This current density level results in an electric field strength of 33.2 V/cm, which is below the minimum level of 100 V/cm cited by Gaylor et al. (1989). To attain field strengths in the limb, the applied voltage could exceed 5000 V. For spinal cord injury to occur, the minimum applied voltage would need to be between 35 kV and 50 kV for a hand-to-foot path. These values were predicted from measurements in the hog given in Tables 10.4 and 10.9 and in Fig. 10.3. From Table 10.9 one notes that a current density of 0.3 mA/cm^2 results when a current of 100 mA is applied from the forelimb to the hindlimb and the spinal cord has a resistivity of 214 Ω cm. Since the electric field strength should be above 100 V/cm, the current density in the cord needed to cause irreversible electroporation would have to be 500 mA/cm^2. To obtain this current density in the spinal cord, an applied current of 167 A between forelimb and hindlimb is needed. To estimate the voltage level for 167 A, refer to Table 10.4: At electrode location 4, nearly 20 A will flow at 6 kV. A simple extrapolation of the voltage-current ratio (6 kV-20 A) shows that 50 kV is needed to generate 167 A in the body. However, resistance decreases with increasing voltage, therefore using the values of 7.2 kV and 25 A from Fig. 10.3 and extrapolating to the 167-A level, the applied voltage needed is 35 kV. The value for humans may be lower, since reports in the clinical literature have cited spinal cord dysfunction at 25 kV (Kanitkar and Roberts, 1988).

10.6 Lightning Injuries

Lightning accidents occur infrequently relative to other electrical incidents, but often enough to be well documented. According to Biegelmeier (1986), one-third of all lightning injuries are fatal. The immense power

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of lightning is shown by the effects of its millions of volts and 5,000 to 200,000 A (Sances et al., 1979; Strasser et al., 1977). Reviews of lightning injury have been given by Taussig (1968) and Silversides (1964). Persons struck by lightning who were clinically dead have been revived, and maladies seen afterward eventually disappear in most cases (Taussig, 1968).

The afflictions commonly encountered with lightning are mostly neurologic. Burns can occur at the entry points and may be accompanied by internal lesions. The burns often have a splashlike or arborlike appearance, assumed to be caused by current tracking over the body (Artz, 1979). Skeletal fractures occur when the person falls or is thrown by muscular contractions. Effects on the nervous system can occur immediately, can be delayed for several hours, or can occur days after.

Immediate effects of lightning strike depend on the severity of the incident. The victims usually undergo a total arrest of all body functions, which slowly return over a given length of time (Taussig, 1968). Fatalities can occur when the victim has a long respiratory and cardiac recovery period and no assistance, such as CPR, is administered (Strasser et al., 1977; Taussig, 1968). Abdominal lesions are also notably fatal, especially when internal hemorrhage is present (Artz, 1979). For the less serious accidents, the heartbeat is present with respiration intact or soon returning, leaving the victim in an unconscious state. Upon arousal, the victim may act disoriented and may have paresis of some or all the limbs (Critchley, 1934; Silversides, 1964). Other, less common deficits are visual, auditory, and speech (Critchley, 1934). Often amnesia occurs with lightning insults (Strasser et al., 1977; Taussig, 1968). Hypertension is normally observed, with anxiety and, at times, neurotic behavior. These symptoms usually vanish within a week (Strasser et al., 1977).

Secondary effects appear within the first few days after the accident. Except for an occasional change in the electrocardiogram or trauma to internal organs, all secondary effects are neurologically oriented, consisting of paralysis (usually of the legs), muscle pain throughout the body, photophobia from the intense light, and various autonomic disturbances. These effects normally vanish within a week. Latent effects (seen after 5 days) usually are resolved within a month after the accident. Neurologic symptoms are thought to be associated mainly with the progression of vascular disease or dysfunction. Neurologic symptoms in this stage are also common to high-voltage power-line injuries, which will be discussed later (Silversides, 1964).

Soft tissue lesions are found more frequently with lightning accidents than in high-voltage accidents (Massello, 1988; Sharma and Smith, 1978). Neurologic lesions often occur where there is an interface between regions

of different resistivities. In lightning accidents one commonly sees splitting of the cortical layers of the brain and petechial and subarachnoid hemorrhage (Critchley, 1934; Silversides, 1964). Several explanations of the lesions have been suggested, but all lack supportive evidence. One hypothesis suggests that the lesions are caused by the heating effects, which produce pockets of gas or steam. This is not generally accepted as a good explanation, since the heat evolved is assumed to be insufficient to cause boiling of the tissue. Following this line of reasoning was the suggestion of fluid electrolysis; however, the time involved and current necessary may exclude this as a possibility. The most acceptable theory is electroporation causing cellular lysis at or near the tissue interfaces. The lesions have been seen more often at tissue interfaces, where charge accumulation can occur (Critchley, 1934; Strasser et al., 1977).

10.7 Clinical Observations

Of all electrical injuries, most occur to those working for electric utility companies. In one report, 95% worked for utility companies, of which 50% or more were linemen (Butler and Gant, 1978). The voltage levels for most of these injuries exceed 1000 V and are at the standard commercial frequency. Reviews of the general aspects of electrical injury have been presented by many (Dixon, 1983; Sances, 1979; Skoog, 1970; Wu, 1979). Clinical reviews have shown common observations among patients (Haberal, 1986; Hammond and Ward, 1988; Luce et al., 1978; Sharma and Smith, 1978; Solem et al., 1977). Some authors have focused reviews on the neurologic sequelae noted in electric accidents (Critchley, 1934; Silversides, 1964; Strasser et al., 1977). Others have reviewed the aspects of electric burns (Artz, 1974; Butler and Gant, 1978; Rosenberg and Nelson, 1988; Rouse and Dimick, 1978).

The various forms of trauma seen with electrical injury are the same as those seen in thermal burns with the addition of others unique to electrical injury. Some aspects of electrical injuries are similar to crush injuries. Clinical reports and reviews present observations in the general areas of burns, lesions, neurologic effects, and cardiovascular effects. The reports and reviews usually focus on one of the areas, while the patients may present symptoms from all areas.

Electrical Burns

The pattern of electrical burns can vary greatly from those seen in thermal injuries (Artz, 1979). Electrical burns follow the current path, whereas thermal burns start at the surface from one location and radiate into the surrounding tissue (Janzekovic, 1975; Luce et al., 1978; Ponten

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et al., 1970; Sances et al., 1979). Deep tissue necrosis is often evident; although tissue may appear viable, it may be damaged and require secondary procedures. The transformation of visibly viable tissue to necrotic tissue has been termed *progressive necrosis*, but experimental studies indicate that the visible viable tissue is actually necrotic from onset of the trauma (Zelt et al., 1988). Artz (1979) has reviewed and presented the various aspects of electrical injury, especially those associated with electric burns. Also, reference is made to internal lesions and renal sequelae. The following is a summary of burn wound observations:

Contact-site wounds usually signify deep tissue destruction locally. The contact sites can be defined in terms of the primary site, which is the contact with the energized source, and the secondary site, which is the contact with the ground or neutral source. The primary wound is usually charred and depressed. The secondary wound is dry, depressed, and has the appearance of the current exploding outward. Massive swelling is evidence of extensive tissue damage caused by heat and electroporation.

Skin injury varies from small circular spots to large areas of charring. Adjacent to the charred tissue is a whitish-yellow ischemic region. Surrounding the ischemic skin is an area darkened by vascular hemorrhage and thrombosis. All three regions are relatively cold and without sensory perception.

Vessel damage may extend beyond the general area of injury. Thrombosis has been noted away from the burn injury. Typically, extreme vascular spasms, thrombosis, and necrosis of vessel walls are observed. In nonthrombotic, damaged vascularization, hemorrhaging may result and lead to serious complications.

Muscular trauma is caused by the direct heating of current or by occlusion of the arterioles supplying the muscle. Damage to the muscle is usually uneven, affecting groups of fibers while not affecting adjacent areas. Uneven damage is characteristic away from the contact sites and may not be noticed initially (Zelt et al., 1988).

Burns caused by arcing imply high temperatures at the contact site and extensive deep tissue destruction. Traumatic limb amputation has been documented (Sances et al., 1979). Cursory burns are caused when arcing ignites the victim's clothing.

Renal failure is more common in electrical injuries than in thermal burns. Renal damage is caused by direct electric involvement of the kidneys and/or renal vessels, or more often by the abnormal breakdown of protein from other injured tissues. Devitalized muscle in electrical injury causes renal complications similar to those seen in severe crush injury (Artz, 1974). There is also a greater occurrence of hemoglobinurea and hematuria in the electrically injured patient. One critical complication is acute tubular necrosis, probably caused by myoglobin breakdown.

Oral burns are most often seen in children and cause severe burns to the lips, tongue, and dentition. This form of electrical burn has been reported extensively particularly in recent years, because of the special treatment needed (Barker and Chiaviello, 1989; Donly and Nowak, 1988; Palin et al., 1987; Sandove et al., 1988; Silverglade, 1983). Of particular concern is tissue contraction of the lips and cheeks, which is prevented by special splints (Sandove et al., 1988).

Most pediatric electrical injuries admitted to the hospital occur to the mouth (35–60%) and most victims of oral burns are under the age of 4 (Baker and Chiaviello, 1989; Palin et al., 1987). Oral burns account for almost all severe burns. Electrical trauma in children results from defective equipment or the momentary lapse of supervision or lack of knowledge on the part of the parent. Nearly all injuries occurring to children are preventable, especially with routine maintenance.

Tissue Lesions

Tissue lesions are evident at the tissue interfaces and are commonly associated with neural dysfunction and abdominal complications. Autopsy upon electrical accident victims often reveals submucosal hemorrhages dispersed throughout the gastrointestinal tract. Abdominal lesions are associated with a high mortality rate. They are difficult to detect and treat. Delayed fatality is usually associated with abdominal lesions of the gastrointestinal tract (Artz, 1979). Typically the patient is comatose, and vital signs degrade over several days until death occurs.

Lesions have the most significance in neural tissues of surviving victims. Once a nerve has been severed, its function seldom returns. Lesions may also be responsible for latent neural dysfunctions that appear up to 3 years after the injury (Sances et al., 1979; Silversides, 1964). When lesions are noted in the spinal cord, they are seldom complete transections. Clinical signs of these lesions are spastic paresis with little or no sensory deficit. The lesions usually are not suspected until the onset of patient ambulation (Baxter, 1970). These afflictions, like many associated with the nervous system, are not well understood and are subject to conjecture.

Neurologic Sequelae

Neurologic sequelae are manifest at all levels of the nervous system and are either permanent or transient. Permanent effects are the result of thermal trauma or lesions, while transient disorders can disappear within days or last for months (Hooshmand et al., 1989). Discussed below are

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the permanent and transient sequelae seen peripherally, seen in the spinal cord, and associated with cortical abnormalities.

Damage to peripheral nerve can be caused by electroporation (lesions) or excessive heating of the tissue. The ulnar, radial, and femoral nerves have the highest incidence of injury due to heating. Occasionally lesions are formed in the peripheral nerves, causing sensory or motor deficits. Some cases have been reported as progressive with time, the victim slowly losing sensation in the limbs and other clinical abnormalities developing (Kinnunen et al., 1988). Injury to the peripheral nerves, as stated above, is permanent, and recovery is minimal. Peripheral nerve damage is usually associated with adjacent tissue injury.

Transient disorders often seen are neurovascular, neuromuscular, and sensory. The neurovascular disorders include vascular constriction and spasmodic reactions, both of which reduce blood flow and vascular dilation (Christiansen et al., 1980; Hooshmand et al., 1989). Vascular spasms cause a reduction of blood flow in an area, usually associated with tingling, numbness, and, at times, paralysis. Vasodilation is believed to be the cause of fainting spells sometimes encountered after electrical injuries. Neuromuscular disorders are paresis, paralysis, hypertension, and muscular pain.

Current having a magnitude great enough to affect the spinal cord or nerve roots has a transthoracic path. The most common transthoracic path is from hand to hand, with hand to foot being nearly as common. Head-to-extremity paths, although not very common, will also affect the spinal cord. With hand-to-hand contact, the current level is greatest in the cervical region (Table 10.9). Hand-to-opposite-foot current paths mostly affect the heart and thoracic spinal cord. Head-to-extremity current paths affect the upper brain centers and cervical spinal cord (Butler and Gant, 1978; Sances et al., 1979; Solem et al., 1977).

Permanent damage to the spinal cord may be caused by vertebral displacement caused by falling or by muscular contractions or by lesions in the cord or nerve roots. Skeletal fractures in electrical injury are normally attributed to falling or being thrown by muscular contraction. Lesions in the spinal cord account for many of the permanent disabilities of motor function. Lesions are seen mainly in cases of power-line contact above 11,000 V (Butler and Gant, 1978). The magnitude of the lesions in the spinal cord is not readily apparent until the onset of ambulation (Baxter, 1970; Solem et al., 1977).

Transient effects of current on the spinal cord appear at all stages of recovery: immediate, secondary, or latent. The immediate effects are loss of consciousness, respiratory arrest, and neural effects on the heart rate. Unconsciousness may cease immediately after current flow has stopped or linger for a day or more (Silversides, 1964). Respiratory arrest occurs from the sustained contraction of intercostal muscles and interruption of the neural respiratory centers. Sustained contractions of the intercostal muscles last only while the current is applied. Spontaneous breathing has been delayed for several hours in some victims, but usually returns within 20 min. Secondary effects of the electric injury involving the spinal cord are temporary paralysis of the limbs, vascular spasms, and muscle pains (Silversides, 1964).

Immediate effects of electrical accidents involving the head may include convulsions, coma, cerebral edema, hysteria, amnesia, tinnitus, deafness, and visual disorders. Convulsions are induced in electrical injury from the passage of current through the cerebral cortex, analogous to those induced in electroconvulsion therapy. Coma is observed in patients who have been in cardiopulmonary arrest for relatively long periods of time. Clinical signs of electric coma are dilated, unresponsive pupils, along with no reflex response. Cerebral edema is seen only in the severest cases (very high voltages and lightning), typified by a softening of the tissue (Critchley, 1934). Hysteria is mentioned throughout the literature; its severity is minimal. Specific hysteric symptoms are agitation, confusion, amnesia, and transitory auditory and visual dysfunction (Critchley, 1934; Silversides, 1964). Amnesia is the most common symptom. Often the cranial nerves are directly affected; tinnitus and deafness are observed in victims, particularly when the victim does not lose consciousness. Permanent deficits in cranial nerves are associated with lesions along the cranial nerves.

Visual disorders include blindness, blurred vision, photophobia, and cataracts (Silversides, 1964). Blindness is caused as a result of current effects on the optic nerve or interference with the photoreceptors in the retina (Al-Rabiah et al., 1987). Permanent blindness is caused by lesions along the optic tract or separation of the retina from the choroid. Blurred vision results when the innervation of the lens musculature and iris have been affected. This condition is typified by dilated pupils. Photophobia occurs when the retina is exposed to intense light from an arc or lightning flash. Cataracts have been known to develop after lightning strikes and very-high-voltage contacts with the head (Moriarty and Char, 1987).

Secondary conditions associated with the cerebrum involve the prolonging and delayed development of the immediate symptoms discussed above. Secondary effects are mainly hysterical complications. In addition to those stated above are speech loss, disorientation, and narcolepsy (Critchley, 1934; Silversides, 1964).

Development of latent effects includes psychosis, hemiplegia, aphasia,

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epilepsy, choreoathetosis, and other hysterical conditions (Critchley, 1934; Silversides, 1964). Psychosis is rare and may be related to preaccident manifestations. Hemiplegia and aphasia (not as common) are seen in conjunction with cerebrovascular disturbances. Prior existence of vascular disease correlates well with hemiplegia and aphasia resulting from electrical accidents. Posthemiplegic Parkinson's disease has been known to develop, either the unilateral or the asymmetric bilateral form (Silversides, 1964). The initial convulsion in a developed epileptic condition may have started during the current flowing in the body. If the current path includes the head, the formation of an epileptic focus is likely. Actual lesions are rare, leaving a diffuse focus as the cause. Victims who developed epilepsy respond well to chemotherapy, which usually is withdrawn over a period of time.

Cardiovascular Effects

Electrical accidents have also produced latent cardiovascular disorders that are usually transient. Some of these affects may be associated with fibrillation and defibrillation of the victim (Wilson et al., 1988). Because these effects are usually less life-threatening than the complications of burn, they are seldom reported. However, the occurrence of cardiovascular complications is frequent (Guinard et al., 1987). High current levels flowing through the chest can cause cardiac arrest, which is then followed by a somewhat normal cardiac rhythm. Most cardiovascular effects follow high-voltage electrical injuries. Latent effects include atrial fibrillation, premature ventricular contractions, bradycardia, tachicardia, ventrical and atrial ectopic foci, conduction branch block, and nonspecific S-T interval and T-wave changes (Butler and Gant, 1977; Jones et al., 1983; Skoog, 1970; Solem et al., 1977).

The causes of latent cardiac effects and delayed arrhythmias is unknown. Some suggested causes include the residual effects of fibrillation, enzymal reactions with the cardiac tissue, neural dysfunction, or coronary artery spasms, The fibrillation of the heart or a sustained myocardial contraction by the current may alter the metabolic activity of the heart and result in altered cardiac rhythm (Solem et al., 1977). Certain enzymes are released from necrotic muscle tissue, such as various forms of creatine kinase, which can alter the function of the cardiac cells or mitochondria and again alter the cardiac rhythm (Ahrenholz et al., 1988). Since various forms of transient neural anomalies have been noted in other areas of the nervous system, neural alterations in the inervation of the heart may also occur (Skoog, 1970). Similarly, the vascular spasms noted in the periphery may also occur in the coronary arteries and lead to altered cardiac rhythm

(Luce and Gottlieb, 1984; Skoog, 1970). Fortunately, these disturbances are usually transient and disappear within a week (Jones et al., 1983; Luce and Gottlieb, 1984).

Latent vascular effects, such as spasms or peripheral coldness, have been attributed to neural disturbances (Kinnunen et al., 1988). Similarly, transient neural disturbances have been attributed to vascular spasms (Silversides, 1974; Skoog, 1970). Some latent effects are attributed to loss of endothelial cells and elasticity in the vessel wall, which leads to vascular impairment (Wang and Zoh, 1983). Also, the vasculature may be impaired by arachidonic acid metabolites, such as thromboxane, that cause vasoconstriction. The latent effects are often a result of the initial trauma, but appear as healing occurs.

10.8 Clinical Treatment

Treatment of electrical injury begins at the scene of the accident with removal of the victim from the electrical source and the observations of vital signs. A lack of pulse or respiration requires immediate cardiopulmonary resuscitation. One should note specific details of the accident, such as the contact voltage, whether the victim fell, if there are fractures, and if there are burns evident at the contact sites. Rapid transportation of the victim to an adequate trauma center is essential (Dixon, 1983).

The potential for considerable fluid loss coincident with deep tissue damage is great, therefore fluid replacement must be started as soon as possible. Intravenous isotonic fluids are administered to maintain the urine output at approximately 100 ml/h. Traditional burn formulas cannot be used to calculate fluid replacement requirements. These formulas underestimate the required fluid volume because they are based only on the skin surface area involved; fluid replacement principles for a crush injury are more appropriate (Artz, 1979; Dixon, 1983). If myoglobinuria is present, sodium bicarbonate is administered to alkalinize the urine, which inhibits pigment precipitation. Also, an osmotic diuretic, usually mannitol, can be used to flush the renal tubules (Baxter, 1970; Dixon, 1983, Hunt et al., 1980; Moncrief and Pruitt, 1971).

The electrocardiogram should be monitored, and echocardiography may be useful in assessing cardiac damage. Monitoring the hemoglobin and hematocrit will indicate the degree of hemolysis, and arterial blood-gas measurements are used to determine the acid-base state of the victim (Artz, 1974; Dixon, 1983).

The external appearance of the electrical burn wound is not indicative of the extent of underlying tissue damage. The electrical burn may be

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masked by flame or flash burns (Moncrief and Pruitt, 1971). Initially, the wounds are thoroughly cleansed. If the initial examination reveals a charred limb, an absent or diminished pulse in a limb, a loss of sensory or motor nerve function in a limb, or evidence of considerable limb swelling, then an escharotomy and fasciotomy should be performed. Fasciotomies have both a therapeutic and diagnostic function, as they may restore circulation and permit the surgeon to inspect the underlying musculature visually (Baxter, 1970; Wang 1985). Amputation of at least one extremity is frequently required following high-voltage injuries. If a limb is clearly necrotic, then amputation should be performed immediately (Parshley et al., 1985). Amputations are generally done in the first week post-injury, after the patient's condition has stabilized. Arteriograms may be helpful in determining the initial level of amputation (Hunt, 1979).

Although there is general agreement that obviously necrotic tissue should be debrided as soon as possible, there is still controversy over the treatment of tissue that is questionably viable (Barnard and Bostwick, 1976; Baxter, 1970; Rouse and Dimick, 1978). The first method advocates early exploaration and debridement, with repeated surgical procedures after 24 to 72 h until all nonviable tissue has been identified and removed (Artz, 1974; Hunt et al., 1980; Luce and Gottlieb, 1984; Parshley et al., 1985). Alternatively, a more conservative approach may be used, where the debridement procedure is delayed until a definite delineation between viable and nonviable tissue becomes evident, usually after 8 to 10 days. Proponents of the aggressive approach claim earlier wound closure and less incidence of infection, while proponents of the conservative approach feel that unnecessary multiple surgical procedures are avoided, the local blood supply is not altered by surgical trauma, and viable tissue is less likely to be removed. Zelt et al. (1988) showed experimentally that all tissue injury is histologically evident at the onset of injury; progressive necrosis does not occur.

Several methods have been advanced to determine the viability of questionable tissue so that excision of the necrotic tissue can be conducted as early as possible. Arteriography has been used to assess vascular damage, but this method does not consistently visualize the smaller arterial and arteriolar vessels in the muscles (Hunt et al., 1980). Thus, only occlusion of the larger vessels can be reliably determined with arteriography. The technetium-99 m pyrophosphate scan has been used to identify the extent of cardiac and skeletal muscle damage, including deep areas of muscle necrosis that may be missed by visual inspection during a fasciotomy (Hunt, 1979). Other studies have suggested that

electrical impedance or nuclear magnetic resonance spectroscopy can be useful in determining tissue necrosis (Chilbert et al., 1985a, 1985b).

Tissue resistivities were compared with histologic changes as well as results of ^{31}P NMR spectroscopy. Abnormalities in anatomic as well as metabolic measures were shown to correspond well to resistivity changes. Measurements of impedance at several frequencies were made to compute the phase-plane plot of muscle tissue (Fig. 10.22). Impedance is unique for each tissue as well as its condition, reflecting traumatic injury, viability, edema, etc. (Ackmann and Seitz, 1984). Likewise, changes in the phase angle are indicative of alterations in tissue, but are more proportionately related to the number of cells present. The relaxation frequency occurs at the point of maximum reactance. These boundary changes (caused by cell lysis) alter the relaxation frequency; loss of cells increases the relaxation frequency. With electrical burn injury, the amount of cell lysis is determined by the amount of heat generated in the tissue. Figure 10.20 shows how muscle resistivity changes with temperature and has been correlated to trauma (Chilbert et al., 1985b). The level of trauma, as indicated by ^{31}P NMR spectroscopy and histology, shows a 75% decrease in resistivity with severely burned tissue, whereas tissue only slightly affected by the electricity showed a decrease of 25% or less. Using impedance techniques

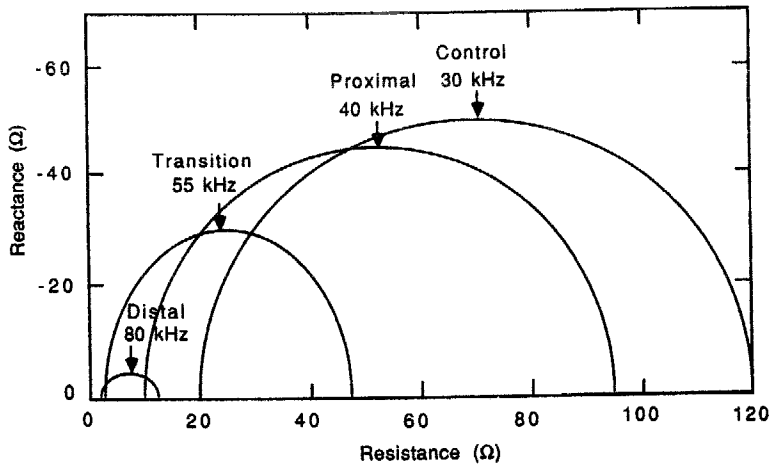


Figure 10.22 Impedance and relaxation frequency changes seen in muscle tissue with electric burn. The proximal tissue impedance curve corresponds to tissue that is only mildly edematous, the transition tissue impedance curve corresponds to tissue showing greater edema and some loss of cell structure, and the distal tissue impedance curve corresponds to tissue that shows gross destruction of cell structure and extensive damage.

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to determine tissue viability allows separation of compartmental changes (edema) and boundary changes (cell lysis) so that tissue vitality is better determined. Figure 10.22 indicates both the impedance change and relaxation frequency change seen in electric burns. Once the probability of tissue survival is determined for a given change in impedance and relaxation frequency, clinical measurements can be performed and appropriate excision of nonviable tissue can be made. This will eventually lead to reduced morbidity in the electric burn patient by minimizing surgical procedures and chances for infection.

It is essential that the bacterial population of the wound be controlled to prevent infection, especially clostridial myositis, which may develop as a result of inadequate excision of necrotic tissue (Artz, 1979; Hunt et al., 1980). Topical antibacterial agents are used rather than systemic agents, because the blood flow is often compromised in the region of the wound. Temporary wound closure can be achieved with porcine xenografts, autografts, or homografts, while permanent wound closure is usually achieved with an autograft. The use of a free muscle flap, utilizing the latissimus dorsi, for immediate coverage of deep electrical injury has been advocated. However, if the debridement prior to grafting is inadequate, then muscle necrosis or infection may be masked by the vascularized muscle flap. A viable cutaneous homograft may be a useful tool to test the readiness of a wound for surgical closure or definitive autografting. Vein grafts, using autotransplantation of the saphenous vein to replace the radial and ulnar arteries, have been used to restore circulation to the hand and prevent limb necrosis (Wang et al., 1984, 1985).

Electrical injuries involving only the scalp may be managed with the same procedures used for soft-tissue electrical burns of other parts of the body (Worthen, 1982). Contrary to earlier procedures for treating an electrical burn of the scalp and skull, a full-thickness scalp flap should be used to cover the exposed skull as soon as possible, regardless of the depth of damage to the skull. The presence of a vascularized cover promotes skull regeneration, as ingrowth and revascularization occur on both the pericranial and meaningeal surfaces (Worthen, 1982). Alternatively, split-thickness skin grafts can be applied to the skull after the cortical bone is removed to expose cancellous bone, although later resurfacing with rotational scalp flaps is required to restore the hair. A graft consisting of autogenous greater omentum covered with autogenous split skin has been used to cover a large irregular area of exposed skull following a high-voltage electrical injury. Extensive destruction of the face requires a multistage reconstructive procedure, which may extend over a period of several years.

11

Standards and Protective Measures

WALTER SKUGGEVIG

Standards and codes are used to judge to risk of electric shock from electrical products offered for sale to the consumer. An appreciation of the role played by these standards and codes can be obtained by understanding the rationale for them. But who writes these standards? What do they cover? Who judges the acceptability of electrical products?

11.1 Codes and Standards

Several organizations cooperate to write safety requirements for electrical products. The National Electrical Safety Code, for example, is published by the Institute of Electrical and Electronics Engineers (IEEE, 1990) and covers supply lines and equipment used by electric power utilities. The IEEE also publishes a guide for safety in AC substation grounding (IEEE, 1986), which contains criteria for proper grounding in order to minimize the risk of electric shock at distribution, transmission, and generating plant substations. The National Electrical Code (NFPA, 1990) is published by the National Fire Protection Association (NFPA) and covers electrical installations in public and private buildings or other structures, from the point of connection to the utility line at the service drop (overhead) or service lateral (underground) to the electrical power outlet.

Safety standards are continually revised to keep them current. For example, the National Electrical Code is revised on a 3-year cycle. Each third year, the public is invited to submit proposed revisions for the Code. Twenty code-making panels consisting of representatives from equipment manufacturers, contractors, installers, large users of electrical equipment, testing laboratories, inspectors, and utilities meet to decide whether to accept or reject each of the submitted proposals. Each new edition of the National Electrical Code is published after the proposed revisions are

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Electrical Stimulation and Electropathology

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The authors have made every attempt to provide an accurate and balanced treatment. However, the material in this book has been drawn from numerous sources, and in matters of critical interpretation the authors suggest that the reader refer to the original sources.

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APPENDIX 21

(b)(4) Third Party Data

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Appendix 22
Animal Study Information and Data

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Appendix 23
Recent Clinical Studies – Percutaneous Electrical Stimulation

Note: Scientific/technical literature referenced in the following discussions are listed in the bibliography in Appendix 28. For convenience, copies of selected references are also included in this Appendix 28.

The following summarizes some recent clinical studies assessing percutaneous electrical stimulation for pain management. The relevance of the studies to the Vertis percutaneous neuromodulation therapy (PNT) is also noted. Contents of this section are as follows:

Topic	pages in this Appendix
Percutaneous Electrical Stimulation - Low Back Pain Studies and Relevance to Vertis PNT	2 –9
• Vertis Modulation (Therapy) Modes	
• Vertis Therapy Duration	
• Vertis Electrode Placement Montage	
• Vertis Electrode Depth	
Percutaneous Electrical Stimulation – Other Recent Studies	10 –11

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Percutaneous Electrical Stimulation - Low Back Pain

Over the years, numerous pharmacological and non-pharmacologic therapies have been used to treat low back pain

Concerns regarding the safety or efficacy of these various modalities have increased interest in percutaneous electrical therapy (1-5). Percutaneous electrical therapy is an analgesic therapy that involves delivery of electrical current directly into the soft tissue to stimulate peripheral nerves at levels corresponding to the local pathology.

In recent years (1997-1999), low back pain (LBP) has been the focus of several randomized, blinded clinical trials performed by researchers at the Eugene McDermott Center for Pain Management at the University of Texas Southwestern Medical Center (UTSW), Dallas Texas. These studies employed percutaneous electrical stimulation. The results of these studies were published in well-respected, peer-reviewed journals.

> Note: Vertis did not sponsor, nor participate, in the UTSW studies. We have some reason to believe that there may have been several variations from protocol, but they should not have affected the study outcomes. These studies were of interest to Vertis and were an important part of the historical and technical basis for the Vertis PNT therapy.

A review of these studies is provided as follows for reference. Relevance of the studies to Vertis PNT therapy is also noted.

- **Study #1:** In a double-blinded, randomized clinical study published in the Journal of American Medical Association (4), percutaneous electrical therapy was shown to be more effective ($P<0.02$) than TENS, exercise therapy, and a sham in providing short-term pain relief and improved physical function in 60 patients with low back pain (Figure 1). In this nine-treatment, 3 week protocol, the percutaneous electrical therapy was not only highly effective in producing acute analgesia, but patients reported more sustained beneficial effects on their level of pain, physical activity, and quality of sleep. Moreover, the use of percutaneous electrical therapy significantly decreased the need for oral, non-opioid analgesic medications in this patient population.

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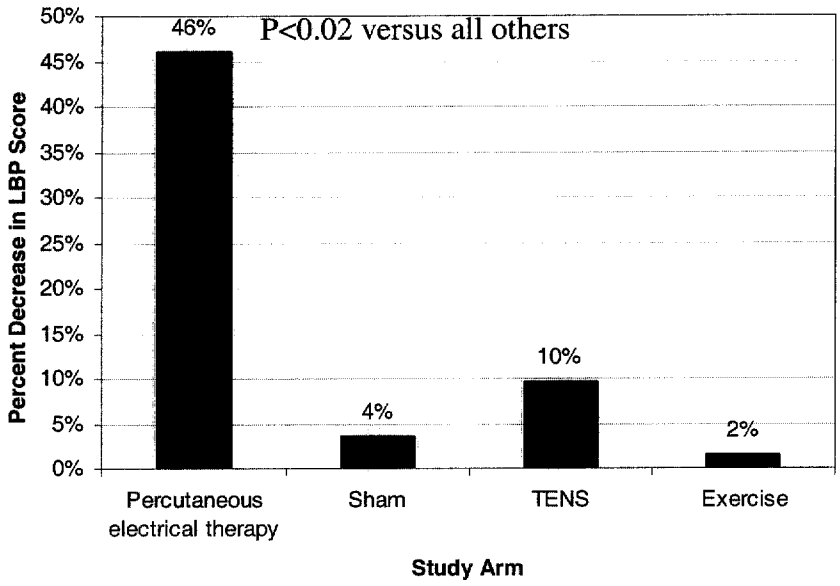


Figure 1. Percent decrease in low back pain (LBP) score from baseline (pre-treatment) level measured 24-hours after the ninth treatment, based on (4).

- **Study #2:** The efficacy of various stimulation frequencies of percutaneous electrical therapy was examined by the same researchers in a separate blinded randomized clinical study involving 68 low back pain patients (5). In this study, percutaneous electrical therapy was delivered in six 30-minutes sessions over a two-week period. Compared with sham stimulation, pulse frequencies of 4 Hz, 15 Hz and 30 Hz alternating in three-second intervals, and 100 Hz produced significantly ($P<0.01$) greater decreases in the degree of pain, improved physical activity and sleep quality, and reduced daily intake of oral analgesic medications.

- **Study #3:** A third randomized study on percutaneous electrical therapy examined the duration of treatment in patients with low back pain (6). Seventy-five patients were randomly assigned to 0, 15, 30, or 45 minute electrical therapy treatment sessions. In a crossover design, each treatment was delivered three times per week for two weeks with a one-week washout period between changes in duration. The 30 or 45 minute electrical therapy sessions were significantly more effective than zero or 15 minutes ($P<0.01$) of treatment in terms of the hypoanalgesic effects. Self-reported physical activity ($P<0.05$), quality of sleep ($P<0.05$), and patient function ($P<0.01$) were also better after the longer duration treatments. The authors recommended that the duration of treatment be 30 minutes, because no additional benefit was observed with 45 minutes of treatment.

- **Study #4:** In this blinded, crossover study, 72 low back pain patients were treated with percutaneous electrical stimulation in four different electrode montages selected in random order (14). The authors concluded that all four electrode montages produced significant improvements in the degree of pain, physical activity, and quality of sleep, as well as a reduction in the daily oral analgesic requirement.

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Summary:

Complications: It is very important to note that these 4 studies involved a fairly large patient population - 275 patients. Furthermore, the design of these clinical studies required delivery of percutaneous electrical stimulation over extended durations (e.g., study #1 involved 9 treatments over 3 weeks). As a result, these 4 studies involved a very significant number of independent percutaneous electrical stimulation sessions ≅ 4,842 treatments. Even with this number of patients and extensive number of percutaneous treatments, *no* complications associated with the use of the percutaneous electrical stimulation (e.g., tissue damage, nerve injury, infection, burns, etc.) were reported in the literature for any of these studies. Vertis followed-up and discussed this issue with the actual clinical Investigators involved in these studies and they confirmed the observation that the studies had no complications or issues that they considered significant. For example, they observed no cutaneous reactions or inflammatory changes at any of the needle insertion sites after the treatment sessions. They reported they had minor issues (e.g., superficial bleeding or soreness at the needle insertion site) in some patients.

Relevance to Vertis PNT:

Vertis PNT parameters: Based on Vertis' internal research efforts and in conjunction with the published studies summarized on pages 2-4, Vertis selected the electrical stimulation parameters for the Vertis version of percutaneous electrical stimulation, called percutaneous neuromodulation therapy (PNT). The correlation of these published studies to Vertis PNT parameters are summarized in Tables A and B (pages 5-9).

Vertis clinical trial: In designing the Vertis PNT System and selecting stimulation parameters, Vertis projected that we would obtain similar clinical results with the Vertis PNT therapy, as was observed in these studies assessing percutaneous electrical stimulation against TENS, a substantially equivalent device. However, to clinically assess PNT therapy and to evaluate potential complications, Vertis conducted a non-significant risk clinical study in pain patients to gain our own clinical data and first-hand knowledge using PNT therapy.

The Vertis clinical trial data, in fact, did demonstrate the safety and effectiveness of PNT therapy. Please refer to Appendix 24 for a detailed discussion of the results of the Vertis clinical study.

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Table A: Percutaneous Electrical Therapy: Summary points from Studies #1-4 (summarized on pages 2-4) and Relevance to Vertis PNT therapy

Summary Point from Studies #1-4	Relevance to Vertis PNT
• The JAMA published double-blinded, randomized clinical study (4) showed percutaneous electrical therapy be more effective than TENS, exercise therapy, and a sham in providing short-term pain relief and improved physical function in patients with low back pain. • The second randomized clinical study demonstrated the effectiveness of a variety of different stimulation pulse frequencies (5).	***Vertis Modulation (Therapy) Modes*** As described in the Vertis PNT Control Unit User's Guide (Appendix 6, page 25), the PNT Control Unit has five pre-programmed modulation (therapy) modes. In designing the Control Unit, three modes Vertis selected (4 Hz Continuous, 15/30 Alternating, and 50 Hz Continuous) were based on the published clinical studies (4, 5). For reference purposes, a comparison of the therapies used in these 2 studies (4, 5) and the Vertis PNT System therapy options is provided in Table B (page 9). The information demonstrates the similarity of the electrical therapy parameters. In the Vertis PNT Control Unit, the remaining two modulation modes (4-10 Hz Periodic Sweep and 4-50 Hz Aperiodic Sweep) were designed by Vertis to deliver therapy that varies dynamically over a range of frequencies. The 4-10 Hz Periodic Sweep was selected as the default modulation mode for the PNT Control Unit based on patient comfort, while staying within a therapeutic range of pulse frequencies. As with any pain treatment , patient comfort and response during treatment is believed to be an important factor towards continued use of the therapy. With the 4-10 Hz Periodic Sweep, patients feel a gradual change from a relatively slow rate of pulses (4 Hz) to a more moderate rate of pulses (10 Hz) and back again over approximately a 33 second cycle. This slow rate of change tends to provide a soothing sensation. At the same time, the range of delivered pulse frequencies stays within the range of previous studied pulse frequencies.
• A third randomized study evaluated the effects of treatment duration and found 30 minutes to be the optimal duration (6).	***Vertis Therapy Duration*** Based on the published treatment duration study (6), Vertis chose a 30 minute suggested treatment duration for PNT. As noted in the Vertis PNT Control Unit User's Guide (Appendix 6, page 24), the Control Unit ships from Vertis with the therapy duration default set at 30 minutes.

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Summary Point from Studies	Relevance to Vertis PNT
• Various percutaneous electrode placement montages may demonstrate improvement in pain when used with electrical stimulation. A dermatomal electrode placement montage was found to be most effective (14).	***Vertis Electrode Placement Montage*** Vertis' recommendation for the placement of Safeguide electrodes for PNT therapy was based on the published study (14). The dermatomal montage selected was statistically more effective. This suggested montage is as noted in the Vertis Safeguide Instructions for Use (Appendix 12, page 5).
• Electrodes in these studies (4, 5, 6, 14) were placed percutaneously (inserted through the skin) to a depth of up to 4 centimeters. These studies report that electrodes were placed at a depth of 2 – 4 centimeters.	***Vertis Electrode Depth*** Electrode placement in the previous studies (4, 5, 6, 14) extended to 4 centimeters; *no* complications were reported with electrode placement (e.g., penetration of a vital organ) or the use of the electrodes (e.g., infection, burns, etc.). However, Vertis chose to be conservative and selected the maximum depth for any PNT Safeguide electrode insertion to be 3 centimeters. As noted in the technical discussion of Safeguide electrodes (Section II, page 12), Vertis will offer electrodes in 0.5 to 3.0 centimeter lengths. For device user ease of use and convenience, electrode kits will be provided as clinical application specific (e.g., a lumbar kit, a cervical kit, etc.). The kit labeling will clearly indicate the kit application (e.g., a lumbar kit). Justification for the safety of these Safeguide electrode lengths derives from three factors related to their design and intended use: • The anatomical ***placement*** of the electrodes relative to vital structures • The ***length*** of the electrodes • The cross-sectional ***diameter*** of the electrodes ***Placement:*** For all Safeguide electrodes, the Instructions for Use will contain a diagram of the recommended placement of the electrodes. For example, refer to Appendix 12 for an example of the Instruction for Use for a lumbar Safeguide electrode kit – the electrode placement diagram is found on page 5 of the Instructions for Use.

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These placement diagrams were developed by Vertis based on clinician's recommendations from experience in routine practice, clinical trials and physician expertise (e.g. neurophysiologists, neurosurgeons, and physical medicine and rehabilitation physicians, etc.). The recommended electrodes placements are carefully selected in order to maximize the efficacy of the treatment (by reaching neural pathways), but ensure safety of electrode insertion. Per the placement diagrams, electrodes will be placed directly over specific anatomical structures that will not be injured by placement of an electrode within them (e.g., muscle groups, etc.).

It is important to note that the literature (provided in Appendix 19) of the substantially equivalent percutaneous electrodes does *not* provide such suggested placement diagrams. Vertis believes that supplying the clinician with suggested electrode placement montages will aid the clinician in the proper use of the electrodes and minimize potential complications.

Length: The length of the Safeguide electrodes (limited to a maximum depth of 3.0 cm) limits the depth of their penetration into the body. The electrode depth is preset for a particular application. For example, electrodes to be used in the cervical region will likely be shorter (e.g., ~1-2 centimeters) than those used in a lumbar region. Similar to electrode placement, electrode depth will be based on clinician's recommendations. The depth will be selected in combination with the recommended anatomical placement, thus aiding to ensure that the electrodes will not be inserted into any vital organs.

It is important to note that substantially equivalent percutaneous electrodes can be 7.5 – 60 centimeters in length (refer to the electrode comparison chart in Appendix 18). Vertis believes that limiting the length of the Safeguide electrode to 3.0 centimeters, mitigates the risk in comparison to the substantially equivalent electrodes.

Diameter: The diameter of the electrodes is 0.25 millimeters. As noted on in 510(k) Section II (page 12), this ultra fine diameter is significantly narrower than any needle currently used for intramuscular injections or intravenous blood drawing. This extraordinarily fine diameter of the electrodes is an important safety feature.

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	According to scientific experts and clinicians who consult with Vertis, even if an artery, nerve, vein, muscle, lung, or other sensitive structure was contacted or punctured by an electrode (for example, if the clinician inadvertently did not place the electrodes according to the labeling diagram), it would be extremely unlikely that such an action would have any adverse consequences. For example, if a nerve were contacted, the electrode would likely simply displace the neural fascicles within the nerve. With this action, there may be a noticeable sensation (e.g. a twinge), and as such the electrode could be removed and repositioned (if necessary) for patient comfort. However, no specific special medical treatment or action would be required or indicated, as there would be no injury of any consequence. It is important to note that electrodes contacting various anatomical structures (e.g., nerves, muscle, etc.) is not unique to the Vertis PNT system. This situation can occur with numerous invasive medical devices and clearly with any of the substantially equivalent percutaneous electrodes used for nerve stimulation (e.g., nerve/muscle contact during placement of an EMG electrode). The substantially equivalent percutaneous electrodes are of a much larger dimension (0.33 – 1.37 millimeters in diameter, per Appendix 18 comparison chart) than the Safeguide electrodes and accordingly, contact with bodily structures with these electrodes would likely be more potentially significant than with the smaller Vertis Safeguide electrodes.

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Table B: Percutaneous Electrical Therapy: published literature vs. Vertis PNT - therapy comparison table

	Published Literature		*Vertis Modulation Mode*				
	Ref. 4	**Ref. 5**	**4-10 Hz Periodic Sweep**	**4 Hz Continuous**	**15/30 Hz Alternating**	**50 Hz Continuous**	**4-50 Hz Aperiodic Sweep**
Pulse repetition frequency	4 Hz	4 Hz, 15/30 Hz, or 100 Hz	Varies between 4 Hz and 10 Hz, inclusive	4 Hz	Alternates between 15 Hz and 30 Hz in 3-second intervals	50 Hz	Varies between 4 Hz and 50 Hz, inclusive
Waveform*	Stated: 0.5 msec unipolar square wave Actual: Asymmetric biphasic, 0.7 msec phase 1, decaying exponential phase 2	Stated: 0.5 msec unipolar square wave Actual: Asymmetric biphasic, 0.7 msec phase 1, decaying exponential phase 2	Symmetric biphasic, 0.2 msec/phase (200 µsec/phase)	Symmetric biphasic, 0.2 msec/phase (200 µsec/phase)	Symmetric biphasic, 0.2 msec/phase (200 µsec/phase)	Symmetric biphasic, 0.2 msec/phase (200 µsec/phase)	Symmetric biphasic, 0.2 msec/phase (200 µsec/phase)
Maximum amplitude	25 mA	25 mA	15 mA	15 mA	12.5 mA	10.2 mA	15 mA

* "Stated" refers to the stimulation parameters reported in the published literature. As part of the development of the Vertis PNT therapy parameters, the researchers at the UTSW were contacted by Vertis Engineering/Research staff and allowed Vertis to evaluate the equipment used in the UTSW studies. The Vertis staff specifically measure the actual device stimulation parameters. This data is recorded in this table as "actual" - meaning what the device system actually delivers.

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Percutaneous Electrical Stimulation – Other recent studies

Although the above studies were specific to low back pain (LBP), the safety and effectiveness of percutaneous electrical stimulation is not limited to low back pain. This is consistent with the historical use of percutaneous electrical stimulation, where the treatment was used in a variety of pain scenarios. For example, the following recent studies have further demonstrated the use of percutaneous electrical stimulation in other acute – chronic pain conditions.

- **Study #5:** An episode of acute LBP accompanied by pain radiating into the buttocks and/or lower extremities is known by clinicians to carry a worse prognosis than LBP pain localized to the lumbosacral region. Numerous studies have documented that—as compared with localized LBP—radiating pain and/or sciatica (pain or neuritis of the sciatic nerve) are associated with increased: 1) pain severity, 2) probability of progression to a chronic state of pain, and 3) disability or loss of ability to participate in activities (7 – 13).

  In a randomized, blinded, sham-controlled investigation comparing therapies for treating sciatica in 64 patients, the authors concluded that percutaneous electrical therapy was more effective than TENS and a sham in providing pain relief and improved functionality (18). The use of the percutaneous electrical therapy improved physical activity and the quality of sleep while decreasing the need for oral non-opioid analgesic medications.

- **Study #6:** In a randomized, blinded study of 50 patients, percutaneous electrical therapy was compared with a standard antiviral regimen (famciclovir) in the treatment of acute herpes zoster (16). In this study, the percutaneous electrical therapy group experienced more rapid resolution of vesicles and complete healing of the lesions. The percent decrease in pain scores for the percutaneous electrical therapy group was 67%, compared with the pharmacological group of 45%. The percent improvement in physical activity and quality of sleep was also greater for the percutaneous electrical therapy patients.

- **Study #7:** Percutaneous electrical therapy was examined in 30 patients suffering form tension headache, migraine or posttraumatic headache symptoms (17). Percutaneous electrode placement was in the posterior cervical region and would not be transcerebrally (a contraindication for Vertis PNT therapy). Compared with a sham control (no electrical stimulation), percutaneous electrical therapy was significantly more effective in decreasing the overall pain levels and produced greater improvement in the patients' physical and quality of sleep. The analgesic response appeared to be independent of the origin of the headache symptoms.

- **Study #8:** In a randomized study of 50 patients, percutaneous electrical therapy was compared with a sham control (no electrical stimulation) in the treatment of diabetic neuropathic pain – a condition experienced by diabetic patients, manifesting as pain in the lower extremities (18). The authors concluded percutaneous electrical therapy was a useful nonpharmacological therapy. In addition to decreasing extremity pain, percutaneous electrical therapy improved

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physical activity and quality of sleep, while reducing the need for oral non-opioid analgesic medication.

Summary:

Complications: These additional 4 studies involved 194 patients. The design of studies #5-8 required delivery of percutaneous electrical stimulation over extended durations (e.g., multiple treatments over multiple weeks). As a result, these 4 studies involved a significant number of independent percutaneous electrical stimulation sessions – 1,506 treatments. Similar to studies #1-4 (summarized on pages 2-4), the authors reported *no* complications associated with the use of the percutaneous electrical stimulation (e.g., tissue damage, nerve injury, infection, burns, etc.) in any of these studies. As with studies #1-4, Vertis followed-up and discussed this issue with the actual clinical Investigators involved in these studies (#5-8) and they confirmed the observation that the studies had no complications or issues that they considered significant. For example, they observed no cutaneous reactions or inflammatory changes at any of the needle insertion sites after the treatment sessions. They reported they had minor issues (e.g., superficial bleeding or soreness at the needle insertion site) in some patients.

Relevance to Vertis PNT: In addition to studies #1-4 in low back pain patients, these additional studies (#5-8) are examples of various other acute-chronic pain conditions in which percutaneous electrical therapy has been shown to benefit patients, with no safety issues reported. Due to the similarity of the PNT stimulation to the therapies deployed in these studies (e.g., see Table B, page 9), Vertis expects PNT to be similarly useful and clearly appropriate for clinician use in pain management for these conditions.

Lastly, it is important to note that many of these studies (#1-8) involved direct comparisons to the substantially equivalent TENS devices. Results showed that percutaneous electrical therapy was, at a minimum, equivalent to TENS as a pain relief modality.

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Appendix 24
Vertis Clinical Trial Information and Data

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Table 6. Investigator determined low back pain diagnoses.
Table 7. Previously tried medications, treatments, and therapies.
Table 8. Results of the responder screen questionnaire prior to 5th treatment.
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Table 14. Patient indication of pain medication intake at follow-up compared with before PNT treatments.

Table 15. Patient perception/satisfaction at follow-up compared with before PNT treatments.

Table 16. Physician assessment at follow-up.

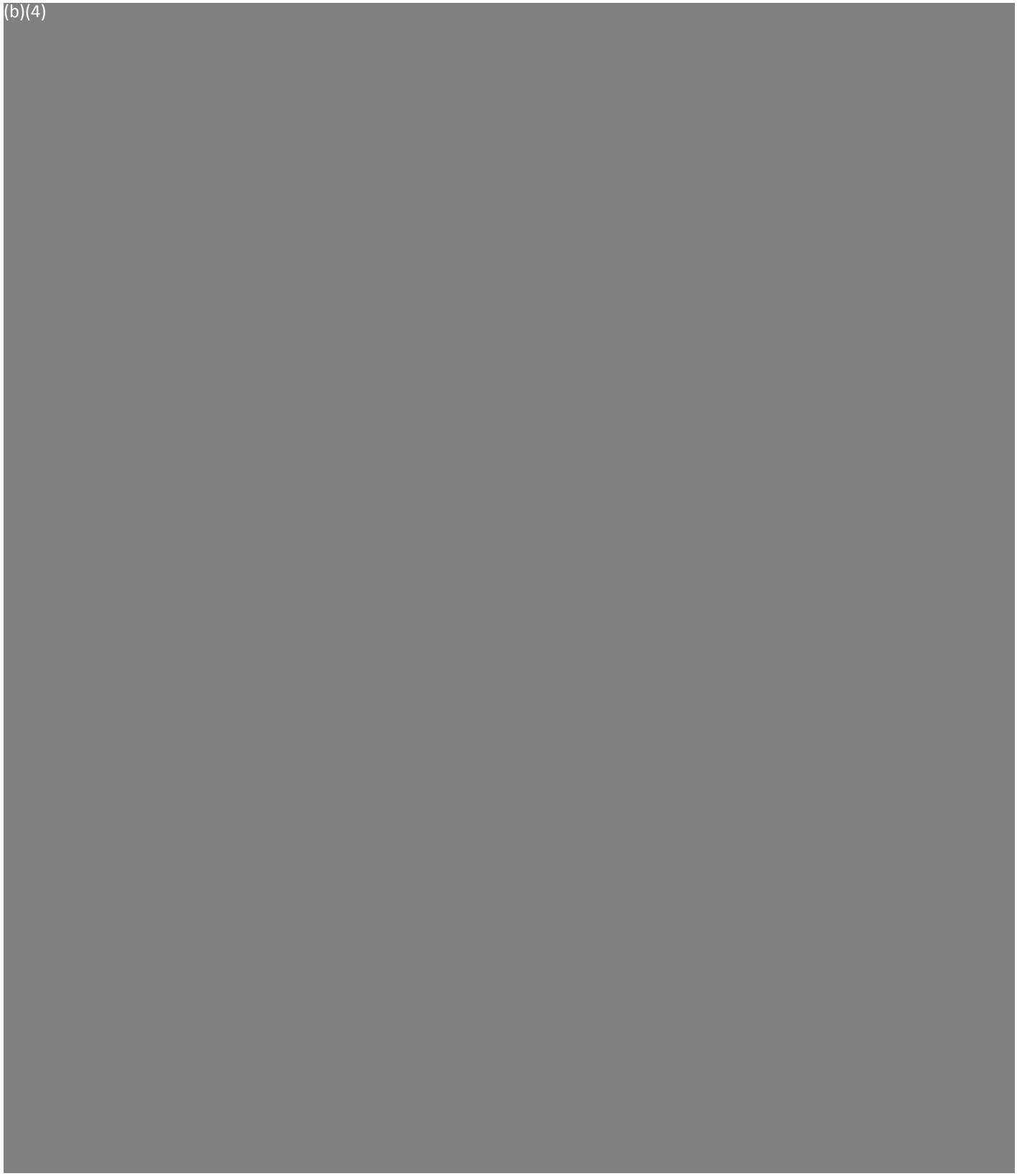
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APPENDIX 24

ATTACHMENT A

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Percutaneous Neuromodulation Therapy (PNT) Low Back Pain Study

INVESTIGATIONAL PLAN

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APPENDIX 24

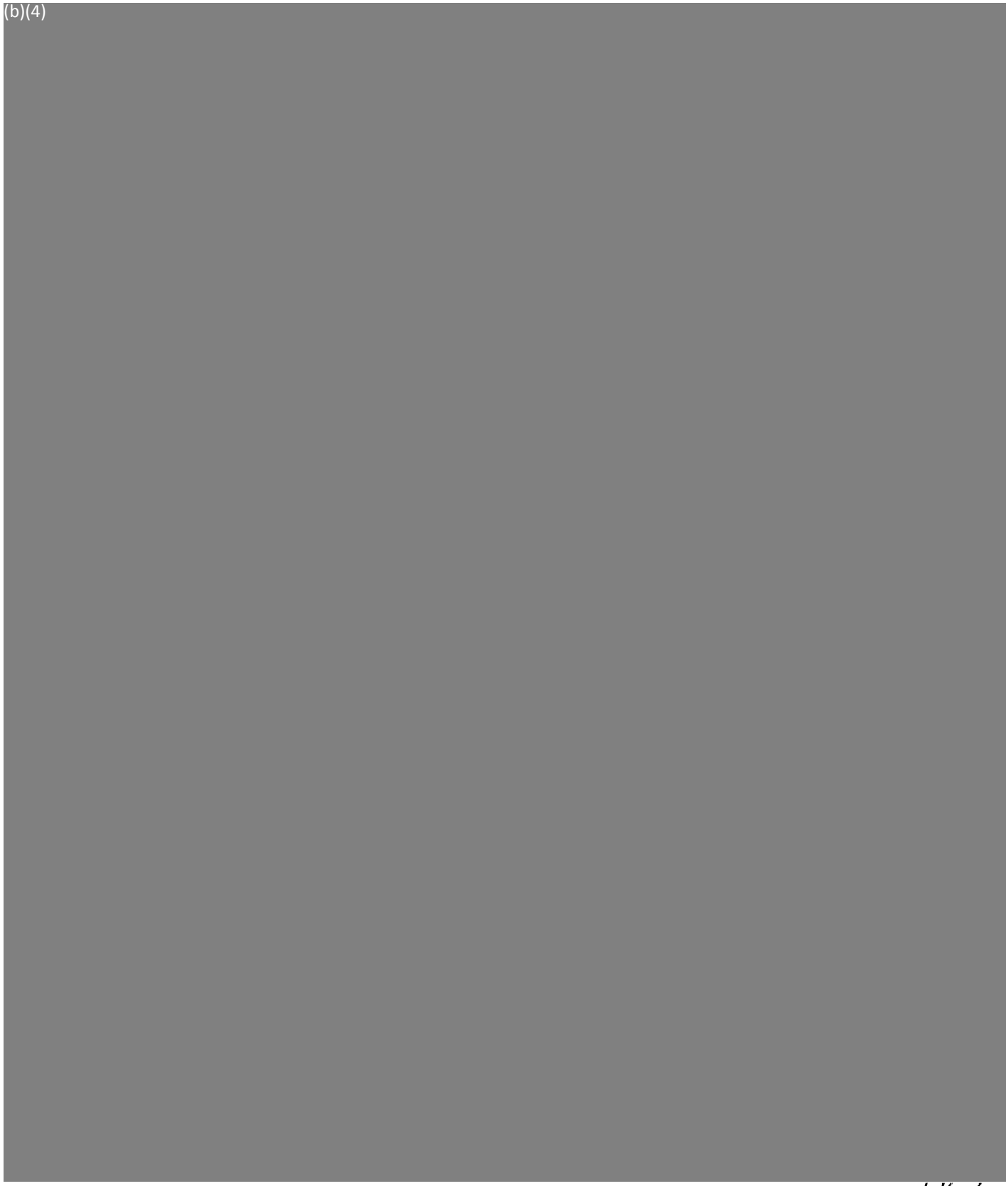
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Appendix 24 – Attachment B
Vertis Clinical Trial – Tables

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ATTACHMENT C

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☐ any proprietary interest in the product tested in the covered study held by the clinical investigator;

☒ any significant equity interest as defined in 21 CFR 54.2(b), held by the clinical investigator in the sponsor of the covered study.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration

Form Approved: OMB No. 0910-0396
Expiration Date: 3/31/02

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical investigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d).

Please mark the applicable checkbox.

☒ (1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator had a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

(b) (6)

☐ (2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).

☐ (3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.

NAME	TITLE
Lori Glastetter	VP Regulatory Affairs and Quality Assurance
FIRM/ORGANIZATION	
Vertis Neuroscience, Inc.	
SIGNATURE	DATE
	12-31-00

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Appendix 25
510(k) Summary of Safety and Effectiveness

Vertis Neuroscience, Inc.
Percutaneous Neuromodulation Therapy (PNT) ™ Control Unit and Accessories

General Information

Classification	Class II
Trade Name	Percutaneous Neuromodulation Therapy (PNT) Nerve Stimulation System
Submitter	Vertis Neuroscience, Inc. 2101 Fourth Avenue, Suite 200 Seattle, Washington, USA 98121
Contact	Lori Glastetter Vice President, Regulatory Affairs/ Quality Assurance

Substantially Equivalent Devices

Manufacturer	Substantially Equivalent devices	510(k)
Empi, Inc. St. Paul, MN	EPIX Tens Device System Model EPIX VT Model EPIX XL	K970203 K951903
Rehabilicare, Inc. New Brighton, MN	SMP-Plus™ Model 4930	K982410
Chattanooga Group, Inc. Hixson, TN	Intelect ® Legend Stim Model IFC2 (catalog #INT002)	K924666
Medtronic, Inc Minneapolis, MN	Mattrix ® Neurostimulation System Receiver model: 3272 Transmitter model: 3210	K982902
TECA Corporation Pleasantville, NY	TECA Disposable Monopolar Needles 902-DMFxx-TP series 892-DMGxx-TP series	K973442
Medtronic, Inc. Minneapolis, MN	DMN™ Disposable Monopolar Needle Electrodes DMFxx series DMNxx series	K950314
Medtronic, Inc. Minneapolis, MN	Resume II Lead Model 3587a	K915540

Intended use

Percutaneous Neuromodulation Therapy (PNT) is indicated for the symptomatic relief and management of chronic, intractable pain and/or as an adjunctive treatment in the management of post-surgical and post-trauma acute pain.

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Device Description

The Vertis PNT System is designed for delivering percutaneous electrical stimulation (termed: Percutaneous Neuromodulation Therapy - PNT). The Vertis PNT System is intended to be used in pain management by a physician (e.g., anesthesiologists or physical medicine and rehabilitation physicians) or on the order of a physician (e.g., by a physical therapist) in a clinic environment. It is not intended for patient use. The device system includes 3 major components:

- the *Vertis PNT Control Unit* - a software-driven, five channel, AC powered nerve stimulator which generates the electrical stimulus;
- the sterile *Safeguides* – which are sterile, needle electrodes, and
- the *Patient Cable* - which interconnects the PNT Control Unit to the electrodes

Bench/Animal Testing

Extensive bench and animal was conducted on the Vertis PNT System and included performance and safety testing. The Vertis PNT System conforms to applicable sections of the technical references and FDA-recognized consensus standards noted below. Additionally, the PNT Control Unit software was validated per recognized validation techniques.

Results: All testing of the products yielded acceptable results prior to commercial distribution.

ANSI/AAMI NS4-1985 Transcutaneous Electrical Nerve Stimulators, approved 5-20-86.
ANSI/AAMI ES1 1993 - Safe Current Limits for Electromedical Apparatus, approved 12-2-93
ANSI/AMI NS15-1995 Implantable Peripheral Nerve Stimulators, approved 2-1-95
IEC60601-1:1993 Medical Electrical Equipment, Part 1: General Requirements for Safety and Amendments A1:1991, A2:1995.
IEC 60601-1-2 First Edition 1993-4 Medical Electrical Equipment, - Part 1: General Requirements for Safety: Electromagnetic Compatibility – Requirements and Tests (tested in accordance to the IEC 61000 series).
IEC 60601-1-4:1996 Medical Electrical Equipment, Part 1: General Requirements for Safety, Part 2: Collateral Standard: Programmable electrical medical systems.
IEC 60601-2-10:1987 Medical Electrical Equipment, Part 2: Particular Requirements for the Safety of Nerve and Muscle Stimulators.
EN (CEN) 1441:1997 Medical Devices – Risk Analysis.

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ANSI/AAMI/ISO 15223: 2000 Medical Devices – Symbols to be used with Medical Device Labels, Labeling and Information to be Supplied, approved 3-13-00.
IEC 60601-2-10:1987 Medical Electrical Equipment, Part 2: Particular Requirements for the Safety of Nerve and Muscle Stimulators.
ANSI/AAMI/ISO 11137: 1994 Sterilization of Health Care Products – Requirements for Validation and Routine Control –Radiation Sterilization; using Method 1 as described per AAMI/ISO TIR No. 13409: 1996 Sterilization of Health care Products – Radiation Sterilization – Substantiation of 25kGy as a Sterilization Dose for Small or Infrequent Production Batches.
ANSI/AAMI/ISO 10993-1:1997, Biological Evaluation of Medical Devices - Part 1: Evaluation and Testing.

Clinical Testing

Under the auspices of an Investigational Device Exemption, Vertis conducted a prospective clinical study evaluating the safety and effectiveness of percutaneous neuromodulation therapy.

The Vertis clinical trial was reviewed and approved in November 2000. The trial commenced shortly thereafter at multiple United States clinical sites. The trial was completed in March 2001. During the multi-week investigational protocol, there were a total of 2150 electrode placements in 215 PNT therapy sessions with patients.

Results: The clinical trial demonstrated the safety and effectiveness of the percutaneous neuromodulation therapy.

Summary of Substantial Equivalence

Therefore, due to the similarity of design features, materials, test results, clinical results and indicated use to other predicate devices, Vertis believes the Vertis PNT System does not raise any new safety or effectiveness issues and is substantially equivalent to currently available nerve stimulators, electrodes and accessories that have been determined to be substantially equivalent to devices in commercial distribution prior to May 28, 1976.

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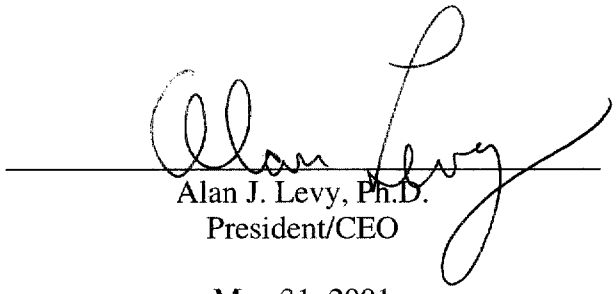
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PREMARKET NOTIFICATION

TRUTHFUL AND ACCURATE STATEMENT

(As Required by 21 CFR 807.87(j))

I certify that, in my capacity as President and Chief Executive Officer of Vertis Neuroscience, Inc., I believe to the best of my knowledge, that all data and information submitted in the premarket notification are truthful and accurate and that no material fact has been omitted.



Alan J. Levy, Ph.D.
President/CEO

May 31, 2001

510(k) Number: _____ (This Notification)

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Appendix 27
Indications for Use

Percutaneous Neuromodulation Therapy (PNT) is indicated for the symptomatic relief and management of chronic, intractable pain and/or as an adjunctive treatment in the management of post-surgical and post-trauma acute pain.

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Appendix 28
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Note: Articles in **bold text** have been included for reference in this Appendix.

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PRELIMINARY COMMUNICATION

Percutaneous Electrical Nerve Stimulation for Low Back Pain

A Randomized Crossover Study

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William F. Craig, MD
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Hesham E. Ahmed, MD
Mohamed A. Hamza, MD
Brent N. Henderson, PhD
Noor M. Gajraj, MD
Philip J. Huber, MD
Robert J. Gatchel, PhD

Context Low back pain (LBP) contributes to considerable disability and lost wages in the United States. Commonly used opioid and nonopioid analgesic drugs produce adverse effects and are of limited long-term benefit in the management of this patient population.

Objective To compare the effectiveness of a novel nonpharmacologic pain therapy, percutaneous electrical nerve stimulation (PENS), with transcutaneous electrical nerve stimulation (TENS) and flexion-extension exercise therapies in patients with long-term LBP.

Design A randomized, single-blinded, sham-controlled, crossover study from March 1997 to December 1997.

Setting An ambulatory pain management center at a university medical center.

Patients Twenty-nine men and 31 women with LBP secondary to degenerative disk disease.

Interventions Four therapeutic modalities (sham-PENS, PENS, TENS, and exercise therapies) were each administered for a period of 30 minutes 3 times a week for 3 weeks.

Main Outcome Measures Pretreatment and posttreatment visual analog scale (VAS) scores for pain, physical activity, and quality of sleep; daily analgesic medication usage; a global patient assessment questionnaire; and Health Status Survey Short Form (SF-36).

Results PENS was significantly more effective in decreasing VAS pain scores after each treatment than sham-PENS, TENS, and exercise therapies (after-treatment mean ± SD VAS for pain, 3.4 ± 1.4 cm, 5.5 ± 1.9 cm, 5.6 ± 1.9 cm, and 6.4 ± 1.9 cm, respectively). The average ± SD daily oral intake of nonopioid analgesics (2.6 ± 1.4 pills per day) was decreased to 1.3 ± 1.0 pills per day with PENS ($P<.008$) compared with 2.5 ± 1.1, 2.2 ± 1.0, and 2.6 ± 1.2 pills per day with sham-PENS, TENS, and exercise, respectively. Compared with the other 3 modalities, 91% of the patients reported that PENS was the most effective in decreasing their LBP. The PENS therapy was also significantly more effective in improving physical activity, quality of sleep, and sense of well-being ($P<.05$ for each). The SF-36 survey confirmed that PENS improved posttreatment function more than sham-PENS, TENS, and exercise.

Conclusions In this sham-controlled study, PENS was more effective than TENS or exercise therapy in providing short-term pain relief and improved physical function in patients with long-term LBP.

JAMA. 1999;281:818-823 www.jama.com

Despite the fact that low back pain (LBP) is one of the most common medical problems in our society,[1] current analgesic therapies remain largely unsatisfactory. Conservative treatment with antiinflammatory drugs and exercise is effective for many patients with acute LBP.[2] However, when the pain symptoms persist, they can interfere with both physical activity and sleep patterns. While analgesic medications can provide temporary pain relief, these drugs may not improve physical function and are associated with well-known adverse effects. Interest in nonpharmacologic alternatives has led to evaluations of transcutaneous electrical nerve stimulation (TENS),[3] acupuncture,[4,5] electroacupuncture,[6] spine manipulation,[7-9] and exercise therapy[9-12] in the management of LBP. However, controversy exists regarding the relative efficacy of these nonpharmacologic therapies in the management of LBP because most of the published studies lacked appropriate control (sham) groups or failed to include relevant comparators.

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Percutaneous electrical nerve stimulation (PENS) is a novel analgesic therapy[13] that combines the advantages of both TENS and electroacupuncture by using acupuncturelike needle probes positioned in the soft tissues and/or muscles to stimulate peripheral sensory nerves at the dermatomal levels corresponding to the local pathology. In a preliminary study,[14] PENS therapy was found to be preferable to TENS and relaxation therapies in the management of pain secondary to osteoarthritis. Therefore, we designed a prospective, randomized, sham-controlled, crossover trial to compare PENS with TENS and exercise therapy in patients with long-term LBP secondary to degenerative disk disease. In addition to assessing the pain response, the patients' physical activity, quality of sleep, sense of well-being, and oral analgesic requirements were evaluated.

METHODS

After obtaining institutional review board approval and written informed consent, 60 patients (29 men and 31 women; mean ± SD age, 43 ± 1.9 years, and weight, 66 ± 1.6 kg) with LBP secondary to radiologically confirmed degenerative disk disease were administered 4 different nonpharmacologic treatment modalities according to a randomized, sham-controlled, crossover study design. The 4 modalities consisted of sham-PENS, PENS, TENS, and flexion-extension exercise. Inclusion criteria included age older than 18 years, absence of any acute or long-term illnesses involving major organ systems, and a history of LBP, which had been maintained at a stable level with oral nonopioid analgesics for at least 3 months prior to enrollment in the study. Exclusion criteria included a history of drug or alcohol abuse, long-term use of opioid-containing medication, a change in the character or severity of the pain within the last 3 months, presence of acute nerve root irritation (sciatica), previous use of nontraditional analgesic therapies (eg, acupuncture), pending medicolegal litigation (or worker's compensation claim), or an inability to complete the health status assessment questionnaires. Patients were told that we were comparing 4 different nonpharmacologic therapies for LBP.

All patients received the 4 treatment modalities according to 1 of 4 different computer-generated sequences: (1) PENS, sham, TENS, and exercise; (2) sham, TENS, exercise, and PENS; (3) TENS, exercise, PENS, and sham; or (4) exercise, PENS, sham, and TENS. Each treatment was administered for 30 minutes 3 times a week (on Monday, Wednesday, and Friday afternoons) for 3 weeks. Upon completion of each 3-week treatment block, the patient was given 1 week off before starting the next modality. The 4 modalities were administered to all patients over the 15-week study period.

Treatment Modalities

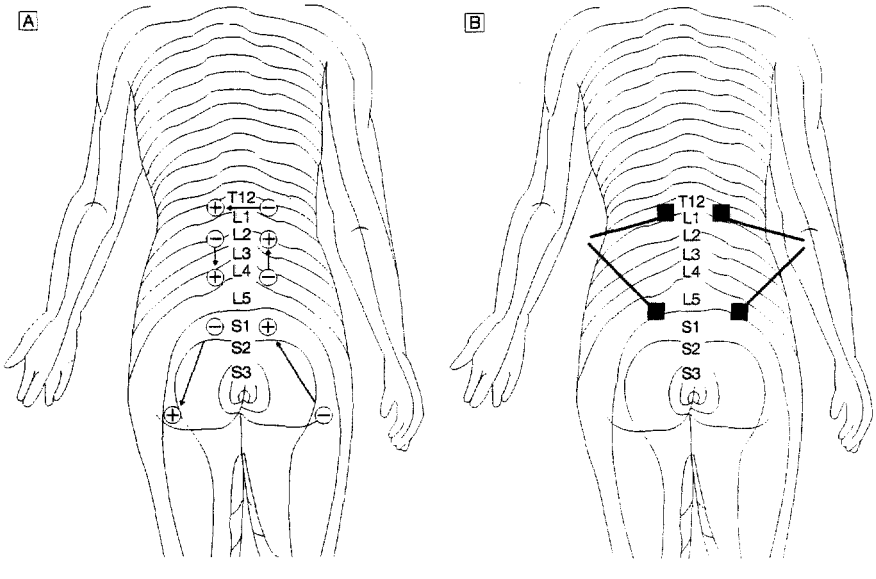
The basic PENS therapy consisted of the placement of ten 32-gauge stainless steel acupuncturelike needle probes into the soft tissue and/or muscle in the lower back region to a 2- to 4-cm depth according to the dermatomal distribution of the pain as illustrated in part A of FIGURE 1. The probes were connected to 5 bipolar leads (with each lead connected to 1 positive and 1 negative probe) from an investigational (not approved by the Food and Drug Administration) low-output (<25 mA) electrical generator, which produced a unipolar square-wave pattern of electrical stimulation at a frequency of 4 Hz with a pulse width of 0.5 milliseconds. The intensity of the electrical stimulation was adjusted to produce the maximum tolerable "tapping" sensation without muscle contractions.

The sham-PENS therapy consisted of the placement of 10 acupuncturelike needle probes in an identical montage (Figure 1, A); however, no electrical stimulation was applied to the probes.

The TENS therapy consisted of the placement of 4 medium-sized (2.5-cm) cutaneous electrode pads (SnapEase, Empi, St Paul, Minn) in a standard dermatomal pattern (Figure 1, B). These electrodes were also stimulated at a frequency of 4 Hz, with a pulse duration of 0.1 milliseconds.

The lower back exercise therapy consisted of spine flexion and extension with

Figure 1. Locations of Needles for PENS and TENS Montage



A, The location of the needles for the sham–percutaneous electrical nerve stimulation (PENS) and PENS treatments. With PENS therapy, each of the 5 bipolar electrical stimulating leads are connected to a pair of needles, alternating the positive and negative positions. B, The location of the 4 cutaneous electrode pads used during the transcutaneous electrical nerve stimulation (TENS) treatments.

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the patient seated on a chair with full abduction of both hips.[15] The patient was instructed to slowly touch the floor with both hands while remaining seated, followed by full extension of the back. This maneuver was repeated a minimum of 30 times during each 30-minute treatment session.

Assessment Procedures

Prior to initiating the first of the 4 treatments, patients were required to complete the Health Status Survey Short Form (SF-36).[16] The physical component summary (PCS) and mental component summary (MCS) scores were used to assess the patient's response to each of the therapeutic modalities.[17] All patients were also asked to assess their baseline level of LBP, physical activity, and quality of sleep during the 48-hour interval prior to each treatment session using standard 10-cm visual analog scales (VASs), with a score of zero equalling the best to a score of 10 equalling the worst (TABLE 1). Repeated VAS assessments of pain, activity, and sleep were performed 3 times a week prior to each treatment session by the patient. In addition, the pain VAS was repeated immediately after completion of each treatment. The SF-36 was repeated 24 hours after completing all 9 treatment sessions with each of the 4 modalities. Patients were instructed not to change the type of nonopioid analgesic medications used during the course of the study. They were also asked to maintain a diary in which they recorded their daily usage of all analgesic medications (eg, pills per day) and any unusual reactions to the investigational therapies. Finally, each patient completed an overall assessment of the relative effectiveness of the 4 different modalities 72 hours after the last treatment session.

Data Analysis

The Number Cruncher Statistical System software program (version 6.0.1 for Windows, Kaysville, Utah) was used for all statistical analyses. An a priori power analysis (α, .05; β, .10; power, 90%; and SD, 2.0) determined that a group size of 60 should be adequate to demonstrate a difference of 25% between the VAS scores for the 4 modalities. The changes in the VAS scores over time were analyzed with repeated measures analysis of variance and t test, with a Bonferroni comparison test (vs control values and pairwise data), applied for multiple comparisons. Analysis of discrete (noncontinuous) data for the 4 treatment modalities was performed using the χ^2 test. The pretreatment and posttreatment changes and the differences between the modalities in the SF-36 scores were analyzed by paired t tests.

RESULTS

The pretreatment SF-36 evaluation suggested that this LBP population reported significantly lower health-related quality-of-life scores compared with the general population. The prestudy scores for this LBP population were 28.4 ± 8.4 and 40.2 ± 5.0 for the PCS and MCS, respectively, compared with general population norms of 50 for these 2 summary scores.[18] The post-PENS treatment SF-36 scores were significantly improved over the prestudy scores for both the PCS (34.2 ± 7.4; $P = .003$) and MCS (42.8 ± 5.2; $P = .007$) components. Both TENS and sham-PENS produced small but statistically significant improvements in the PCS (29.6 ± 8.4 and 29.4 ± 8.6, respectively) and MCS (41.1 ± 5.5 and 41.0 ± 5.4, respectively) scores ($P<.02$). When the changes in the SF-36 scores with the PENS therapy were compared with the other 3 modalities, PENS was found to produce significantly greater improvement in posttherapy function (eg, PENS vs sham-PENS differences were +4.97 ± 2.99 and +1.84 ± 3.56 for PCS and MCS, respectively; PENS vs TENS differences were +4.66 ± 2.85 and +1.7 ± 4.19 for PSC and MCS, respectively; and PENS vs exercise differences were +5.82 ± 2.93 and +1.84 ± 3.56 for PCS and MSC, respectively).

The VAS scores for pain, physical activity, and quality of sleep prior to the first treatment session (baseline) and 24 hours after the last treatment session with each of the 4 modalities are summarized in Table 1. Compared with the baseline values, posttreatment VAS scores for pain, physical activity, and quality of sleep were improved by 46% ± 18%, 42% ± 19%, and 44% ± 20%, respectively, with PENS therapy ($P<.007$). TENS also produced significant decreases in the degree of pain and improvement in physical activity after 6 of 9 treatment sessions ($P<.03$) with an average overall improvement in the degree of pain and physical activity (from the baseline values) of 11% ± 14% and 15% ± 16%, respectively. No significant pain-relieving effects were demonstrated with either the sham-PENS or exercise therapies. Comparing the effects of the 4 treatment modalities on VAS scores for pain, physical activity, and sleep quality revealed that PENS produced significantly greater improve-

Table 1. Comparison of the Average Visual Analog Scale Scores for Low Back Pain, Level of Activity, and Quality of Sleep Prior to Receiving the First Treatment and at 24 Hours After the Ninth Treatment With Each of the 4 Modalities*

Treatment	Sham-PENS	PENS	TENS	Exercise
Degree of pain				
Before	5.7 (1.8)	6.3 (1.5)	6.2 (1.7)	6.5 (1.4)
After	5.5 (1.9)	3.4 (1.4)†	5.6 (1.9)‡	6.4 (1.9)
Level of activity				
Before	5.1 (2.1)	5.5 (2.0)	5.5 (2.1)	5.7 (1.8)
After	4.9 (2.1)	3.2 (1.7)†	4.7 (1.9)‡	5.7 (1.8)
Quality of sleep				
Before	5.0 (2.3)	5.5 (1.9)	5.6 (2.1)	5.8 (1.9)
After	5.0 (2.1)	3.1 (1.6)†	5.3 (2.2)	5.5 (1.9)

*Values are mean (SD) centimeters. PENS indicates percutaneous electrical nerve stimulation; TENS, transcutaneous electrical nerve stimulation.
†Significantly different from value prior to receiving the first treatment (before), $P<.03$, and from sham-PENS, TENS, and exercise therapies, $P<.02$.
‡Significantly different from value prior to receiving the first treatment (before), $P<.04$.

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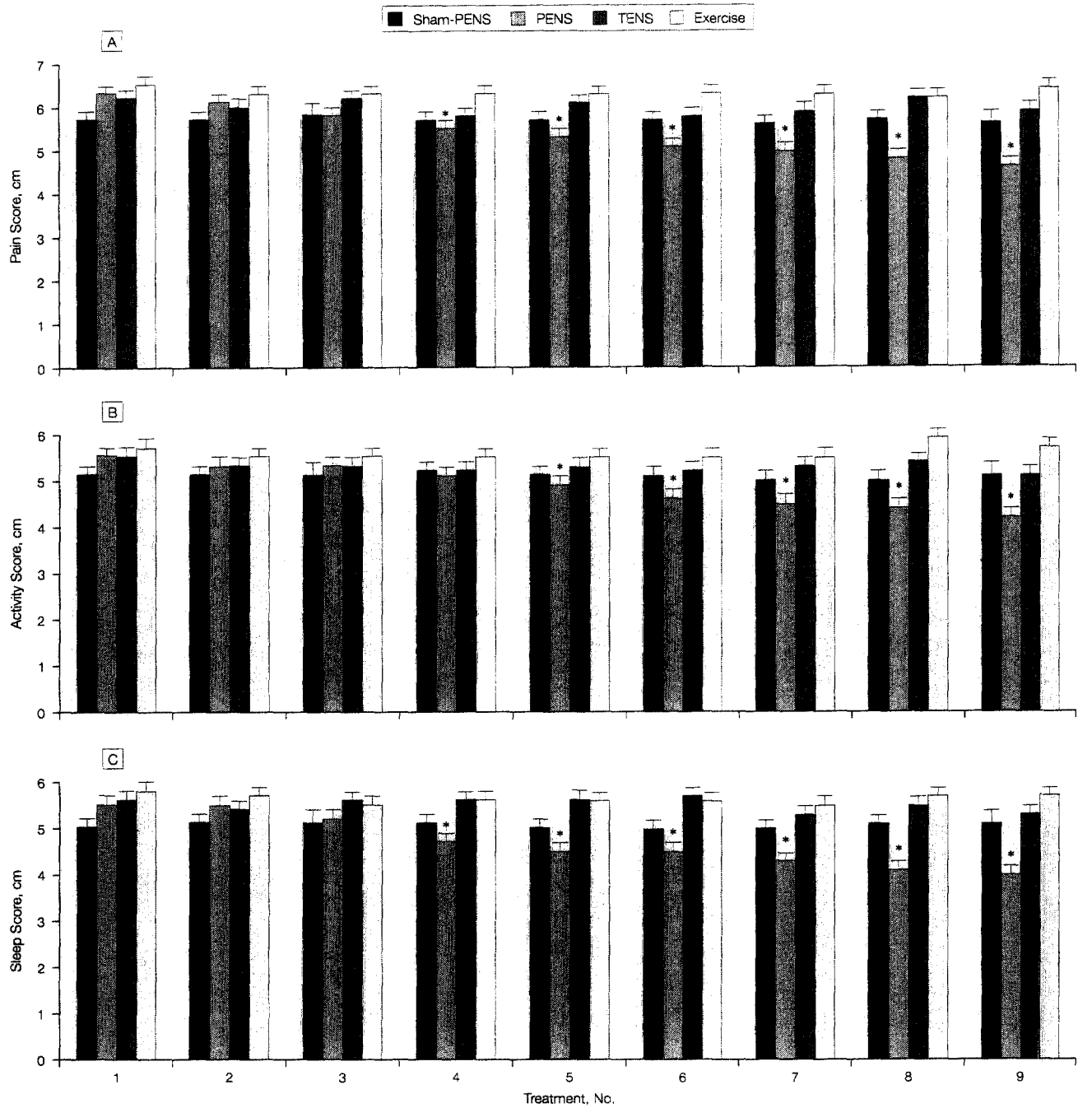
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ments than sham-PENS, TENS, or exercise therapies ($P<.02$).

PENS produced an acute analgesic effect immediately after each treatment session (with an average 82% ± 23% decrease in the pain VAS scores vs 26% ± 19%, 9% ± 15%, and 4% ± 11% decreases with TENS, sham-PENS, and exercise, respectively). After 3 to 4 treatments with PENS, patients began reporting significant improvement in their pretreatment VAS scores for pain, activity, and sleep compared with their baseline values (FIGURE 2). PENS also significantly decreased the consumption of oral

Figure 2. Visual Analog Scale Scores



Visual analog scale scores for low back pain (A), physical activity (B), and quality of sleep (C) before each of the 9 treatment sessions with the 4 study modalities. Values are mean (SEM). Asterisk indicates value is significantly different from baseline value ($P<.03$). PENS indicates percutaneous electrical nerve stimulation; TENS, transcutaneous electrical nerve stimulation.

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nonopioid analgesic medication ($P<.009$) (FIGURE 3). Compared with the prestudy values, PENS therapy was associated with a 50% reduction in the daily oral analgesic requirement. In contrast, TENS therapy decreased the need for analgesic medication on only 6 days during the 3-week study period ($P<.04$). Neither sham-PENS nor exercise therapies altered the patients' usage of their oral analgesic medication.

Finally, the overall evaluation of the 4 treatment modalities indicated that PENS was the preferred therapy in 91% of the study patients (TABLE 2). In addition, PENS was reportedly more effective than TENS and exercise therapies in improving the patients' physical activity and sense of well-being. More than 80% of the patients indicated that they would be willing to pay extra money (out-of-pocket) to receive PENS therapy in the future.

COMMENT

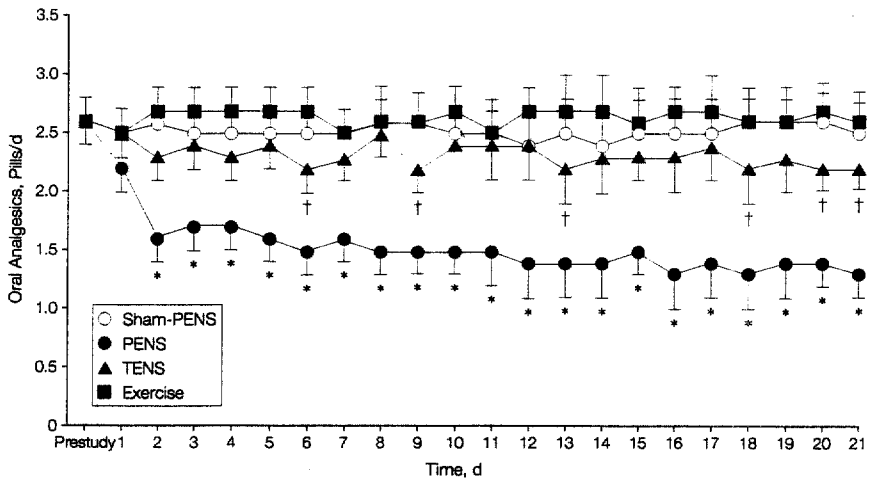
This crossover, sham-controlled study demonstrated that PENS was more effective than TENS and exercise therapies in providing short-term relief of pain and in improving function in patients with stable LBP of at least 3 months' duration. PENS was also significantly more effective than TENS and exercise therapies in reducing the need for oral analgesic medications. These findings are consistent with earlier studies by Deyo et al[19] and Marchand et al,[20] suggesting that TENS therapy is only marginally more effective than a placebo treatment (eg, sham-PENS) in this patient population. Of interest, Moore and Shurman[21] reported that combined neuromuscular electrical stimulation with TENS was significantly more effective than TENS alone in the management of long-term back pain.

PENS therapy was also highly effective in producing acute analgesia in this LBP population. More importantly, the patients began to report more sustained beneficial effects on their level of pain and physical activity, as well as their quality of sleep, after 3 to 4 PENS treatments. Due to the apparent cumulative effects of PENS over the course of the 3-week treatment period, these data would suggest that the use of this treatment modality over a longer period of time has the potential to produce prolonged beneficial effects in patients with long-term LBP. However, a more prolonged period of PENS therapy with careful follow-up at 3-, 6-, and 12-month intervals would be required to assess the long-term effects of this novel therapeutic modality in improving patient outcome.

Enhanced physical activity may be the most important outcome variable in the treatment of LBP.[19,22,23] To achieve the maximal benefit from nonpharmacologic (so-called complementary) analgesic therapies such as PENS, it is recommended that PENS be used as part of a multimodality rehabilitation program, which also includes an ongoing exercise program. Although the simple spine flexion-extension exercise used in this investigation failed to produce a significant improvement in patient well-being when administered alone, this may be a reflection of the lack of effectiveness of this particular exercise maneuver or an inadequate period of exercising. In contrast to our findings, other investigators have found a more extensive exercise program to be as effective as TENS in reducing pain scores and disability in workers with acute LBP.[24] Future studies need to evaluate the effectiveness of PENS therapy in combination with a comprehensive exercise program.

The results of the SF-36 psychological assessments further support and strengthen the clinical findings by providing additional outcome measures, which demonstrates the superiority of PENS over the other

Figure 3. Effect of Sham-PENS, TENS, and Exercise Therapies on the Daily Oral Analgesic Requirements



Change in the daily oral intake of nonopioid analgesic medications during the 3-week treatment period with each of the 4 study modalities. Values are mean (SEM). Asterisk indicates value is significantly different from prestudy value ($P<.008$) and from sham-percutaneous electrical nerve stimulation (PENS), transcutaneous electrical nerve stimulation (TENS), and exercise therapy values ($P<.03$). Dagger indicates value is significantly different from prestudy value ($P<.04$).

Table 2. Overall Patient Evaluation of the Relative Effectiveness of Sham-PENS, PENS, TENS, and Exercise Therapies After Receiving all 4 Treatment Modalities*

Result	Sham-PENS	PENS	TENS	Exercise
Most desirable modality	1 (2)	55 (91)†	4 (7)	0 (0)
Improved physical activity	2 (4)	31 (51)†	5 (8)	0 (0)
Improved sense of well-being	7 (12)	46 (76)†	10 (16)	6 (10)
Preferred pain therapy	1 (2)	55 (91)†	4 (7)	0 (0)
Willing to pay extra for therapy	4 (6)	49 (81)†	5 (9)	2 (4)

*PENS indicates percutaneous electrical nerve stimulation; TENS, transcutaneous electrical nerve stimulation. Values are expressed as number (percentage) of patients.
†Significantly different from sham-PENS, TENS, and exercise therapies, $P<.02$.

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nonpharmacologic treatments used in this study. These data suggest that PENS therapy was the most beneficial modality in improving the physical (eg, fewer limitations in self-care, less severe body pain) and mental (eg, less psychological distress, less disability due to emotional problems) health and well-being of these patients with long-term LBP.

The nature of the electrical (tapping) sensations precluded our ability to perform the treatments in a double-blind fashion. In an attempt to minimize investigator bias, all patient assessments were performed by individuals not involved in administering the therapies. To avoid prejudicing patients in favor of PENS therapy, the sham treatment was described to the patients as an acupuncturelike therapy. Since the needles for the sham-PENS treatments were placed in a dermatomal montage rather than at specific acupoints, it would be inappropriate to conclude that classic Chinese acupuncture is of no benefit in this patient population.

Another potential criticism of the study design relates to the selection of a low-stimulus frequency (4 Hz) for 30-minute intervals for both the PENS and TENS treatments. However, Walsh et al[25] reported that the hypoalgesic effect of TENS was more effective at 4 Hz than 110 Hz. Other investigators have found that more prolonged periods of stimulation (>40 minutes) may be associated with the development of tolerance to the analgesic effect of the electrical stimulus.[26]

Future studies are clearly needed to determine the relative effectiveness of different frequencies and durations of electrical stimulation with PENS therapy. Preliminary experience with PENS in other patient populations suggests that an improved analgesic response may be achieved by using higher (50-100 Hz) or mixed (15 Hz and 30 Hz) stimulating frequencies at subsequent treatment sessions.[13,14] Similarly, this dermatomal montage was selected as a starting point for PENS therapy because it was found to be highly effective in this patient population during our pilot studies. However, depending on the associated manifestations of the pain (eg, radiation down the leg), other needle locations may prove to be more effective for subsequent PENS treatments.

Since long-term LBP is extremely costly to society and can have debilitating effects on both patients and their families, this patient population is increasingly turning to unconventional alternative medical practices (including various forms of nonpharmacologic analgesic therapies).[27] In determining the cost benefit of any new analgesic therapy, it is important to carefully consider both the pertinent costs (eg, equipment, disposables, personnel requirements) and the consequences or outcome of the treatment (eg, patient satisfaction, quality of life, resumption of normal activities) in monetary terms.[28] Future studies should be designed to examine the cost benefit of using PENS therapy as part of a multimodal approach, which would also include anti-inflammatory analgesic drugs and a low back exercise program.

In conclusion, this sham-controlled study demonstrated that PENS is more effective in improving short-term outcomes than TENS and exercise therapies in patients with long-term LBP. The use of PENS therapy significantly decreased the need for oral nonopioid analgesic medications in this patient population.

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The Effect of Stimulus Frequency on the Analgesic Response to Percutaneous Electrical Nerve Stimulation in Patients with Chronic Low Back Pain

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Low back pain (LBP) is one of the most common medical problems in our society. Increasingly, patients are turning to nonpharmacologic analgesic therapies such as percutaneous electrical nerve stimulation (PENS). We designed this sham-controlled study to compare the effect of three different frequencies of electrical stimulation on the analgesic response to PENS therapy. Sixty-eight consenting patients with LBP secondary to degenerative lumbar disc disease were treated with PENS therapy at 4 Hz, alternating 15 Hz and 30 Hz (15/30 Hz), and 100 Hz, as well as sham-PENS (0 Hz), according to a randomized, cross-over study design. Each treatment was administered for a period of 30 min three times per week for 2 wk. The pre- and posttreatment assessments included the health status survey short form and visual analog scales for pain, physical activity, and quality of sleep. After receiving all four treatments, patients completed a global assessment questionnaire. The sham-PENS treatments failed to produce changes in the degree of pain, physical activity, sleep quality, or daily intake of oral analgesic medications. In contrast, 4-Hz, 15/30-Hz, and 100-Hz stimulation all produced significant decreases in the severity of pain, increases in physical activity, improvements in the quality of sleep, and decreases in oral analgesic requirements ($P < 0.01$). Of the three frequencies, 15/30 Hz was the most effective in decreasing pain, increasing physical activity, and improving the quality of sleep ($P < 0.05$). In the global assessment, 40% of the patients reported that 15/30 Hz was the most desirable therapy, and it was also more effective in improving the patient's sense of well-being. We conclude that the frequency of electrical stimulation is an important determinant of the analgesic response to PENS therapy. Alternating stimulation at 15-Hz and 30-Hz frequencies was more effective than either 4 Hz or 100 Hz in improving outcome measures in patients with LBP. **Implications:** The frequency of electrical stimulation seems to be an important determinant of the analgesic efficacy of percutaneous electrical nerve stimulation. Mixed low- and high-frequency stimulation was more effective than either low or high frequencies alone in the treatment of patients with low back pain.

(Anesth Analg 1999;88:841–6)

Low back pain (LBP) is second only to the common cold as a cause for primary care clinic visits (1–4), and it is the second most common cause of absence from work in adults <55 yr of age (5). The current therapies for LBP include physical therapy, epidural steroid injections, opioid and nonopioid analgesic medications, implantable spinal cord-stimulating devices, as well as various psychological and behavioral modification programs.

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Concerns regarding the efficacy and side effects associated with these treatment modalities have increased interest in nonpharmacologic neuromodulation therapies such as transcutaneous electrical nerve stimulation (TENS) (6), acupuncture (7,8), electroacupuncture (9), and percutaneous electrical nerve stimulation (PENS) (10–12). Unfortunately, most of the published studies involving the use of electrical stimulation devices have used arbitrarily chosen treatment variables.

Therefore, we designed a randomized, sham-controlled, cross-over study to evaluate the effect of stimulation frequency on the acute analgesic response to PENS therapy. The comparative effects of three different frequencies of stimulation (4 Hz, alternating

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15 Hz and 30 Hz, and 100 Hz) on pain scores, physical activity, quality of sleep, and the patient's sense of well-being were evaluated in patients with LBP.

Methods

After obtaining institutional review board approval and written informed consent, 68 patients (30 men and 38 women) with LBP associated with radiologically confirmed degenerative lumbar disc disease were enrolled in this randomized, sham-controlled, investigator-masked, cross-over study. Each patient was treated with sham-PENS (no electrical stimulation) and PENS at 4 Hz, alternating 15 Hz and 30 Hz (15/30 Hz) (a mixed frequency using both frequencies at each cycle with the stimulation pulses switched on and off every 3 s), and 100 Hz for a period of 30 min, three times per week for 2 consecutive wk in a random sequence (with 1 wk off between each treatment modality). Inclusion criteria included a history of LBP that has remained unchanged on a stable oral nonopioid analgesic regimen for a period of at least 3 mo before enrolling in the study. Exclusion criteria included LBP with a radicular component (sciatica), a history of drug or alcohol abuse, major organ disease, a change in the character or severity of the pain within the last 3 mo, and an inability to reliably complete the health status survey short form (SF-36), the daily assessment tools, or the global assessment questionnaire.

The basic therapy consists of the placement of ten 32-gauge (0.2 mm) stainless steel acupuncture-like needle probes (ITO, Tokyo, Japan) into the soft tissue and/or muscle in the low back region to a depth of 2–4 cm according to the dermatomal distribution of the pain as illustrated in Figure 1. The 10 probes were connected to five bipolar leads (with each lead connected to one positive and one negative probe) from an investigational (non-Food and Drug Administration-approved), low-output electrical generator, which was calibrated before each series of treatments. The maximal amplitude of the electrical stimulation produced by the generator was 25 mA, with a unipolar square-wave pattern and a pulse width of 0.5 ms. The electrical current was DC, and the duty cycle was continuous. These probes were then stimulated at one of four different frequencies: 0 Hz (sham), 4 Hz, 15/30 Hz, or 100 Hz. The intensity of the electrical stimulation was adjusted to produce the highest tolerable electrical sensation without muscle contractions (except for the sham treatments).

Before initiating the first of the four (frequency) treatment modalities, patients were required to complete the SF-36 (13). The physical component summary (PCS) and mental component summary (MCS) scores were used to assess the patient's response to each of the therapeutic modalities (14). The baseline level of pain, physical activity, and quality of sleep was evaluated before the first treatment with each

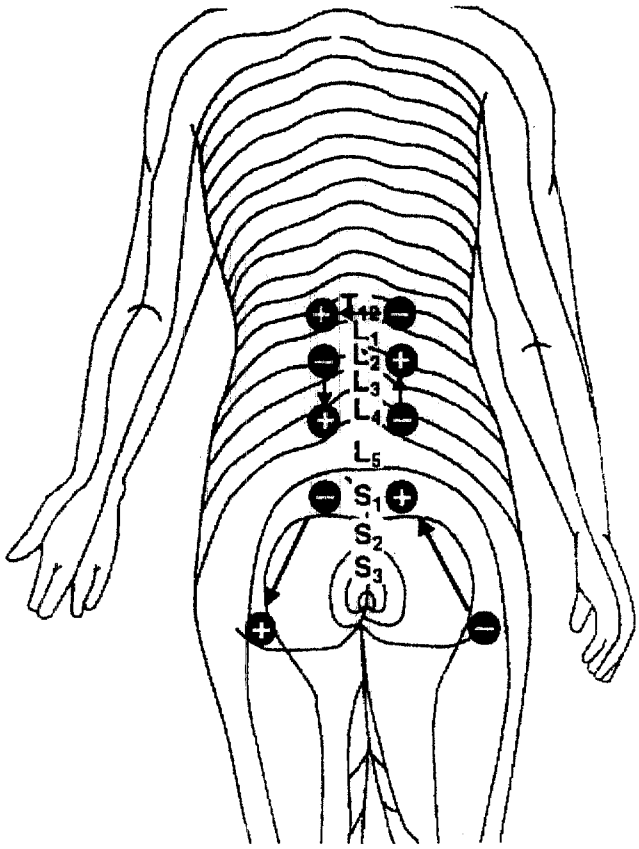


Figure 1. The location of the needle probes for the percutaneous electrical nerve stimulation (PENS) and sham-PENS treatments. With PENS therapy, each of the five bipolar leads from the low-output electrical generator was connected to a pair of needle probes, alternating the positive and negative positions as shown.

modality using standard 10-cm visual analog scales (VAS), with 0 = best to 10 = worst. Repeat VAS assessments of pain, activity, and sleep were performed three times per week before each treatment session. In addition, the pain VAS was repeated 5–10 min after each treatment session. The daily oral analgesic requirements (pills per day) were recorded in the patient's diary during each phase of the study. The SF-36 questionnaire was repeated after completing all six treatment sessions with each of the four frequency modalities. Finally, each patient completed a global assessment questionnaire comparing the relative effectiveness of the sham and the three stimulation frequencies 72 h after the final treatment session.

The NCSS software package (version 6.0.1; NCSS, Kaysville, UT) was used for all statistical analyses. An *a priori* power analysis with $\alpha = 0.05$, $\beta = 0.10$ (power 90%) and SD of 2.0 determined that a group size of 60 should be adequate to demonstrate a difference of 25% among the pain VAS scores for the four frequencies

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studied. The changes in the VAS scores were analyzed using repeated-measures analysis of variance and Student's *t*-test, with a Bonferroni correction applied for multiple comparisons. Analysis of discrete data was performed by using the χ^2 test. Changes and differences in the SF-36 scores were analyzed by using paired sample *t*-tests. Data are presented as mean values ± SD, median values, and percentages. $P < 0.05$ was considered statistically significant.

Results

The prestudy SF-36 evaluation suggested that this LBP patient population (age 46 ± 21 yr) reported significantly lower health-related quality of life scores compared with the general population. The median prestudy scores were 29.8 and 41.4 for the PCS and MCS, respectively, compared with general population norms of 50 for these two variables. The posttreatment SF-36 test results revealed that the 4-Hz, 15/30-Hz, and 100-Hz frequencies produced significant improvements over the prestudy scores for both the PCS and the MCS components ($P < 0.01$). Moreover, the absolute (mean) magnitude of the changes in PCS and MCS components at the end of each treatment period were similar with 4 Hz (7.0 and 2.8, respectively), 15/30 Hz (7.3 and 3.2, respectively), and 100 Hz (7.1 and 3.1, respectively). In contrast, the sham treatments did not show any significant improvement in posttreatment functionality.

All three frequencies of electrical stimulation produced significant decreases in the pain scores immediately after each treatment (Table 1). Compared with the sham treatments, the 4-Hz, 15/30-Hz, and 100-Hz frequencies of PENS therapy also produced statistically greater decreases in the degree of pain and improved physical activity and sleep quality at the end of the 2-wk treatment period (Fig. 2). However, the overall percent changes in pain, physical activity, and quality of sleep scores were significantly greater after electrical stimulation at 15/30 Hz compared with 4 Hz or 100 Hz.

The daily requirements for nonopioid analgesic medications are summarized in Figure 3. Compared with baseline values 24 h before starting each frequency modality, the need for oral analgesic medications was significantly decreased over the course of the 2-wk treatment period with 4 Hz, 15/30 Hz, and 100 Hz, but not with the sham treatments. Moreover, the overall percent decrease in the oral analgesic requirements was greater with 15/30 Hz (48%) than with 4 Hz (35%) or 100 Hz (33%).

Finally, the global assessment of the four modalities indicated that 15/30 Hz was the therapy preferred by 40% of the patients, whereas 28%, 30%, and 2% favored the 4 Hz, 100 Hz, and sham treatments, respectively (Table 2). In addition, the 15/30-Hz treatments were significantly more effective in improving the patient's physical activity and sense of well-being compared with the 4-Hz, 100-Hz, and sham treatments. Given a hypothetical situation, patients indicated that they would be more willing to pay out-of-pocket for the PENS treatment when it was administered at a frequency of 15/30 Hz (versus the sham treatment).

Table 1. Comparison of the Effects of the Four Frequency (F) Modalities on the VAS Pain Scores

Treatment	Sham	F 4	F 15/30	F 100
1				
Pre	5.8 ± 1.5	6.4 ± 1.6	6.0 ± 1.7	5.7 ± 1.6
Post	5.6 ± 1.8	2.3 ± 1.2*	2.5 ± 1.3*	2.7 ± 1.5*
2				
Pre	5.9 ± 1.8	6.1 ± 1.7	5.4 ± 1.7	5.4 ± 1.8
Post	5.5 ± 1.6	2.1 ± 1.4*	2.3 ± 1.3*	2.5 ± 1.3*
3				
Pre	5.8 ± 1.7	5.9 ± 1.8	5.1 ± 2.0	5.1 ± 1.9
Post	5.7 ± 1.8	2.5 ± 1.2*	2.5 ± 1.4*	2.2 ± 1.5*
4				
Pre	5.6 ± 1.6	5.1 ± 1.5	4.9 ± 1.6	5.0 ± 1.7
Post	5.5 ± 1.9	1.8 ± 1.2*	1.7 ± 1.3*	1.7 ± 1.5*
5				
Pre	5.9 ± 1.7	4.9 ± 1.8	4.5 ± 1.9	4.7 ± 1.8
Post	5.8 ± 1.9	1.4 ± 1.4*	1.3 ± 1.3*	1.6 ± 1.3*
6				
Pre	5.7 ± 1.7	4.7 ± 1.6	4.0 ± 1.4	4.5 ± 1.5
Post	5.5 ± 1.8	1.2 ± 1.2*	1.1 ± 1.4*	1.2 ± 1.5*

Values are mean ± SD.
VAS = visual analog scale, with 0 = no pain to 10 = worst pain imaginable.
* Significantly different from values before (pre) each treatment session ($P < 0.01$).

Discussion

Analogous to previously reported findings in animals with electroacupuncture (15), these data suggest that the frequency of electrical stimulation influences the analgesic response to PENS therapy in patients with chronic LBP. Compared with low- (4 Hz) and high- (100 Hz) frequency stimulation, a mixed pattern (15/30 Hz) of electrical stimulation produced the greatest decrease in pain and improvement in physical activity and quality of sleep at the end of a 2-wk treatment period.

Using a rat model for studying electroacupuncture, Chen et al. (15) reported that the dense-disperse mode of electrical stimulation (alternating 2 Hz and 15 Hz) was more effective than a fixed frequency of stimulation at either 2 Hz or 100 Hz in producing experimental analgesia. According to Sun and Han (16), the enhanced analgesia produced by alternating frequencies results from the differing effects of the frequency of stimulation on the pattern of neurotransmitter release within the central nervous system (CNS). At

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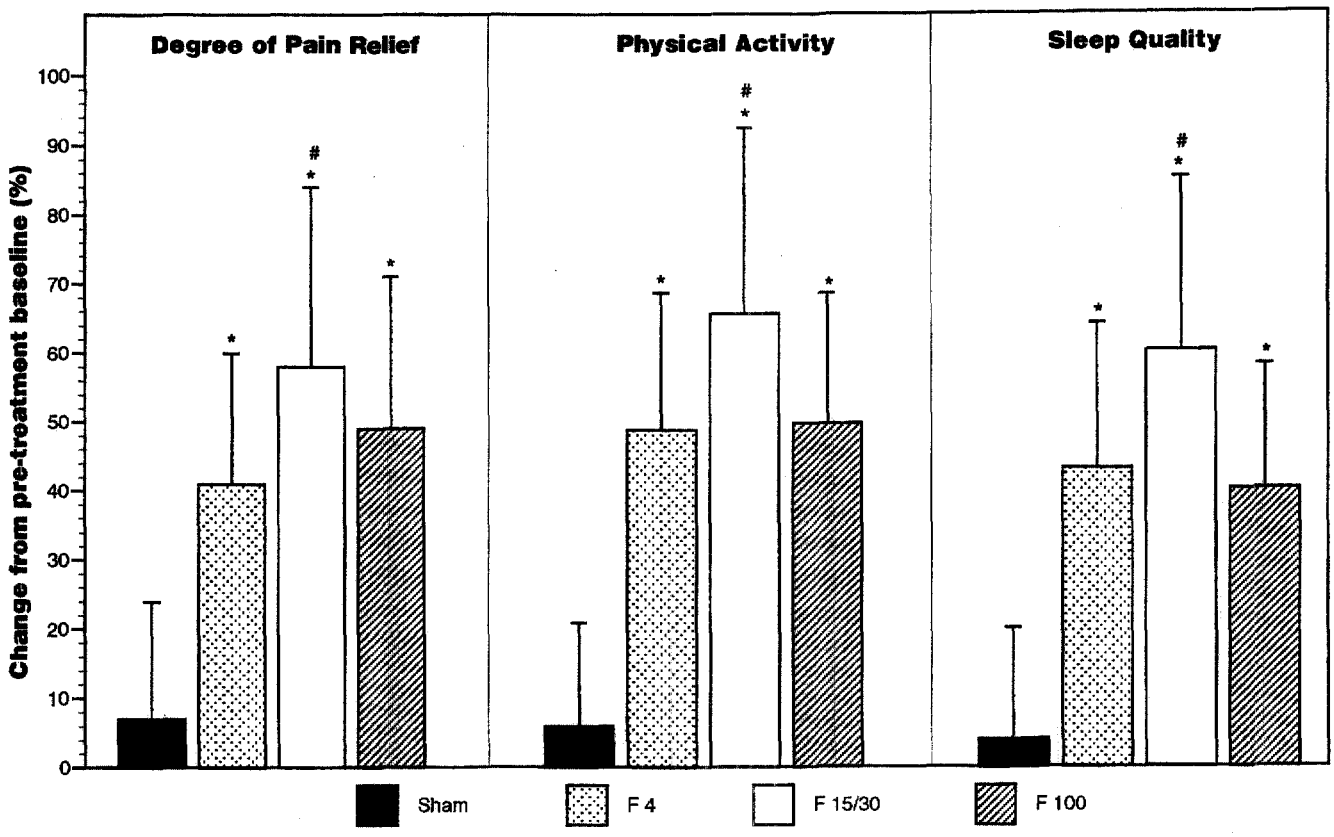


Figure 2. Comparison of the percent changes from baseline value (24 h before the first treatment session with each modality) in the degree of pain relief, physical activity, and sleep quality at the end of each 2-wk treatment period. Data are mean values ± SD. * $P < 0.05$ compared with the sham-percutaneous electrical nerve stimulation values. # $P < 0.05$ compared with F4 and F100 values.

2 Hz, analgesia was alleged to be mediated by stimulation of μ and δ opioid receptors, whereas, at 100 Hz, analgesia was reportedly mediated by activation of κ opioid receptors in the CNS (16).

In studying the effect of the frequency of electroacupuncture stimulation on the release of substance P in the spinal cord, Chen et al. (17) also found that 15 Hz was more effective than either lower (2, 4, or 8 Hz) or higher (30 or 100 Hz) frequencies of electrical stimulation. Analogous to the findings of Sun and Han (16), Goldstein and Naidu (18) also reported that high-frequency (100 Hz) electroacupuncture-induced analgesia was mediated by the activation of κ opioid receptors, whereas low-frequency stimulation (2 Hz) activated μ and δ opioid receptors. One might speculate that using a combination of intermediate frequencies (e.g., alternating 15 Hz and 30 Hz) would activate both subtypes of opioid receptors. However, opioid receptor binding studies would have to be performed to determine the pattern of opioid receptor activation that occur when mixed frequencies of electrical stimulation are used to produce electroanalgesia in humans.

Controversy still surrounds the optimal frequency of electrical stimulation for TENS therapy (19). For example, Walsh et al. (20) reported that a low frequency (4 Hz) of stimulation had a greater hypoalgesic effect than high-frequency (100 Hz) stimulation using an experimental pain model. However, Johnson et al. (21) reported that using high-frequency stimulation (20–80 Hz) produced greater analgesic effects than low-frequency stimulation (10 Hz). Consistent with our findings using PENS therapy, Hansson and Ekblom (22) reported significant pain relief at both high and low frequencies of electrical stimulation. In a recent TENS study, Hamza et al. (23) found that mixed-frequency electrical stimulation at 2 and 100 Hz produced greater postoperative analgesic-sparing effects than either 2 Hz or 100 Hz alone. Thus, it seems that both PENS and TENS therapies are most effective when administered using mixed frequencies of electrical stimulation.

The deficiencies in the current study design relate to an inability to effectively blind the patients, although a sham treatment was included because of the unique nature of the electrical sensation produced by the active PENS treatments. In an attempt to minimize investigator bias, all patient assessments were performed by one of the investigators not involved in actually administrating the PENS therapy. To avoid

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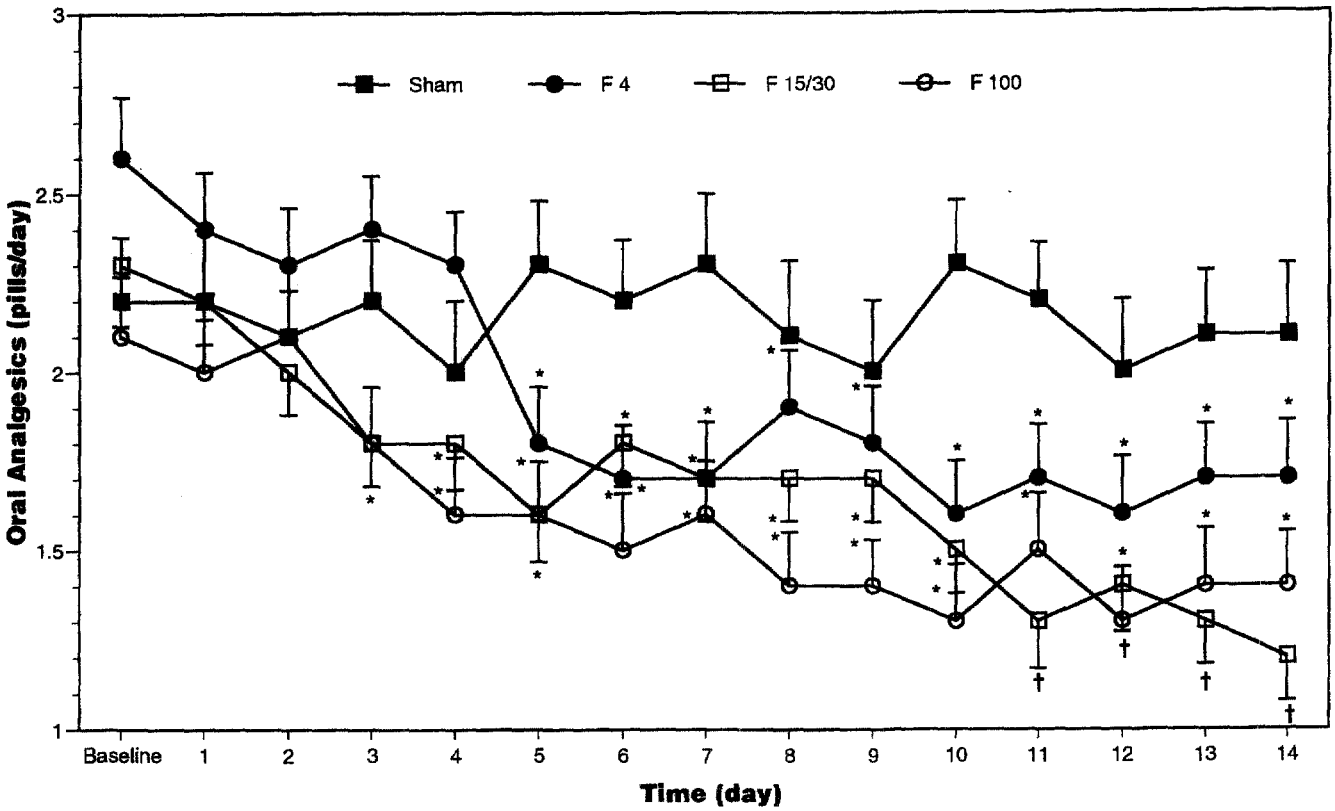


Figure 3. Changes in the daily oral intake of nonopioid analgesic medications (pills per day) during the 2-wk treatment period with each of the four frequency modalities. Data are mean values ± SEM. * $P < 0.05$ and † $P < 0.01$ compared with values 24 h before the first treatment (baseline).

Table 2. Overall Patient Evaluation of the Relative Effectiveness of the Three Different Frequencies (F) and Sham Therapies After All Six Treatment Sessions with Each Modality

	Sham	F 4	F 15/30	F 100
Most desirable modality	2	28*	40*†‡	30*
Improved physical activity	3	30*	38*†‡	29*
Improved sense of well-being	5	23*	44*†‡	28*
Preferred pain therapy	2	28*	40*†‡	30*
Willing to pay extra for therapy	3	25*	45*†‡	27*

Values are expressed as percentages.
* Significantly different from the sham treatments ($P < 0.05$).
† Significantly different from the F4 treatments ($P < 0.05$).
‡ Significantly different from the F100 treatments ($P < 0.05$).

prejudicing patients in favor of the active PENS treatments, the sham treatment was described to the patients as "acupuncture-like" therapy. Because the needles for the sham-PENS treatments were placed in the same dermatomal montage used for the PENS therapy, rather than at specific acupoints, it would be inappropriate to conclude that classic Chinese acupuncture is of no benefit based on these findings. In addition, the use of alternating 15-Hz and 30-Hz frequencies (rather than alternating 4 Hz and 100 Hz) may be a limitation because of the limitations of the electrical generator used in this study. The study was designed to cover the widest possible frequency range (4–100 Hz), but the stimulating device was not able to combine these frequencies when used in the alternating stimulation mode. In a future study, it would be of interest to compare 15-Hz and 30-Hz frequencies of electrical stimulation alone with an alternating 15/30-Hz pattern.

Given the interest of both patients and healthcare providers in unconventional (or so-called complementary) medical therapies (24,25), it is not surprising that nonpharmacologic electroanalgesic therapies (e.g., PENS, electroacupuncture) are increasing in popularity. Future studies in patients with LBP should focus on the effects of these nontraditional modalities on long-term outcome measures (e.g., chronic analgesic use, return to work) when used to supplement conventional analgesic medications and physical therapy as part of a multimodal treatment program (26).

In conclusion, using a mixed frequency (alternating 15 Hz and 30 Hz) of PENS was more effective than either low (4 Hz) or high (100 Hz) frequencies alone in improving short-term outcome measures in patients with LBP.

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Effect of the Duration of Electrical Stimulation on the Analgesic Response in Patients with Low Back Pain

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Background: **Electrical stimulation of peripheral nerves produces acute analgesic effects. This randomized, sham-controlled, crossover study was designed to evaluate the effect of differing durations of electrical stimulation on the analgesic response to percutaneous electrical nerve stimulation in 75 consenting patients with low back pain.**

Methods: **All patients received electrical stimulation for four different time intervals (0, 15, 30, and 45 min) in a random sequence over the course of an 11-week study period. All active percutaneous electrical nerve stimulation treatments were administered using alternating frequencies of 15 and 30 Hz three times per week for 2 consecutive weeks. The prestudy assessments included the health status survey short form questionnaire and 10-cm visual analog scale scores for pain, physical activity, and quality of sleep, with 0 being the best and 10 being the worst. The pain scoring was repeated 5–10 min after each 60-min study session and 24 h after the last treatment session with each of the four methods. The daily oral analgesic requirements were assessed during each of the four treatment blocks. At the end of each 2-week treatment block, the questionnaire was repeated.**

Results: **Electrical stimulation using percutaneously placed needles produced short-term improvements in the visual analog scale pain, physical activity, and quality of sleep scores, and a reduction in the oral analgesic requirements. The 30-min and 45-min durations of electrical stimulation produced similar hypoalgesic effects (48 ± 21% and 46 ± 19%, respectively) and were significantly more effective than either 15 min (21 ± 17%) or 0 min (10 ± 11%). The 30- and 45-min treatments were also more effective in improving physical activity and sleep scores over the course of the 2-week treatment period. In contrast to the sham treatment (0 min), the health status survey short form revealed that electrical stimulation for 15 to 45 min three times per week for 2 weeks improved patient function.**

Conclusion: **The recommended duration of electrical stimulation with percutaneous electrical nerve stimulation therapy is 30 min. (Key words: Electroanalgesia; lumbago; stimulation interval.)**

THERAPIES for low back pain (LBP) include physical therapy, epidural steroid injections, opioid and nonopioid analgesic medications, implantable spinal cord–stimulating devices, and various psychologic and behavioral modification programs. Although these therapeutic methods may be effective for patients with acute LBP,[1] they are unsatisfactory for many patients with chronic LBP. If pain symptoms persist, the use of pharmacologic therapy can interfere with physical activity and sleep patterns and produce unwanted side effects.[2] These concerns have increased interest in nonpharmacologic therapies for LBP, including transcutaneous electrical nerve stimulation (TENS),[3] acupuncture,[4] electroacupuncture,[5] and percutaneous electrical nerve stimulation (PENS).[6-8]

Percutaneous electrical nerve stimulation is a novel, nonpharmacologic analgesic therapy that combines the advantages of transcutaneous electrical nerve stimulation (*i.e.*, peripheral dermatomal-based electrical nerve stimulation) and electroacupuncture (*i.e.*, electrical stimulation at specific acupoints *via* percutaneously placed needles). This therapy involves the placement of acupuncture needle probes in the soft tissues or muscles to stimulate peripheral sensory nerves at the dermatomal (or sclerotomal) levels corresponding to the local dis-

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ease. The effect of the duration of the electrical stimulation on the short-term analgesic response to PENS therapy has not been studied previously.

Therefore, we designed a randomized, single-blind, crossover study to evaluate the analgesic effectiveness of different durations of electrical stimulation of PENS therapy in patients with LBP. In addition, the comparative effects of the different durations of stimulation on the patients' levels of physical activity and quality of sleep, as well as daily oral analgesic requirements, were assessed over each 2-week treatment interval.

Materials and Methods

After obtaining local institutional review board approval and written informed consent, 75 patients (34 men and 41 women, ranging between 21 and 76 yr of age) with LBP secondary to radiologically confirmed degenerative lumbar disk disease received electrical stimulation *via* acupuncture needle probes for periods of 0, 15, 30, and 45 min, according to a randomized, single-blind, crossover study design. Inclusion criteria included age older than 18 yr and a history of LBP related to degenerative lumbar disk disease with a pain level that remained unchanged over a period of at least 3 months before enrolling in the study. Forty-two percent of the study patients had undergone previous back surgery. Exclusion criteria included LBP with a radicular component (sciatica), a history of drug or alcohol abuse, previous experience with acupuncture, a change in the character or severity of the pain within the last 3 months, a recent change in analgesic medications (or current use of opioid-containing drugs), and the inability to reliably complete the health status survey short form (SF-36),[9] daily assessment tools, or the global assessment questionnaire.

All patients were told that each treatment session would last for 60 min, with varying periods of electrical stimulation (producing either no sensation or a light tapping sensation), three times per week (on Monday, Wednesday, and Friday afternoons) for 2 consecutive weeks, with 1 week "off" before each treatment modality. Patients were exposed to all four stimulation intervals in a random sequence over the course of the 11-week study period.

Treatment Methods

Ten 32-gauge stainless steel acupuncture needle probes (ITO, Tokyo, Japan) were placed into the soft tissue or muscle to a depth of 2–4 cm in the low back region according to the dermatomal (or sclerotomal) distribution of the pain for a period of 60 min, as shown in figure 1. The 10 probes were connected to five bipolar leads (with each lead connected to one positive and one negative probe) from an investigational low-output electrical generator and stimulated for a period of 0, 15, 30, or 45 min at an alternating frequency of 15 and 30 Hz.[10] The intensity of the electrical stimulation was adjusted to produce a tolerable tapping sensation without muscle contractions. The maximum amplitude of the electrical stimulation produced by the generator was 25 mA using a unipolar square-wave pattern and a pulse width of 0.5 ms. The electrical current was direct and the duty cycle was continuous.

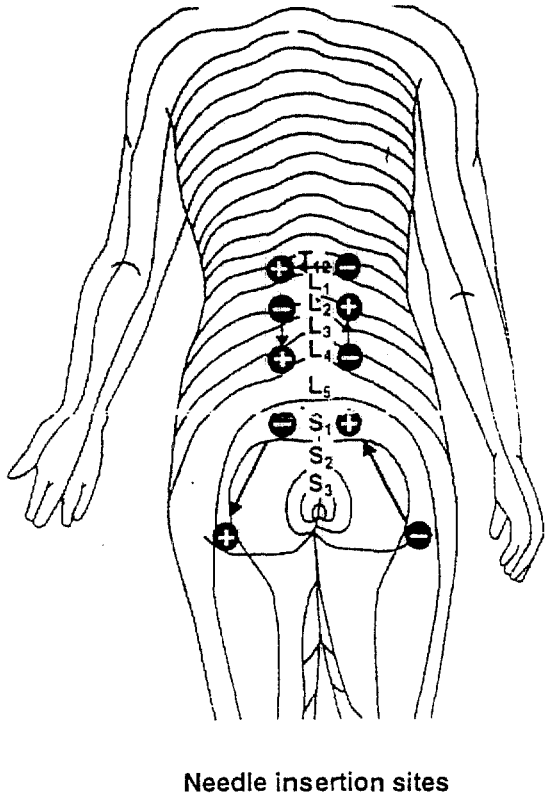


Fig. 1. The location of the needle probes for the percutaneous electrical nerve stimulation and nonelectrical ("sham") needle treatments. Each of the five bipolar leads are connected to a pair of needles, alternating the positive (+) and negative (-) connections as shown in the illustration.

Assessment Procedures

Before initiating any of the four treatments, patients were required to complete the SF-36 questionnaire.[9] The physical component summary and mental component summary scores of the SF-36 were used to assess patient

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response to each of the different stimulation intervals.[11] All patients were also asked to assess their level of LBP, physical activity, and quality of sleep during the 24-h interval before the first treatment and after the last (sixth) treatment for each of the four different timing intervals, using three separate 10-cm visual analog scales (VAS), with 0 being the best and 10 being the worst score. Subsequent VAS assessments of the degree of pain, physical activity, and quality of sleep were performed three times per week before each treatment session. In addition, the pain VAS assessment was repeated 5–10 min after completion of each treatment session to determine the acute analgesic response to the therapy. Patients were instructed to record in their diaries (which were checked by the investigators at each clinic visit) the number of oral nonopioid analgesic pills they used each day. The SF-36 questionnaire was again filled out after completing all six treatment sessions with each of the four stimulation intervals.

Data Analysis

The Number Cruncher Statistical System (NCSS) software package (NCSS 6.0.1 statistical system for Windows; NCSS, Kaysville, UT) was used for all statistical analysis. An *a priori* power analysis with $\alpha = 0.05$, $\beta = 0.10$ (power = 90%), and standard deviations of 2.0 and 1.5 determined that a group size of 75 should be adequate to show differences of 20 and 10% between the VAS scores and the daily oral analgesic requirements (pills per day), respectively, for the four treatment intervals studied. The changes in the VAS scores and daily oral analgesic medication usage were analyzed using repeated measures analysis of variance (ANOVA) and the Student *t* test. Changes and differences in the SF-36 scores were analyzed by paired *t* tests. Data are presented as mean values (± SD for tables and ± SEM for figures) and percentages, with $P < 0.05$ considered significant.

Results

Seventy-five patients with a mean age of 47 ± 18 yr, a mean baseline VAS pain score of 7.4 ± 2.2, and a mean duration of pain of 38 ± 13 months, were enrolled in this study. The prestudy SF-36 evaluation suggested that this LBP population reported significantly lower health-related "quality-of-life" scores compared with the general population. The mean prestudy scores were 32.7 ± 7.6 and 41.8 ± 5.9 for the physical and mental component summaries, respectively, compared with general population norms of 50 for these two variables. The post-treatment SF-36 test results revealed that electrical stimulation for 15 to 45 min produced significant improvements compared with the sham (0 min) treatments with respect to the physical and the mental components of the survey ($P < 0.01$ for 15 min and $P < 0.001$ for 30- and 45-min stimulation intervals). However, the absolute mean magnitude of the changes in physical and mental components with the 30-min (+7.4 and +3.1, respectively) and 45-min (+7.1 and +2.9, respectively) stimulation intervals were significantly greater than with the 15-min stimulation interval (+5.4 and +2.1, respectively; $P < 0.01$). Although the improvements after the 30-min interval were greater than those after the 45-min interval, the differences were not statistically significant.

Table 1. Comparison of the Acute Analgesic Effects of the Four Stimulation Intervals on the VAS Pain Scores Immediately before (Pre) and After (Post) Each Treatment Session

Treatment Number	0 min	15 min	30 min	45 min
1 Pre	6.2 ± 1.9	6.8 ± 1.7	6.4 ± 1.9	6.3 ± 1.9
Post	5.8 ± 1.7	5.9 ± 1.9	3.9 ± 1.8†	3.8 ± 1.8†
2 Pre	6.3 ± 1.7	6.2 ± 1.7	5.8 ± 1.8	5.9 ± 1.8
Post	5.8 ± 1.9	4.9 ± 1.8*	3.1 ± 1.7†	3.2 ± 1.7†
3 Pre	6.1 ± 1.8	5.5 ± 2.0	5.4 ± 1.9	5.4 ± 1.7
Post	5.7 ± 2.1	3.8 ± 1.8*	2.9 ± 1.7†	2.9 ± 2.0†
4 Pre	6.2 ± 1.9	4.9 ± 1.6	4.6 ± 2.2	4.9 ± 1.6
Post	5.6 ± 1.9	3.0 ± 2.0*	2.2 ± 1.8†	2.3 ± 1.9†
5 Pre	6.1 ± 2.2	4.3 ± 1.9	4.5 ± 1.8	4.2 ± 1.8
Post	5.5 ± 1.5	2.7 ± 1.7*	2.0 ± 1.7†	1.9 ± 1.6†
6 Pre	6.0 ± 1.6	3.8 ± 1.9	4.5 ± 2.1	4.6 ± 1.5
Post	5.4 ± 1.9	2.0 ± 1.7*	1.6 ± 1.8†	1.5 ± 1.4†

Values are mean ± SD.

VAS = Visual analog scale; 0 = the best to 10 = the worst.

* Significantly different from values before (pre) each treatment session ($P < 0.05$).

† Significantly different from values before (pre) each treatment session ($P < 0.01$).

Electrical stimulation produced significant decreases in pain scores immediately after each treatment, with $P < 0.05$ for the 15-min and $P < 0.01$ for the 30- and 45-min stimulation intervals (table 1). Compared with the values 24 h after the completion of the sixth treatment with each method, mean (overall) percentage changes in the degree of pain, physical activity, and quality of sleep from the baseline values 24 h before starting each treatment block were statistically significant for the 15-min interval ($P < 0.05$) and the 30- and 45-min stimulation

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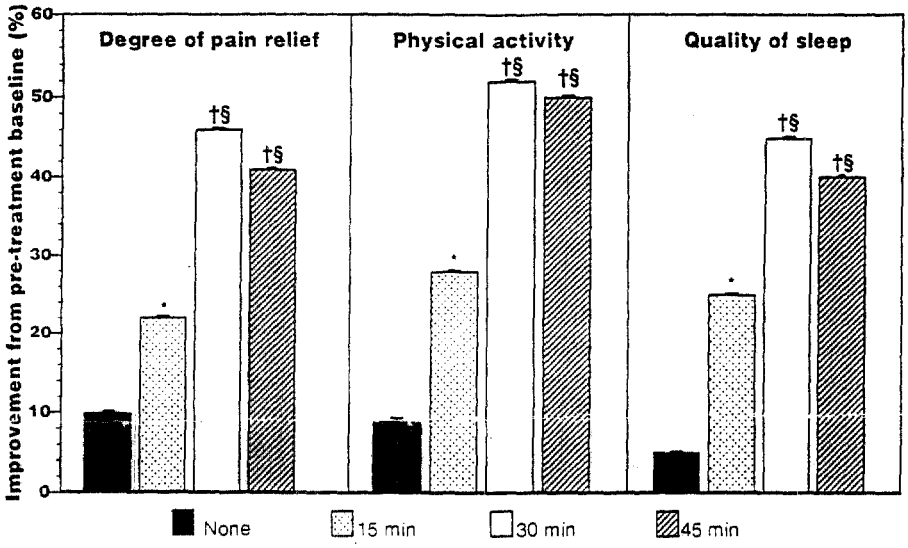


Fig. 2. Comparison of the percentage improvements from the baseline (24 h before and after the first treatment session with each method) in the degree of pain, physical activity, and sleep quality at the end of each 2-week treatment period. Data are mean values ± SEM. Significant differences compared with nonelectrical needle therapy values are designated as follows: *$P < 0.05$; †$P < 0.01$. Significant differences compared with 15-min values are designated by §$P < 0.05$.

intervals ($P < 0.01$) (fig. 2). In addition, there were significant differences between the 30- and 45-min treatment intervals compared with the 15-min treatment interval.

The daily requirements for oral nonopioid analgesic medications (pills per day) are summarized in figure 3. Compared with baseline values, the need for oral analgesic medications was decreased by an average of 8 ± 11%, 21 ± 13 %, 38 ± 16%, and 35 ± 17% over the course of the 2-week treatment period for the 0-, 15-, 30-, and 45-min stimulation intervals, respectively. Compared with no electrical stimulation, it was found that a 15-min stimulation interval ($P < 0.05$) and both the 30- and the 45-min stimulation intervals ($P < 0.01$) were more effective in decreasing the daily oral analgesic requirements. Moreover, the overall decrease in the daily oral analgesic requirements was greater with the 30- and 45-min (*vs.* 15-min) stimulation intervals ($P < 0.05$).

Discussion

Preliminary studies with PENS therapy showed that this therapy produces short-term benefits in patients with chronic LBP secondary to osteoarthritis[6] and degenerative disk disease,[8] and acute herpes zoster pain.[7] This crossover study showed that the duration of electrical stimulation with PENS therapy influences the degree of

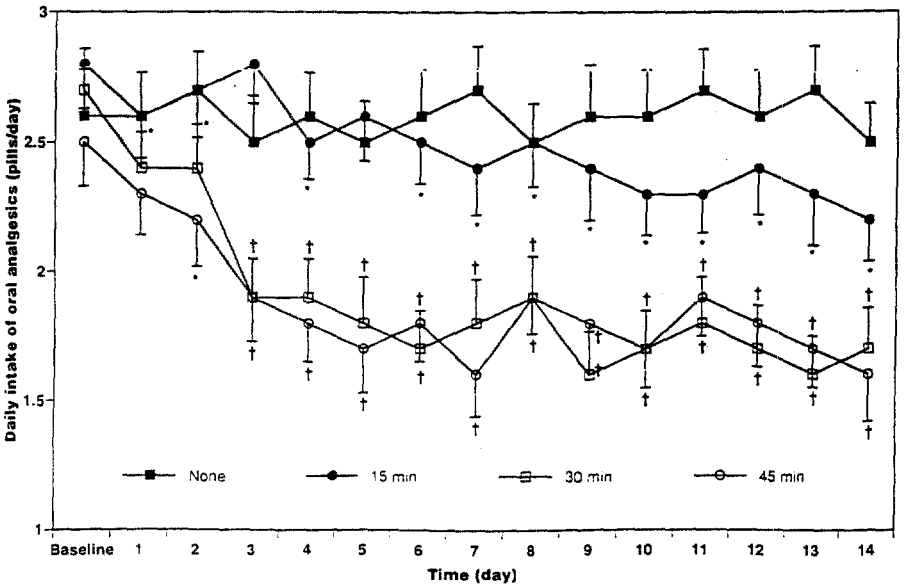


Fig. 3. Changes in the daily oral intake of nonopioid analgesic medications (pills per day) during the 2-week treatment period with each of the four methods. Data are mean values ± SEM. Significant changes from the values 24 h before the first treatment (baseline) are indicated as follows: *$P < 0.05$; †$P < 0.01$.

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acute pain relief and the improvement in function over a 2-week treatment period. Although there were no significant differences between the 30- and 45-min durations of electrical stimulation, both intervals were more effective than the 15-min interval and the no-electrical-stimulation ("sham") treatments. These data suggest that the recommended duration of electrical stimulation for PENS therapy should be 30 min because no additional benefit was achieved with a longer stimulation interval.

These findings are consistent with a study by Romita *et al.*[12] in rodents. Using a rat model to study electroacupuncture-induced analgesia, these investigators found that electrical stimulation for a period of 20 min elicited a greater and longer lasting antinociceptive effect than 10- or 40-min intervals of stimulation. Moreover, a study by Chung *et al.*[13] showed that a 5-min train of electrical stimulation elicited a poststimulation inhibition of spinothalamic tract cells lasting less than 2 min. If the same stimulus was maintained for 15 min, these investigators reported, the inhibition persisted for up to 30 min.[14] These data suggest that more prolonged stimulation may allow summation of central mechanisms, thereby producing a more persistent analgesic effect. However, with continuous electroacupuncture the evoked antinociceptive effect appears to gradually decrease as a function of the time of stimulation.[15] Although short-term electroacupuncture stimulation produces marked analgesic effects, prolonged electroacupuncture stimulation appears to result in the development of tolerance.[16] Other investigators also have reported that prolonged periods of electrical stimulation are associated with the development of tolerance to the electroanalgesic effect.[17]

It has been proposed that the accumulation of antiopioid substances within the central nervous system may account for the development of tolerance to electroacupuncture.[18,19] During prolonged electroacupuncture stimulation, release of endogenous opioids activates the cholecyctokinin octapeptide system, which can counteract the analgesia produced by endogenous opioid substances. Moreover, electroacupuncture appears to enhance the release of endogenous orphanin FQ[20] in the brain, which can also antagonize electroacupuncture-induced analgesia. Therefore, orphanin FQ may play an important role in the development of tolerance to the analgesic effects of electrical stimulation.

In electroacupuncture studies, the effects of the duration of electrical stimulation on the analgesic response also have been reported to be highly variable. For example, it was found that 30 min of stimulation produced hypoalgesic effects lasting several hours,[21–23] whereas a 40-min period of stimulation produced analgesia lasting for only 30 min.[24] If the electrical stimulation was applied for 75 min, the duration of analgesia lasted for only 15 min[24,25] Consistent with these electroacupuncture studies, our data suggest that 30 min is the optimal stimulation interval for PENS therapy. The results of the SF-36 assessment further support this clinical finding by providing an additional outcome measure that shows the superiority of the 30-min electrical stimulation interval (*vs.* intervals ≤ 15 min). These data revealed that if PENS therapy was administered for 30 min at each treatment session, it was more effective in improving the physical (*e.g.*, fewer limitations in self-care, less severe body pains) and mental (*e.g.*, less psychologic distress, less disability resulting from emotional problems) health and well-being of patients with chronic LBP compared with shorter stimulation intervals.

The major limitations in the study design include (1) potential bias because of inability to "blind" the patient to the electrical stimulus, (2) the "placebo effect," resulting from placement of the needles, and (3) the failure to show a sustained analgesic effect after the PENS treatments, with the pain levels returning to baseline values within 1 week after discontinuing each method. Although the investigator collecting these data was blinded to the duration of the electrical stimulation, it was not possible to blind the patients. However, the patients were told that they "may or may not actually feel the stimulus" and they were not informed as to the duration of the electrical stimulation they received at each session. All treatment sessions lasted for 60 min. The placebo (analgesic) effect of the needles alone appeared to be very limited, consistent with previous studies involving PENS therapy.[8,10] Finally, the short-term analgesic effects of PENS are consistent with previous studies in this patient population.[8,10] Future studies need to evaluate the long-term effect of PENS therapy.

In conclusion, this study shows that the duration of electrical stimulation influences the short-term outcome with PENS therapy. Of the different durations of electrical stimulation studied, the 30-min interval appears to be the most suitable for this LBP patient population.

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The Effect of Montage on the Analgesic Response to Percutaneous Neuromodulation Therapy

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The analgesic response to percutaneous neuromodulation therapy (PNT) is influenced by the location, frequency, and duration of electrical stimulation. We evaluated the effect of different patterns of stimulation (montages) on the acute analgesic response to PNT when applied at the same dermatomal levels in 72 consenting patients with low back pain. All of the patients received a standardized montage (I) and three alternative montage (II–IV) patterns according to a randomized, single-blinded, crossover study design. All of the PNT treatments were administered at identical alternating stimulation frequencies of 15 and 30 Hz for a period of 30 min, three times per week for two consecutive weeks, with 1 wk "off" between each modality. Pretreatment assessments included the health status survey short form (SF-36) questionnaire, as well as visual analog scale scores for pain, physical activity, and quality of sleep (with 0 = the best to 10 = the worst). The pain visual analog scale was repeated 5–10 min after each treatment session. The daily oral analgesic usage was recorded in a patient diary. All four montages produced significant improvements in pain (42%–64%), physical activity (35%–51%), and quality of sleep (28%–46%), as well as 23% to 47% reductions in the daily oral analgesic usage. However, Montage II was significantly more effective than the standard (Montage I) and the other two montages studied. These data suggest that the pattern of stimulation (i.e., montage) can influence the acute analgesic response to PNT.

(Anesth Analg 2001;92:483–7)

Recent studies involving percutaneous neuromodulation therapy (PNT), formerly referred to as percutaneous electrical nerve stimulation, have demonstrated the analgesic efficacy of this therapy in the short-term management of low back pain (LBP), sciatica, headaches, and diabetic neuropathic pain (1–4). The response to PNT is influenced by the frequency of the electrical stimulus (5), as well as the duration (6) and location (7) of the percutaneously applied electrical stimulation. For example, the use of mixed stimulating frequencies alternating at 15 and 30 Hz (15/30) is more effective than either low- or high-frequency electrical stimulation alone (5), and the optimal duration of the electrical stimulation is determined to be 30–45 min (6). Furthermore, stimulation of the dermatomal levels corresponding to the patients' pain symptoms was more effective than stimulating nonrelated (remote) dermatomes (7). The effect of the specific pattern of electrical stimulation (i.e., montage) when administered at the same dermatomal levels has not been studied.

Therefore, we designed a randomized, single-blinded, cross-over study to test the hypothesis that the pattern of electrical stimulation influences the acute analgesic response to PNT when applied at the same dermatomal levels in patients with LBP. The short-term analgesic efficacy of three different PNT montages was compared with the standard montage used in previous studies (1,5,6). In addition, the comparative effects of the four different montages on the patients' physical activity, quality of sleep, and need for supplemental oral analgesic medication were assessed over the 11-wk study period.

Methods

After obtaining local IRB approval and written informed consent, 72 patients (31 men and 41 women ranging between 21 and 76 yr of age) with LBP of >6-mo duration, were treated with four different PNT montages according to a randomized, single-blinded, crossover study design. Inclusion criteria included age over 18 yr and radiologically confirmed degenerative lumbar spine disease, with a "stable" level of LBP and

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analgesic usage for at least 3 mo before entering the study. Exclusion criteria included LBP with a radicular component (sciatica), history of drug or alcohol abuse, change in the character or severity of the pain within the last 3 mo, recent change in analgesic medications, and inability to reliably complete the health status survey Short-Form (SF-36), or the daily assessment tools.

Each PNT treatment was administered for 30 min, three times per week (on Monday, Wednesday, and Friday afternoons) for 2 consecutive wk, with a 1 wk "washout" period between each treatment modality. All of the patients received the four different montages over the course of the 11-wk study period. Any missed treatment sessions were completed before switching to the next montage. Montage I (Fig. 1A) was used in our preliminary PNT studies, and this standard montage was compared with three other montages (II–IV) when applied at the same dermatomal levels (Fig. 1B–D). The basic PNT procedure consists of the placement of 10 32-gauge stainless steel acupuncture needles into the soft tissue and/or muscle in the low back region to a depth of 2–4 cm. The 10 needles used with all 4 montages were connected to 5 bipolar leads (with each lead connected to one positive and one negative probe) by using a low-output battery-powered generator. The maximal amplitude of the electrical stimulation produced by the generator was 37 mA with an asymmetric biphasic waveform pattern, a pulse width of 0.7 ms, and a continuous duty cycle. The intensity of the electrical stimulation was adjusted to produce the maximal tolerable "tapping" sensation without eliciting muscle contractions.

Before initiating any of the treatment modalities, the patients were required to complete the SF-36 (8). The physical component summary (PCS) and mental component summary (MCS) scores were used to assess the patient's psychological response to each of the different montages (9). All of the patients were asked to assess their level of LBP, physical activity, and quality of sleep during the 24-h interval before the first treatment session by using three separate 10-cm visual analog scales (VAS), with a response of 0 = the best to 10 = the worst. The VAS assessments of pain, physical activity, and quality of sleep were performed three times per week before each treatment session. In addition, the pain VAS was repeated 5–10 min after completion of each individual treatment to assess the acute analgesic response. The daily oral analgesic requirements were recorded in a patient diary. Finally, the SF-36 was repeated 24 h after completing all six treatment sessions with each of the four montages.

The Number Cruncher Statistical System software package (NCSS 6.0.1 Statistical System for Windows; NCSS Statistical Software, Kaysville, UT) was used for all statistical analyses. An *a priori* power analysis with $\alpha = 0.05$, $\beta = 0.10$ (power = 90%), and standard deviation of 2 cm, suggested that a group size of 72 should be adequate to demonstrate a 17% difference among the pain VAS scores. The changes in the VAS scores over time were analyzed with repeated measures analysis of variance and Student's *t*-test, with a Bonferroni test applied for multiple comparisons. Analysis of discrete data was performed using the χ^2 test. Changes and differences in the SF-36 scores were analyzed by paired *t*-tests. Data were presented as mean values ± SD or SEM and percentages, with P values <0.05 considered statistically significant.

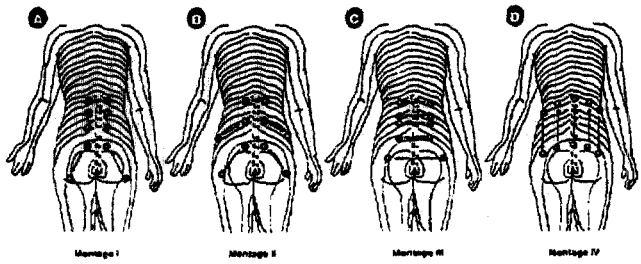


Figure 1. The needle insertion positions and electrode pairing patterns used for the four different PNT montages. Montage I (A) was the standard montage used in all of the earlier PNT studies involving patients with low back pain (1,5,6).

Results

The prestudy SF-36 evaluation suggested that this LBP population reported significantly lower health-related "quality-of-life" scores compared with an age-matched general population without chronic diseases. The prestudy baseline scores were 32.7 and 41.8 for the PCS and MCS, respectively, compared with general population norms of 50 for these two health status survey scores. A comparison of the posttreatment SF-36 test results revealed that all four PNT montages produced significant improvements compared with the baseline scores for both the PCS and the MCS components of the survey ($P < 0.01$). However, the mean magnitude of the changes in the PCS and MCS components with the standard Montage I (+7.1 and +2.9, respectively) and Montage II (+7.6 and +3.2, respectively) were significantly greater than with Montages III (+5.9 and +1.9, respectively) and IV (+5.7 and +1.8, respectively) ($P < 0.05$).

All four montages produced similar 25% to 68% decreases in pain VAS scores immediately after each treatment session (Table 1). However, the cumulative effects over the course of the 2-wk treatment period indicated a better efficacy with Montage II compared with the other three montages (Table 1). Furthermore, the overall percentage changes at the end of the 2-wk treatment period in the VAS pain, physical activity, and quality-of-sleep scores with Montage II (64%,

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Table 1. Comparison of the Effects of the Four Montages of Electrical Stimulation on the Pain VAS Scores Before and After Each of the Six Consecutive Treatment Sessions

Treatment no.	Montage I	Montage II	Montage III	Montage IV
1				
Pretreatment	6.0 ± 1.6	6.1 ± 1.7	5.5 ± 1.9	5.5 ± 1.9
Posttreatment	3.8 ± 1.7*	3.2 ± 1.5†	3.9 ± 1.8*	4.1 ± 1.8*
2				
Pretreatment	5.9 ± 1.7	5.3 ± 1.7‡	5.8 ± 1.8	5.9 ± 1.8
Posttreatment	3.2 ± 1.9†	2.9 ± 1.8†	3.7 ± 1.7*	3.9 ± 1.7*
3				
Pretreatment	5.3 ± 1.8‡	5.1 ± 2.0‡	5.4 ± 1.9	5.4 ± 1.7
Posttreatment	2.8 ± 1.9†	2.5 ± 1.8†	2.9 ± 1.7†	3.6 ± 2.0*
4				
Pretreatment	5.1 ± 1.5‡	4.9 ± 1.6‡	5.2 ± 1.7	5.3 ± 1.6
Posttreatment	2.8 ± 1.9†	1.9 ± 1.6†	2.2 ± 1.8†	2.5 ± 1.9†
5				
Pretreatment	4.7 ± 1.8‡	4.3 ± 1.9‡	4.8 ± 1.8‡	5.0 ± 1.8
Posttreatment	1.9 ± 1.5†	1.6 ± 1.5†	2.0 ± 1.7†	1.9 ± 1.6†
6				
Pretreatment	4.4 ± 1.6‡	3.8 ± 1.4‡	4.5 ± 1.5‡	4.6 ± 1.5‡
Posttreatment	1.4 ± 1.3†	1.2 ± 1.7†	1.6 ± 1.5†	1.5 ± 1.4†

Pretreatment = VAS score 5–10 min before the start of each treatment session.
Posttreatment = VAS score 5–10 min after the end of each treatment session.
VAS = visual analog scale. Mean (±SD) VAS scores, with 0 = the best to 10 = the worst.
* Significantly different from the pretreatment score, $P < 0.05$.
† Significantly different from the pretreatment score, $P < 0.01$.
‡ Significantly different from values before treatment session 1, $P < 0.05$.

51%, and 46%, respectively) were significantly greater compared with the standard (Montage I) (47%, 42%, and 30%, respectively), as well as Montages III (43%, 37%, and 28%, respectively) and IV (42%, 35%, and 29%, respectively) (Table 2). Although the need for oral analgesic medications was decreased over the course of the 2-wk treatment period with all four PNT montages (Fig. 2), the percentage of decrease over the course of the 2-wk treatment period with Montages I (43% ± 23%) and II (47% ± 21%) were significantly greater than with Montages III (27% ± 23%) and IV (23% ± 23%) ($P < 0.05$).

Discussion

Consistent with the previous PNT studies in patients with chronic LBP (1,5,6), Montage I produced both acute and cumulative analgesic effects over the course of the two-week treatment period. This "standard" montage also produced comparable improvements in physical activity and quality of sleep, as well as a reduction in the need for supplemental oral (nonopioid) analgesic medication, as reported in the previous studies involving a similar patient population. These data also support the hypothesis that electrical stimulation of myotomes and sclerotomes at dermatomal levels corresponding to the local pathology is an important factor in the analgesic response to PNT.

In contrast to the previous study (7), in which we evaluated the effect of local-versus-remote dermatomal stimulation, we evaluated the acute analgesic response to PNT when it was administered using different patterns of electrical stimulation at the *same* dermatomal levels. These data suggest that the pattern of stimulation or montage (as determined by electrode placement) influences the acute analgesic response even when the same electrical current is applied at identical dermatomal levels.

Of interest, stimulating along the involved nerve roots at the dermatomal levels corresponding to the patients' pain symptoms (Montage II) was found to be more effective for the acute and short-term pain-reducing effects of PNT, as well as in improving the patients' perceived levels of physical activity and quality of sleep. Although the precise mechanism of PNT-induced analgesia is not known, we speculate that the stimulation pattern used with Montage II produces more effective electrical stimulation of the involved myotomes and/or sclerotomes. On the basis of the PNT studies performed to date, it is recommended to start the therapy using Montage II. If this montage fails to achieve the expected benefits, the patient should be switched to Montage I or one of the other two montages studied.

The failure to conduct the study in a double-blinded manner is a valid criticism of the study. However, all of the evaluations were performed by an independent observer who was unaware of the montage. Another concern relates to the potential residual ("carryover")

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Table 2. Comparison of the Average VAS Scores, as Well as the Percentage Changes, for the Degree of Pain, Level of Activity, and Quality of Sleep During the 24-Hr Period Before Receiving the First Treatment (Before) and 24 Hr After the Last Treatment (After) With Each of the Four Montages

	Montage I	Montage II	Montage III	Montage IV
Degree of pain				
Before (cm)	6.0 ± 1.6	6.1 ± 1.7	6.1 ± 1.6	6.2 ± 1.7
After (cm)	3.2 ± 1.2*	2.2 ± 1.3*	3.5 ± 1.5*	3.6 ± 1.5*
Change (%)	47 ± 2	64 ± 2†	43 ± 2	42 ± 2
Level of activity				
Before	6.2 ± 1.6	6.1 ± 1.7	6.3 ± 1.8	6.3 ± 1.7
After (cm)	3.6 ± 1.4*	3.0 ± 1.3*	4.0 ± 1.3*	4.1 ± 1.5*
Change (%)	42 ± 2	51 ± 2‡	37 ± 2	35 ± 2
Quality of sleep				
Before (cm)	5.4 ± 1.8	5.2 ± 1.7	5.3 ± 1.9	5.5 ± 1.7
After (cm)	3.8 ± 1.2*	2.8 ± 1.4*	3.8 ± 1.5*	3.9 ± 1.5*
Change (cm)	30 ± 2	46 ± 2§	28 ± 2	29 ± 2

Mean (± SD) VAS scores, with 0 = the best to 10 = the worst.
VAS = visual analog scale.
* Significantly different from the 24-h period before the first treatment, $P < 0.05$.
† Significantly different from the 24-hr period before the first treatment, $P < 0.01$.
‡ Significantly different from Montages III and IV, $P < 0.05$.
§ Significantly different from Montages I, III, and IV, $P < 0.05$.

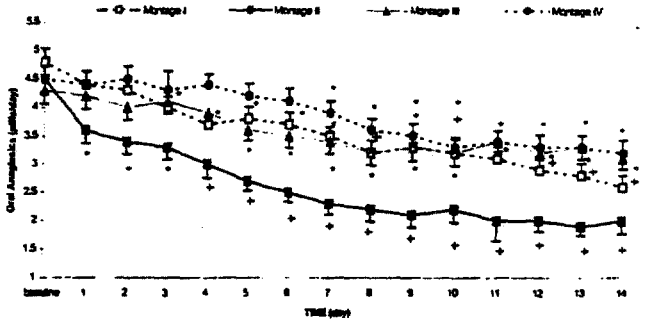


Figure 2. The daily nonopioid analgesic usage (pills per day) during the 2-wk treatment period with each of the four different montages. Baseline refers to the average number of pills consumed per day before entering the study. Values are means ± SEM *Significantly different from the baseline, $P < 0.05$. +Significantly different from Montages III and IV, $P < 0.05$.

effect of the previous montages. To minimize this effect, the montages were evaluated in random order, and a one-week washout period was allowed between the different montages. Finally, the failure to distinguish between the different types of nonopioid analgesic drugs used by the patients may have confounded the interpretation of the effects of the montages on the patient's oral analgesic requirement.

In future studies involving this chronic pain population, the long-term effects of PNT should be evaluated by using the treatment variables that have been established in the preliminary studies (1,5,6). These studies should not only assess pain, physical activity, sleep, and oral analgesic requirements, but also more important outcome measures such as resumption of normal activities and patient satisfaction. Another important area for future investigation is the

beneficial effects of using PNT as a complementary therapy in a multimodal rehabilitation program (10). Finally, the availability of a simple, inexpensive, disposable electrode system would facilitate the use of PNT in the management of both acute and chronic pain disorders.

We conclude that the pattern of electrical stimulation can influence the effects of PNT even when applied at the same dermatomal levels. Peripheral stimulation along the involved nerve roots appears to be the most effective approach in patients with LBP.

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Percutaneous electrical nerve stimulation: an alternative to TENS in the management of sciatica

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Abstract

Sciatica is a common pain problem and current pharmacologic therapies have proven inadequate for many patients. The objective of this sham-controlled investigation was to compare a novel non-pharmacologic technique, percutaneous electrical nerve stimulation (PENS), to transcutaneous electrical nerve stimulation (TENS) in the management of the radicular pain associated with sciatica. Sixty-four consenting patients with sciatica due to lumbar disc herniation were treated with PENS, TENS and sham-PENS according to a randomized, single-blinded, cross-over study. All patients had been maintained on a stable oral non-opioid analgesic regimen for at least 6 weeks prior to entering the study. Each treatment modality was administered for a period of 30 min three times per week for 3 weeks, with 1 week 'off' between each modality. Both PENS and TENS treatments were administered using a stimulation frequency of 4 Hz. The pre-treatment assessment included the health status survey short form (SF-36), as well as visual analog scales (VAS) for radicular pain, physical activity and quality of sleep. The pain VAS was also repeated after each treatment session. At the end of each 3-week treatment block, the SF-36 was repeated. After receiving all three treatment modalities, a global assessment questionnaire was completed. Both PENS (42%) and TENS (23%) were significantly more effective than the sham (8%) treatments in decreasing VAS pain scores. The daily oral analgesic requirements were also significantly reduced compared to the pre-treatment values with PENS ($P < 0.01$) and TENS ($P < 0.05$). However, PENS was significantly more effective than TENS (and sham-PENS) in improving physical activity and quality of sleep. The SF-36 evaluation confirmed the superiority of PENS (versus TENS and sham-PENS) with respect to post-treatment functionality. In the overall assessment, 73% of the patients reported that PENS was the most desirable modality (versus 21% for TENS and 6% for sham-PENS). Finally, 71% of the patients stated that they would be willing to pay extra to receive PENS therapy compared to 22% and 3% for TENS and sham-PENS, respectively. In this sham-controlled study, we concluded that PENS was more effective than TENS when administered at a stimulation frequency of 4 Hz in providing short-term pain relief and improved functionality in patients with sciatica. © 1999 International Association for the Study of Pain. Published by Elsevier Science B.V.

Keywords: Percutaneous electrical nerve stimulation; Transcutaneous electrical nerve stimulation; Sciatica; Radicular leg pain

1. Introduction

Sciatica due to a herniated nucleus pulposus is a common cause of pain and constitute an important socioeconomic problem in our society (Frymoyer, 1988), with a lifetime prevalence of 40% (Frymoyer et al., 1983;Stevenson and Anderson, 1983). Although epidural steroid injections provide short-term improvement in the leg pain associated with a herniated disc, this treatment offers no significant functional benefit and does not reduce the need for surgery (Carelette et al., 1997). While analgesic medications can provide temporary pain relief, both opioid and non-opioid analgesics are associated with well-known side effects.

Increasingly, patients are turning to unconventional 'alternative' medical practices [including non-pharmacologic analgesic therapies like transcutaneous electrical nerve stimulation (TENS) and electroacupuncture] (Eisenberg et al., 1993). Percutaneous electrical nerve stimulation (PENS) is a novel analgesic therapy which combines the advantages of both TENS and electroacupuncture by utilizing acupuncture-like needle probes positioned in the soft tissues and/or muscles to stimulate peripheral sensory nerves at the dermatomal levels corresponding to the local pathology. A recent study demonstrated that electrical stimulation at the dermatomal level was equivalent to acupoint stimulation with

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respect to its analgesic effects (Chen et al., 1998). In a recently published sham-controlled study involving PENS therapy (Ghoname et al., 1999a), it was found to be preferable to TENS and exercise therapy in the management of chronic low back pain.

Therefore, we designed a randomized, sham-controlled, cross-over study to compare PENS to TENS therapy when used in the management of radicular pain associated with sciatica. In addition to assessing the pain response, the patients' physical activity, quality of sleep, sense of 'well-being,' and daily oral analgesic requirements were evaluated.

2. Methods

After obtaining institutional review board approval and written informed consent, 64 patients (30 males and 34 females, mean age 43 ± 19 years) with typical radicular pain lasting for 6–28 months (mean duration of 21 ± 9 months) due to radiologically-confirmed lumbar disc herniation were administered three different non-pharmacologic analgesic modalities (namely, sham-PENS, PENS and TENS) according to a randomized, single (investigator)-blinded, cross-over protocol. The mean (±SD) pre-study pain score was 7.6 ± 2.1 cm on a 10 cm visual analog scale (VAS), with 0 = none to 10 = worst pain imaginable. Inclusion criteria included age greater than 18 years, absence of any acute or chronic illnesses involving major organ systems, and a history of sciatica (defined as the presence of constant or intermittent pain in one leg radiating below the knee, a positive straight-leg raising test, evidence of nerve-root compression at the L5-S1 level confirmed by radiologic testing) which had been maintained at a stable level with non-opioid anti-inflammatory analgesics for a period of at least 6 weeks. Exclusion criteria included a history of drug or alcohol abuse, a change in the character or severity of the pain within the last 6 weeks, and an inability to complete the health status survey short form (SF-36), the daily assessment tools, or the global questionnaire.

All patients received the three modalities according to one of three different sequences: (1) Sham – PENS – TENS; (2) PENS – TENS – Sham; or (3) TENS – Sham – PENS. Each treatment was administered for 30 min three times per week (on Monday, Wednesday, and Friday afternoons) for 3 weeks (Ghoname, 1999b). Upon completion of each three-week treatment block, patients were given 1 week 'off' before starting the next modality. All three modalities were administered over an 11 week period.

2.1. Treatment modalities

The basic PENS therapy consisted of the placement of 10, 32 gauge stainless steel acupuncture-like needle probes into the soft tissue and/or muscle in the symptomatic leg to a depth of 2–4 cm as illustrated in Fig. 1A. The 10 needle probes were connected to 5 bipolar leads (with each lead connected to one positive and one negative probe) from a low-output electrical generator and stimulated at 4 Hz (Ghoname et al., 1999c). The intensity of the electrical stimulation was adjusted to produce the highest tolerable electrical 'tapping' sensation without muscle contractions. The maximum amplitude of the electrical stimulation produced by the generator was 250 μAmps with a unipolar square-wave pattern and a pulse width of 0.1 s. The electrical current was DC and the duty cycle was continuous.

The sham-PENS therapy consisted of the placement of 10 acupuncture-like needle probes in an identical montage (Fig. 1A); however, no electrical stimulation was applied to the probes.

The standard TENS therapy consisted of the placement of four medium-sized (2.5 cm) cutaneous electrode pads (SnapEase®, Empi, St. Paul, Minnesota) in a standardized dermatomal pattern (Fig. 1B). These electrodes were also stimulated at a frequency of 4 Hz, with a pulse duration of 0.1 s (Walsh et al., 1995). The intensity of the electrical stimulation was adjusted to the maximum tolerated amplitude without producing muscle contractions.

2.2. Assessment procedures

Prior to initiating the non-pharmacologic treatments, patients were required to complete the SF-36 (Ware and Sherbourne, 1992). The physical component summary (PCS) and mental component summary (MCS) scores were utilized to assess the patient's response to each of the therapeutic modalities (Ware et al., 1995). All patients

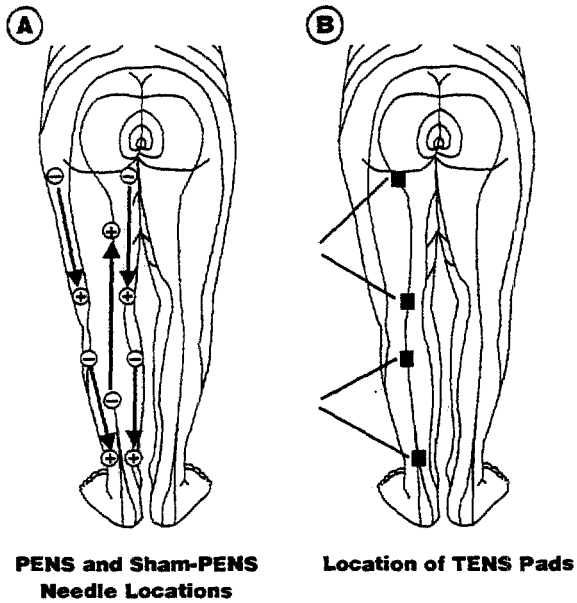


Fig. 1. (A) The peripheral leg montage, with position of needles for sham-PENS and PENS treatments. With PENS therapy, each of the 5 bipolar electrical stimulating leads are connected to a pair of probes, alternating the positive (+) and negative (−) positions as shown in the illustration. (B) The location of the four cutaneous electrode pads used for the TENS treatments.

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were also asked to assess their baseline level of leg pain, physical activity and quality of sleep during the 24 h interval prior to each treatment session using standard 10 cm VAS, with 0 = best to 10 = worst. Repeat VAS assessments for the degree of pain, physical activity and quality of sleep were performed three times per week prior to each treatment session. In addition, the pain VAS was repeated immediately after completion of each treatment session. The daily intake of oral non-opioid analgesic medication (i.e. number of pills per day) was recorded in the patient's diary. The SF-36 was repeated 24 h after completing all nine-treatment sessions with each modality. Finally, each patient completed a global assessment questionnaire to determine the relative effectiveness of the three different modalities 72 h after the last treatment session.

2.3. Data analysis

The NCSS software package (version 6.0.1 statistical system for Windows, NCSS, Kaysville, UT) was utilized for all statistical analyses. An a priori power analysis with $\alpha = 0.05$, $\beta = 0.10$ (power = 90%), and SD of 2.0, determined that a group size of 60 should be adequate to demonstrate a difference of 25% between the VAS scores for the three treatment modalities. The changes in the VAS scores over time were analyzed with repeated measures analysis of variance (ANOVA) and Students' *t*-test, with a Bonferroni correction applied for multiple comparisons. A multivariate ANOVA was used to analyze between (e.g. PENS versus sham-PENS) and within subjects factors (e.g. time). Analysis of discrete (non-continuous) data for the four treatment modalities was performed using the Chi-square test. Pre- versus post-treatment changes and differences between modalities in the SF-36 scores were analyzed using paired *t*-tests. Data are presented as mean values (±SD (Tables), ± SEM (Figs. 1–4)), and percentages, with *P*-values < 0.05 considered statistically significant.

3. Results

The pre-study SF-36 evaluation suggested that this study population reported significantly lower health-related 'quality of life' scores on the physical component summary (PCS) and mental component summary (MCS) compared to general population norms of 50 for both of the summary scores. The pre-study (baseline) scores for this patient population were 26.7 ± 7.6 and 39.5 ± 5.2 for the PCS and MCS, respectively. Compared to the baseline scores, PENS therapy resulted in the most significant improvements in both the PCS (35.3 ± 8.2) and MCS (44.2 ± 6.4) components ($P < 0.001$). Both TENS (29.6 ± 7.4 and 42.1 ± 6.0)

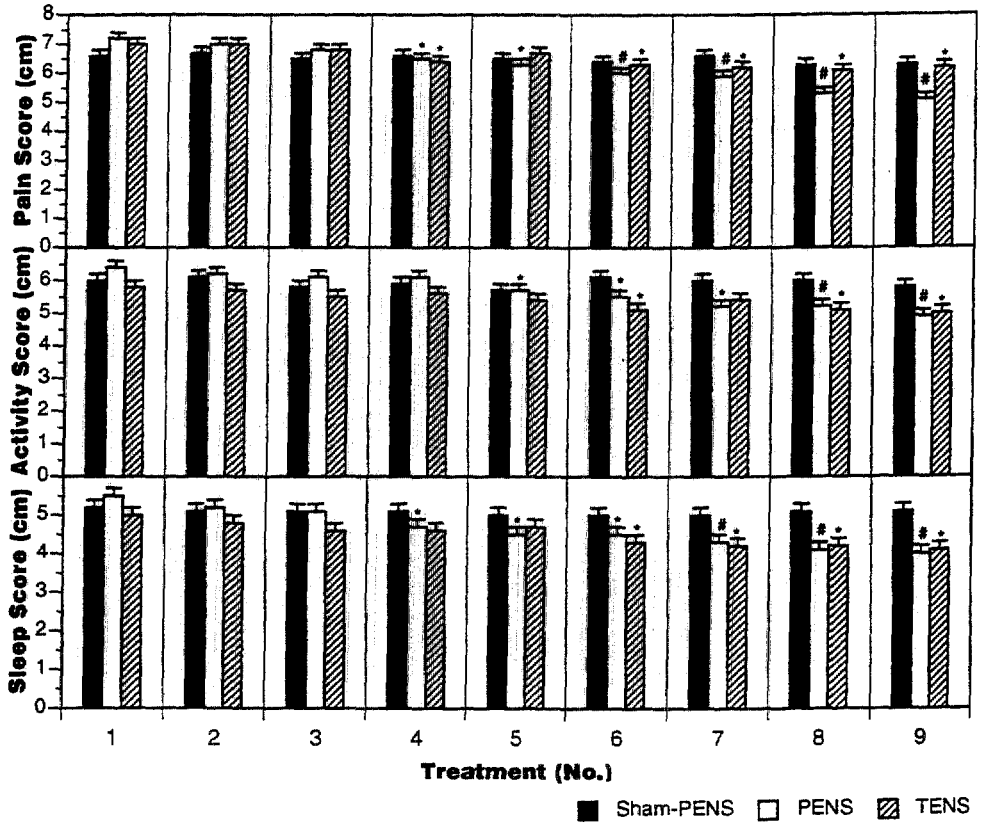


Fig. 2. Visual analog scale scores (cm) for radicular leg pain, physical activity and quality of sleep before each of the nine treatment sessions with the three modalities. Scores of 0 = best to 10 = worst. Data are mean values ± SEM. Symbols indicate significant changes from the values prior to the first treatment. *P-value < 0.05 and #P-value < 0.01.

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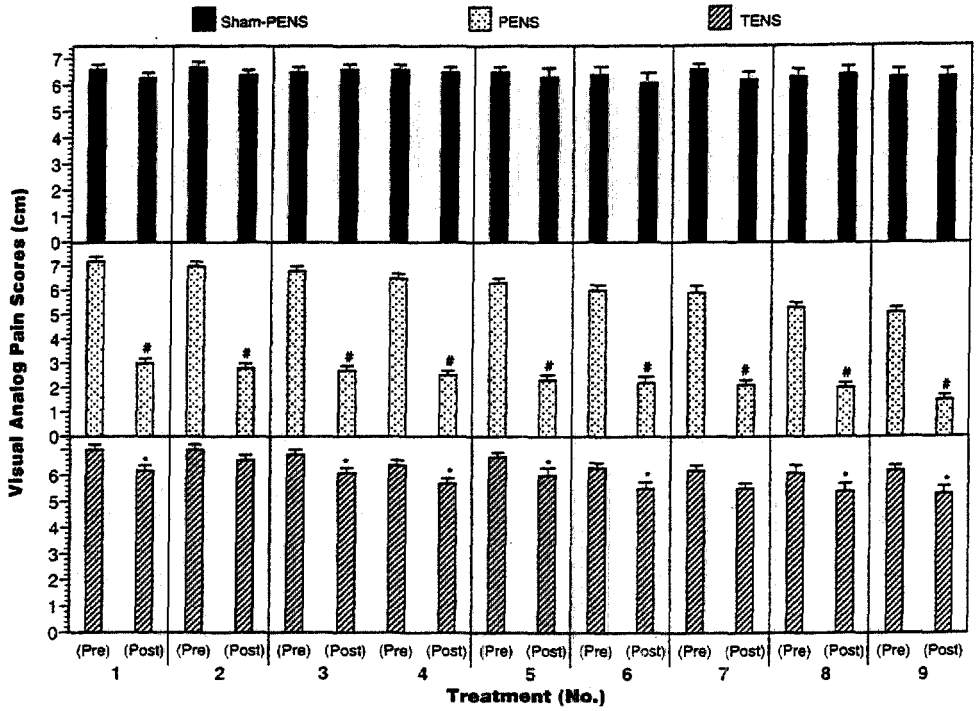


Fig. 3. Visual analog scale (VAS) pain scores with 0 = best to 10 = worst immediately before (pre) and after (post) each of the nine treatment sessions with the three modalities. Data are mean values ± SEM. Symbols indicate significant differences from the pre-treatment values, *P-value < 0.05 and #P-value < 0.01.

and sham-PENS (28.4 ± 6.7 and 41.7 ± 6.2) therapies produced smaller, but statistically significant improvements in the PCS and MCS scores, respectively ($P < 0.05$). Moreover, when PENS therapy was compared to each of the other therapeutic modalities, significantly greater improvement in post-treatment functionality was found (+5.7 and +2.1 versus TENS and +6.9 and +2.5 versus sham-PENS with respect to PCS and MCS scores, respectively).

The VAS scores for pain, physical activity and quality of sleep 24 h prior to the first treatment session and 24 h after the last treatment session with each of the three modalities are summarized in Table 1. The average decrease in the VAS pain scores 24 h after the last treatment session was significantly greater with PENS therapy (42 ± 18 versus 23 ± 16% for TENS and 8 ± 11% for sham-PENS). After three to four treatments, patients receiving PENS also reported significant improvement in their pre-treatment VAS scores for both activity and sleep (Fig. 2). Although TENS was also associated with improvement in the VAS scores for the degree of pain, physical activity and sleep quality, the magnitude of the changes were less than with PENS ($P < 0.05$). In addition, PENS therapy produced the greatest decrease in VAS pain scores immediately after each treatment ($P < 0.01$) (Fig. 3). However, TENS also produced a significant decrease in VAS pain scores immediately after eight of the nine treatment sessions ($P < 0.05$).

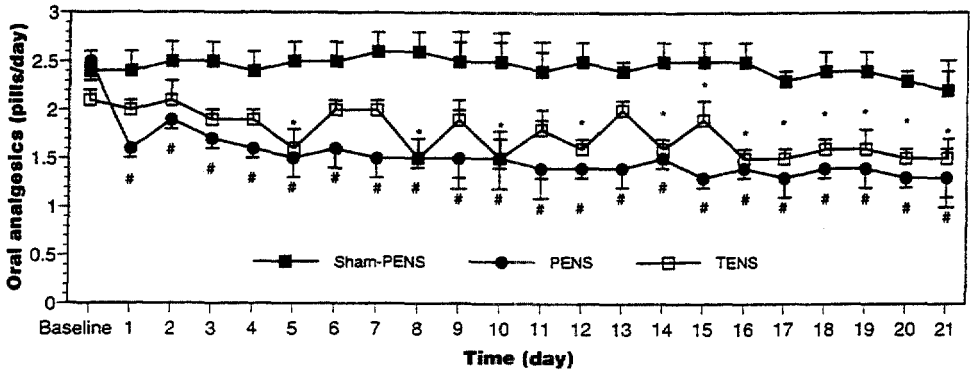


Fig. 4. Daily oral intake (pills/day) of non-opioid analgesic medications during the 3-week treatment period with each of the three modalities. Data are mean values ± SEM. Symbols indicate significant differences from baseline values 24 h prior to the first treatment with each modality, *P-value < 0.05 and #P-value < 0.01.

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Table 1
Comparison of visual analog scale (VAS) scores for sciatic pain, level of activity and quality of sleep 24 h prior to receiving the first treatment (before) and 24 h after the last treatment (after) with each modality, with 0 = best to 10 = worst[a]

	Sham-PENS	PENS	TENS
Degree of pain			
Before (cm)	6.6 ± 1.9	7.2 ± 1.8	7.0 ± 1.9
After (cm)	6.1 ± 1.9	4.1 ± 1.4[b,c]	5.4 ± 1.9*
Level of activity			
Before (cm)	6.0 ± 1.9	6.4 ± 2.1	5.8 ± 1.7
After (cm)	5.5 ± 2.1	4.0 ± 1.7[b,c]	4.5 ± 1.7[b]
Quality of sleep			
Before (cm)	5.2 ± 2.1	5.5 ± 1.9	5.0 ± 2.0
After (cm)	4.9 ± 1.9	3.1 ± 1.9[b,c]	4.0 ± 2.0[b]

[a] Values are means ± SD. PENS, Percutaneous electrical nerve stimulation; TENS, Transcutaneous electrical nerve stimulation.
[b] Significantly different from 'baseline' prior to receiving treatment No. 1, P-value < 0.05.
[c] Significantly different from sham-PENS and TENS, P-value < 0.01.

The daily intake of oral non-opioid anti-inflammatory analgesic medication (pills per day) is displayed in Fig. 4. Compared to the pre-treatment values (24 h before starting each treatment modality), PENS therapy was associated with a 50 ± 19 percent reduction in the daily oral analgesic requirements over the 3-week interval. In contrast, TENS and sham-PENS therapies decreased the oral analgesic intake by 29 ± 17 and 8 ± 13%, respectively.

Finally, the overall evaluation of the three modalities indicated that PENS was the preferred therapy by 73% of the study patients compared to 21 and 6% for TENS ($P < 0.05$) and sham-PENS ($P < 0.01$), respectively (Table 2). In addition, PENS was significantly more effective than sham-PENS ($P < 0.01$) and TENS ($P < 0.05$) therapies in improving the patients' sense of 'well-being.' Compared to TENS (22%) and sham-PENS (3%) therapies, 71% of the patients indicated that they would be willing to pay extra money ('out of pocket') to receive PENS therapy in the future.

Table 2
Overall patient evaluation of the relative effectiveness of sham-PENS, PENS and TENS therapies after receiving all three modalities

	Sham-PENS	PENS	TENS
Most desirable modality (%)	6	73[a,b]	21[a]
Improved sense of 'well-being' (%)	8	66[a,b]	26[a]
Preferred pain therapy (%)	6	73[a,b]	21[a]
Willing to pay extra for therapy (%)	3	71[a,b]	22[a]

[a] Significantly different from the Sham-PENS group, P-value < 0.05.
[b] Significantly different from the TENS group, P-value < 0.05.

4. Discussion

Many patients with sciatica have been successfully treated with conservative medical management consisting of bed rest, anti-inflammatory analgesic drugs and epidural steroids (Frymoyer, 1988). Although this approach can effectively decrease the radicular pain, improvement in functionality has been more difficult to demonstrate. If the pain associated with sciatica can be adequately controlled, spontaneous regression of the herniated nucleus pulposus has been reported to occur in the vast majority of patients (Bush et al., 1992).

The use of peripheral electrical stimulation with TENS units has previously been reported to be beneficial in treating the pain associated with radiculopathies, including sciatica (Woolf and Thompson, 1994). Blockade of the sciatic nerve distal to the site of the lesion with local anesthetics has also been reported to produce long-lasting relief of radicular leg pain (Xavier et al., 1988). Although the current study confirmed the efficacy of TENS, it was significantly less effective than PENS therapy in providing short-term relief of pain and improvement in functionality in patients with sciatica due to herniation of a lumbar disc. These findings indicating the superior efficacy of PENS (versus TENS) are consistent with the preliminary studies by Sun et al. (1997); Ghoname et al. (1999a) in patients with low back pain due to osteoarthritis and degenerative disc disease, respectively. The more limited efficacy of TENS is related in part to the cutaneous pain associated with the higher amplitudes of electrical stimulation required with TENS because of the skin resistance to the transmission of the electrical impulses. Although the tapping sensation produced by PENS was not considered uncomfortable by the patients, some preferred TENS because it was less invasive (i.e. did not require placement of needle probes).

Sciatic neuralgia has also been successfully treated with acupuncture stimulation (Leung, 1973; Jiang et al., 1984). Although many of the reports describing the effectiveness of acupuncture (or electroacupuncture) have failed to include a placebo (sham) treatment arm, Duplan et al. (1983) performed a double blind, placebo-controlled study of acupuncture in patients with acute sciatica. These investigators reported that acupuncture stimulation produced statistically significant improvement in the Lasegue sign and a reduction in oral analgesic usage. Analogous to the earlier findings of Duplan and colleagues, PENS therapy proved to be highly effective in this patient population.

In order to determine the role of PENS in the long-term management of sciatica, longitudinal studies are required. However, this sham-controlled study indicates that PENS produced profound acute analgesic effects and the pain relieving effects appeared to accumulate over the course of the three-week treatment period. These data suggest that the use of this non-pharmacologic analgesic modality over a longer period of time has the potential to produce long-term beneficial effects in patients with sciatica. To test

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this hypothesis, a more prolonged period of PENS therapy with careful follow-up at 3, 6 and 12 month intervals would be required.

While this was a sham-controlled study, the unique tapping sensation associated with PENS therapy precluded our ability to perform the study in a double-blind fashion. In order to minimize investigator bias, all patient assessments were performed by an individual not involved in administering the therapies. In addition, to avoid prejudicing patients in favor of PENS therapy, the sham treatment was described to the patients as an 'acupuncture-like' therapy. However, since the sham-PENS needles were placed in a dermatomal montage rather than at specific acupoints, it would be incorrect to conclude that classical Chinese acupuncture (or electroacupuncture) would be of no benefit in patients with sciatica.

Another potential criticism of the study design relates to the selection of a low stimulus frequency (4 Hz) for 30 min intervals for both PENS and TENS treatments. These variables were chosen because it was previously reported that low frequency (4 Hz) is more effective than high frequency (>100 Hz) stimulation in producing hypoalgesic effects with TENS using an experimental pain model (Walsh et al., 1995). Moreover, recent studies in humans using TENS (Hamza et al., 1999) and PENS (Ghoname et al., 1999a) have found no significant differences in the analgesic responses to high and low frequency stimulation. A 30 min period of stimulation was selected because more prolonged periods of stimulation (>30 min) may be associated with the development of tolerance to the electrical stimulation (Romita et al., 1997). When using PENS therapy, we also found no additional benefit when the stimulation intervals were increased from 30 to 45 min (Ghoname et al., 1999b). However, additional studies with PENS are needed to determine the relative analgesic effectiveness of different frequencies and durations of electrical stimulation in this patient population.

Experience with PENS in other patient populations [e.g. chronic osteoarthritis (Sun et al., 1997), acute herpes zoster (Ahmed et al., 1998) and low back pain (Ghoname et al., 1999c)] has suggested that improved analgesic responses may be achieved by using higher (50–100 Hz) or mixed (15/30 Hz) frequencies of electrical stimulation at subsequent treatment sessions. Similarly, the standardized montage used in this study was based on anecdotal clinical experience (W.F. Craig, unpublished data). However, depending on the associated manifestations of the pain symptoms (e.g. bilateral radicular leg pain, low back pain), other needle montages may prove to be more effective for subsequent treatment sessions.

The results of the psychological (SF-36) assessment further support and strengthen the clinical findings by providing an additional outcome measure which demonstrates the superiority of PENS over TENS and sham therapies. These data suggest that PENS was the most beneficial modality in improving the physical (e.g. fewer limitations in self-care, less severe body pain) and mental (e.g. less psychological stress, less disability due to emotional problems) health and well-being of patients with sciatica.

In order to determine the cost-benefit of any new analgesic therapy, long-term outcome studies are needed which carefully consider the pertinent costs (e.g. stimulating device, disposables, personnel requirements), as well as the consequences or outcomes of the treatment (e.g. patient satisfaction, quality of life, resumption of normal activities) in monetary terms (Watcha and White, 1997). Long-term outcome studies should be designed to examine the cost-benefit of using PENS therapy as part of a multi-modal rehabilitation program which also includes anti-inflammatory drugs and specific low back exercises.

In conclusion, this sham-controlled study demonstrates that PENS is more effective than TENS in improving short-term outcome in patients with sciatica. The use of PENS therapy improves physical activity and the quality of sleep while decreasing the need for oral non-opioid analgesic medications.

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Percutaneous Electrical Nerve Stimulation: An Alternative to Antiviral Drugs for Acute Herpes Zoster

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Antiviral drugs decrease the pain and enhance the resolution of acute herpes zoster lesions in immunocompetent patients (1–6). However, the effect of antiviral therapy on postherpetic neuralgia (PHN) remains controversial. Whereas some studies reported a lower incidence of prolonged pain with antiviral therapy (4), others found no benefit with respect to prolonged pain (5). In an attempt to improve patient comfort and long-term outcome with respect to PHN, combinations of different drugs have also been evaluated (5–7).

Anecdotal reports have suggested that electroacupuncture may be helpful in the management of herpes-related pain (8,9). Clinical experience with a novel form of electroanalgesia known as percutaneous electrical nerve stimulation (PENS) in the treatment of patients with acute herpes zoster suggested that it is effective in decreasing herpes-related pain and is associated with rapid resolution of the cutaneous lesions (Craig WF, Taylor SM, Fort Worth Center for Pain Management, personal communication, 1997). Therefore, we designed this clinical study to compare PENS therapy with a standard antiviral regimen with respect to the severity of the associated pain, impact on the patient's physical activity and quality of sleep, resolution of the herpes lesions, and incidence and severity of PHN.

Methods

After obtaining institutional review board approval and written, informed consent, 50 adult patients (27 female and 23 male) with the recent acute onset (<72 h) of herpes zoster lesions were administered one of two different treatment modalities according to a randomized, single-blind study design. Exclusionary criteria included known hypersensitivity to the antiviral drugs, preexisting neurological impairment, women who were pregnant or nursing, any previous experience with acupuncture-like therapies, the presence of the zoster rash for >72 h, or secondary complications from the viral infection.

The patients were randomly assigned using a computer-based program to either the control group (which received famciclovir 500 mg three times a day for 1 wk) or the experimental group (which received PENS therapy for 30 min three times a week for 2 wk). The PENS therapy consisted of the placement of 32-gauge stainless steel acupuncture-like needle probes into the soft tissue to a depth of 1–2 cm at dermatomes one level above and below the cutaneous lesions (Figures 1 and 2). The needle probes were connected to a low-output (5 mAmp) electrical generator and stimulated at frequencies ranging from 4 to 100 Hz. Patients in both treatment groups were evaluated daily by a physician (HEA) not involved in either the famciclovir or PENS treatments. The patients were instructed not to use any topical medications or systemic treatments during the 2-wk study period.

Before receiving the study treatments, all patients were asked to assess their baseline degree of pain, level of physical activity, and quality of sleep using three separate 100-mm visual analog scales (VAS), with 0 = minimal (lowest) to 100 = maximal (highest). All patients were instructed to return to the medical center daily during the 2-wk study period to assess the appearance of their cutaneous lesions and to complete the pain, physical activity, and quality of sleep VASs. At the end of the study period, all patients were asked to complete a global assessment questionnaire to evaluate the change in pain, physical activity, and quality of sleep using the VASs.

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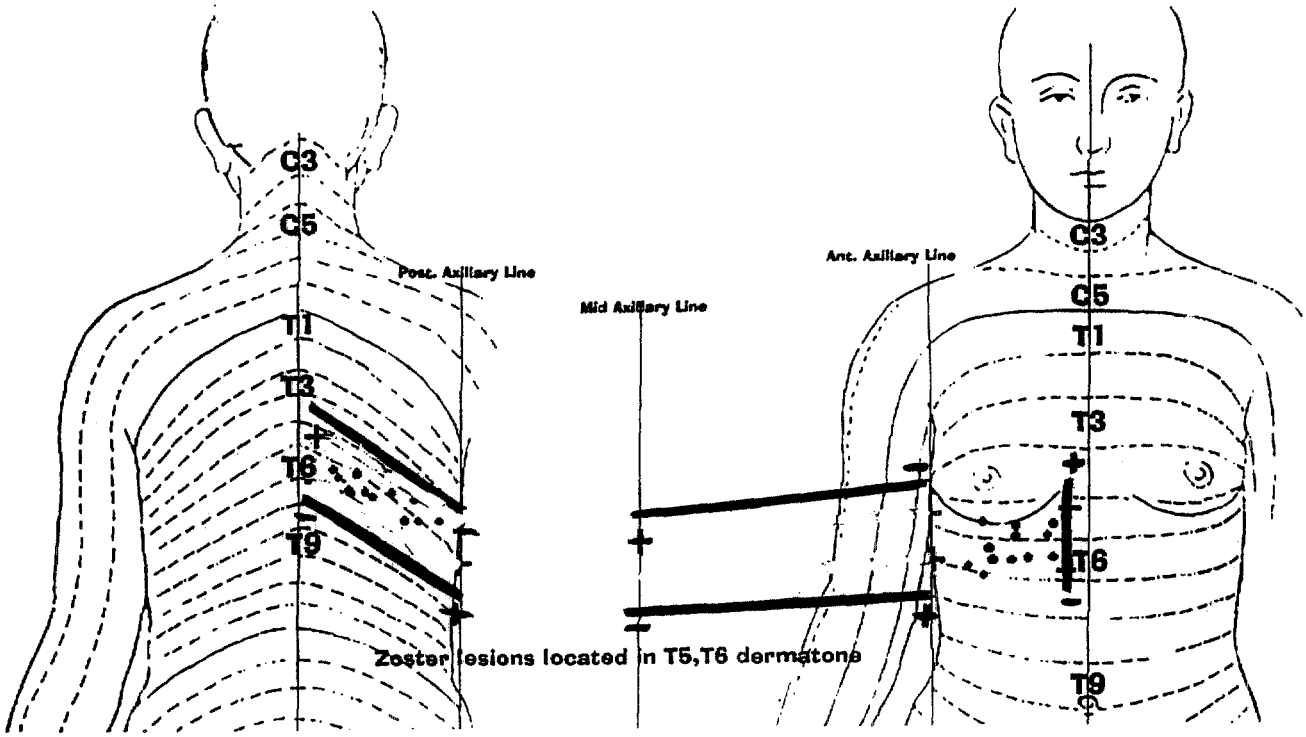


Figure 1. The "arc" montage was applied initially when the lesions were wet during the first week of therapy, consisting of bipolar leads connected to needle probes placed in the soft tissues at one dermatomal level above and below the acute lesions. Each lead was connected to a pair of needles, alternating the positive (+) and the negative (−) electrode positions as shown.

The assessment of the cutaneous lesions was performed by a blind observer and included: 1) location of the rash; 2) severity of the rash (i.e., number of the lesions in the involved dermatomes) using the following classification system: mild (<25), moderate (25–50), or severe (> 50); 3) the last day that new lesions appeared; 4) the first day without any new lesions; 5) the first day with full crusting of the lesions; and 6) the time to complete healing of the lesions. All patients were contacted at 3-, 6-, and 9-mo intervals to inquire about the presence of pain in a dermatomal pattern corresponding to the level of the acute lesions (i.e., PHN). The severity of the PHN pain was quantified using the 100-mm pain VAS.

Changes in the VAS scores were analyzed by using analysis of variance, with *t*-tests used to determine intergroup differences and Bonferroni's adjustment for multiple comparisons. Analysis of discrete data was performed using the χ^2 test, with P values <0.05 considered statistically significant.

Results

The two treatment groups were similar with respect to demographic characteristics, including the location and severity of the herpetic lesions (Table 1). The PENS group experienced more rapid resolution of the vesicles and complete healing of the lesions (Table 2). The VAS pain scores were consistently lower in the PENS group during the 2-wk observation period (Table 3). On the global assessment questionnaire, the percent decrease in the VAS pain score was 67% in the PENS group compared with 45% in the control group ($P < 0.05$). The percent improvement in the VAS physical activity and quality of sleep scores (78% vs 60% and 55% vs 37%, respectively) was also greater in the PENS- versus famciclovir-treated patients at the end of the second week. The older patients (≥50 yr) were more likely to develop PHN symptoms, and PENS therapy was associated with a decrease in the severity of pain at 3 and 6 mo in this subpopulation (Table 2). However, no differences in PHN symptoms were apparent at the 9-mo follow-up assessment period.

Discussion

This comparative study suggests that PENS, a novel, nonpharmacologic analgesia technique, may be a viable alternative to antiviral drugs for the treatment of acute herpes zoster lesions. The use of PENS therapy provided pain relief, increased physical activity, and an improved quality of sleep that compared favorably

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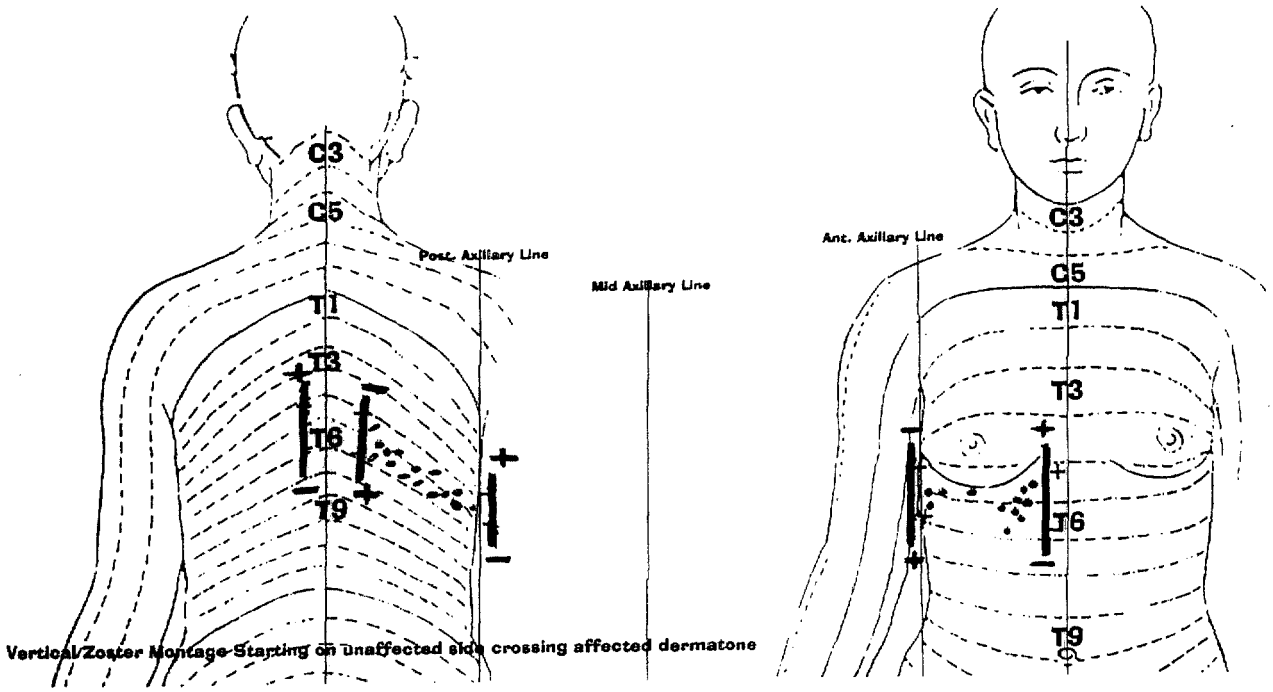


Figure 2. The "vertical" montage was applied after the lesions became crusted during the second week of therapy, consisting of bipolar leads stimulating across the dermatomal region from C4 to C7. Each lead was connected to a pair of needles, alternating the positive (+) and the negative (−) positions as shown.

Table 1. Demographic Characteristics of Patients with Acute Herpes Zoster Receiving Antiviral Drug (Control) or PENS Therapy

	Control	PENS
Patients (*n*)	25	25
Male/female (%)	44/56	48/52
Age (yr), mean ± SD	53 ± 15	56 ± 15
≤50 yr (%)	32	28
≥50 yr (%)	68	72
Location of rash (%)		
Thoracic	56	60
Cervical	16	12
Lumbar	16	16
Cranial	0	4
Sacral	12	8
Severity of rash (%)		
Mild (<25 lesions)	32	20
Moderate (25–50 lesions)	40	48
Severe (>50 lesions)	28	32

PENS = percutaneous electrical nerve stimulation.

Table 2. Effect of Antiviral Drug (Control) or PENS Therapy on Resolution of Acute Herpes Zoster Lesions and the Incidence and Severity of Postherpetic Neuralgia

	Control	PENS
Vesicles (days)	5.6 ± 0.7	4.6 ± 0.5*
Ulcers (days)	7.3 ± 0.7	6.4 ± 0.5
Crusting (days)	7.8 ± 0.5	7.4 ± 0.8
Healing (days)	18.8 ± 1.4	16.9 ± 0.9*
Postherpetic neuralgia		
At 3 mo (n)	9	6
Age (yr)	66 ± 8	65 ± 5
Pain severity (mm)	44 ± 8	32 ± 4*
At 6 mo (n)	6	3
Age (yr)	64 ± 6	66 ± 5
Pain severity (mm)	46 ± 8	30 ± 2*
At 9 mo (n)	3	2
Age (yr)	65 ± 6	65 ± 4
Pain severity (min)	55 ± 13	49 ± 11

Values are means ± SD or *n*.
Pain severity was measured on a scale from 0 = minimal to 100 = maximal.
PENS = percutaneous electrical nerve stimulation.
* Significantly different from control group ($P < 0.05$).

with a standard antiviral therapy. In this preliminary study, PENS therapy was also more effective than famciclovir in preventing PHN-related pain symptoms 3 and 6 mo after resolution of the cutaneous lesions.

Although this study can be criticized because it did not include a placebo (or sham) group, the benefits of antiviral therapy have been firmly established during the acute phase of the illness, and other investigators (4) have suggested that it would be unethical to include a placebo treatment group. The outcome assessments were blinded because the physician making the assessment was unaware of the treatment that the patients were receiving. Furthermore, the small cutaneous needle puncture sites (0.2 mm) produced by the PENS probes were not apparent to the individual

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Table 3. Effect of Antiviral Drug (Control) or PENS Therapy on Pain Scores, Physical Activity, and Quality of Sleep in Patients with Acute Herpes Zoster

	Control	PENS
Pain score (mm)		
Baseline	58 ± 15	61 ± 11
1 wk	46 ± 13	39 ± 8*
2 wk	32 ± 8*	20 ± 9*†
Activity score (mm)		
Baseline	47 ± 13	46 ± 13
1 wk	62 ± 13	67 ± 10
2 wk	75 ± 11*	83 ± 8*
Sleep score (mm)		
Baseline	55 ± 15	53 ± 15
1 wk	65 ± 12	70 ± 12
2 wk	76 ± 9*	83 ± 10*

Values are mean ± SD of visual analog scale scores, 0 = minimal (lowest) to 100 = maximal (highest).
PENS = percutaneous electrical nerve stimulation.
* Significantly different from the baseline value ($P < 0.05$).
† Significantly different from the control group ($P < 0.05$).

performing the clinical assessments. Nevertheless, future studies should include a sham PENS group that receives the antiviral therapy in combination with the needle probes but without electrical stimulation. Unfortunately, the inclusion of a sham PENS group would not blind the patients because it does not mimic the sensation provided by the electrical stimulation associated with PENS therapy.

The improved physical activity and quality of sleep during the second week of treatment in the PENS group may be secondary to the decrease in the intensity of pain. Although the mechanism of PENS-induced analgesia is not known, it may be related to both neural modulation produced by the electrical stimulus (10) and an increase in endogenous morphine-like substances (e.g., dynorphins, endorphins, enkephalins) within the central nervous system (11). Using a rat model for studying electroacupuncture, Chen et al. (12) reported that an alternating 2-Hz and 15-Hz pattern of electrical stimulation was more effective than a fixed frequency of stimulation at either 2 Hz or 100 Hz in producing experimental analgesia. In a clinical study, Han et al. (11) reported that low- and high-frequency electrical stimulation resulted in increased cerebrospinal fluid levels of met-enkephalin and dynorphin, respectively. Further studies are clearly needed to determine the precise central nervous system mechanism(s) of PENS-induced analgesia.

Because herpes zoster is caused by a reactivation of the varicella virus residing in the sensory ganglia and spinal cord after the primary viral infection, the beneficial effects of PENS therapy may also be related to electrical stimulation of the involved peripheral sensory nerves. The electrical current can produce localized vasodilation and may stimulate the release of antiinflammatory mediators at the site of injury. Further studies evaluating the efficacy of PENS therapy in immunosuppressed patients would be helpful in understanding the basis for its apparent analgesic and antiinflammatory activity. However, PENS therapy should be evaluated as a supplement to antiviral therapy in this high-risk patient population.

In conclusion, PENS therapy is a unique nonpharmacologic approach to treating immunocompetent patients with acute herpes zoster that compared favorably with standard antiviral drug therapy in this preliminary study.

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Use of Percutaneous Electrical Nerve Stimulation (PENS) in the Short-term Management of Headache

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Objective.–To evaluate the short-term effects of percutaneous electrical nerve stimulation (PENS) in the management of three types of chronic headache.

Background.–Traditional electroanalgesic therapies have been reported to be effective in the management of acute headache symptoms. However, no controlled studies have been performed in patients with chronic headache.

Methods.–Thirty patients with either tension headache, migraine, or posttraumatic headache symptoms of at least 6 months' duration were randomized to receive PENS (needles with electricity) or "needles alone" according to a crossover study design. All treatments were administered for 30 minutes, three times a week for 2 consecutive weeks with 1 week off between the two different treatments. For the PENS treatments, an alternating electrical stimulation frequency of 15 and 30 Hz was used. Pain, activity, and sleep scores were assessed using a 10-cm visual analog scale, with 0 corresponding to the best and 10 to the worst, during the 48-hour period prior to the beginning of the two treatments, immediately before and after each treatment session, and 48 hours after completing each treatment modality.

Results.–Compared with the needles alone, PENS therapy was significantly more effective in decreasing the overall VAS pain scores for tension-type headache, migraine and posttraumatic headache (58%, 59%, and 52% versus 20%, 15%, and 20%, respectively). Similarly, PENS therapy produced greater improvement in the patients' physical activity (41% to 58% for PENS versus 11% to 21% for needles only) and quality of sleep (41% to 48% for PENS versus 12% to 20% for needles only). However, there were no differences in the pattern of the response to PENS therapy among the three headache groups.

Conclusions.–Percutaneous electrical nerve stimulation appears to be a useful complementary therapy to analgesic and antimigraine drugs for the short-term management of headache. Interestingly, the analgesic response to PENS therapy appears to be independent of the origin of the headache symptoms.

Key words: tension-type headache, migraine, posttraumatic headache, percutaneous electrical nerve stimulation, PENS, electroanalgesia

Abbreviations: TENS transcutaneous electrical nerve stimulation, PENS percutaneous electrical nerve stimulation, SF-36 short-form health status survey, MCS mental component summary, PCS physical component summary, VAS visual analog scale

(*Headache* 2000;40:311-315)

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Headache is one of the most common pain problems. Although a wide variety of pharmacological therapies have been used in the management of headache, these drugs are of limited efficacy in relieving headache symptoms and many produce unwanted side effects.[1-3] Nonpharmacological therapies such as biofeedback, relaxation, hypnosis,[4-6] and physical therapy[7] have also been used, but there have been

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few well-controlled clinical trials evaluating their efficacy.

Electrical stimulation techniques (so-called electroanalgesia) have become increasingly popular as alternative (or complementary) therapies in the management of acute and chronic pain syndromes. Both transcutaneous electrical nerve stimulation (TENS)[8] and electroacupuncture[9] have been reported to be effective in the management of headache symptoms. Recently, we described the use of percutaneous electrical nerve stimulation (PENS) for the treatment and prevention of migrainelike headaches associated with electroconvulsive therapy (ECT).[10] This therapy involved the insertion of needle probes, akin to those used in acupuncture, in the soft tissues at the dermatomal levels corresponding to the location of the headache symptoms and then applying low levels of electrical current.

Based on the results of our preliminary study,[10] we hypothesized that PENS therapy could also prove beneficial in the management of other more common types of headache. Therefore, we designed a study to evaluate the efficacy of PENS (versus needles alone) for the management of chronic tension headache, migraine, and posttraumatic headache.

METHODS

After obtaining institutional review board approval and written, informed consent, 30 patients (18 women and 12 men), aged from 24 to 56 years, with long-standing headache symptoms were enrolled in this single-blind, crossover study. The patients received both PENS and "needles-only" treatments in a random sequence for 30 minutes, three times per week for 2 consecutive weeks, with 1 week off between the two modalities. Inclusion criteria included a history of severe headache occurring four or more times per week and managed with oral nonopioid analgesics for a period of at least 6 months. Exclusion criteria included patients younger than 18 years, a history of cluster-type headache, and an inability to understand or perform the daily assessments or the patient preference questionnaire.

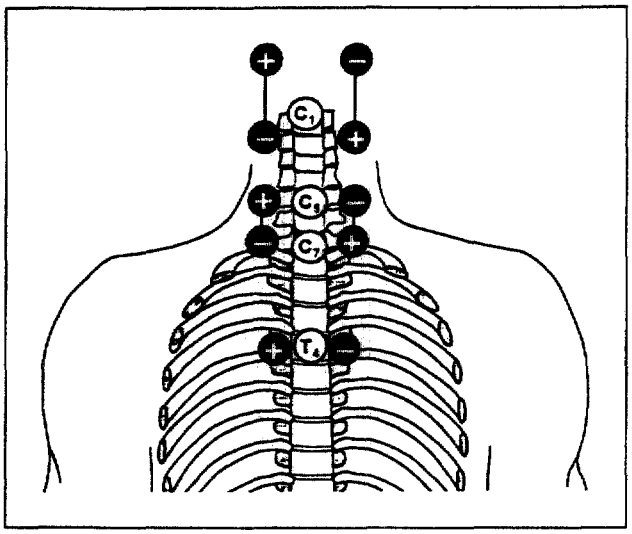
Thirteen patients were diagnosed as having chronic tension-type headache according to the criteria of the International Headache Society classification system. The diagnostic criteria included a headache frequency of greater than or equal to 15 days a month and at least two of the following pain characteristics: (1) a pressing or tightening quality, (2) mild or moderate severity, (3) bilateral location and involving the posterior aspect of the head and neck, and (4) no aggravation by routine physical activity. Twelve patients had chronic headache transformed into migraine characterized by a past history of episodic migraine, positive family history of migraine, headache symptoms beginning in the late teens or early twenties, associated symptoms of photophobia and nausea, menstrual aggravation in women, identifiable trigger factors, and unilateral headache occurring every 1 to 2 days (>15 days per month), with an average duration of 4 hours if untreated. Finally, five patients had chronic posttraumatic headaches characterized by a history of head or neck trauma, with headache beginning as a new symptom less than 14 days after the trauma and lasting longer than 6 months.

Treatment Modalities.–Both the PENS and "needles-only" therapies consisted of the placement of ten 32-gauge (0.2 mm), 15-mm-long, stainless steel needle probes (ITO, Tokyo, Japan), like those used in acupuncture, into the soft tissue in the back of the neck (C2, C5, C7, and T4) and scalp in a standardized montage as illustrated in Figure 1. For active PENS treatments, the needle probes were connected to five bipolar leads, with each lead connected to one positive and one negative probe. The leads were connected to an investigational low-output electrical generator and stimulated at an alternating frequency of 15 Hz and 30 Hz (15/30 Hz).[11] The maximum amplitude of the electric stimulation produced by the generator was 25 mA with a unipolar, square pattern and a pulse width of 0.5 milliseconds. The intensity of the electrical stimulation was adjusted to produce the highest tolerable "tapping" sensation without eliciting a muscle contraction. For the needles-only treatments, the probes and leads were connected in an identical manner and the generator was turned on (lights flashing), but the amplitude of each lead was set at zero.

Assessment Procedures.–A detailed headache history was obtained, including the duration and frequency of symptoms, the total number of headaches,

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The positions of the acupuncturelike probes used for the treatment of headaches with percutaneous electrical nerve stimulation (PENS) or needles-only (sham) therapies. Ten 32-gauge acupuncture-type needles were positioned in the soft tissue to a depth of 1 to 3 cm and connected to five pairs of positive (+) and negative (−) leads, which were stimulated at an alternating frequency of 15 and 30 Hz for the active PENS treatments.

the location, quality, and intensity of pain, impact on physical activity and quality of sleep, occurrence of associated symptoms (eg, nausea, vomiting, photophobia), and history of head or neck trauma. Prior to initiating any of the treatment modalities, patients were asked to complete the short-form health status survey (SF-36) questionnaire. The physical component summary (PCS) and the mental component summary (MCS) scores were used to assess the patient's response to each treatment modality. All the patients were asked to assess their baseline level of pain, physical activity, and quality of sleep 48 hours prior to starting treatment using standard 10-cm visual analog scales (VAS), where 0 corresponds to best and 10 to worst and repeat VAS assessments were performed three times a week prior to each treatment session. The pain VAS was also repeated 5 to 10 minutes after each treatment session. The average number of pills taken for headaches during the 2-week interval prior to entering the study (baseline) and daily oral analgesic requirements were recorded in the patient's diary. After receiving both treatment modalities, patients completed a preference questionnaire comparing the relative effectiveness of the active PENS and the needles-only treatments.

Data Analysis.–The NCSS software package (NCSS 6.0.1 statistical system for Windows, Kaysville, UT) was used for all statistical analyses. An a priori power analysis determined that a group size of 18 should be adequate to demonstrate a difference of 25% in pain VAS scores between the active PENS and needles-only treatments ($\alpha = 0.05$ and $\beta = 0.10$). The changes in the VAS scores were analyzed with repeated measures of analysis of variance (ANOVA) and Student *t* test, with the Bonferroni correction for multiple comparisons. Analysis of discrete (noncontinuous) data for the two treatment modalities was performed using the chi-square test. Data are presented as mean values (±SD), and percentages, with $P<.05$ considered statistically significant.

RESULTS

The demographic characteristics of the patients are summarized in Table 1. Percutaneous electrical nerve stimulation therapy was found to reduce significantly pain scores and improve activity and sleep scores compared with the needles-only treatments (Table 2). Compared with the pretreatment pain scores, the pain assessments 48 hours after completing each treatment modality demonstrated overall

Table 1.–Demographic Characteristics of the Study Patients and the Frequency and Duration of Chronic Headache Symptoms

	Tension Headache	Migraine	Posttraumatic Headache
No. of patients	13	12	5
Sex (F/M)	7/6	8/4	3/2
Mean age, y (±SD)	38 ± 11	38 ± 13	41 ± 12
Mean duration of symptoms, y (±SD)	4 ± 1	11 ± 3	4 ± 1
No. of headaches per week (±SD)			
Baseline	6 ± 2	6 ± 1	6 ± 3
Post-PENS*	3 ± 1†	3 ± 2†	4 ± 2
Post–needles only	6 ± 2	6 ± 2	6 ± 3

*PENS indicates percutaneous electrical nerve stimulation.
†Significantly different from baseline value, $P<.05$.

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Table 2.–Visual Analog Scale Scores for Pain, Physical Activity, and Quality of Sleep

	Baseline	Needles Only	PENS
Tension headache			
Pain	7.1 ± 1.0*	6.3 ± 0.9	3.1 ± 0.7†‡
Activity	6.4 ± 0.9	5.8 ± 0.9	3.0 ± 0.7†‡
Sleep	5.2 ± 1.1	4.3 ± 0.8	2.9 ± 0.6†‡
Migraine headache			
Pain	7.6 ± 1.1	6.5 ± 0.9	3.0 ± 0.7†‡
Activity	5.8 ± 1.0	5.1 ± 0.9	2.8 ± 0.7†‡
Sleep	5.2 ± 0.8	4.2 ± 0.9	2.9 ± 0.6†‡
Posttraumatic headache			
Pain	7.3 ± 1.0	5.7 ± 0.9	3.1 ± 0.6†‡
Activity	6.0 ± 0.8	5.3 ± 1.0	3.0 ± 0.6†‡
Sleep	4.5 ± 1.0	4.1 ± 0.8	2.7 ± 0.6†‡

Scores calculated 48 hours before the first treatment session (baseline) and 48 hours after completing the last treatment session.
*Values are means ± SD.
†Value is significantly different from needles-only treatment ($P<.05$).
‡Value is significantly different from pretreatment baseline value ($P<.05$).

decreases of 58%, 59%, and 52% for PENS therapy and 20%, 15%, and 20% for the needles-only treatments in the tension headache, migraine, and posttraumatic headache groups, respectively. Similarly, there were significant improvements in physical activity (41% to 58% for PENS versus 11% to 21% for the needles only) and quality of sleep (41% to 48% for PENS versus 12% to 20% for the needles only) compared with baseline scores with PENS (versus needles only) treatments in all three headache groups.

A significant reduction in the frequency of headaches was noted after the PENS therapy in two of the three groups (Table 1). The average daily requirement for oral analgesic (headache) medication was reduced by over 50% during PENS therapy compared with only a 13% to 23% reduction with the needles-only treatments. Assessment of PCS and MCS scores revealed significant lower baseline scores (35.4 ± 5.2 and 33.7 ± 4.3 for PCS and MCS, respectively) than the norms for the general population ($P<.05$). Compared with needles-only treatments, the posttreatment assessments revealed significantly greater improvements after PENS treatments (43.2 ± 4.6 and 43.1 ± 3.7 versus 38.9 ± 5.1 and 39.3 ± 3.9, $P<.01$). There were no significant differences among the three headache groups after PENS treatment with respect to pain, activity, sleep, and posttreatment SF-36 scores.

COMMENTS

Similar to our preliminary findings in patients with ECT-evoked headache, this study demonstrated that PENS therapy decreases pain scores, improves physical activity and quality of sleep, and decreases analgesic drug requirements in a population of patients with chronic tension headache, migraine, and posttraumatic headache. These results are consistent with the findings of Costantini et al[12] in a study involving the use of electroacupuncture for the management of craniofacial pain. Using TENS therapy, Farina et al[13] reported an improvement of greater than 60% in headache symptoms in up to 80% of the cases. Similarly, Solomon et al[8] reported that 55% of patients with tension headaches or migraines reported improvement after TENS therapy compared with only 18% of those receiving placebo (sham) treatments.

Although the precise mechanism of PENS-induced analgesia is not known, it has been speculated that both alterations in neural modulation produced by electrical stimulation,[14] as well as an increase in endogenous morphinelike substances within the central nervous system (CNS),[15,16] contribute to PENS-induced analgesia. Previous studies have reported that electroacupuncture-induced analgesia can be blocked by an opioid receptor antagonist.[17,18] Using experimental pain models, investigators have suggested that three types of CNS opioid receptors (ie, mu, sigma, and kappa) are important mediators of analgesia produced by electroacupuncture and TENS.[15,16]

The psychological (SF-36) assessment further supports and strengthens the clinical findings by providing additional outcome measurements. The superiority of active PENS therapy over the nonelectrical ("sham") needle therapy was demonstrated with respect to improvement in the physical (eg, fewer limitations to self care, less severe body pain) and mental (eg, less psychological distress, less disability due to emotional problems) health and well-being of this pa-

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tient population with long-term headaches. It is clear that additional studies will be required to evaluate the long-term effects of PENS therapy in the management of chronic headaches.

One deficiency of our study design related to the fact that the so-called sham (needles-only) treatments were necessarily administered without any form of electrical stimulus. Since the patients were not blinded, the possibility exists that they could be biased in favor of active PENS therapy. To minimize this bias, the needles-only treatments were described to the patients as "acupuncturelike" therapy. Although the needles-only treatments decreased the pain scores compared with the prestudy (baseline) values, the changes were significantly less than with PENS therapy and may represent the residual ("carry-over") effect of PENS therapy in those patients who received the active treatments first. Given the small group sizes, it was not possible to compare the responses to active PENS versus needles-only treatments in the initial phase of the study (ie, prior to the crossover). Since the needles were placed in a dermatomal pattern rather than at specific acupoints, the placebo effect of the needles-only treatments should not be considered equivalent to classic Chinese acupuncture therapy.

In conclusion, PENS therapy would appear to be a useful complementary therapy for the short-term management of patients with debilitating recurrent headache symptoms.

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Percutaneous Electrical Nerve Stimulation

A novel analgesic therapy for diabetic neuropathic pain

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OBJECTIVE — To evaluate the use of percutaneous electrical nerve stimulation (PENS) in the management of patients with painful diabetic peripheral neuropathy.

RESEARCH DESIGN AND METHODS — A total of 50 adult patients with type 2 diabetes and peripheral neuropathic pain of >6 months duration involving the lower extremities were randomly assigned to receive active PENS (needles with electrical stimulation at an alternating frequency of 15 and 30 Hz) and sham (needles only) treatments for 3 weeks. Each series of treatments was administered for 30 min three times a week according to a standardized protocol. After a 1-week washout period, all patients were subsequently switched to the other modality. A 10-cm visual analog scale (VAS) was used to assess pain, physical activity, and quality of sleep before each session. The changes in VAS scores and daily requirements for oral analgesic medication were determined during each 3-week treatment period. Patients completed the MOS 36-Item Short-Form Health Survey (SF-36), the Beck Depression Inventory (BDI), and the Profile of Mood States (POMS) before and after completion of each treatment modality. At the end of the crossover study, a patient preference questionnaire was used to compare the effectiveness of the two modalities.

RESULTS — Compared with the pain VAS scores before active (6.2 ± 1.0) and sham (6.4 ± 0.9) treatments, pain scores after treatment were reduced to 2.5 ± 0.8 and 6.3 ± 1.1, respectively. With active PENS treatment, the VAS activity and sleep scores were significantly improved from 5.2 ± 1.0 and 5.8 ± 1.3 to 7.9 ± 1.0 and 8.3 ± 0.7, respectively. The VAS scores for pain, activity, and sleep were unchanged from baseline values after the sham treatments. Patients' daily oral nonopioid analgesic requirements decreased by 49 and 14% after active and sham PENS treatments, respectively. The post-treatment physical and mental components of the SF-36, the BDI, and the POMS all showed a significantly greater improvement with active versus sham treatments. Active PENS treatment improved the neuropathic pain symptoms in all patients.

CONCLUSIONS — PENS is a useful nonpharmacological therapeutic modality for treating diabetic neuropathic pain. In addition to decreasing extremity pain, PENS therapy improved physical activity, sense of well-being, and quality of sleep while reducing the need for oral nonopioid analgesic medication.

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Abbreviations: BDI, Beck Depression Inventory; MCS, Mental Component Summary; PCS, Physical Component Summary; PENS, percutaneous electrical nerve stimulation; POMS, Profile of Mood States; SF-36, MOS 36-Item Short-Form Health Survey; TENS, transcutaneous electrical nerve stimulation; VAS, visual analog scale.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

Peripheral neuropathy is the most common complication of type 2 diabetes, occurs in the distal extremities, and typically affects the sensory, motor, and autonomic systems (1,2). In diabetic patients, chronic hyperglycemia can produce neuropathic changes that affect peripheral nerve function and produce extremity pain (3,4). The persistence of these painful symptoms can interfere with the patient's physical activity and sleep pattern.

Conventional pharmacotherapy for painful diabetic neuropathy remains largely symptomatic. Analgesics, tricyclic antidepressants, and anticonvulsants are the mainstays of therapy (5). Nonpharmacological therapies such as transcutaneous electrical nerve stimulation (TENS) (6), acupuncture (7), and spinal cord stimulation (8) have also been used successfully to alleviate the pain and discomfort associated with peripheral neuropathy. Percutaneous electrical nerve stimulation (PENS) is a novel electroanalgesic therapy that combines the advantages of both TENS and electroacupuncture by using percutaneously placed disposable acupuncture-like needle probes to stimulate peripheral sensory nerves innervating the region of neuropathic pain. This therapy has recently been reported to be highly effective in the short-term management of a wide variety of acute and chronic pain syndromes (9–13).

The present randomized sham-controlled crossover study was designed to evaluate the effectiveness of PENS therapy in diabetic patients with peripheral neuropathic pain. In addition to examining the acute analgesic effects of PENS, changes in physical activity, quality of sleep, and requirements for analgesic medication were examined during a 3-week treatment period.

RESEARCH DESIGN AND METHODS

Study patients

After local institutional review board approval and after patients gave their written informed consent, 50 adult diabetic patients (28 women and 22 men), ranging in age from 34 to 71 years (means ± SD 55 ± 9

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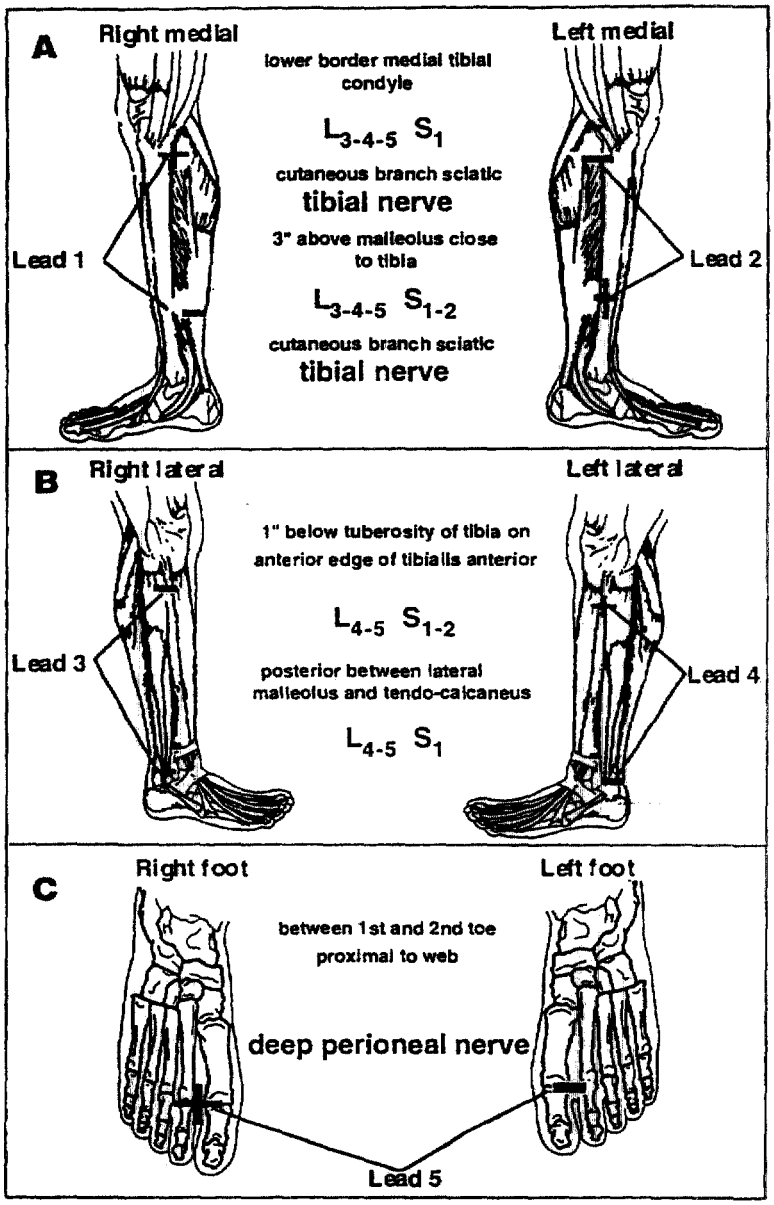


Figure 1—The needle locations for each pair of positive (+) and negative (−) lead. A total of 10 needles were connected to five sets of leads.

years) and in body weight from 46 to 113 kg (70 ± 17 kg) were enrolled in this sham-controlled investigator-blinded crossover study. The patients had longstanding type 2 diabetes associated with painful peripheral neuropathic symptoms of >6 months (18 ± 7) duration involving both lower extremities. The study patients were referred from the diabetes clinic with a diagnosis of peripheral neuropathy confirmed by an abnormal nerve conduction study. These patients complained of burning pain with paresthesia in both legs. Neurological examination of the patients revealed sensory abnormalities in both lower extremities. Exclusion criteria included pregnancy, cardiac arrhythmias or cardiac pacemakers, infection or gangrene, history of vascular insufficiency in the legs, drug or alcohol abuse, psychiatric disease, major organ disease, radicular pain (sciatica), psychiatric disease, and inability to complete the psychological assessment forms reliably. Patients receiving steroids, dilantin, or chemotherapeutic agents were also excluded. All patients were stable regarding control of their diabetes, and their medical management was unchanged during the study period. The patients were instructed to use their current nonopioid analgesic medications on an as-needed basis.

Study design

The patients were randomly assigned to receive active PENS (needles with electrical stimulation) or sham PENS treatment (needles only). The crossover study design mandated a 1-week recovery (washout) period after completing the initial series of treatments. The protocol also stipulated 30 min of active or sham electrical stimulation treatment three times a week for 3 consecutive weeks. Each treatment session required placement of 10 32-gauge (0.2-mm) stainless steel acupuncture-like needle probes (ITO, Tokyo, Japan) to a depth of 1–3 cm into the soft tissue and/or muscle in the leg and foot bilaterally as illustrated in Fig. 1A–C. The 10 needle probes were connected to five bipolar leads from an investigational (i.e., not approved by the U.S. Food and Drug Administration) low-output electrical generator. These probes were stimulated at alternating frequencies of 15 and 30 Hz every 3 s or at 0 Hz for the active and sham treatments, respectively. The generator produced a maximum of 25 m ampheres electrical stimulation with a biphasic square-wave pattern and a pulse width of 0.5 ms in a continuous duty cycle. The intensity of the electrical stimulation was adjusted to the highest tolerable level without producing muscle contractions.

Before initiating either treatment modality, patients completed a baseline psychological assessment. Both the Physical Component Summary (PCS) and the Mental Component Summary (MCS) scores of the MOS 36-Item Short-Form Health Survey (SF-36) (14) were determined 24 h before the first treatment and were repeated 48 h after completing the 3-week treatment session with each modality. The Beck Depression Inventory (BDI) (15) and the Profile of Mood Status (POMS) (16) were also administered at these same three time points. As a result of questionnaire completion problems, only 46 BDI and 44 POMS tests were analyzed. For all other measures, data from all 50 subjects were analyzed. Before the first treatment session, all patients were asked to record their baseline levels of pain, physical activity, and quality of sleep by using three separate 10-cm visual analog scales (VASs), where 0 = minimal (lowest) and 10 = maximal (highest). In addition, each patient was asked to record the number of doses of oral analgesic medication taken each day. Repeat

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VAS assessments of pain, activity, and sleep were performed before each treatment session, after each week of treatment, and again at the end of the 3-week treatment period with each modality. Daily oral analgesic requirements were recorded in the patient's diary. At 24 h after the final treatment session, each patient completed a questionnaire assessing the relative effectiveness of the two treatment modalities.

Statistical analysis

The NCSS software package (Version 6.0.1 for Windows, Kaysville, UT) was used for all statistical analyses. An a priori power analysis with $\alpha = 0.05$ and $\beta = 0.10$ (power = 90%) determined that a group size of 40 should be adequate to demonstrate a 25% change in the VAS pain scores between the two treatment modalities. The changes in the VAS scores and oral analgesic medications over time were analyzed by using repeated measures of analyses of variance and Student's t test. Analysis of discrete data was performed by using the χ^2 test. Changes and differences in the psychological assessment were analyzed by using t tests. Data are means ± SD and percentages, and P values <0.05 were considered statistically significant.

RESULTS

The demographic characteristics and treatment effects after the initial 3-week study period are summarized in Table 1. The post-treatment VAS scores for extremity pain, physical activity, and quality of sleep were significantly improved after each week of PENS treatment compared with baseline values ($P < 0.05$), but no significant changes were evident after the sham treatments (Table 1). The overall percentage reduction in pain after the 3-week treatment with active PENS (56 ± 17%) was significantly greater than with sham (14 ± 11%) treatments (Table 2). Similarly, the overall average percentage increases in physical activity and quality of sleep were also significantly higher after active PENS (48 ± 19 and 41 ± 22%, respectively) compared with sham treatments (13 ± 16 and 11 ± 13%, respectively) ($P < 0.05$). Moreover, a cumulative effect of PENS therapy was noted during the course of the 3-week treatment block.

Evaluation of pretreatment SF-36 values suggested that the study population had significantly lower health-related scores compared with the general population. The prestudy scores were 31.2 ± 7.3 and 41 ± 5.8 for the PCS and MCS, respectively, compared with the general population norm of 50. With PENS therapy, the SF-36 scores were significantly improved compared with the prestudy scores for both the PCS (36.8 ± 6.7) and MCS (43.9 ± 5.6) components ($P < 0.01$). Although the sham treatments also produced an improvement in the SF-36 regarding both PCS (32.4 ± 7.5) and MCS (42 ± 5.5) scores ($P < 0.05$), the effect was significantly less than with active PENS therapy ($P < 0.05$).

Analysis of the pretreatment BDI scores indicated that the study population had a mean depression level of 30.2 ± 11.6, which reflects a severe level of depression. The post-PENS treatment BDI scores revealed a significant improvement in the level of depression (8.1 ± 4.6) relative to the pretreatment score ($P < 0.01$). Although the post-sham treatment BDI score was also significantly decreased compared with the prestudy baseline value (20.7 ± 8.2), this level is still in the moderately depressed range. Finally, a comparative analysis revealed that the decrease in the BDI scores was significantly greater after PENS versus sham treatments ($P < 001$).

The overall results of the POMS evaluation are summarized in Table 3. A multivariate analysis of variance revealed a significant multivariate effect (Hotelling's T^2 revealed $P < 0.01$) that justified univariate analyses of the individual POMS measures. These t tests revealed that, relative to pretreatment values, the postactive and post-sham PENS treatments displayed significant improvement on all POMS measures except for the vigor activity measure. More importantly, the postactive PENS treatment was associated with greater decreases on all POMS measures relative to the post-sham treatment ($P < 0.05$).

In addition to its salutary analgesic effects, active PENS treatments significantly

Table 1—Demographic characteristics and effects of sham and active PENS treatments on VASs for pain, activity, and sleep and on oral nonopioid analgesic intake after each week of the initial 3-week treatment block (before crossover to the second modality)

	PENS	
	Sham	Active
n	25	25
Age (years)	54 ± 9	56 ± 8
Weight (kg)	70 ± 16	68 ± 19
Duration of diabetes (years)	9 ± 2	10 ± 3
Duration of symptomatic neuropathy (months)	17 ± 6	19 ± 8
Pain score (cm)*		
Baseline	6.4 ± 0.9	6.2 ± 1.0
Week 1	5.9 ± 1.1	3.6 ± 1.2†‡
Week 2	6.1 ± 1.2	3.3 ± 1.1†‡
Week 3	6.3 ± 1.1	2.5 ± 0.9†‡§‖
Activity score (cm)*		
Baseline	5.3 ± 0.9	5.2 ± 1.0
Week 1	5.7 ± 1.0	6.4 ± 0.8†‡
Week 2	5.9 ± 1.1	6.8 ± 0.9†‡
Week 3	6.0 ± 1.1	7.9 ± 1.0†‡§‖
Sleep score (cm)*		
Baseline	6.0 ± 1.5	5.8 ± 1.3
Week 1	6.9 ± 1.2	7.5 ± 0.9†‡
Week 2	6.7 ± 1.3	7.8 ± 0.8†‡
Week 3	6.6 ± 1.3	8.3 ± 0.7†‡§‖
Oral analgesics (pills/day)		
Baseline	3.1 ± 1.1	3.3 ± 1.3
Week 1	2.8 ± 0.9	2.2 ± 0.9†‡
Week 2	2.7 ± 1.0	2.0 ± 0.8†‡
Week 3	2.9 ± 0.8	1.3 ± 0.6†‡§‖

Data are n or means ± SD. *VASs (0 = minimal [lowest] to 10 = maximal [highest]); †significantly different from the baseline ($P < 0.05$); ‡significantly different from sham ($P < 0.05$); §significantly different from week 1 ($P < 0.05$); ‖significantly different from week 2 ($P < 0.05$).

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Table 2—Comparative effects of sham versus active PENS treatments after completion of the crossover study

	PENS	
	Sham	Active
Pain score (cm)		
Baseline	5.2 ± 1.6	6.2 ± 1.3†
Week 1	4.6 ± 1.5	3.8 ± 1.2*
Week 2	4.6 ± 1.4	3.5 ± 1.0*
Week 3	4.8 ± 1.2	2.6 ± 0.9*‡§
Activity score (cm)		
Baseline	5.9 ± 1.3	4.8 ± 1.2†
Week 1	6.4 ± 1.1	6.5± 0.8*
Week 2	6.2 ± 1.3	7.0 ± 1.0*
Week 3	6.3 ± 1.2	7.8 ± 1.1*‡§
Sleep score (cm)		
Baseline	6.8 ± 1.5	5.7 ± 1.3†
Week 1	7.3 ± 1.3	7.5 ± 1.2*
Week 2	7.0 ± 1.1	7.9 ± 1.0*
Week 3	7.1 ± 1.2	8.6 ± 1.0*‡§

Scores are for pain, physical activity, and quality of sleep 24 h before receiving the first treatment (baseline) and at the end of the first, second, and third weeks of each treatment after completion of the crossover study. Data are means ± SD. VASs (0 = minimal [lowest] to 10 = maximal [highest]. *Significantly different from the baseline ($P < 0.05$); †significantly different from sham baseline ($P < 0.05$); ‡significantly different from Week 1 ($P < 0.05$); §significantly different from Week 2 ($P < 0.05$).

decreased the need for daily oral (nonopioid) analgesic medication during each of the 1st, 2nd, and 3rd weeks of treatment ($P < 0.05$), whereas sham treatments produced no significant change in the patients' use of oral analgesic medications (Fig. 2). The overall reduction in the analgesic medication requirement was significantly greater with active (49 ± 19%) than with sham (14 ± 10%) PENS treatments.

Finally, the poststudy evaluation of the two treatment modalities revealed that active PENS was clearly the preferred therapy (92%) for alleviating the pain and numbness in the lower extremities. In addition, 88% of the patients reported an improved sense of well-being after PENS treatment, and 92% of the patients expressed a willingness to "pay extra money" for PENS therapy in the future. No side effects were reported with either therapeutic modality.

CONCLUSIONS — In this prospective crossover sham-controlled study, PENS provided highly effective short-term pain relief for patients with diabetic peripheral neuropathy. The beneficial effects of the active versus sham PENS treatments were remarkably similar before and after the crossover treatments were performed. However, a carry-over effect was evident from the prior PENS therapy, despite the 1-week recovery (washout) period, as evidenced by the lower overall baseline pain scores in the sham group (Table 2). These findings support earlier publications that described the beneficial effects of electroanalgesic therapy in diabetes-induced neuropathic symptoms (6–8). In addition, the apparent cumulative benefits of PENS therapy over time suggest that this therapy may have long-term benefits consistent with the experimental findings of Mo et al. (17) involving electroacupuncture and TENS in animals with experimental (drug-induced) diabetes and associated neuropathic changes.

Although the precise mechanism of PENS-induced analgesia is not known at this time, it appears to be related to both neural modulation (18) and an increase in endogenous opioid-like substances (e.g., dynorphins, endorphins, enkephalins) within the central nervous system (19). Interestingly, both Cameron et al. (20) and Mo et al. (17), have reported that peripheral electrical stimulation can normalize the changes in nerve conduction velocity when using an experimental diabetic rat model. Walsh et al. (21) also observed a decrease in nerve conduction latency and mechanical pain threshold when TENS was applied directly over the nerve. In addition, clinical studies have suggested that the use of electrotherapy in diabetic patients produces decreases in mechanical pain threshold, a local vasodilatory effect, and enhanced wound healing (21–24).

Active PENS treatments produced significant pain relief, increased levels of mood and physical activity, and improved quality of sleep compared with the sham treatments during the course of the 3-week treatment period. Improvements in activity level and sleep quality may be secondary to improved pain control with PENS therapy. Interestingly, pain relief appeared to be maximal at the end of the 3rd week of treatment. However, within 1 week of the last PENS treatment session, the pain scores began to return to pretreatment (baseline) levels. These data suggest that the use of PENS will require a maintenance treatment program to achieve a more sustained beneficial effect, which is consistent with the findings of Kumar and Marshall (6), that involved using TENS to treat neuropathic pain. In the future, a randomized crossover study involving PENS and TENS therapies in the management of diabetic neuropathic pain should be performed.

Previous studies involving the use of PENS in patients with chronic pain syndromes showed that alternating low- and high-frequency stimulation for 30–45 min produced the optimal analgesic effect (25,26). Therefore, we chose to use stimulus frequencies of 15 and 30 Hz at 30-min intervals during each of the active PENS treatment sessions. Because the natural course of neuropathic symptoms is highly variable, these data supporting the short-term benefits of PENS therapy must be interpreted with caution. To minimize investigator and patient bias, all assessments were performed by a blinded observer, and the patients, none of whom had ever undergone acupuncture, were told that the needle-only (sham) treatments represented an acupuncture-like therapy. Nevertheless, these preliminary data clearly require validation by a follow-up study that replicates these findings.

Although neuropathic pain is most commonly treated with a combination of antidepressants, opioids, and nonopioid

Table 3—Pretreatment (baseline) and post-treatment POMS scores for the active and sham PENS treatments after completion of the crossover study

	Baseline	After sham	After active PENS
Tension-anxiety	54.6 ± 7.4	50.4 ± 7.1	44.1 ± 5.6
Depression-dejection	58.6 ± 9.4	56.1 ± 10.8	47.5 ± 7.2
Anger-hostility	62.9 ± 12.2	59.3 ± 12.1	51.1 ± 9.1
Vigor-activity	53.1 ± 6.1	50.6 ± 7.7	50.9 ± 12.4
Fatigue-inertia	56.1 ± 6.6	51.4 ± 6.8	43.3 ± 7.1*
Confusion-bewilderment	53.5 ± 7.4	50.2 ± 8.3	44.4 ± 6.3*
Total mood disturbance	71.3 ± 32.1	57.8 ± 34.4	29.5 ± 27.6*

Data are means ± SD. *Significantly greater decrease from baseline values after active PENS (vs. sham) treatment ($P < 0.01$).

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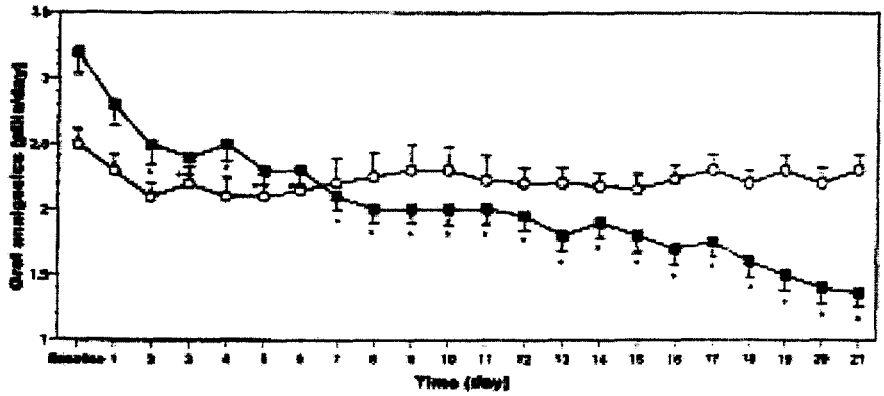


Figure 2—Effect of active (■) and sham (○) PENS therapies on daily oral analgesic requirements (changes in the daily intake of nonopioid analgesic medication during the 3-week treatment period). Data are means ± SEM. *Data are significantly different from prestudy data ($P < 0.05$).

analgesics, gastrointestinal side effects and excessive sedation can be problematic in patients with diabetes (27). Analogous to our earlier findings with PENS in chronic pain conditions (10,13), these data suggest that this form of electroanalgesia can significantly decrease a diabetic patient's daily oral analgesic requirements. The analgesic-sparing effects of PENS may also minimize the side effects of commonly used pharmacological agents.

The improvements in post-treatment SF-36 and mood levels (as assessed by the BDI and POMS questionnaires) suggest that the beneficial effects of PENS may also be related to an antidepressant action. These psychological data further support the clinical utility of PENS as a nonpharmacological treatment modality in this patient population. After completing the crossover study, these patients also reported that PENS produced an improved sense of well-being, and most patients expressed a willingness to pay additional money (out of pocket) to receive PENS therapy in the future. Many of the patients have elected to continue with PENS treatments on a less frequent basis as part of a maintenance therapy program. The need for further treatments to maintain the beneficial effects of PENS therapy is consistent with the findings for other forms of electrotherapy in this patient population (6,7).

The deficiencies of the study design include: 1) the possibility of patient bias as a result of our inability to perform the study in a double-blind fashion because we could not "blind" the patients regarding the electrical sensation; 2) the failure to monitor serial blood glucose and glycated hemoglobin levels and nerve conduction velocities; and 3) the decrease in the beneficial effects of PENS over time will necessitate a maintenance treatment program to achieve a sustained effect. Long-term outcome studies are needed to ascertain the cumulative effects of PENS in this patient population. Comparative studies involving PENS and other forms of electroanalgesic therapy (e.g., TENS, electroacupuncture) and interaction studies involving pharmacological modalities (28) should be performed in the future. Although clearly less invasive than spinal cord stimulation, PENS is more complex than TENS.

In conclusion, PENS therapy produces short-term pain relief; improves mood, functionality, and quality of sleep; and decreases the oral nonopioid analgesic requirements in patients with painful peripheral diabetic neuropathy. However, PENS should be viewed as a supplementary (or complementary) therapy rather than as an alternative to conventional pharmacological therapy.

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Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTAT@cdrh.fda.hhs.gov or 301-796-8618

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FDA/CDRH IMAGING SYSTEM

Page Count Discrepancy Information

The page behind page 187 was not numbered.
The page behind the page marked 223 was not numbered
The page behind the page marked 225 was not numbered
The page behind the page marked 250 was not numbered.
The page behind the page marked 289 was not numbered.
The page behind the page marked 308 was not numbered.
The page behind the page marked 309 was not numbered.
The page behind the page marked 440 was not numbered.
The page behind the page marked 465 was not numbered.

Verifiers Initials CAB

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

DEC 21 2001

Lori J. Glastetter
Vice President, Regulatory Affairs/Quality Assurance
Vertis Neuroscience, Inc.
2101 Fourth Avenue, Suite 200
Seattle, Washington 98121

Re: K011702/S1
Trade/Device Name: Vertis Percutaneous Neuromodulation Therapy (PNT) Stimulation System (Vertis PNT Control Unit and Vertis PNT Lumbar Safeguard Kit)
Regulation Number: 21 CFR 882.5890 and 21 CFR 882.1350
Regulation Name: Transcutaneous Electrical Nerve Stimulator for Pain Relief and Needle Electrode
Regulatory Class: Class II
Product Code: NHI and GXZ
Dated: September 24, 2001
Received: September 25, 2001

Dear Ms. Glastetter:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 21 CFR Part 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4659. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address
http://www.fda.gov/cdrh/dsma/dsmamain.html

Sincerely yours,

Celia M. Witten, Ph.D., M.D.
Director
Division of General, Restorative
and Neurological Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

510(k) Number (if known): K011702

Device Name: Vertis PNT System

Indications For Use:

Percutaneous Neuromodulation Therapy (PNT) is indicated for the symptomatic relief and management of chronic or intractable low back pain and/or as an adjunctive treatment in the management of post-surgical low back pain and post-trauma low back pain.

The PNT Control Unit is to be used with a PNT Safeguide Kit – Lumbar.

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

(Division Sign-Off)
Division of General, Restorative and Neurological Devices

(Optional Format 3-10-98)

510(k) Number K011702

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

DEPARTMENT OF HEALTH & HUMAN SERVICES — Public Health Service
Food and Drug Administration

Memorandum

m: Reviewer(s) - Name(s) KRISTEN BOWSHER

Subject: 510(k) Number K011702/S1

To: The Record - It is my recommendation that the subject 510(k) Notification:

- ☐ Refused to accept.
- ☐ Requires additional information (other than refuse to accept).
- ☒ Is substantially equivalent to marketed devices.
- ☐ NOT substantially equivalent to marketed devices.
  - De Novo Classification Candidate? ☐ YES ☒ NO
- ☐ Other (e.g., exempt by regulation, not a device, duplicate, etc.)

Is this device subject to Postmarket Surveillance?	☐ YES	☒ NO
Is this device subject to the Tracking Regulation?	☐ YES	☒ NO
Was clinical data necessary to support the review of this 510(k)?	☒ YES	☐ NO
Is this a prescription device?	☒ YES	☐ NO
Was this 510(k) reviewed by a Third Party?	☐ YES	☒ NO
Special 510(k)?	☐ YES	☒ NO
Abbreviated 510(k)? Please fill out form on H Drive 510k/boilers	☐ YES	☒ NO

This 510(k) contains:

Truthful and Accurate Statement ☐ Requested ☒ Enclosed
(required for originals received 3-14-95 and after)

☒ A 510(k) summary OR ☐ A 510(k) statement

NA ☐ The required certification and summary for class III devices

☒ The indication for use form (required for originals received 1-1-96 and after)

Material of Biological Origin ☐ YES ☐ NO

The submitter requests under 21 CFR 807.95 (doesn't apply for SEs):

☐ No Confidentiality ☐ Confidentiality for 90 days ☐ Continued Confidentiality exceeding 90 days

NHI - new procode for PENS

Predicate Product Code with class: GZJ, Class II 882.5890 Transcutaneous Electrical Nerve Stimulator for Pain Relief

Additional Product Code(s) with panel (optional): GXZ, Class II 882.1350 Needle Electrode

Review: _____ (Branch Chief) RED (Branch Code) 12/4/07 (Date)

Final Review: _____ (Division Director) 12/20/01 (Date)

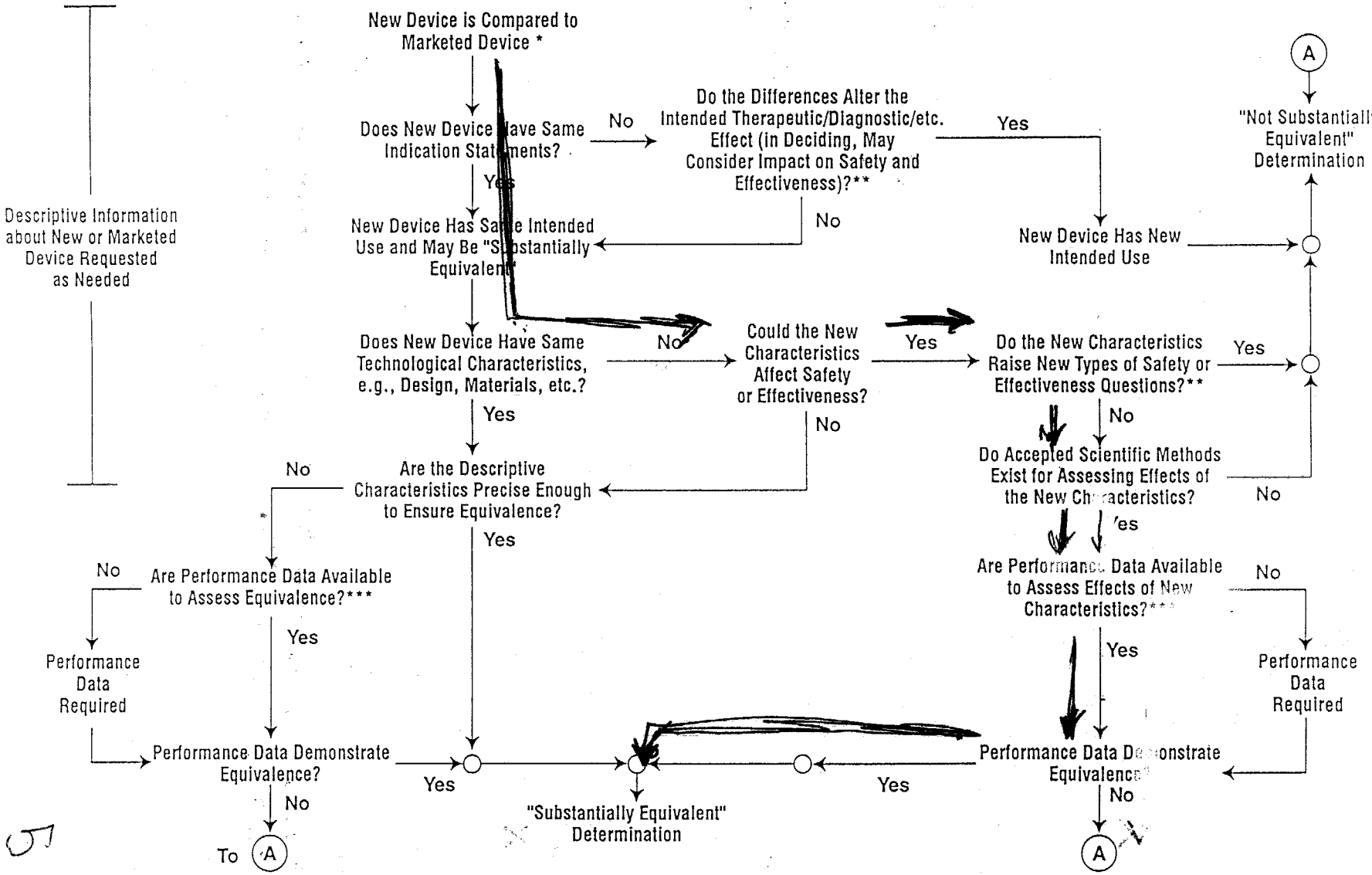
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Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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510(k) "Substantial Equivalence" Decision-Making Process (Detailed)



* 510(k) Submissions Compare New Devices to Marketed Devices. FDA Requests Additional Information if the Relationship Between Marketed and "Predicate" (Pre-Amendments or Reclassified Post-Amendments) Devices is Unclear.

** This Decision is Normally Based on Descriptive Information Alone, But Limited Testing Information is Sometimes Required.

*** Data May Be in the 510(k), Other 510(k)s, The Center's Classification Files, or the Literature.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

510(k) MEMO

DATE: 8-23-01

FROM: Kristen A. Bowsher, Ph.D., Biomedical and Electrical Engineer KAB
ODE/DGRD/REDB

SUBJECTS: Vertis Neuroscience, Inc. – Percutaneous Neuromodulation Therapy (PNT) System

TO: K011702

Background

On August 29, 2001 the FDA sent the sponsor a "Cannot Respond in 30 Days" letter. The sponsor called me after receipt of that letter and stated that they believed they could respond in 30 days. I stated that if they felt they could respond to our concerns they should go ahead and submit a supplement. This supplement thus, is in response to our August 29, 2001 letter to the company.

August 29, 2001 Letter

The following are the concerns voiced in the letter to the sponsor. Please refer to the review from the original submission for detail.

Although you have provided results from a clinical study for your device, due to significant study design flaws, conclusions cannot be drawn with respect to the safety and effectiveness of your device as compared to legally marketed predicate devices. Particularly, the study's design did not attempt to compare the new device to a legally marketed predicate device and did not attempt to differentiate between the device effect and placebo/sham effect, i.e., a sham control was not used. Therefore, you should perform a new clinical study to determine whether your device is as safe and effective as legally marketed predicate devices. We recommend performing a study that directly compares the Vertis PNT device to a legally marketed predicate device to which you are claiming equivalence (e.g., a legally marketed TENS device with surface electrodes). Prior to conducting a future study, we highly recommend that you contact us to discuss your study protocol. The following information should be considered in a new study protocol:

(b) (4)

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

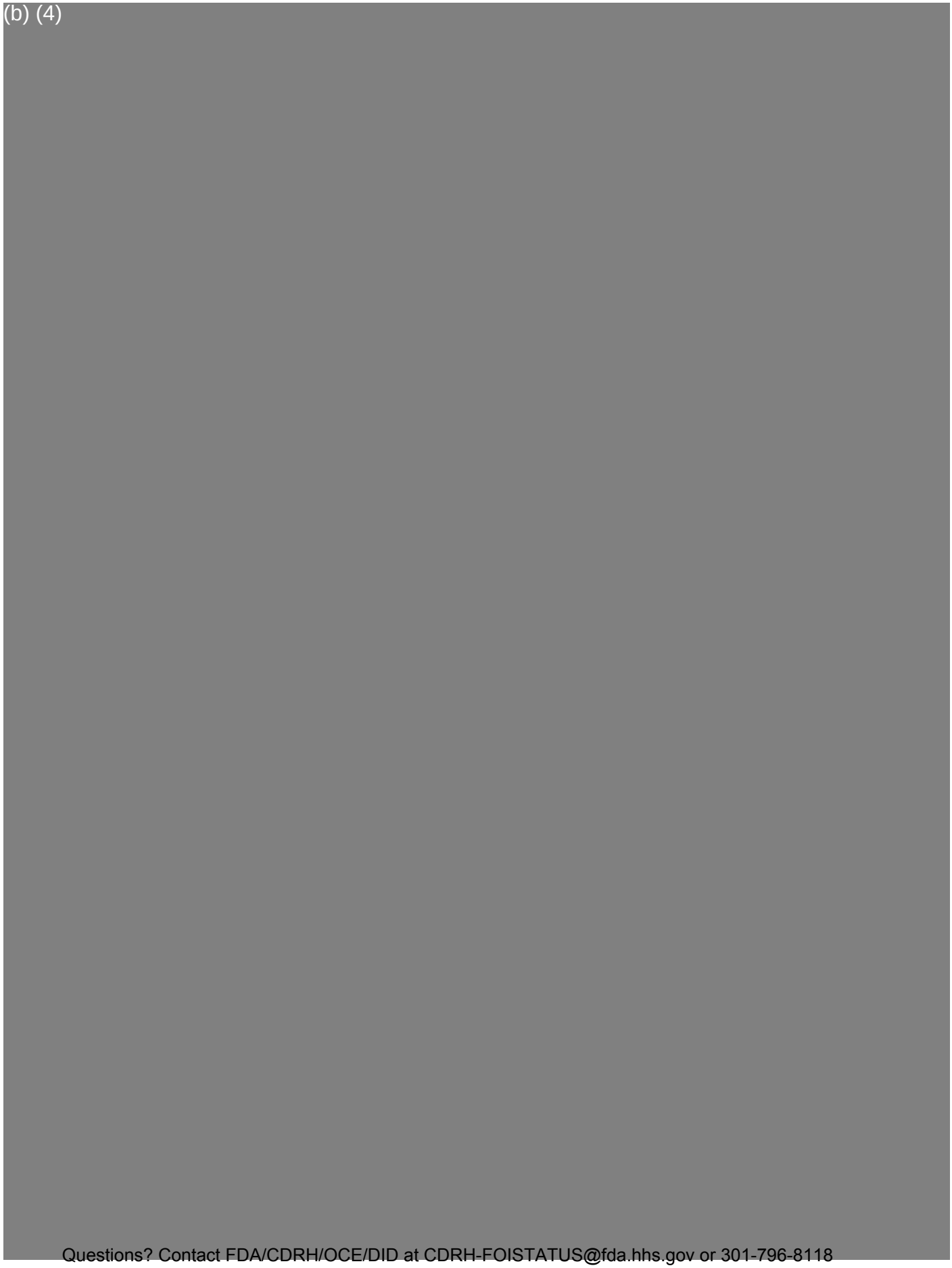
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(b) (4)

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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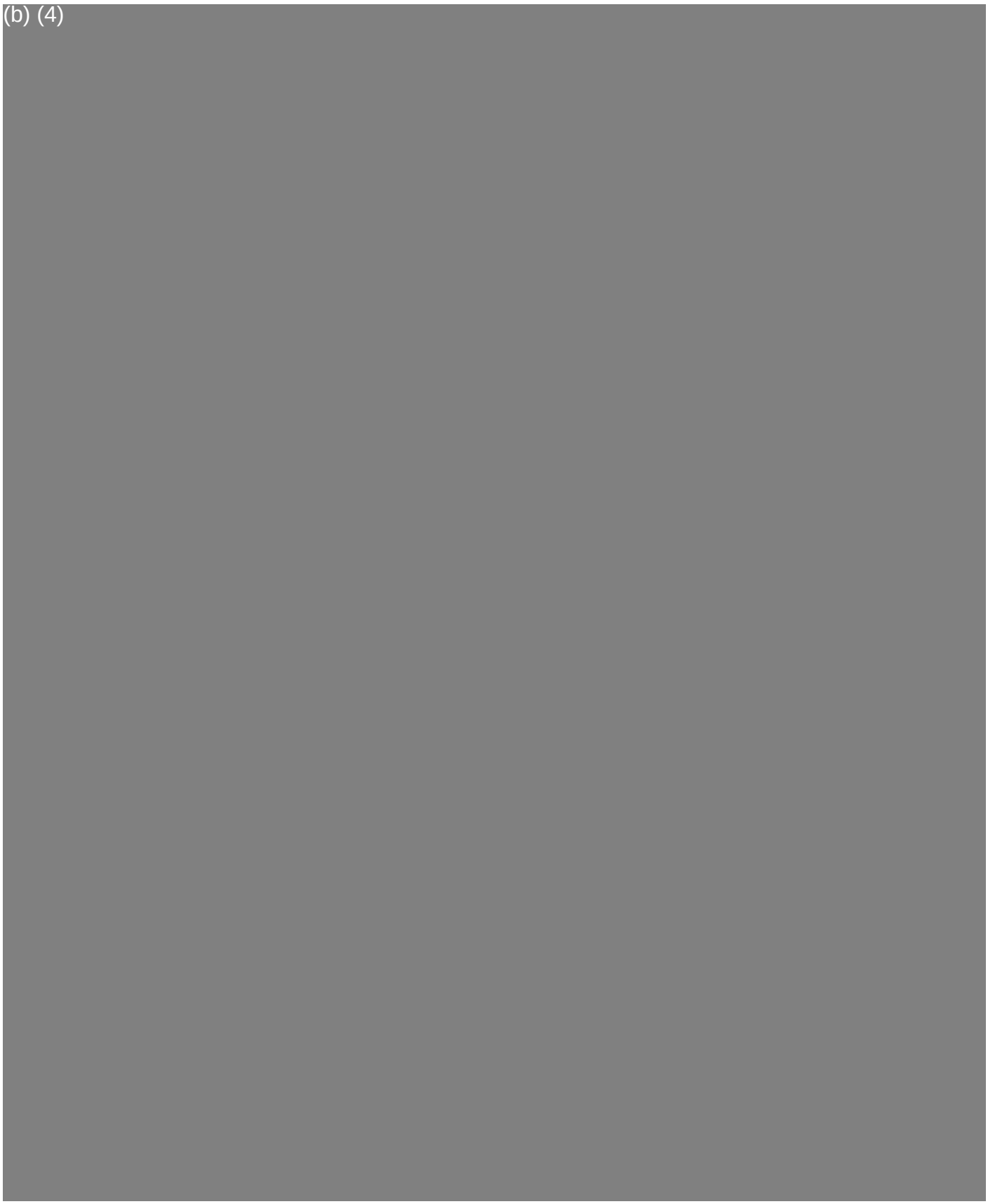
(b) (4)



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(b) (4)



Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Product Code

Since the percutaneous electrodes represent a new technology for TENS devices I requested a new product code. A Percutaneous Electrical Nerve Stimulator (PENS) is a device used for the treatment of pain. Unlike the classified Transcutaneous Electrical Nerve Stimulator that apply an electrical current to electrodes on a patient's skin to deliver stimulation a PENS uses electrodes that are placed percutaneously to deliver stimulation.

The new product code is: NHI - Nerve, Stimulator, Electrical, Percutaneous (PENS) for Pain Relief

The PNT Lumbar Safeguard kit is substantially equivalent to needle electrodes and thus the PNT Stimulation System will also have the product code GXZ.

RECOMMENDATION

I recommend that the Vertis Percutaneous Neuromodulation Therapy (PNT) Stimulation System (Vertis PNT Control Unit and Vertis PNT Lumbar Safeguard Kit) be found substantially equivalent to legally-marketed TENS for Pain Relief devices (21 CFR 882.5890, Class II) and legally marketed Needle Electrodes (21 CFR 882.1350, Class II).

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Appendix 25 - *revised*
510(k) Summary of Safety and Effectiveness

Vertis Neuroscience, Inc.
Percutaneous Neuromodulation Therapy (PNT) ™ Control Unit and Accessories

General Information

Classification	Class II
Trade Name	Percutaneous Neuromodulation Therapy (PNT) Nerve Stimulation System
Submitter	Vertis Neuroscience, Inc. 2101 Fourth Avenue, Suite 200 Seattle, Washington, USA 98121
Contact	Lori Glastetter Vice President, Regulatory Affairs/ Quality Assurance

Substantially Equivalent Devices

Manufacturer	Substantially Equivalent devices	510(k)
Empi, Inc. St. Paul, MN	EPIX Tens Device System Model EPIX VT Model EPIX XL	K970203 K951903
Rehabilicare, Inc. New Brighton, MN	SMP-Plus™ Model 4930	K982410
Chattanooga Group, Inc. Hixson, TN	Intelect ® Legend Stim Model IFC2 (catalog #INT002)	K924666
Medtronic, Inc Minneapolis, MN	Mattrix ® Neurostimulation System Receiver model: 3272 Transmitter model: 3210	K982902
TECA Corporation Pleasantville, NY	TECA Disposable Monopolar Needles 902-DMFxx-TP series 892-DMGxx-TP series	K973442
Medtronic, Inc. Minneapolis, MN	DMN™ Disposable Monopolar Needle Electrodes DMFxx series DMNxx series	K950314
Medtronic, Inc. Minneapolis, MN	Resume II Lead Model 3587a	K915540

Intended use

Percutaneous Neuromodulation Therapy (PNT) is indicated for the symptomatic relief and management of chronic or intractable low back pain and/or as an adjunctive treatment in the management of post-surgical low back pain and post-trauma low back pain.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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The PNT Control Unit is to be used with a PNT Safeguide Kit – Lumbar.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Device Description

The Vertis PNT System is designed for delivering percutaneous electrical stimulation (termed: Percutaneous Neuromodulation Therapy - PNT). The Vertis PNT System is intended to be used in pain management by a physician (e.g., anesthesiologists or physical medicine and rehabilitation physicians) or on the order of a physician (e.g., by a physical therapist) in a clinic environment. It is not intended for patient use. The device system includes 3 major components:

- the *Vertis PNT Control Unit* - a software-driven, five channel, AC powered nerve stimulator which generates the electrical stimulus;
- the sterile *Safeguides* – which are sterile, needle electrodes, and
- the *Patient Cable* - which interconnects the PNT Control Unit to the electrodes

Bench/Animal Testing

Extensive bench and animal was conducted on the Vertis PNT System and included performance and safety testing. The Vertis PNT System conforms to applicable sections of the technical references and FDA-recognized consensus standards noted below. Additionally, the PNT Control Unit software was validated per recognized validation techniques.

Results: All testing of the products yielded acceptable results prior to commercial distribution.

ANSI/AAMI NS4-1985 Transcutaneous Electrical Nerve Stimulators, approved 5-20-86.
ANSI/AAMI ES1 1993 - Safe Current Limits for Electromedical Apparatus, approved 12-2-93
ANSI/AMI NS15-1995 Implantable Peripheral Nerve Stimulators, approved 2-1-95
IEC60601-1:1993 Medical Electrical Equipment, Part 1: General Requirements for Safety and Amendments A1:1991, A2:1995.
IEC 60601-1-2 First Edition 1993-4 Medical Electrical Equipment, - Part 1: General Requirements for Safety: Electromagnetic Compatibility – Requirements and Tests (tested in accordance to the IEC 61000 series).
IEC 60601-1-4:1996 Medical Electrical Equipment, Part 1: General Requirements for Safety, Part 2: Collateral Standard: Programmable electrical medical systems.
IEC 60601-2-10:1987 Medical Electrical Equipment, Part 2: Particular Requirements for the Safety of Nerve and Muscle Stimulators.
EN (CEN) 1441:1997 Medical Devices – Risk Analysis.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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ANSI/AAMI/ISO 15223: 2000 Medical Devices – Symbols to be used with Medical Device Labels, Labeling and Information to be Supplied, approved 3-13-00.
IEC 60601-2-10:1987 Medical Electrical Equipment, Part 2: Particular Requirements for the Safety of Nerve and Muscle Stimulators.
ANSI/AAMI/ISO 11137: 1994 Sterilization of Health Care Products – Requirements for Validation and Routine Control –Radiation Sterilization; using Method 1 as described per AAMI/ISO TIR No. 13409: 1996 Sterilization of Health care Products – Radiation Sterilization – Substantiation of 25kGy as a Sterilization Dose for Small or Infrequent Production Batches.
ANSI/AAMI/ISO 10993-1:1997, Biological Evaluation of Medical Devices - Part 1: Evaluation and Testing.

Clinical Testing

Under the auspices of an Investigational Device Exemption, Vertis conducted a prospective clinical study evaluating the safety and effectiveness of percutaneous neuromodulation therapy.

The Vertis clinical trial was reviewed and approved in November 2000. The trial commenced shortly thereafter at multiple United States clinical sites. The trial was completed in March 2001. During the multi-week investigational protocol, there were a total of 2150 electrode placements in 215 PNT therapy sessions with patients.

Results: The clinical trial demonstrated the safety and effectiveness of the percutaneous neuromodulation therapy.

Summary of Substantial Equivalence

Therefore, due to the similarity of design features, materials, test results, clinical results and indicated use to other predicate devices, Vertis believes the Vertis PNT System does not raise any new safety or effectiveness issues and is substantially equivalent to currently available nerve stimulators, electrodes and accessories that have been determined to be substantially equivalent to devices in commercial distribution prior to May 28, 1976.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

510(k) Appendix 27 - *revised*
Indications for Use

Percutaneous Neuromodulation Therapy (PNT) is indicated for the symptomatic relief and management of chronic or intractable low back pain and/or as an adjunctive treatment in the management of post-surgical low back pain and post-trauma low back pain.

The PNT Control Unit is to be used with a PNT Safeguide Kit – Lumbar.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

Bowsher, Kristen
From: Lori Glastetter [lglastetter@vertisneuro.com]
Sent: Thursday, December 20, 2001 3:53 PM
To: Kristen A. Bowsher Ph. D. (E-mail)
Subject: patient population

Per your request, this confirms that Vertis treated post-surgical and post-trauma pain patients with PNT therapy in the Vertis clinical trial. This information is contained in Appendix 24 of the 510(k).

Furthermore, we observed no difference in safety or effectiveness of the therapy in these patients versus any other patient group.

Accordingly, we would like the "post-surgical and post-trauma pain" clause to remain in our indications for use.

Lori

LORI GLASTETTER
VP, Regulatory Affairs & Quality Assurance
lglastetter@vertisneuro.com
Direct line: 206.902.1902
Fax: 206.902.0140

Vertis Neuroscience
2101 Fourth Avenue, Suite 200
Seattle, WA 98121-2329
www.vertisneuro.com

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015



2101 Fourth Avenue, Suite 200
Seattle, Washington 98121-2329
Tel: 206.728.1477
Fax: 206.902-0140

To: Kristen Bowsher, Ph.D. FDA,
DGRND, ODE

From: Lori Glastetter, Vertis

Date: 12-20-01

Re: For 510(k) K011702 – per 12-20-01 telephone conversation

Comments:

Kristen,

Per our telephone conversation today (12-20-01) and as we discussed, Vertis agrees to the following with respect the Vertis PNT System labeling:

- The device Indications (that is in the PNT Control Unit User's Guide) is revised to:

  Percutaneous Neuromodulation Therapy (PNT) is indicated for the symptomatic relief and management of chronic, intractable low back pain and/or as an adjunctive treatment in the management of post-surgical acute low back pain and post-trauma acute low back pain.

  The PNT Control Unit is to be used with a PNT Safeguide Kit – Lumbar.

I made these changes to the Indications for Use form and 510(k) summary. Revised copies of these documents are included with this memo.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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- The following Warning is added to the PNT Control Unit User's Guide (page 31):

  Warning: Children *— Keep out of the reach of children.*

- The following Warning (that is currently on page 6 of the Safeguide Instructions for Use) is repeated at the front of the Safeguide Instructions under the heading *Using Vertis PNT Safeguide Electrodes*:

  Warning: Safeguide Use*—Each Safeguide is designed to deploy a small gauge needle electrode into the tissue to a depth of 3 cm. To avoid patient injuries or complications, use appropriate clinical judgment in patient selection (e.g., body morphology) and tissue/site selection for electrode placement. For example, in extremely thin patients, consider repositioning the electrode to a location of sufficient tissue mass or possibly exclude the patient from treatment.*

- The following instructions are added to the Safeguide Instructions for Use under the heading *Disconnecting the Patient from the Lumbar Patient Cable:*

  In the event the electrode breaks during removal, use appropriate clinical judgment and all efforts to retrieve the electrode. If the electrode is unable to be retrieved, the patient should be monitored appropriately.

With this information, Vertis believes we have provided all information that you have requested, and all information that is necessary in order to make a substantial equivalence determination. We respectfully request that you finalize the 510(k) process as quickly as possible.

Thank you.

Lori Glastetter

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Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8148

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2101 Fourth Avenue, Suite 200
Seattle, Washington 98121-2329
Tel: 206.728.1477
Fax: 206.902-0140

To:	Kristen Bowsher, Ph.D. FDA, DGRND, ODE	**Recipient's Fax:**	301-594-2358
From:	Lori Glastetter, Vertis	**Sender's Phone:**	206-902-1902
Date:	12-18-01	**Pages:**	3 pages – including cover
Re:	For 510(k) K011702 - FDA requests from 12-17-01 telephone conversations		

Comments:

Kristen,

Per our telephone conversation yesterday (12-17-01) afternoon, the following information is provided as you requested.

With this information, Vertis strongly believes we have provided all information that you have requested, and all information that is necessary in order to make a substantial equivalence determination. As a small company, time is extremely critical to us and thus, we respectfully request that you finalize the 510(k) process as quickly as possible. Thank you.

Lori Glastetter

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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(b) (4)

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Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

(b) (4)

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

MEMORANDUM

DATE December 7, 2001

FROM Director, Regulatory Review Officer, DGRND

SUBJECT K011702/S1 – Vertis Percutaneous Neuromodulation Therapy (PNT)

TO Kristen Bowsher, Ph. D., Lead Reviewer, Electrical & Biomedical Engineer

Comments

The White study may not be adequate for demonstrating that percutaneous stimulation of equivalent to transcutaneous electrical nerve stimulation (TENS).

It appears that the stimuli applied and the areas treated were different. While the publication states that both TENS and percutaneous electrical nerve stimulation (PENS) were applied at 4 Hz, the pulse width was 0.5 milliseconds for the PENS and 0.1 milliseconds for the TENS. The publication does not report more specific output stimulus characteristics so it's not clear that the electrical stimuli are equivalent. From what is reported, they appear to be different. Additionally, while the article clearly states, "The intensity of the electrical stimulation [for the active PENS] was adjusted to produce the maximum tolerable 'tapping' sensation without muscle contractions," it does not state that this was done for the TENS. If the stimuli were different, then this is not a fair comparison. It's hard to understand why they would not utilize the same electrical stimulus to avoid confounding the results. To keep this option alive as potential substantiation that PENS is equivalent to TENS, this would have to be resolved...but I don't know how they could do this. Even if TENS were adjusted to produce the maximum tolerable tapping sensation without muscle contractions, the different pulse width could have had an effect on the perceived sensation and may have been responsible for the difference in pain relief.

Additionally, the electrode placements were not standardized for the PENS and TENS. The PENS used more electrodes and covered a larger area as compared to the TENS. Again this covariate confounds the issue. The sites and overall area treated can affect results.

Note also that this study also confounded results concerning the exercise group because the exercises that the patients were to perform were not standard of care and in fact would likely aggravate LBP since they were performed in the sitting position. The literature demonstrates that the sitting position creates the greatest intradiscal pressures and usually sitting is avoided or minimized to avoid aggravating LBP. It's not surprising that the exercise group did not get better.

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Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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The article also reports mean changes in pain pre- to post-treatment during the same session (page 821 of the article), but the variability is larger than the changes for the sham and the exercise groups. Individual data might reveal whether some were actually made worse by these treatments.

I am concerned that the type of stimulus applied by the TENS and the manner of adjusting the intensity, did not allow for fair comparison the PENS stimulus and manner of application. If the company does come up with a reasonable way of analyzing the effect of the above mentioned covariates, which I don't think is possible, then we would have to get the investigational plan (including the protocol, statistical plan, copies of case report forms) and the individual data. We could then evaluate the study design and data to see if it is adequate for substantiating that the PENS was equivalent or better than the TENS. Additionally, we would need some substantiation that the depth of penetration (3 cm vs a range to 2-4cm) does not make a difference in ability to achieve pain relief.

Marie A. Schroeder, MS, PT

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

MEMORANDUM

DATE November 16, 2001

FROM Director, Regulatory Review Officer, DGRND

SUBJECT K011702/S1 – Vertis Percutaneous Neuromodulation Therapy (PNT)

TO Kristen Bowsher, Ph. D., Lead Reviewer, Electrical & Biomedical Engineer

Recommendation

The additional information supplied in this supplement does not adequately address my concerns originally outlined in my memo dated August 2, 2001. My recommendation remains the same, i.e., due to the significant study design flaws mentioned in my August 2, 2001 memo, conclusions regarding the safety and effectiveness of this device can not be made. Additionally, the publications do not assure that this new device is substantially equivalent to a legally marketed device or to standard-of-care. They do not assure that the new device is better than placebo. Since this is an invasive device which can be used only in the clinic, the benefits should be greater than achieved with TENS which is not invasive and which can be worn during daily activities and provide continuing pain relief.

I have some concern that this device might actually caused more harm than benefit, since it may be that only 12.8% (5/39) of the patients had clinically meaningful benefit in light of the very few patients who experienced more than a *little* benefit. I would have expected more patients to have clinically meaningful benefit from placebo alone. Note that the sponsor reports that **5** patients reported that they got ***a lot better*** from **massage** which is a non-invasive therapy (it's not clear what the denominator was for this massage group). Only **3** patients reported getting ***very much benefit*** and **2** patients reported ***much benefit*** from the Vertis PNT device.

Scope of Review of Supplement 1

I reviewed the section labeled ***Main Text*** (supplement 1) which is the response to our concerns. I also re-reviewed references 4 and 5 that had been previously provided and reviewed with the original submission.

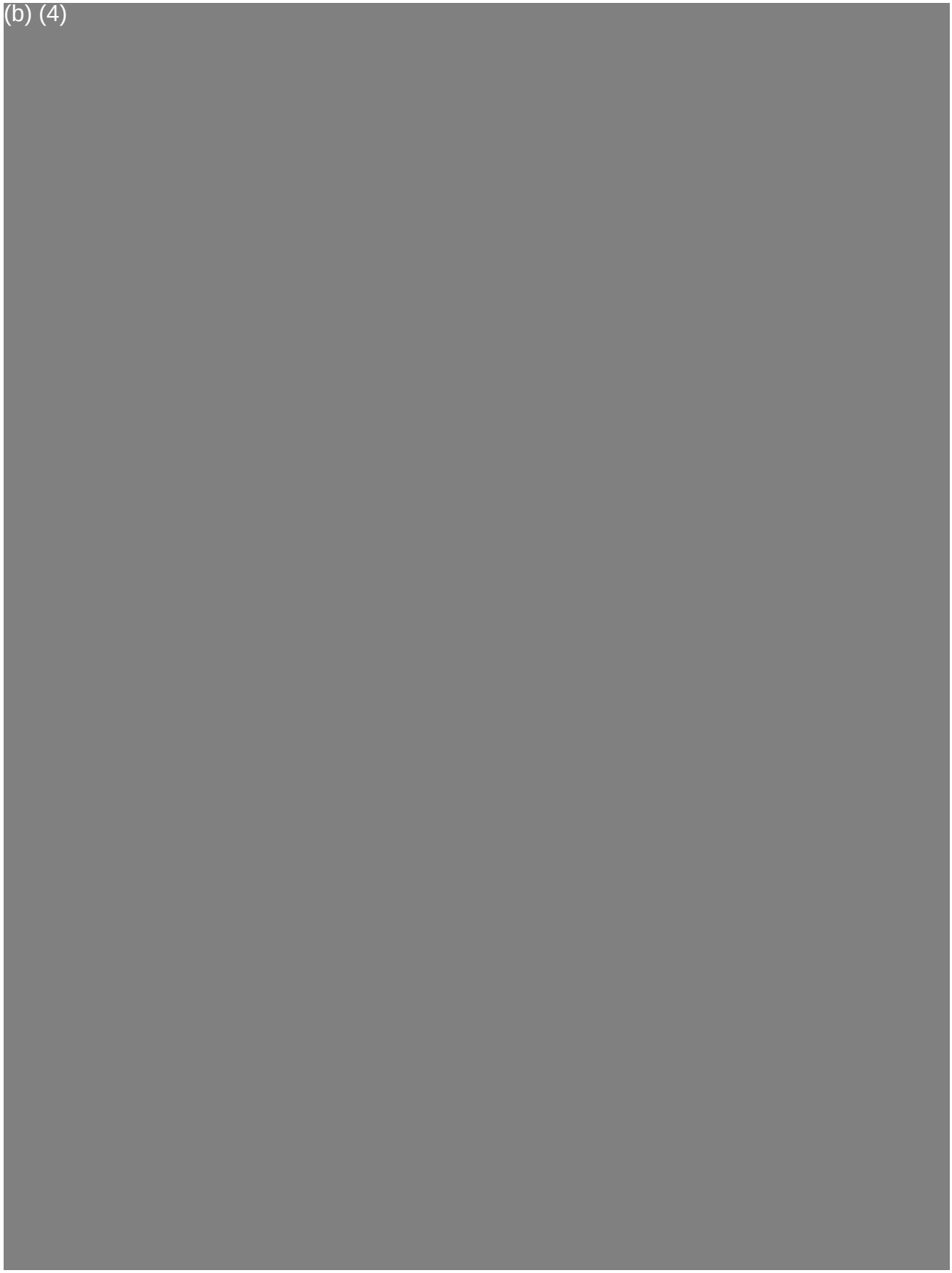
Comments

(b) (4)

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

(b) (4)



Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

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Marie A. Schroeder, MS, PT

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

MEMORANDUM

DATE August 2, 2001

FROM Director, Regulatory Review Officer, DGRND

SUBJECT K011702 – Vertis Percutaneous Neuromodulation Therapy (PNT)

TO Kristen Bowsher, Ph. D., Lead Reviewer, Electrical & Biomedical Engineer

Recommendation

Due to the significant study design flaws mentioned below, conclusions regarding the safety and effectiveness of this device can not be made. I have some concern that this device might actually caused more harm than benefit, since it may be that only 12.8% (5/39) of the patients had clinically meaningful benefit. I would have expected more patients to have clinically meaningful benefit from placebo alone. Note that the sponsor reports that **5** patients reported that they got ***a lot better*** from **massage** which is a non-invasive therapy (it's not clear what the denominator was for this massage group). Only **3** patients reported getting ***very much benefit*** and **2** patients reported ***much benefit*** from the Vertis PNT device. The background information was very well presented and appeared to support the feasibility of effectiveness for this device. However, because of the uncertainties mentioned below, it's hard to say for sure what happened in this trial.

Due to the apparent new design of the needle electrodes with a safety feature to minimize clinician sticks, this electrode design should be reviewed by General Hospital Devices Branch.

Scope of Review

I reviewed Appendix 23, Appendix 24 and Attachment B of Appendix 24.

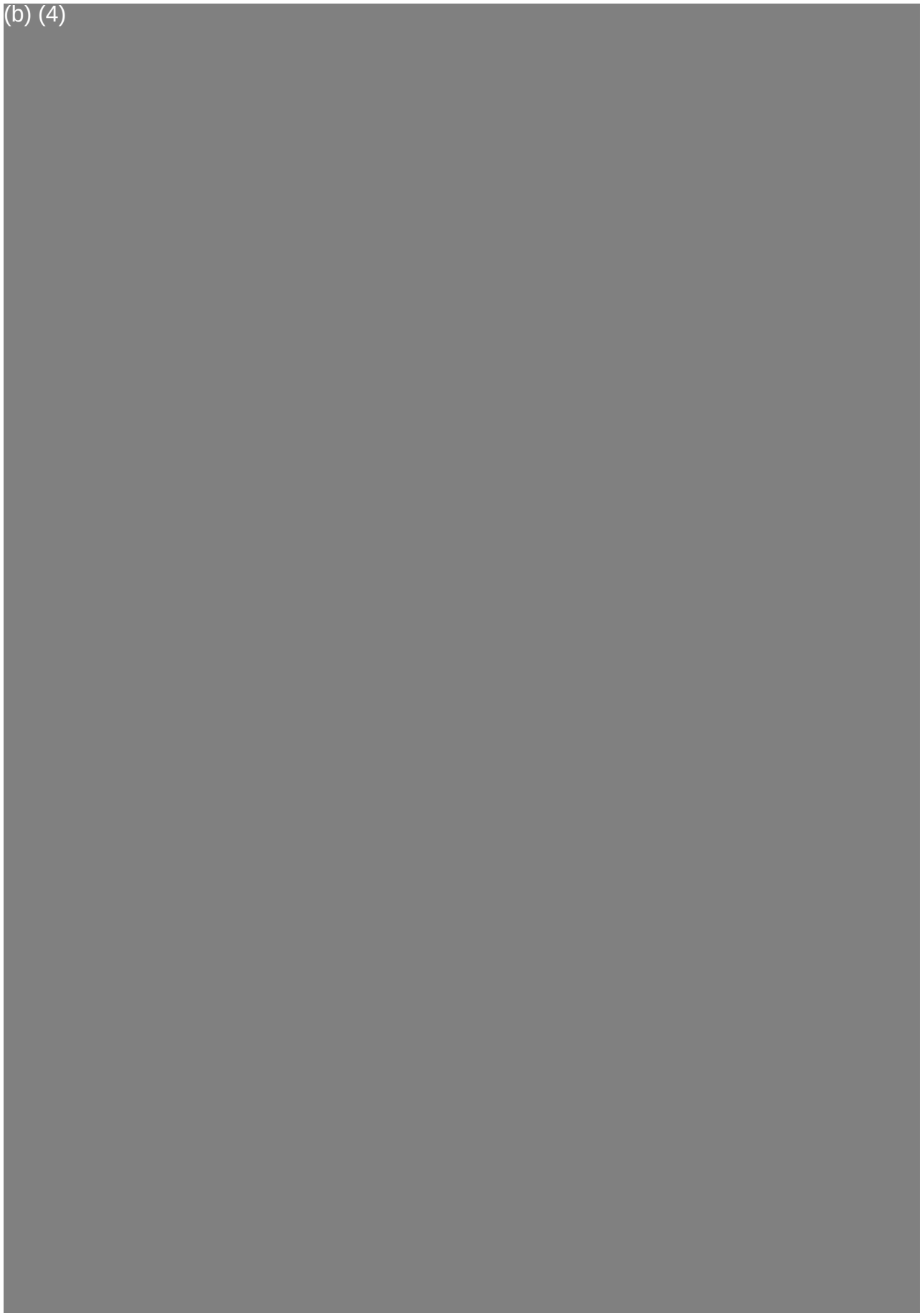
Comments

(b) (4)

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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[redacted]

Future Considerations

Prior to conducting a future study, the sponsor should consider submitting a pre-IDE to FDA for comments. Future studies should eliminate the bias mentioned above. Validated and reliable assessment tools should be provided along with the validation data (e.g., peer reviewed literature may be provided). In order to support a general claim of reducing low back pain (LBP), sufficient numbers of patients should be studied in a sufficient number of subsets (with respect to etiology of LBP). Justification as to why the subsets included adequately support a general claim should be provided.

Premarketing applications should include case report forms and individual patient listings of data (actual scores and changes from baseline). The results should include the numbers and percentages of patients who passed unbiased success criteria as well as those who failed, e.g. worsening, no change and improvements should be reported. ITT analyses should be done as per our statistician's recommendation. Justification that the success criteria are clinically meaningful must also be provided.

The statistician was silent regarding the pooling, whether the p-value was appropriate in light of the 3 chances to succeed, and whether there were adequate numbers of patients in the subsets. In light of the most significant deficiencies, it is pointless to address these for this document. However, these issues should be addressed in a future application.

The Vertis PNT device has several modes/output signals. Data should support all output options. Likewise, if multiple body sites are to be treated, data should support multiple sites.

Marie A. Schroeder, MS, PT

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

Schroeder, Marie
From: Bourke, Tracey C.
Sent: Friday, December 07, 2001 10:09 AM
To: Schroeder, Marie
Subject: FW: TUCO

-----Original Message-----
From: Costello, Ann
Sent: Friday, December 07, 2001 9:27 AM
To: Bourke, Tracey C.
Subject: RE: TUCO

We did not ask them to do separate analyses of sprain and spasm since we are going to just give them minor pain which can result from any of those etiologies even osteoarthritis. We can't control what it will be used for or how it will be used therefore I will recommend single use for temporary minor pain but I know that is not how it will be used.

Ann

-----Original Message-----
From: Bourke, Tracey C.
Sent: Wednesday, December 05, 2001 3:34 PM
To: Costello, Ann
Subject: TUCO

Hi Ann,

I've got a question for you - since the incl/excl criteria for the diagnoses of muscle sprain and cervical sprain strain made it possible to include more than 1 etiology for the pain (e.g., spasm could be due to sprain, strain, cervical disc compression or arthritis encroachment on a nerve root, etc., how are we assuring that the statistical differences between groups are due to the device and not the underlying etiology differences (which may have different prognoses)?
Did you find any more specific information in the document that addresses this concern?

I ask because we're trying to figure out what to tell the current laser PMA company (Acculaser) in terms of their current and any future study, and the TUCO study is being sort of looked at for some help. The PMA results are awful; they would not support a 510k.

I'll probably be touching base for the TUCO response to the deficiency letter (came in 11/20/01).

Thanx,
Tracey

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

DEPARTMENT OF HEALTH AND HUMAN SERVICES Public Health Service

Food and Drug Administration
Center for Devices and
Radiological Health
Office of Device Evaluation
Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, Maryland 20850

September 26, 2001

VERTIS NEUROSCIENCE, INC.
2101 FOURTH AVE STE 200
SEATTLE, WA 98121
ATTN: LORI GLASTETTER

510(k) Number: K011702
Product: VERTIS PNT
CONTROL UNIT,
VERTIS PNT
SAFEGUIDE KIDS,

The additional information you have submitted has been received.

We will notify you when the processing of this submission has been completed or if any additional information is required. Please remember that all correspondence concerning your submission MUST be sent to the Document Mail Center (HFZ-401) at the above letterhead address. Correspondence sent to any address other than the one above will not be considered as part of your official premarket notification submission. Because of equipment and personnel limitations we cannot accept telefaxed material as part of your official premarket notification submission, unless specifically requested of you by an FDA official.

The Safe Medical Devices Act of 1990, signed on November 28, states that you may not place this device into commercial distribution until you receive a letter from FDA allowing you to do so. As in the past, we intend to complete our review as quickly as possible. Generally we do so 90 days. However, the complexity of a submission or a requirement for additional information may occasionally cause the review to extend beyond 90 days. Thus, if you have not received a written decision or been contacted within 90 days of our receipt date you may want to check with FDA to determine the status of your submission.

If you have procedural or policy questions, please contact the Division of Small Manufacturers International and Consumer Assistance (DSMICA) at (301) 443-6597 or at their toll-free number (800) 638-2041, or contact me at (301) 594-1190.

Sincerely yours,

Marjorie Shulman
Supervisory Consumer Safety Officer
Premarket Notification Section
Office of Device Evaluation
Center for Devices and
Radiological Health

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Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-5[illegible] Released by CDRH on 09-10-2015

K011702/S1

Vertis
neuroscience

2101 Fourth Avenue, S Seattle, WA 98121-2329
Tel 206.728. x 206.728.1497
www .com

September 24, 2001

Office of Device Evaluation
510(k) Document Mail Center (HFZ-4[illegible]
Center for Devices and Radiological H[illegible]
Food and Drug Administration
9200 Corporate Blvd.
Rockville, MD 20850

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FDA/CDRH/OCE/DID

Reference: **510(k) Notification K011702 - Supplement #1**
Vertis Neuroscience, Inc. Nerve Stimulator, Electrodes and Accessories

Attention: **Kristen A. Bowsher, Ph.D.**

Dear Document Mail Center and Device Evaluation Staff:

In accordance to a recent discussion with FDA Division of General, Restorative and Neurological Devices (DGRND) staff member Dr. Kristen Bowsher, this data is being supplied as additional information in support of 510(k) Notification K011702. As Dr. Bowsher is the reviewer for this 510(k) Notification, we request that this Supplement be forwarded to Dr. Bowsher's attention.

Specifically, this Supplement provides information discussed with, and requested by, Dr. Bowsher in a telephone conversation with Vertis staff on 9-7-01. This Supplement is being provided by Vertis within 30 days of receipt of a FDA deficiency letter (dated 8-29-01). As such, in accordance to 21 CFR 807.87(l), we respectfully request the continued review of our 510(k) Notification (K011702), in conjunction with the new additional information contained in this Supplement.

For the convenience of the FDA Document Mail Center and Device Evaluation staffs, Vertis has enclosed (at the front of this binder) the CDRH Premarket Submission Cover Sheet to aid FDA in the rapid processing of this Supplement.

This information is provided in accordance to 21 CFR 807. Based on the information provided in the 510(k) Notification and this supporting Supplement, we believe the Vertis *PNT™ Control Unit* and Accessories to be substantially equivalent to devices in commercial distribution prior to May 28, 1976.

SK 35 32

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

Statement of Confidentiality

The information provided in this Supplement is considered by Vertis Neuroscience, Inc. to be confidential information as it relates to our intention to market this product in the future. We have not, to our knowledge, released this information through advertising or any other manner to anyone outside the employ of, or under contract to, Vertis Neuroscience, Inc. Vertis has taken precautions to protect the confidentiality of this information under Section 21CFR 807.95, Confidentiality of Information. We ask that this Supplement be treated as confidential in accordance with the Freedom of Information Act.

Should you require any additional information or have any questions regarding this Supplement, please do not hesitate to contact me at (206) 902-1902. Your attention to this Supplement is sincerely appreciated.

Sincerely,

Lori J. Glastetter
Vice President, Regulatory Affairs/Quality Assurance
Vertis Neuroscience, Inc.

Vertis PNT is a trademark of Vertis Neuroscience, Inc.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

Note: Submission of this information does not affect the need to submit a 2891 or 2891a Device Establishment Registration form.	FDA Document Number: **K011702**

Section H Manufacturing/Packaging/Sterilization Sites Relating to a Submission

☒ Original ☐ Add ☐ Delete	FDA establishment registration number: (b) (4)	☐ Manufacturer ☐ Contract manufacturer	☒ Contract sterilizer ☐ Repackager / relabeler
Company/Institution name: (b) (4)		Establishment registration number: (b) (4)	
Division name (if applicable):		Phone number (include area code): (b) (4)	
Street address: (b) (4)		FAX number (include area code): (b) (4)	
City: (b)	State/Province: (b)	Country: **USA**	
Contact name: (b) (4)			
Contact title: **Manager RA/QS**		Contact e-mail address: (b) (4)	

☒ Original ☐ Add ☐ Delete	FDA establishment registration number: (b) (4)	☐ Manufacturer ☒ Contract manufacturer	☐ Contract sterilizer ☐ Repackager / relabeler
Company/Institution name: (b) (4)		Establishment registration number: (b) (4)	
Division name (if applicable):		Phone number (include area code): (b) (4)	
Street address: (b) (4)		FAX number (include area code): (b) (4)	
City: (b) (4)	State/Province: (b) (4)	Country: **USA**	
Contact name: (b) (4)			
Contact title: **QA Manager**		Contact e-mail address: (b) (4)	

☐ Original ☐ Add ☐ Delete	FDA establishment registration number:	☐ Manufacturer ☐ Contract manufacturer	☐ Contract sterilizer ☐ Repackager / relabeler
Company/Institution name: **N/A**		Establishment registration number:	
Division name (if applicable):		Phone number (include area code): ( )	
Street address:		FAX number (include area code): ( )	
City:	State/Province:	Country:	
Contact name:			
Contact title:		Contact e-mail address:	

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

CDRH SUBMISSION COVER SHEET

Date of Submission: **September 24, 2001** FDA Document Number: **K011702**

Section A Type of Submission

PMA	PMA Supplement	PDP	510(k)	Meeting
☐ Original submission	☐ Regular	☐ Presubmission summary	☐ Original submission:	☐ Pre-IDE meeting
☐ Modular submission	☐ Special	☐ Original PDP	☐ Traditional	☐ Pre-PMA meeting
☐ Amendment	☐ Panel Track	☐ Notice of intent to start clinical trials	☐ Special	☐ Pre-PDP meeting
☐ Report	☐ 30-day Supplement	☐ Intention to submit Notice of Completion	☐ Abbreviated	☐ 180-day meeting
☐ Report Amendment	☐ 30-day Notice	☐ Notice of Completion	☒ Additional information:	☐ Other (specify):
	☐ 135-day Supplement	☐ Amendment to PDP	☒ Traditional	
	☐ Real-time Review	☐ Report	☐ Special	
	☐ Amendment to PMA Supplement		☐ Abbreviated	

IDE	Humanitarian Device Exemption	Class II Exemption	Evaluation of Automatic Class III Designation	Other Submission
☐ Original submission	☐ Original submission	☐ Original submission	☐ Original submission	Describe submission:
☐ Amendment	☐ Amendment	☐ Additional information	☐ Additional information	
☐ Supplement	☐ Supplement			
	☐ Report			

Section B Applicant or Sponsor

Company/Institution name: **Vertis Neuroscience, Inc.**	Establishment registration number: **Not Yet Assigned**
Division name (if applicable): **N/A**	Phone number (include area code): **(206) 902-1902**
Street address: **2101 Fourth Avenue, Suite 200**	FAX number (include area code): **(206) 728-1497**
City: **Seattle** State/Province: **WA**	Country: **USA**
Contact name: **Lori Glastetter**	
Contact title: **Vice President, RA/QA**	Contact e-mail address: **lglastetter@vertisneuro.com**

Section C Submission correspondent (if different from above)

Company/Institution name: **Same as above**	Establishment registration number:
Division name (if applicable):	Phone number (include area code): ( )
Street address:	FAX number (include area code): ( )
City: State/Province:	Country:
Contact name:	
Contact title:	Contact e-mail address:

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

Section D1 Reason for Submission—PMA, PDP, or HDE

- ☐ New device
- ☐ Withdrawal
- ☐ Additional or expanded indications
- ☐ Licensing agreement
- ☐ Process change
  - ☐ Manufacturing
  - ☐ Sterilization
  - ☐ Packaging
  - ☐ Other (specify below)
- ☐ Response to FDA correspondence:
  - ☐ Request for applicant hold
  - ☐ Request for removal of applicant hold
  - ☐ Request for extension
  - ☐ Request to remove or add manufacturing site
- ☐ Other reason (specify):
- ☐ Change in design, component, or specification:
  - ☐ Software
- ☐ Color Additive
  - ☐ Material
  - ☐ Specifications
- ☐ Other (specify below)
- ☐ Labeling change:
  - ☐ Indications
  - ☐ Instructions
  - ☐ Performance Characteristics
- ☐ Shelf life
- ☐ Trade name
- ☐ Other (specify below)
- ☐ Location change:
  - ☐ Manufacturer
  - ☐ Sterilizer
  - ☐ Packager
    - ☐ Distributor
- ☐ Report submission:
  - ☐ Annual or periodic
  - ☐ Post-approval study
  - ☐ Adverse reaction
  - ☐ Device defect
  - ☐ Amendment
- ☐ Change in ownership
  - ☐ Change in correspondent

Section D2 Reason for Submission—IDE

- ☐ New device
- ☐ Addition of institution
- ☐ Expansion / extension of study
- ☐ IRB certification
- ☐ Request hearing
- ☐ Request waiver
- ☐ Termination of study
- ☐ Withdrawal of application
- ☐ Unanticipated adverse effect
- ☐ Notification of emergency use
- ☐ Compassionate use request
- ☐ Treatment IDE
- ☐ Continuing availability request
- ☐ Other reason (specify):
- ☐ Change in:
  - ☐ Correspondent
  - ☐ Design
  - ☐ Informed consent
  - ☐ Manufacturer
  - ☐ Manufacturing process
  - ☐ Protocol – feasibility
  - ☐ Protocol – other
  - ☐ Sponsor
- ☐ Report submission:
  - ☐ Current investigator
  - ☐ Annual progress
  - ☐ Site waiver limit reached
  - ☐ Final
- ☐ Response to FDA letter concerning:
  - ☐ Conditional approval
  - ☐ Deemed approved
  - ☐ Deficient final report
  - ☐ Deficient progress report
  - ☐ Deficient investigator report
  - ☐ Disapproval
  - ☐ Request extension of time to respond to FDA
  - ☐ Request meeting

Section D3 Reason for Submission—510(k)

- ☒ New device
- ☐ Additional or expanded indications
- ☐ Other reason (specify):
- ☐ Change in technology
- ☐ Change in design
- ☐ Change in materials
- ☐ Change in manufacturing process

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

Section E Additional Information on 510(k) Submissions

Product codes of devices to which substantial equivalence is claimed:

1 **GZJ**	2 **GZF**	3 **GZB**	4 **LIH**
5 **GXZ**	6 **IKT**	7 **GXY**	8

Summary of, or statement concerning, safety and effectiveness data:
- ☒ 510(k) summary attached
- ☐ 510(k) statement

Information on devices to which substantial equivalence is claimed:

	510(k) Number	Trade or proprietary or model name	Manufacturer
1	**K970203 K951903**	**EPIX TENS Device System**	**Empi, Inc.**
2	**K982410**	**SMP-Plus™**	**Rehabilicare**
3	**K924666**	**Intelect® Legend Stim**	**Chattanooga Group, Inc.**
4	**K973442**	**TECA Disposable Monopolar Needles**	**TECA Corporation**
5	**K950314**	**DMN™ Disposable Monopolar Needle Electrodes**	**Medtronic, Inc.**
6	**K982902 K915540**	**Mattrix Neurostimulation System Resume II Lead**	**Medtronic, Inc.**

Section F Product Information—Applicable to All Applications

Common or usual name or classification name: **Nerve Stimulator, Peripheral Nerve Stimulator, or Electrical Nerve Stimulator and Accessories**

	Trade or proprietary or model name	Model number
1	**Vertis PNT Control Unit**	**CU100**
2	**Vertis PNT Safeguide Kits**	**SGXXX**
3		
4		
5		

FDA document numbers of all prior related submissions (regardless of outcome):

1 **K970203**	2 **K951903**	3 **K982410**	4 **K924666**	5 **K973442**	6 **K950314**
7 **K982902**	8 **K915540**	9	10	11	12

Data included in submission: ☒ Laboratory testing ☒ Animal trials ☒ Human trials

Section G Product Classification—Applicable to All Applications

Product Code **GZJ** **GZF**

C.F.R. Section: **21 CFR 882.5890** **21 CFR 882.5870**

Device Class:
- ☐ Class I
- ☒ Class II
- ☐ Class III
- ☐ Unclassified

Classification panel: **General Restorative and Neurological**

Indications (from labeling): **Percutaneous Neuromodulation Therapy (PNT) is indicated for the symptomatic relief and management of chronic, intractable pain and/or as an adjunctive treatment in the management of post-surgical and post-trauma acute pain.**

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-5070; Released by CDRH on 09-10-2015

Note: Submission of this information does not affect the need to submit a 2891 or 2891a Device Establishment Registration form.	FDA Document Number: **K011702**

Section H Manufacturing/Packaging/Sterilization Sites Relating to a Submission

☒ Original ☐ Add ☐ Delete	FDA establishment registration number: (b) (4)	☐ Manufacturer ☒ Contract manufacturer	☐ Contract sterilizer ☐ Repackager / relabeler
Company/Institution name: (b) (4)		Establishment registration number: (b) (4)	
Division name (if applicable):		Phone number (include area code): (b) (4)	
Street address: (b) (4)		FAX number (include area code): (b) (4)	
City: (b) (4)	State/Province: (b) (4)	Country: **USA**	
Contact name: (b) (4)			
Contact title: **Quality/Regulatory Manager**		Contact e-mail address: (b) (4)	

☒ Original ☐ Add ☐ Delete	FDA establishment registration number: (b) (4)	☐ Manufacturer ☒ Contract manufacturer	☐ Contract sterilizer ☐ Repackager / relabeler
Company/Institution name: (b) (4)		Establishment registration number: (b) (4)	
Division name (if applicable):		Phone number (include area code): (b) (4)	
Street address: (b) (4)		FAX number (include area code): (b) (4)	
City: (b) (4)	State/Province: (b) (4)	Country: **USA**	
Contact name: (b) (4)			
Contact title: **President**		Contact e-mail address: (b) (4)	

☒ Original ☐ Add ☐ Delete	FDA establishment registration number: (b) (4)	☐ Manufacturer ☐ Contract manufacturer	☒ Contract sterilizer ☐ Repackager / relabeler
Company/Institution name: (b) (4)		Establishment registration number: (b) (4)	
Division name (if applicable):		Phone number (include area code): (b) (4)	
Street address: (b) (4)		FAX number (include area code): (b) (4)	
City: (b) (4)	State/Province: (b) (4)	Country: **USA**	
Contact name: (b) (4)			
Contact title: **Manager of Regulatory Affairs and Quality Systems**		Contact e-mail address: (b) (4)	

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Note: Submission of this information does not affect the need to submit a 2891 or 2891a Device Establishment Registration form.	FDA Document Number: **K011702**

Section H Manufacturing/Packaging/Sterilization Sites Relating to a Submission

☒ Original ☐ Add ☐ Delete	FDA establishment registration number: (b) (4)	☐ Manufacturer ☐ Contract manufacturer	☒ Contract sterilizer ☐ Repackager / relabeler
Company/Institution name: (b) (4)		Establishment registration number: (b) (4)	
Division name (if applicable):		Phone number (include area code): (b) (4)	
Street address: (b) (4)		FAX number (include area code): (b) (4)	
City: (b) (4)	State/Province: (b) (4)	Country: **USA**	
Contact name: (b) (4)			
Contact title: **Manager RA/QS**		Contact e-mail address: (b) (4)	

☒ Original ☐ Add ☐ Delete	FDA establishment registration number: (b) (4)	☐ Manufacturer ☒ Contract manufacturer	☐ Contract sterilizer ☐ Repackager / relabeler
Company/Institution name: (b) (4)		Establishment registration number: (b) (4)	
Division name (if applicable):		Phone number (include area code): (b) (4)	
Street address: (b) (4)		FAX number (include area code): (b) (4)	
City: (b) (4)	State/Province: (b)	Country: **USA**	
Contact name: (b) (4)			
Contact title: **QA Manager**		Contact e-mail address: (b) (4)	

☐ Original ☐ Add ☐ Delete	FDA establishment registration number:	☐ Manufacturer ☐ Contract manufacturer	☐ Contract sterilizer ☐ Repackager / relabeler
Company/Institution name: **N/A**		Establishment registration number:	
Division name (if applicable):		Phone number (include area code): ( )	
Street address:		FAX number (include area code): ( )	
City:	State/Province:	Country:	
Contact name:			
Contact title:		Contact e-mail address:	

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510(k) Notification # K011702 - Supplement #1

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Appendix 2: Assessment Tools and Success Criteria

Appendix 3: Revision to 510(k) Appendix 16

Appendix 4: Bibliography - Copies of Selected Literature

Scientific/technical literature referenced in the following discussions are listed in the bibliography in this Appendix 4. For convenience, copies of selected references are also included in this Appendix 4.

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Introduction

Regarding 510(k) K011702, Vertis received FDA's deficiency letter (dated 8-29-01). The concerns FDA raised in the letter were exclusively about the Vertis clinical study and clinical data provided in the 510(k). Specifically, FDA indicated, "conclusions cannot be drawn with respect to the safety and effectiveness of your device as compared to legally marketed predicate devices".

A subsequent telephone discussion occurred on 9-7-01 between FDA scientific reviewer Kristen Bowsher, Ph.D. and Vertis staff (Lori Glastetter, VP, RA/QA and Brad Gliner, Director, Research). Vertis found this phone discussion extremely helpful and appreciated Dr. Bowsher taking the time to discuss the 510(k) and FDA letter with us.

In our phone discussion with Dr. Bowsher, and in response to the concerns raised in the deficiency letter, Vertis had discussed the purpose of the Vertis clinical study. Vertis believes that the study's role was another piece, among many pieces in the 510(k) Notification, that supports a substantial equivalence decision. In this Supplement, Vertis has documented how we had intended the Vertis study to support the 510(k) and has attempted to clarify any misunderstanding that may have occurred as to the study's intent in relation to substantial equivalence. We have also discussed the importance of other published clinical studies in relation to substantial equivalence. We regret not making these points clearer in the original 510(k) Notification.

Summary: In summary, this Supplement documents issues discussed with Dr. Bowsher by phone and specifically provides the information she requested or that Vertis offered to provide to her.

Vertis strongly believes the 510(k) Notification and the additional information contained in this Supplement support a substantial equivalence decision. In comparison to substantially equivalent devices, Vertis has provided a substantial amount of bench, animal and clinical data in the 510(k) and this Supplement. Since Vertis believes our data more than adequately responds to FDA's questions and concerns, we do <u>not</u> believe a new clinical study as suggested in the August FDA deficiency letter is necessary, nor appropriate, to achieve a finding of substantial equivalence.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Appendix 1

Information from 510(k) – Published Clinical Studies

Appendix 23 in the 510(k) Notification contained considerable information regarding prior published clinical studies.

For FDA's convenience, a duplicate copy of that original Appendix 23 information (11 pages total) is enclosed in this Appendix.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Appendix 23
Recent Clinical Studies – Percutaneous Electrical Stimulation

Note: Scientific/technical literature referenced in the following discussions are listed in the bibliography in Appendix 28. For convenience, copies of selected references are also included in this Appendix 28.

The following summarizes some recent clinical studies assessing percutaneous electrical stimulation for pain management. The relevance of the studies to the Vertis percutaneous neuromodulation therapy (PNT) is also noted. Contents of this section are as follows:

Topic	pages in this Appendix
Percutaneous Electrical Stimulation - Low Back Pain Studies and Relevance to Vertis PNT	2 –9
• Vertis Modulation (Therapy) Modes	
• Vertis Therapy Duration	
• Vertis Electrode Placement Montage	
• Vertis Electrode Depth	
Percutaneous Electrical Stimulation – Other Recent Studies	10 –11

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Percutaneous Electrical Stimulation - Low Back Pain

Over the years, numerous pharmacological and non-pharmacologic therapies have been used to treat low back pain

Concerns regarding the safety or efficacy of these various modalities have increased interest in percutaneous electrical therapy (1-5). Percutaneous electrical therapy is an analgesic therapy that involves delivery of electrical current directly into the soft tissue to stimulate peripheral nerves at levels corresponding to the local pathology.

In recent years (1997-1999), low back pain (LBP) has been the focus of several randomized, blinded clinical trials performed by researchers at the Eugene McDermott Center for Pain Management at the University of Texas Southwestern Medical Center (UTSW), Dallas Texas. These studies employed percutaneous electrical stimulation. The results of these studies were published in well-respected, peer-reviewed journals.

> Note: Vertis did not sponsor, nor participate, in the UTSW studies. We have some reason to believe that there may have been several variations from protocol, but they should not have affected the study outcomes. These studies were of interest to Vertis and were an important part of the historical and technical basis for the Vertis PNT therapy.

A review of these studies is provided as follows for reference. Relevance of the studies to Vertis PNT therapy is also noted.

- **Study #1:** In a double-blinded, randomized clinical study published in the Journal of American Medical Association (4), percutaneous electrical therapy was shown to be more effective ($P<0.02$) than TENS, exercise therapy, and a sham in providing short-term pain relief and improved physical function in 60 patients with low back pain (Figure 1). In this nine-treatment, 3 week protocol, the percutaneous electrical therapy was not only highly effective in producing acute analgesia, but patients reported more sustained beneficial effects on their level of pain, physical activity, and quality of sleep. Moreover, the use of percutaneous electrical therapy significantly decreased the need for oral, non-opioid analgesic medications in this patient population.

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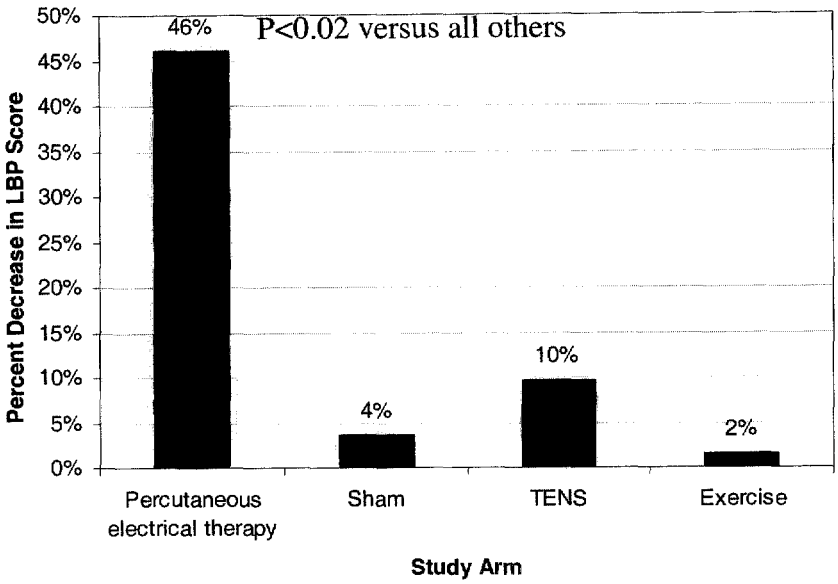


Figure 1. Percent decrease in low back pain (LBP) score from baseline (pre-treatment) level measured 24-hours after the ninth treatment, based on (4).

- **Study #2:** The efficacy of various stimulation frequencies of percutaneous electrical therapy was examined by the same researchers in a separate blinded randomized clinical study involving 68 low back pain patients (5). In this study, percutaneous electrical therapy was delivered in six 30-minutes sessions over a two-week period. Compared with sham stimulation, pulse frequencies of 4 Hz, 15 Hz and 30 Hz alternating in three-second intervals, and 100 Hz produced significantly ($P<0.01$) greater decreases in the degree of pain, improved physical activity and sleep quality, and reduced daily intake of oral analgesic medications.

- **Study #3:** A third randomized study on percutaneous electrical therapy examined the duration of treatment in patients with low back pain (6). Seventy-five patients were randomly assigned to 0, 15, 30, or 45 minute electrical therapy treatment sessions. In a crossover design, each treatment was delivered three times per week for two weeks with a one-week washout period between changes in duration. The 30 or 45 minute electrical therapy sessions were significantly more effective than zero or 15 minutes ($P<0.01$) of treatment in terms of the hypoanalgesic effects. Self-reported physical activity ($P<0.05$), quality of sleep ($P<0.05$), and patient function ($P<0.01$) were also better after the longer duration treatments. The authors recommended that the duration of treatment be 30 minutes, because no additional benefit was observed with 45 minutes of treatment.

- **Study #4:** In this blinded, crossover study, 72 low back pain patients were treated with percutaneous electrical stimulation in four different electrode montages selected in random order (14). The authors concluded that all four electrode montages produced significant improvements in the degree of pain, physical activity, and quality of sleep, as well as a reduction in the daily oral analgesic requirement.

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Summary:

Complications: It is very important to note that these 4 studies involved a fairly large patient population - 275 patients. Furthermore, the design of these clinical studies required delivery of percutaneous electrical stimulation over extended durations (e.g., study #1 involved 9 treatments over 3 weeks). As a result, these 4 studies involved a very significant number of independent percutaneous electrical stimulation sessions ≅ 4,842 treatments. Even with this number of patients and extensive number of percutaneous treatments, *no* complications associated with the use of the percutaneous electrical stimulation (e.g., tissue damage, nerve injury, infection, burns, etc.) were reported in the literature for any of these studies. Vertis followed-up and discussed this issue with the actual clinical Investigators involved in these studies and they confirmed the observation that the studies had no complications or issues that they considered significant. For example, they observed no cutaneous reactions or inflammatory changes at any of the needle insertion sites after the treatment sessions. They reported they had minor issues (e.g., superficial bleeding or soreness at the needle insertion site) in some patients.

Relevance to Vertis PNT:

Vertis PNT parameters: Based on Vertis' internal research efforts and in conjunction with the published studies summarized on pages 2-4, Vertis selected the electrical stimulation parameters for the Vertis version of percutaneous electrical stimulation, called percutaneous neuromodulation therapy (PNT). The correlation of these published studies to Vertis PNT parameters are summarized in Tables A and B (pages 5-9).

Vertis clinical trial: In designing the Vertis PNT System and selecting stimulation parameters, Vertis projected that we would obtain similar clinical results with the Vertis PNT therapy, as was observed in these studies assessing percutaneous electrical stimulation against TENS, a substantially equivalent device. However, to clinically assess PNT therapy and to evaluate potential complications, Vertis conducted a non-significant risk clinical study in pain patients to gain our own clinical data and first-hand knowledge using PNT therapy.

The Vertis clinical trial data, in fact, did demonstrate the safety and effectiveness of PNT therapy. Please refer to Appendix 24 for a detailed discussion of the results of the Vertis clinical study.

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Table A: Percutaneous Electrical Therapy: Summary points from Studies #1-4 (summarized on pages 2-4) and Relevance to Vertis PNT therapy

Summary Point from Studies #1-4	Relevance to Vertis PNT
• The JAMA published double-blinded, randomized clinical study (4) showed percutaneous electrical therapy be more effective than TENS, exercise therapy, and a sham in providing short-term pain relief and improved physical function in patients with low back pain. • The second randomized clinical study demonstrated the effectiveness of a variety of different stimulation pulse frequencies (5).	***Vertis Modulation (Therapy) Modes*** As described in the Vertis PNT Control Unit User's Guide (Appendix 6, page 25), the PNT Control Unit has five pre-programmed modulation (therapy) modes. In designing the Control Unit, three modes Vertis selected (4 Hz Continuous, 15/30 Alternating, and 50 Hz Continuous) were based on the published clinical studies (4, 5). For reference purposes, a comparison of the therapies used in these 2 studies (4, 5) and the Vertis PNT System therapy options is provided in Table B (page 9). The information demonstrates the similarity of the electrical therapy parameters. In the Vertis PNT Control Unit, the remaining two modulation modes (4-10 Hz Periodic Sweep and 4-50 Hz Aperiodic Sweep) were designed by Vertis to deliver therapy that varies dynamically over a range of frequencies. The 4-10 Hz Periodic Sweep was selected as the default modulation mode for the PNT Control Unit based on patient comfort, while staying within a therapeutic range of pulse frequencies. As with any pain treatment , patient comfort and response during treatment is believed to be an important factor towards continued use of the therapy. With the 4-10 Hz Periodic Sweep, patients feel a gradual change from a relatively slow rate of pulses (4 Hz) to a more moderate rate of pulses (10 Hz) and back again over approximately a 33 second cycle. This slow rate of change tends to provide a soothing sensation. At the same time, the range of delivered pulse frequencies stays within the range of previous studied pulse frequencies.
• A third randomized study evaluated the effects of treatment duration and found 30 minutes to be the optimal duration (6).	***Vertis Therapy Duration*** Based on the published treatment duration study (6), Vertis chose a 30 minute suggested treatment duration for PNT. As noted in the Vertis PNT Control Unit User's Guide (Appendix 6, page 24), the Control Unit ships from Vertis with the therapy duration default set at 30 minutes.

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Summary Point from Studies	Relevance to Vertis PNT
• Various percutaneous electrode placement montages may demonstrate improvement in pain when used with electrical stimulation. A dermatomal electrode placement montage was found to be most effective (14).	***Vertis Electrode Placement Montage*** Vertis' recommendation for the placement of Safeguide electrodes for PNT therapy was based on the published study (14). The dermatomal montage selected was statistically more effective. This suggested montage is as noted in the Vertis Safeguide Instructions for Use (Appendix 12, page 5).
• Electrodes in these studies (4, 5, 6, 14) were placed percutaneously (inserted through the skin) to a depth of up to 4 centimeters. These studies report that electrodes were placed at a depth of 2 – 4 centimeters.	***Vertis Electrode Depth*** Electrode placement in the previous studies (4, 5, 6, 14) extended to 4 centimeters; *no* complications were reported with electrode placement (e.g., penetration of a vital organ) or the use of the electrodes (e.g., infection, burns, etc.). However, Vertis chose to be conservative and selected the maximum depth for any PNT Safeguide electrode insertion to be 3 centimeters. As noted in the technical discussion of Safeguide electrodes (Section II, page 12), Vertis will offer electrodes in 0.5 to 3.0 centimeter lengths. For device user ease of use and convenience, electrode kits will be provided as clinical application specific (e.g., a lumbar kit, a cervical kit, etc.). The kit labeling will clearly indicate the kit application (e.g., a lumbar kit). Justification for the safety of these Safeguide electrode lengths derives from three factors related to their design and intended use: • The anatomical ***placement*** of the electrodes relative to vital structures • The ***length*** of the electrodes • The cross-sectional ***diameter*** of the electrodes ***Placement:*** For all Safeguide electrodes, the Instructions for Use will contain a diagram of the recommended placement of the electrodes. For example, refer to Appendix 12 for an example of the Instruction for Use for a lumbar Safeguide electrode kit – the electrode placement diagram is found on page 5 of the Instructions for Use.

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These placement diagrams were developed by Vertis based on clinician's recommendations from experience in routine practice, clinical trials and physician expertise (e.g. neurophysiologists, neurosurgeons, and physical medicine and rehabilitation physicians, etc.). The recommended electrodes placements are carefully selected in order to maximize the efficacy of the treatment (by reaching neural pathways), but ensure safety of electrode insertion. Per the placement diagrams, electrodes will be placed directly over specific anatomical structures that will not be injured by placement of an electrode within them (e.g., muscle groups, etc.).

It is important to note that the literature (provided in Appendix 19) of the substantially equivalent percutaneous electrodes does *not* provide such suggested placement diagrams. Vertis believes that supplying the clinician with suggested electrode placement montages will aid the clinician in the proper use of the electrodes and minimize potential complications.

Length: The length of the Safeguide electrodes (limited to a maximum depth of 3.0 cm) limits the depth of their penetration into the body. The electrode depth is preset for a particular application. For example, electrodes to be used in the cervical region will likely be shorter (e.g., ~1-2 centimeters) than those used in a lumbar region. Similar to electrode placement, electrode depth will be based on clinician's recommendations. The depth will be selected in combination with the recommended anatomical placement, thus aiding to ensure that the electrodes will not be inserted into any vital organs.

It is important to note that substantially equivalent percutaneous electrodes can be 7.5 – 60 centimeters in length (refer to the electrode comparison chart in Appendix 18). Vertis believes that limiting the length of the Safeguide electrode to 3.0 centimeters, mitigates the risk in comparison to the substantially equivalent electrodes.

Diameter: The diameter of the electrodes is 0.25 millimeters. As noted on in 510(k) Section II (page 12), this ultra fine diameter is significantly narrower than any needle currently used for intramuscular injections or intravenous blood drawing. This extraordinarily fine diameter of the electrodes is an important safety feature.

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	According to scientific experts and clinicians who consult with Vertis, even if an artery, nerve, vein, muscle, lung, or other sensitive structure was contacted or punctured by an electrode (for example, if the clinician inadvertently did not place the electrodes according to the labeling diagram), it would be extremely unlikely that such an action would have any adverse consequences. For example, if a nerve were contacted, the electrode would likely simply displace the neural fascicles within the nerve. With this action, there may be a noticeable sensation (e.g. a twinge), and as such the electrode could be removed and repositioned (if necessary) for patient comfort. However, no specific special medical treatment or action would be required or indicated, as there would be no injury of any consequence. It is important to note that electrodes contacting various anatomical structures (e.g., nerves, muscle, etc.) is not unique to the Vertis PNT system. This situation can occur with numerous invasive medical devices and clearly with any of the substantially equivalent percutaneous electrodes used for nerve stimulation (e.g., nerve/muscle contact during placement of an EMG electrode). The substantially equivalent percutaneous electrodes are of a much larger dimension (0.33 – 1.37 millimeters in diameter, per Appendix 18 comparison chart) than the Safeguide electrodes and accordingly, contact with bodily structures with these electrodes would likely be more potentially significant than with the smaller Vertis Safeguide electrodes.

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Table B: Percutaneous Electrical Therapy: published literature vs. Vertis PNT - therapy comparison table

	Published Literature		*Vertis Modulation Mode*				
	Ref. 4	**Ref. 5**	**4-10 Hz Periodic Sweep**	**4 Hz Continuous**	**15/30 Hz Alternating**	**50 Hz Continuous**	**4-50 Hz Aperiodic Sweep**
Pulse repetition frequency	4 Hz	4 Hz, 15/30 Hz, or 100 Hz	Varies between 4 Hz and 10 Hz, inclusive	4 Hz	Alternates between 15 Hz and 30 Hz in 3-second intervals	50 Hz	Varies between 4 Hz and 50 Hz, inclusive
Waveform*	Stated: 0.5 msec unipolar square wave Actual: Asymmetric biphasic, 0.7 msec phase 1, decaying exponential phase 2	Stated: 0.5 msec unipolar square wave Actual: Asymmetric biphasic, 0.7 msec phase 1, decaying exponential phase 2	Symmetric biphasic, 0.2 msec/phase (200 µsec/phase)	Symmetric biphasic, 0.2 msec/phase (200 µsec/phase)	Symmetric biphasic, 0.2 msec/phase (200 µsec/phase)	Symmetric biphasic, 0.2 msec/phase (200 µsec/phase)	Symmetric biphasic, 0.2 msec/phase (200 µsec/phase)
Maximum amplitude	25 mA	25 mA	15 mA	15 mA	12.5 mA	10.2 mA	15 mA

* "Stated" refers to the stimulation parameters reported in the published literature. As part of the development of the Vertis PNT therapy parameters, the researchers at the UTSW were contacted by Vertis Engineering/Research staff and allowed Vertis to evaluate the equipment used in the UTSW studies. The Vertis staff specifically measure the actual device stimulation parameters. This data is recorded in this table as "actual" - meaning what the device system actually delivers.

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Percutaneous Electrical Stimulation – Other recent studies

Although the above studies were specific to low back pain (LBP), the safety and effectiveness of percutaneous electrical stimulation is not limited to low back pain. This is consistent with the historical use of percutaneous electrical stimulation, where the treatment was used in a variety of pain scenarios. For example, the following recent studies have further demonstrated the use of percutaneous electrical stimulation in other acute – chronic pain conditions.

- **Study #5:** An episode of acute LBP accompanied by pain radiating into the buttocks and/or lower extremities is known by clinicians to carry a worse prognosis than LBP pain localized to the lumbosacral region. Numerous studies have documented that—as compared with localized LBP—radiating pain and/or sciatica (pain or neuritis of the sciatic nerve) are associated with increased: 1) pain severity, 2) probability of progression to a chronic state of pain, and 3) disability or loss of ability to participate in activities (7 – 13).

  In a randomized, blinded, sham-controlled investigation comparing therapies for treating sciatica in 64 patients, the authors concluded that percutaneous electrical therapy was more effective than TENS and a sham in providing pain relief and improved functionality (18). The use of the percutaneous electrical therapy improved physical activity and the quality of sleep while decreasing the need for oral non-opioid analgesic medications.

- **Study #6:** In a randomized, blinded study of 50 patients, percutaneous electrical therapy was compared with a standard antiviral regimen (famciclovir) in the treatment of acute herpes zoster (16). In this study, the percutaneous electrical therapy group experienced more rapid resolution of vesicles and complete healing of the lesions. The percent decrease in pain scores for the percutaneous electrical therapy group was 67%, compared with the pharmacological group of 45%. The percent improvement in physical activity and quality of sleep was also greater for the percutaneous electrical therapy patients.

- **Study #7:** Percutaneous electrical therapy was examined in 30 patients suffering form tension headache, migraine or posttraumatic headache symptoms (17). Percutaneous electrode placement was in the posterior cervical region and would not be transcerebrally (a contraindication for Vertis PNT therapy). Compared with a sham control (no electrical stimulation), percutaneous electrical therapy was significantly more effective in decreasing the overall pain levels and produced greater improvement in the patients' physical and quality of sleep. The analgesic response appeared to be independent of the origin of the headache symptoms.

- **Study #8:** In a randomized study of 50 patients, percutaneous electrical therapy was compared with a sham control (no electrical stimulation) in the treatment of diabetic neuropathic pain – a condition experienced by diabetic patients, manifesting as pain in the lower extremities (18). The authors concluded percutaneous electrical therapy was a useful nonpharmacological therapy. In addition to decreasing extremity pain, percutaneous electrical therapy improved

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physical activity and quality of sleep, while reducing the need for oral non-opioid analgesic medication.

Summary:

Complications: These additional 4 studies involved 194 patients. The design of studies #5-8 required delivery of percutaneous electrical stimulation over extended durations (e.g., multiple treatments over multiple weeks). As a result, these 4 studies involved a significant number of independent percutaneous electrical stimulation sessions – 1,506 treatments. Similar to studies #1-4 (summarized on pages 2-4), the authors reported *no* complications associated with the use of the percutaneous electrical stimulation (e.g., tissue damage, nerve injury, infection, burns, etc.) in any of these studies. As with studies #1-4, Vertis followed-up and discussed this issue with the actual clinical Investigators involved in these studies (#5-8) and they confirmed the observation that the studies had no complications or issues that they considered significant. For example, they observed no cutaneous reactions or inflammatory changes at any of the needle insertion sites after the treatment sessions. They reported they had minor issues (e.g., superficial bleeding or soreness at the needle insertion site) in some patients.

Relevance to Vertis PNT: In addition to studies #1-4 in low back pain patients, these additional studies (#5-8) are examples of various other acute-chronic pain conditions in which percutaneous electrical therapy has been shown to benefit patients, with no safety issues reported. Due to the similarity of the PNT stimulation to the therapies deployed in these studies (e.g., see Table B, page 9), Vertis expects PNT to be similarly useful and clearly appropriate for clinician use in pain management for these conditions.

Lastly, it is important to note that many of these studies (#1-8) involved direct comparisons to the substantially equivalent TENS devices. Results showed that percutaneous electrical therapy was, at a minimum, equivalent to TENS as a pain relief modality.

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Appendix 2
Assessment Tools and Success Criteria

Assessment Tools

Vertis and FDA are both aware that in the design of clinical trials it is important to select assessment tools (outcome measures) that have been validated for the tools intended use in the study.

For both the Vertis clinical trial (discussed on pages 2-11 of this Supplement) and the other published clinical trials conducted at the University of Texas Southwestern - UTSW (discussed on pages 12-29 of this Supplement), the assessment tools used were well-respected pain research tools and had been validated in pain research for their intended use in the clinical studies. A brief summary of the tools used and their validation (as documented in scientific publications) is as follows:

Visual Analog Scale (VAS)

The primary endpoint in the multiple published clinical studies on percutaneous electrical stimulation (references 4,5,6 and 14) and the Vertis clinical study was a measurement in the reduction in low back pain or an improvement in activity. Intensity of low back pain and level of activity were measured using a 10-cm visual analog scale (VAS scale).

Visual analog scales - VAS scales - have been used in hundreds of clinical studies on pain and physical function. For example, a recent search of the Medline medical/scientific publication database using the search terms "back pain" and "visual analog scale" yielded 858 citations. Thus, the VAS scale has been widely used and has been the standard of measurement in pain research for the past several decades, with excellent validity.

In a landmark publication (Deyo, et. al., reference 34), an international group of back pain researchers assessed and proposed *standardized* outcome measures to be used in clinical trials/clinical outcomes specific to research in patients with back pain. They proposed a "core set" of outcome measurement instruments for clinical researchers (Table 4 in the publication). This core set specifically included and recommended the use of visual analog scales to assess pain symptoms. With respect to the use of VAS scales, they noted:

> Pain symptoms (such as bothersomeness or severity and frequency of low back pain and leg pain) were to be assessed as follows: "The severity of low back pain and leg pain could also be measured using conventional visual analog scales, a type of measurement more familiar to some investigators. Guyett, et. al. demonstrated nearly identical statistical measures of responsiveness for 7-point Likert Scales and Visual Analog Scales".
>
> "Similarly, visual analog pain scales have enjoyed wide use and similar evidence of construct validity has accrued".

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In addition to the Deyo publication, numerous other publications have continued to support the validity of using VAS scales in pain research. Specifically:

Roach, et. al. (35) in 1997 studied the test-retest reliability of a visual analogue scale measure of pain intensity. They concluded "the reliability of these pain measures is sufficient to permit their use in making clinical decisions and measuring treatment outcomes".

Triano, et. al. (36) in 1993 compared the reliability and validity of six different potential outcome measures in 186 back pain patients. They noted "Overall, the Oswestry and Visual Analogue Pain Scale were the most reliable" and concluded "The Oswestry and Visual Analogue Pain Scale were both more reliable and valid than other instruments".

Health Status Survey Short Form (SF-36) and Oswestry Disability Questionnaire

A secondary endpoint in the published clinical studies was a global patient assessment measurement. For this assessment, the researchers used the well-known Health Status Survey Short Form (SF-36) tool. Similarly, in the Vertis clinical study, a measurement of impaired function was used. Patient status in the Vertis trial was measured by using the Oswestry Disability Questionnaire (as modified by the American Academy of Orthopedic Surgeons - AAOS).

Similar to VAS, both the SF-36 and the Oswestry questionnaire have been used in excess of 20 years in numerous clinical studies has become recognized as excellent, validated tools to assess patient status. The SF-36 is a tool that is normally associated with evaluating patient's general well being; Oswestry is a more disease-specific tool more applicable for back-related functional assessments.

In the Deyo 1998 publication (reference 34, previously discussed in the context of VAS scales), Deyo, et. al., assessed and proposed standardized outcome measures to be used in clinical trials/clinical outcomes specific to research in patients with back pain. To assess "back-related function", they proposed the use of the Oswestry Disability questionnaire (or adaptations) and SF-12 (a condensed version of the SF-36) to evaluate "generic well-being" as part of the "core set" of outcome measurement instruments for clinical researchers (Table 4 in the publication).

With respect to the use of the Oswestry and the SF-36, they noted:

"With regard to functional status, the use of either the Roland and Morris Disability Scale (or its adaptations) or the Oswestry Disability Questionnaire (and its adaptations) is recommended. These are among the most widely used and well validated of functional status questionnaires, and both would be highly acceptable".

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"The Oswestry Disability Questionnaire may be most useful in specialty care settings or in situations in which the disability is likely to remain relatively high throughout the trial (e.g., chronic severe low back pain)".

"In addition, a modest adaptation of the Oswestry Disability Questionnaire has been developed and validated for use in the AAOS and NASS [North American Spine Society] outcome questionnaires".

"With regard to generic well-being, inclusion of either the SF-12 (adapted from the SF-36) or the EuroQol is tentatively recommended". Their tentative recommendation is based on their conclusion that the SF-12 may have limited responsiveness, "although the larger S-36 has been found to be responsive".

In addition to the Deyo publication, numerous other publications have continued to support the validity of using the SF-36 and Oswestry tools in clinical research assessing function. Specifically:

The SF-36 is a well-established measurement tool. Ware, et. al (37) in the SF-36 User's Manual presents substantial information regarding the SF-36 scale use, including assumptions underlying the use of the SF-36 physical and mental health scales, scoring of the scales, reliability, precision and data quality, validation and interpretation guidelines. They devote 2 entire chapters ("Reliability and Statistical Power" and "Empirical Validation") discussing the validation of the SF-36 for use in research. The SF-36 Health Survey Bibliography (38) lists 446 publications that employed the use of the SF-36 in research studies. Many of these publications specifically used the SF-36 in low back pain patients:

> Garratt , et. al., (39) reported on the reliability and validity of the SF-36 in "low back pain patients, menorrhagia, suspected peptic ulcer, or varicose veins. The data from these patients were used to test the internal consistency, clinical validity, and construct validity of the SF-36 in a British population.". They concluded the "SF-36 proved reliable and showed strong clinical construct validity..." "Clinical validity was also supported by strong relationships between the SF-36 scale scores and physician ratings of severity."

Fairbank, et. al. (40) reviewed the use of the Oswestry Disability tool 20 years after its inception. They noted it "has become one of the principal condition-specific outcome measures used in the management of spinal disorders" and concluded it "remains a valid and vigorous measure and has been a worthwhile outcome measure".

And as previously noted in discussing the selection of the use of VAS scales (page 1), Triano, et. al. (36) compared the reliability and validity of six different potential outcome measures in 186 back pain patients. They noted "Overall, the Oswestry and Visual Analogue Pain Scale were the most reliable" and concluded "The Oswestry and Visual Analogue Pain Scale were both more reliable and valid than other instruments".

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Success Criteria

Similar to the importance of the validity of assessment tools, Vertis and FDA are both aware that in the design of clinical trials it is important to select success criteria for the study that are clinically meaningful.

For the published clinical studies, a success criteria was not identified in the publications and accordingly, Vertis cannot comment on the Investigator's criteria selection. However, for the Vertis clinical trial a valid success criteria was identified for the study. A discussion of the criteria is as follows:

> The Investigational Plan (document V0040) for the Vertis clinical trial was provided in the 510(k) Notification (Appendix 24, Attachment A). In developing this Investigational Plan, Vertis consulted with our Scientific and Medical Advisors and many of the world's leading researchers in pain. With the help of these individuals, the primary endpoint was defined based on clinically relevant thresholds of treatment response.
>
> With respect to the primary endpoint and clinical relevance, text from the Investigational Plan (page 14) is provided here for reference and is as follows (italics emphasis added):
>
> Primary endpoint
>
> The primary endpoint of the study is the percentage of patients (who have passed the responder screen) that have at least a 30% improvement at follow-up as compared with baseline. *A 30% or more improvement has been shown to have clinical relevance (27).* For the primary endpoint, improvement is defined as at least a 30% reduction in low back pain, at least a 30% improvement in activity, or a combined pain/activity improvement of at least 30%. Intensity of low back pain and level of activity are measured using 10-cm visual analog scales (VAS).
>
> Reference #27 (equivalent to reference #33 in this Supplement) in the Investigational Plan was from the November 2000 American Pain Society Meeting, where Young, et. al. presented on the clinical relevance of changes to a numerical pain rating scale. They reported the following:
>
> "Pain is frequently measured on an 11-point numerical rating scale (NRS), where 0 = no pain and 10 = worst possible pain. However, it is difficult to interpret the clinical relevance of changes from baseline on this scale (such as 2- or 3-point decreases). We attempted to determine clinical relevance by associating changes and percent changes in the NRS to patients' global assessments of change."
>
> The authors studied 2,724 patients from 10 studies and concluded "NRS [numerical rating scale] percent decreases of 30% or more represent clinically relevant improvement."

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Summary

The Vertis staff, Vertis clinical Investigators, Vertis Scientific and Medical Advisors and UTSW clinical Investigators believe that the assessment tools (outcome measures) employed in the Vertis and UTSW clinical trials were the appropriate tools for the studies. The tools used (the VAS scale, the SF-36 and the Oswestry Disability Questionnaire) are the identical tools recommended in the peer-reviewed literature to be used in pain research. As the referenced literature reports, these tools have been used for decades in hundreds of clinical studies similar to the Vertis and UTSW clinical trials and are considered validated for their intended use.

Similarly, Vertis believes that the success criteria established for the Vertis clinical trial is a valid criteria as documented by recent pain research.

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Appendix 3
(Appendix 16 from 510(k) Notification – *Revised*)

Company	**Vertis Neuroscience, Inc. Seattle, WA**	**Empi, Inc. St. Paul, MN**	**Rehabilicare, Inc. New Brighton, MN**	**Chattanooga Group, Inc. Hixson, TN**	**Medtronic, Inc Minneapolis, MN**
Product	**Vertis PNT System**	**EPIX TENS Device**	**SMP-Plus™**	**Intelect® Legend Stim**	**Mattrix® Neurostimulation System**
Model/Catalog No(s)	Model: CU 100	Model: EPIX VT Model: EPIX XL	Model 4930	Model IFC2 (catalog no. INT002)	Receiver model: 3272 Transmitter model: 3210
510(k) References	N/A – This submission	K970203, K951903	K982410	K924666	K982902
Indications for Use	Indicated for the symptomatic relief and management of chronic intractable pain and/or as an adjunctive treatment in the management of post-surgical and post-trauma acute pain.	Indicated for the symptomatic relief and management of chronic, intractable pain and/or adjunctive treatment for post-surgical and post-trauma acute pain.	Indicated for the symptomatic relief and management of chronic intractable pain and/or as an adjunctive treatment in the management of post-surgical and post-traumatic pain.	Indicated for symptomatic relief of chronic, intractable pain and management of pain associated with post-traumatic or post-operative conditions.	Indicated for spinal cord stimulation and for peripheral nerve stimulation. Indicated for treatment of chronic, intractable pain of the trunk or limbs.
Intended User	Clinician (e.g., physician, physical therapist) use.	Clinician use or patient use under the supervision of a clinician.	Clinician use or patient use under the supervision of a clinician.	Clinician use.	Implant procedure: Clinician Ongoing use: patient with clinician supervision.
Examples of Therapy Applications	Lumbar pain Cervical pain Thoracic pain ~~Sciatica~~ ~~Shingles (zoster)~~ ~~Diabetic neuropathy~~ ~~Headache~~ ~~Other neuropathies~~	Low back pain Arthritis Chronic strains and sprains Neuralgia Reflex sympathetic dystrophy Shingles (zoster) Degenerative joint disease Intractable migraine	Cervical, thoracic, lumbar, and sacral syndromes Neuropathies Causalgias Neuralgias Nerve root/plexus injuries Phantom limb syndromes Spinal stenosis Arthritis Reflex sympathetic dystrophy	Not disclosed in manufacturer's literature.	Chronic limb pain Complex regional pain syndrome Failed back syndrome Arachnoiditis Painful neuropathies

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Company	**Vertis Neuroscience, Inc. Seattle, WA**	**Empi, Inc. St. Paul, MN**	**Rehabilicare, Inc. New Brighton, MN**	**Chattanooga Group, Inc. Hixson, TN**	**Medtronic, Inc Minneapolis, MN**
Product	**Vertis PNT System**	**EPIX TENS Device**	**SMP-Plus™**	**Intelect® Legend Stim**	**Mattrix® Neurostimulation System**
How Therapy Delivered	Percutaneous stimulation of peripheral nerves	Cutaneous stimulation of peripheral nerves	Cutaneous stimulation of peripheral nerves	Cutaneous stimulation of peripheral nerves	Pulses transmitted across skin to receiver and electrodes to stimulate peripheral nerves or spinal cord.
System Components & Accessories	Nerve stimulator Electrodes Patient Cables	Nerve stimulator Electrodes Lead Wires Batteries Battery Charger	Nerve stimulator Electrodes Patient cables Batteries	Nerve stimulator Electrodes Lead	Receiver Transmitter Antenna Electrodes/leads
Specifications					
Physical					
size (H x W x D)	4.7" x 9.65" x 9.5"	3.7" x 2.5" x 0.94"	3.75" x 2.5" x 1"	3" x 8" x 12"	2.75" x 2" x .5"
approximate weight	6.0 lbs.	4.0 oz with battery	4.8 oz with battery	7.0 lbs	Not disclosed in manufacturer's literature.
portable	yes	yes	yes	yes	yes
power supply	AC, configurable to either 115 or 240V	DC, 9V alkaline or rechargeable battery	DC, 9V alkaline or rechargeable battery	AC, configurable to either 120 or 220/240V	DC, 9V alkaline or rechargeable battery
Therapeutic					
waveform	charge-balanced, rectangular biphasic	balanced asymmetrical biphasic, constant current, constant voltage	biphasic asymmetrical with zero net DC	sinusoidal	Not disclosed in manufacturer's literature.
phase duration/pulse width	200 μSec	0-400 μSec	40-300 μSec	NA (with sinusoidal waveform)	50-500 μSec
maximum output amplitude	15 mA into 500 Ohm load	60 mA into 1000 Ohm load (>60 mA into 500 Ohm load – but actual data not disclosed in manufacturer's literature)	60 mA into 500 Ohm load	50 mA into a 500 Ohm load	24 mA into a 500 Ohm load
frequency range	4–50 Hz	2–150 Hz	2-125 Hz	0-200 Hz	5-240 Hz
maximum output charge per pulse	7.2 μC	20 μC	18 μC	NA (with sinusoidal waveform)	12 μC

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Product	**Vertis PNT System**	**EPIX TENS Device**	**SMP-Plus™**	**Intelect® Legend Stim**	**Mattrix® Neurostimulation System**
# of output channels	1 - 5	1 – 2	1 – 2	1-2	2
Features					
on/off activation	button	button	touch pad	touch pad	button
text prompts	on LCD screen	on LCD screen	on LCD screen	on LCD screen	on LCD screen
intensity control	knob/dial	button	touch pad	touch pad	push-button
data recording	Yes (e.g., # of sessions used, therapy mode delivered, length of therapy session, etc.)	Yes (e.g., # of sessions used, therapy mode delivered, length of therapy session, % of sessions with pain relief, etc.)	Yes (e.g., stores parameter setting from most recent session)	Yes (e.g., stores parameters)	Not disclosed in manufacturer's literature.
Safety					
output protection	automatic channel disable for high voltage (open-circuit) load condition	automatic channel disable for high amplitude (open-circuit load) condition	automatic shut off with disconnect of electrode or lead wire	automatic channel disable when excessive current change.	Not disclosed in manufacturer's literature.
patient isolated	yes	yes	yes	yes	yes
safety standards compliance	AAMI NS 4 AAMI NS 15	AAMI NS 4	AAMI NS 4	AAMI NS 4	AAMI NS 15

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Appendix 4
Bibliography - Copies of Selected Literature

Note: References 1 - 33 in this Appendix are a duplicate of Appendix 28 originally provided in the 510(k) Notification. Full copies of references 4-6 and 14-18 were originally provided in Appendix 28 in the 510(k).

For this Amendment, references 34 - 50 have been added. Copies of the articles in **bold text** have been included for reference in this Amendment's Appendix.

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PRELIMINARY COMMUNICATION

Percutaneous Electrical Nerve Stimulation for Low Back Pain

A Randomized Crossover Study

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Context Low back pain (LBP) contributes to considerable disability and lost wages in the United States. Commonly used opioid and nonopioid analgesic drugs produce adverse effects and are of limited long-term benefit in the management of this patient population.

Objective To compare the effectiveness of a novel nonpharmacologic pain therapy, percutaneous electrical nerve stimulation (PENS), with transcutaneous electrical nerve stimulation (TENS) and flexion-extension exercise therapies in patients with long-term LBP.

Design A randomized, single-blinded, sham-controlled, crossover study from March 1997 to December 1997.

Setting An ambulatory pain management center at a university medical center.

Patients Twenty-nine men and 31 women with LBP secondary to degenerative disk disease.

Interventions Four therapeutic modalities (sham-PENS, PENS, TENS, and exercise therapies) were each administered for a period of 30 minutes 3 times a week for 3 weeks.

Main Outcome Measures Pretreatment and posttreatment visual analog scale (VAS) scores for pain, physical activity, and quality of sleep; daily analgesic medication usage; a global patient assessment questionnaire; and Health Status Survey Short Form (SF-36).

Results PENS was significantly more effective in decreasing VAS pain scores after each treatment than sham-PENS, TENS, and exercise therapies (after-treatment mean ± SD VAS for pain, 3.4 ± 1.4 cm, 5.5 ± 1.9 cm, 5.6 ± 1.9 cm, and 6.4 ± 1.9 cm, respectively). The average ± SD daily oral intake of nonopioid analgesics (2.6 ± 1.4 pills per day) was decreased to 1.3 ± 1.0 pills per day with PENS ($P<.008$) compared with 2.5 ± 1.1, 2.2 ± 1.0, and 2.6 ± 1.2 pills per day with sham-PENS, TENS, and exercise, respectively. Compared with the other 3 modalities, 91% of the patients reported that PENS was the most effective in decreasing their LBP. The PENS therapy was also significantly more effective in improving physical activity, quality of sleep, and sense of well-being ($P<.05$ for each). The SF-36 survey confirmed that PENS improved posttreatment function more than sham-PENS, TENS, and exercise.

Conclusions In this sham-controlled study, PENS was more effective than TENS or exercise therapy in providing short-term pain relief and improved physical function in patients with long-term LBP.

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DESPITE THE FACT THAT LOW back pain (LBP) is one of the most common medical problems in our society,[1] current analgesic therapies remain largely unsatisfactory. Conservative treatment with antiinflammatory drugs and exercise is effective for many patients with acute LBP.[2] However, when the pain symptoms persist, they can interfere with both physical activity and sleep patterns. While analgesic medications can provide temporary pain relief, these drugs may not improve physical function and are associated with well-known adverse effects. Interest in nonpharmacologic alternatives has led to evaluations of transcutaneous electrical nerve stimulation (TENS),[3] acupuncture,[4,5] electroacupuncture,[6] spine manipulation,[7-9] and exercise therapy[9-12] in the management of LBP. However, controversy exists regarding the relative efficacy of these nonpharmacologic therapies in the management of LBP because most of the published studies lacked appropriate control (sham) groups or failed to include relevant comparators.

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Percutaneous electrical nerve stimulation (PENS) is a novel analgesic therapy[13] that combines the advantages of both TENS and electroacupuncture by using acupuncturelike needle probes positioned in the soft tissues and/or muscles to stimulate peripheral sensory nerves at the dermatomal levels corresponding to the local pathology. In a preliminary study,[14] PENS therapy was found to be preferable to TENS and relaxation therapies in the management of pain secondary to osteoarthritis. Therefore, we designed a prospective, randomized, sham-controlled, crossover trial to compare PENS with TENS and exercise therapy in patients with long-term LBP secondary to degenerative disk disease. In addition to assessing the pain response, the patients' physical activity, quality of sleep, sense of well-being, and oral analgesic requirements were evaluated.

METHODS

After obtaining institutional review board approval and written informed consent, 60 patients (29 men and 31 women; mean ± SD age, 43 ± 1.9 years, and weight, 66 ± 1.6 kg) with LBP secondary to radiologically confirmed degenerative disk disease were administered 4 different nonpharmacologic treatment modalities according to a randomized, sham-controlled, crossover study design. The 4 modalities consisted of sham-PENS, PENS, TENS, and flexion-extension exercise. Inclusion criteria included age older than 18 years, absence of any acute or long-term illnesses involving major organ systems, and a history of LBP, which had been maintained at a stable level with oral nonopioid analgesics for at least 3 months prior to enrollment in the study. Exclusion criteria included a history of drug or alcohol abuse, long-term use of opioid-containing medication, a change in the character or severity of the pain within the last 3 months, presence of acute nerve root irritation (sciatica), previous use of nontraditional analgesic therapies (eg, acupuncture), pending medicolegal litigation (or worker's compensation claim), or an inability to complete the health status assessment questionnaires. Patients were told that we were comparing 4 different nonpharmacologic therapies for LBP.

All patients received the 4 treatment modalities according to 1 of 4 different computer-generated sequences: (1) PENS, sham, TENS, and exercise; (2) sham, TENS, exercise, and PENS; (3) TENS, exercise, PENS, and sham; or (4) exercise, PENS, sham, and TENS. Each treatment was administered for 30 minutes 3 times a week (on Monday, Wednesday, and Friday afternoons) for 3 weeks. Upon completion of each 3-week treatment block, the patient was given 1 week off before starting the next modality. The 4 modalities were administered to all patients over the 15-week study period.

Treatment Modalities

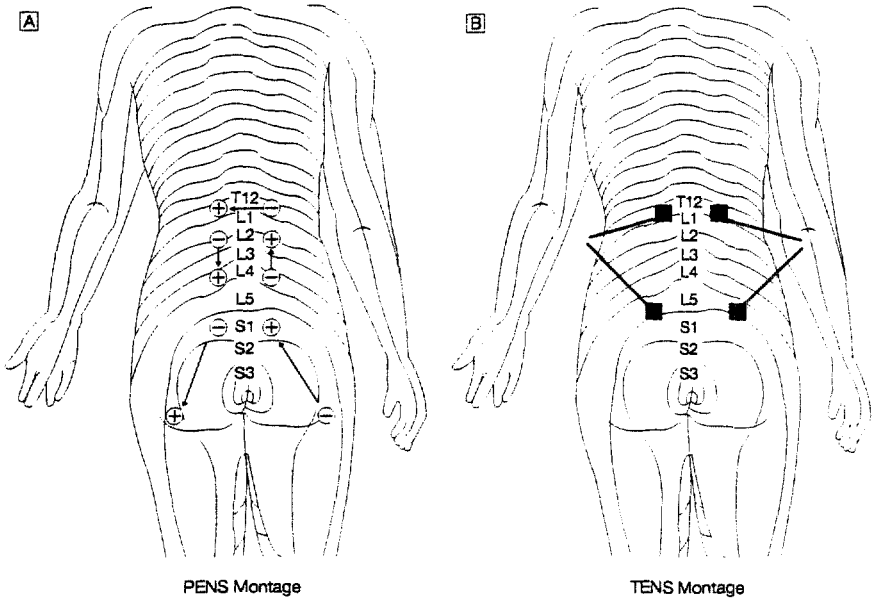
The basic PENS therapy consisted of the placement of ten 32-gauge stainless steel acupuncturelike needle probes into the soft tissue and/or muscle in the lower back region to a 2- to 4-cm depth according to the dermatomal distribution of the pain as illustrated in part A of FIGURE 1. The probes were connected to 5 bipolar leads (with each lead connected to 1 positive and 1 negative probe) from an investigational (not approved by the Food and Drug Administration) low-output (<25 mA) electrical generator, which produced a unipolar square-wave pattern of electrical stimulation at a frequency of 4 Hz with a pulse width of 0.5 milliseconds. The intensity of the electrical stimulation was adjusted to produce the maximum tolerable "tapping" sensation without muscle contractions.

The sham-PENS therapy consisted of the placement of 10 acupuncturelike needle probes in an identical montage (Figure 1, A); however, no electrical stimulation was applied to the probes.

The TENS therapy consisted of the placement of 4 medium-sized (2.5-cm) cutaneous electrode pads (SnapEase, Empi, St Paul, Minn) in a standard dermatomal pattern (Figure 1, B). These electrodes were also stimulated at a frequency of 4 Hz, with a pulse duration of 0.1 milliseconds.

The lower back exercise therapy consisted of spine flexion and extension with

Figure 1. Locations of Needles for PENS and TENS Montage



A, The location of the needles for the sham–percutaneous electrical nerve stimulation (PENS) and PENS treatments. With PENS therapy, each of the 5 bipolar electrical stimulating leads are connected to a pair of needles, alternating the positive and negative positions. B, The location of the 4 cutaneous electrode pads used during the transcutaneous electrical nerve stimulation (TENS) treatments.

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the patient seated on a chair with full abduction of both hips.[15] The patient was instructed to slowly touch the floor with both hands while remaining seated, followed by full extension of the back. This maneuver was repeated a minimum of 30 times during each 30-minute treatment session.

Assessment Procedures

Prior to initiating the first of the 4 treatments, patients were required to complete the Health Status Survey Short Form (SF-36).[16] The physical component summary (PCS) and mental component summary (MCS) scores were used to assess the patient's response to each of the therapeutic modalities.[17] All patients were also asked to assess their baseline level of LBP, physical activity, and quality of sleep during the 48-hour interval prior to each treatment session using standard 10-cm visual analog scales (VASs), with a score of zero equalling the best to a score of 10 equalling the worst (TABLE 1). Repeated VAS assessments of pain, activity, and sleep were performed 3 times a week prior to each treatment session by the patient. In addition, the pain VAS was repeated immediately after completion of each treatment. The SF-36 was repeated 24 hours after completing all 9 treatment sessions with each of the 4 modalities. Patients were instructed not to change the type of nonopioid analgesic medications used during the course of the study. They were also asked to maintain a diary in which they recorded their daily usage of all analgesic medications (eg, pills per day) and any unusual reactions to the investigational therapies. Finally, each patient completed an overall assessment of the relative effectiveness of the 4 different modalities 72 hours after the last treatment session.

Data Analysis

The Number Cruncher Statistical System software program (version 6.0.1 for Windows, Kaysville, Utah) was used for all statistical analyses. An a priori power analysis (α, .05; β, .10; power, 90%; and SD, 2.0) determined that a group size of 60 should be adequate to demonstrate a difference of 25% between the VAS scores for the 4 modalities. The changes in the VAS scores over time were analyzed with repeated measures analysis of variance and t test, with a Bonferroni comparison test (vs control values and pairwise data), applied for multiple comparisons. Analysis of discrete (noncontinuous) data for the 4 treatment modalities was performed using the χ^2 test. The pretreatment and posttreatment changes and the differences between the modalities in the SF-36 scores were analyzed by paired t tests.

RESULTS

The pretreatment SF-36 evaluation suggested that this LBP population reported significantly lower health-related quality-of-life scores compared with the general population. The prestudy scores for this LBP population were 28.4 ± 8.4 and 40.2 ± 5.0 for the PCS and MCS, respectively, compared with general population norms of 50 for these 2 summary scores.[18] The post-PENS treatment SF-36 scores were significantly improved over the prestudy scores for both the PCS (34.2 ± 7.4; $P = .003$) and MCS (42.8 ± 5.2; $P = .007$) components. Both TENS and sham-PENS produced small but statistically significant improvements in the PCS (29.6 ± 8.4 and 29.4 ± 8.6, respectively) and MCS (41.1 ± 5.5 and 41.0 ± 5.4, respectively) scores ($P<.02$). When the changes in the SF-36 scores with the PENS therapy were compared with the other 3 modalities, PENS was found to produce significantly greater improvement in posttherapy function (eg, PENS vs sham-PENS differences were +4.97 ± 2.99 and +1.84 ± 3.56 for PCS and MCS, respectively; PENS vs TENS differences were +4.66 ± 2.85 and +1.7 ± 4.19 for PSC and MCS, respectively; and PENS vs exercise differences were +5.82 ± 2.93 and +1.84 ± 3.56 for PCS and MSC, respectively).

The VAS scores for pain, physical activity, and quality of sleep prior to the first treatment session (baseline) and 24 hours after the last treatment session with each of the 4 modalities are summarized in Table 1. Compared with the baseline values, posttreatment VAS scores for pain, physical activity, and quality of sleep were improved by 46% ± 18%, 42% ± 19%, and 44% ± 20%, respectively, with PENS therapy ($P<.007$). TENS also produced significant decreases in the degree of pain and improvement in physical activity after 6 of 9 treatment sessions ($P<.03$) with an average overall improvement in the degree of pain and physical activity (from the baseline values) of 11% ± 14% and 15% ± 16%, respectively. No significant pain-relieving effects were demonstrated with either the sham-PENS or exercise therapies. Comparing the effects of the 4 treatment modalities on VAS scores for pain, physical activity, and sleep quality revealed that PENS produced significantly greater improve-

Table 1. Comparison of the Average Visual Analog Scale Scores for Low Back Pain, Level of Activity, and Quality of Sleep Prior to Receiving the First Treatment and at 24 Hours After the Ninth Treatment With Each of the 4 Modalities*

Treatment	Sham-PENS	PENS	TENS	Exercise
Degree of pain				
Before	5.7 (1.8)	6.3 (1.5)	6.2 (1.7)	6.5 (1.4)
After	5.5 (1.9)	3.4 (1.4)†	5.6 (1.9)‡	6.4 (1.9)
Level of activity				
Before	5.1 (2.1)	5.5 (2.0)	5.5 (2.1)	5.7 (1.8)
After	4.9 (2.1)	3.2 (1.7)†	4.7 (1.9)‡	5.7 (1.8)
Quality of sleep				
Before	5.0 (2.3)	5.5 (1.9)	5.6 (2.1)	5.8 (1.9)
After	5.0 (2.1)	3.1 (1.6)†	5.3 (2.2)	5.5 (1.9)

*Values are mean (SD) centimeters. PENS indicates percutaneous electrical nerve stimulation; TENS, transcutaneous electrical nerve stimulation.
†Significantly different from value prior to receiving the first treatment (before), $P<.03$, and from sham-PENS, TENS, and exercise therapies, $P<.02$.
‡Significantly different from value prior to receiving the first treatment (before), $P<.04$.

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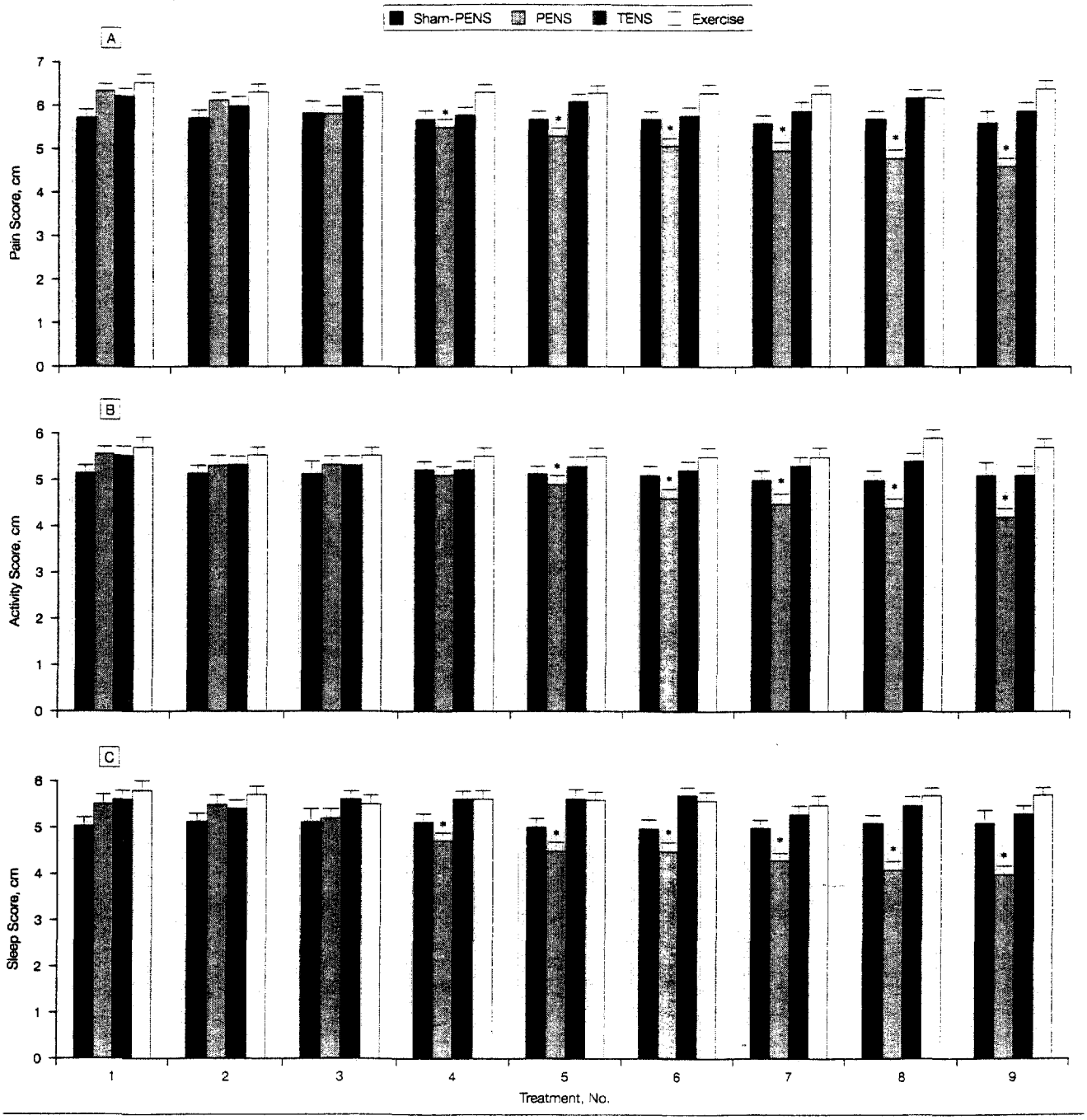
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ments than sham-PENS, TENS, or exercise therapies ($P<.02$).

PENS produced an acute analgesic effect immediately after each treatment session (with an average 82% ± 23% decrease in the pain VAS scores vs 26% ± 19%, 9% ± 15%, and 4% ± 11% decreases with TENS, sham-PENS, and exercise, respectively). After 3 to 4 treatments with PENS, patients began reporting significant improvement in their pretreatment VAS scores for pain, activity, and sleep compared with their baseline values (FIGURE 2). PENS also significantly decreased the consumption of oral

Figure 2. Visual Analog Scale Scores



Visual analog scale scores for low back pain (A), physical activity (B), and quality of sleep (C) before each of the 9 treatment sessions with the 4 study modalities. Values are mean (SEM). Asterisk indicates value is significantly different from baseline value ($P<.03$). PENS indicates percutaneous electrical nerve stimulation; TENS, transcutaneous electrical nerve stimulation.

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nonopioid analgesic medication ($P<.009$) (FIGURE 3). Compared with the prestudy values, PENS therapy was associated with a 50% reduction in the daily oral analgesic requirement. In contrast, TENS therapy decreased the need for analgesic medication on only 6 days during the 3-week study period ($P<.04$). Neither sham-PENS nor exercise therapies altered the patients' usage of their oral analgesic medication.

Finally, the overall evaluation of the 4 treatment modalities indicated that PENS was the preferred therapy in 91% of the study patients (TABLE 2). In addition, PENS was reportedly more effective than TENS and exercise therapies in improving the patients' physical activity and sense of well-being. More than 80% of the patients indicated that they would be willing to pay extra money (out-of-pocket) to receive PENS therapy in the future.

COMMENT

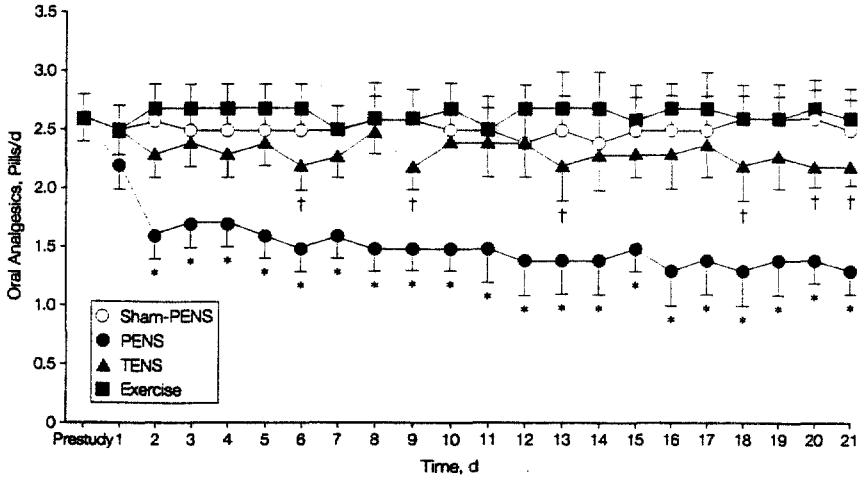
This crossover, sham-controlled study demonstrated that PENS was more effective than TENS and exercise therapies in providing short-term relief of pain and in improving function in patients with stable LBP of at least 3 months' duration. PENS was also significantly more effective than TENS and exercise therapies in reducing the need for oral analgesic medications. These findings are consistent with earlier studies by Deyo et al[19] and Marchand et al,[20] suggesting that TENS therapy is only marginally more effective than a placebo treatment (eg, sham-PENS) in this patient population. Of interest, Moore and Shurman[21] reported that combined neuromuscular electrical stimulation with TENS was significantly more effective than TENS alone in the management of long-term back pain.

PENS therapy was also highly effective in producing acute analgesia in this LBP population. More importantly, the patients began to report more sustained beneficial effects on their level of pain and physical activity, as well as their quality of sleep, after 3 to 4 PENS treatments. Due to the apparent cumulative effects of PENS over the course of the 3-week treatment period, these data would suggest that the use of this treatment modality over a longer period of time has the potential to produce prolonged beneficial effects in patients with long-term LBP. However, a more prolonged period of PENS therapy with careful follow-up at 3-, 6-, and 12-month intervals would be required to assess the long-term effects of this novel therapeutic modality in improving patient outcome.

Enhanced physical activity may be the most important outcome variable in the treatment of LBP.[19,22,23] To achieve the maximal benefit from nonpharmacologic (so-called complementary) analgesic therapies such as PENS, it is recommended that PENS be used as part of a multimodality rehabilitation program, which also includes an ongoing exercise program. Although the simple spine flexion-extension exercise used in this investigation failed to produce a significant improvement in patient well-being when administered alone, this may be a reflection of the lack of effectiveness of this particular exercise maneuver or an inadequate period of exercising. In contrast to our findings, other investigators have found a more extensive exercise program to be as effective as TENS in reducing pain scores and disability in workers with acute LBP.[24] Future studies need to evaluate the effectiveness of PENS therapy in combination with a comprehensive exercise program.

The results of the SF-36 psychological assessments further support and strengthen the clinical findings by providing additional outcome measures, which demonstrates the superiority of PENS over the other

Figure 3. Effect of Sham-PENS, TENS, and Exercise Therapies on the Daily Oral Analgesic Requirements



Change in the daily oral intake of nonopioid analgesic medications during the 3-week treatment period with each of the 4 study modalities. Values are mean (SEM). Asterisk indicates value is significantly different from prestudy value ($P<.008$) and from sham–percutaneous electrical nerve stimulation (PENS), transcutaneous electrical nerve stimulation (TENS), and exercise therapy values ($P<.03$). Dagger indicates value is significantly different from prestudy value ($P<.04$).

Table 2. Overall Patient Evaluation of the Relative Effectiveness of Sham-PENS, PENS, TENS, and Exercise Therapies After Receiving all 4 Treatment Modalities*

Result	Sham-PENS	PENS	TENS	Exercise
Most desirable modality	1 (2)	55 (91)†	4 (7)	0 (0)
Improved physical activity	2 (4)	31 (51)†	5 (8)	0 (0)
Improved sense of well-being	7 (12)	46 (76)†	10 (16)	6 (10)
Preferred pain therapy	1 (2)	55 (91)†	4 (7)	0 (0)
Willing to pay extra for therapy	4 (6)	49 (81)†	5 (9)	2 (4)

*PENS indicates percutaneous electrical nerve stimulation; TENS, transcutaneous electrical nerve stimulation. Values are expressed as number (percentage) of patients.
†Significantly different from sham-PENS, TENS, and exercise therapies, $P<.02$.

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nonpharmacologic treatments used in this study. These data suggest that PENS therapy was the most beneficial modality in improving the physical (eg, fewer limitations in self-care, less severe body pain) and mental (eg, less psychological distress, less disability due to emotional problems) health and well-being of these patients with long-term LBP.

The nature of the electrical (tapping) sensations precluded our ability to perform the treatments in a double-blind fashion. In an attempt to minimize investigator bias, all patient assessments were performed by individuals not involved in administering the therapies. To avoid prejudicing patients in favor of PENS therapy, the sham treatment was described to the patients as an acupuncturelike therapy. Since the needles for the sham-PENS treatments were placed in a dermatomal montage rather than at specific acupoints, it would be inappropriate to conclude that classic Chinese acupuncture is of no benefit in this patient population.

Another potential criticism of the study design relates to the selection of a low-stimulus frequency (4 Hz) for 30-minute intervals for both the PENS and TENS treatments. However, Walsh et al[25] reported that the hypoalgesic effect of TENS was more effective at 4 Hz than 110 Hz. Other investigators have found that more prolonged periods of stimulation (>40 minutes) may be associated with the development of tolerance to the analgesic effect of the electrical stimulus.[26]

Future studies are clearly needed to determine the relative effectiveness of different frequencies and durations of electrical stimulation with PENS therapy. Preliminary experience with PENS in other patient populations suggests that an improved analgesic response may be achieved by using higher (50-100 Hz) or mixed (15 Hz and 30 Hz) stimulating frequencies at subsequent treatment sessions.[13,14] Similarly, this dermatomal montage was selected as a starting point for PENS therapy because it was found to be highly effective in this patient population during our pilot studies. However, depending on the associated manifestations of the pain (eg, radiation down the leg), other needle locations may prove to be more effective for subsequent PENS treatments.

Since long-term LBP is extremely costly to society and can have debilitating effects on both patients and their families, this patient population is increasingly turning to unconventional alternative medical practices (including various forms of nonpharmacologic analgesic therapies).[27] In determining the cost benefit of any new analgesic therapy, it is important to carefully consider both the pertinent costs (eg, equipment, disposables, personnel requirements) and the consequences or outcome of the treatment (eg, patient satisfaction, quality of life, resumption of normal activities) in monetary terms.[28] Future studies should be designed to examine the cost benefit of using PENS therapy as part of a multimodal approach, which would also include anti-inflammatory analgesic drugs and a low back exercise program.

In conclusion, this sham-controlled study demonstrated that PENS is more effective in improving short-term outcomes than TENS and exercise therapies in patients with long-term LBP. The use of PENS therapy significantly decreased the need for oral nonopioid analgesic medications in this patient population.

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The Effect of Stimulus Frequency on the Analgesic Response to Percutaneous Electrical Nerve Stimulation in Patients with Chronic Low Back Pain

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Low back pain (LBP) is one of the most common medical problems in our society. Increasingly, patients are turning to nonpharmacologic analgesic therapies such as percutaneous electrical nerve stimulation (PENS). We designed this sham-controlled study to compare the effect of three different frequencies of electrical stimulation on the analgesic response to PENS therapy. Sixty-eight consenting patients with LBP secondary to degenerative lumbar disc disease were treated with PENS therapy at 4 Hz, alternating 15 Hz and 30 Hz (15/30 Hz), and 100 Hz, as well as sham-PENS (0 Hz), according to a randomized, cross-over study design. Each treatment was administered for a period of 30 min three times per week for 2 wk. The pre- and posttreatment assessments included the health status survey short form and visual analog scales for pain, physical activity, and quality of sleep. After receiving all four treatments, patients completed a global assessment questionnaire. The sham-PENS treatments failed to produce changes in the degree of pain, physical activity, sleep quality, or daily intake of oral analgesic medications. In contrast, 4-Hz, 15/30-Hz, and 100-Hz stimulation all produced significant decreases in the severity of pain, increases in physical activity, improvements in the quality of sleep, and decreases in oral analgesic requirements ($P < 0.01$). Of the three frequencies, 15/30 Hz was the most effective in decreasing pain, increasing physical activity, and improving the quality of sleep ($P < 0.05$). In the global assessment, 40% of the patients reported that 15/30 Hz was the most desirable therapy, and it was also more effective in improving the patient's sense of well-being. We conclude that the frequency of electrical stimulation is an important determinant of the analgesic response to PENS therapy. Alternating stimulation at 15-Hz and 30-Hz frequencies was more effective than either 4 Hz or 100 Hz in improving outcome measures in patients with LBP. **Implications:** The frequency of electrical stimulation seems to be an important determinant of the analgesic efficacy of percutaneous electrical nerve stimulation. Mixed low- and high-frequency stimulation was more effective than either low or high frequencies alone in the treatment of patients with low back pain.

(Anesth Analg 1999;88:841–6)

Low back pain (LBP) is second only to the common cold as a cause for primary care clinic visits (1–4), and it is the second most common cause of absence from work in adults <55 yr of age (5). The current therapies for LBP include physical therapy, epidural steroid injections, opioid and nonopioid analgesic medications, implantable spinal cord-stimulating devices, as well as various psychological and behavioral modification programs.

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Concerns regarding the efficacy and side effects associated with these treatment modalities have increased interest in nonpharmacologic neuromodulation therapies such as transcutaneous electrical nerve stimulation (TENS) (6), acupuncture (7,8), electroacupuncture (9), and percutaneous electrical nerve stimulation (PENS) (10–12). Unfortunately, most of the published studies involving the use of electrical stimulation devices have used arbitrarily chosen treatment variables.

Therefore, we designed a randomized, sham-controlled, cross-over study to evaluate the effect of stimulation frequency on the acute analgesic response to PENS therapy. The comparative effects of three different frequencies of stimulation (4 Hz, alternating

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15 Hz and 30 Hz, and 100 Hz) on pain scores, physical activity, quality of sleep, and the patient's sense of well-being were evaluated in patients with LBP.

Methods

After obtaining institutional review board approval and written informed consent, 68 patients (30 men and 38 women) with LBP associated with radiologically confirmed degenerative lumbar disc disease were enrolled in this randomized, sham-controlled, investigator-masked, cross-over study. Each patient was treated with sham-PENS (no electrical stimulation) and PENS at 4 Hz, alternating 15 Hz and 30 Hz (15/30 Hz) (a mixed frequency using both frequencies at each cycle with the stimulation pulses switched on and off every 3 s), and 100 Hz for a period of 30 min, three times per week for 2 consecutive wk in a random sequence (with 1 wk off between each treatment modality). Inclusion criteria included a history of LBP that has remained unchanged on a stable oral nonopioid analgesic regimen for a period of at least 3 mo before enrolling in the study. Exclusion criteria included LBP with a radicular component (sciatica), a history of drug or alcohol abuse, major organ disease, a change in the character or severity of the pain within the last 3 mo, and an inability to reliably complete the health status survey short form (SF-36), the daily assessment tools, or the global assessment questionnaire.

The basic therapy consists of the placement of ten 32-gauge (0.2 mm) stainless steel acupuncture-like needle probes (ITO, Tokyo, Japan) into the soft tissue and/or muscle in the low back region to a depth of 2–4 cm according to the dermatomal distribution of the pain as illustrated in Figure 1. The 10 probes were connected to five bipolar leads (with each lead connected to one positive and one negative probe) from an investigational (non-Food and Drug Administration-approved), low-output electrical generator, which was calibrated before each series of treatments. The maximal amplitude of the electrical stimulation produced by the generator was 25 mA, with a unipolar square-wave pattern and a pulse width of 0.5 ms. The electrical current was DC, and the duty cycle was continuous. These probes were then stimulated at one of four different frequencies: 0 Hz (sham), 4 Hz, 15/30 Hz, or 100 Hz. The intensity of the electrical stimulation was adjusted to produce the highest tolerable electrical sensation without muscle contractions (except for the sham treatments).

Before initiating the first of the four (frequency) treatment modalities, patients were required to complete the SF-36 (13). The physical component summary (PCS) and mental component summary (MCS) scores were used to assess the patient's response to each of the therapeutic modalities (14). The baseline level of pain, physical activity, and quality of sleep was evaluated before the first treatment with each

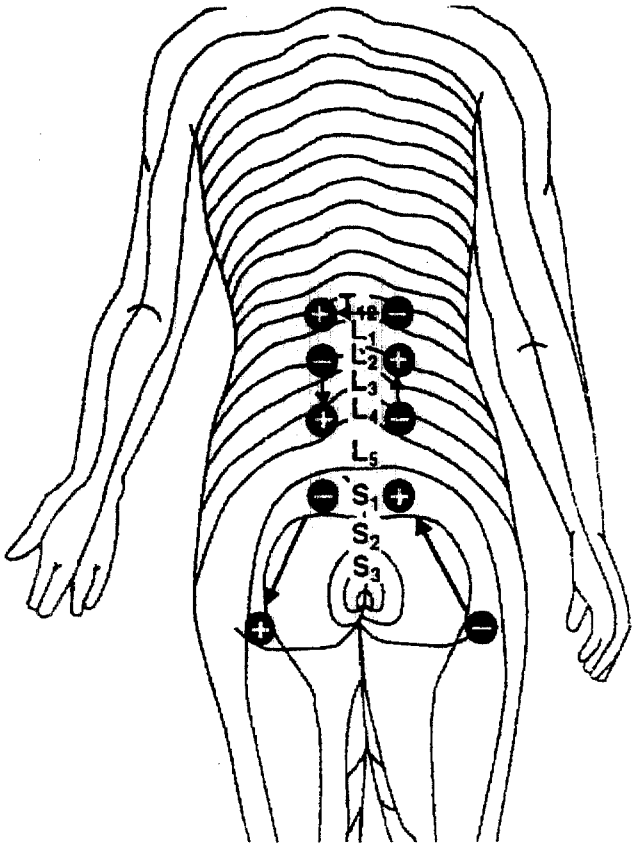


Figure 1. The location of the needle probes for the percutaneous electrical nerve stimulation (PENS) and sham-PENS treatments. With PENS therapy, each of the five bipolar leads from the low-output electrical generator was connected to a pair of needle probes, alternating the positive and negative positions as shown.

modality using standard 10-cm visual analog scales (VAS), with 0 = best to 10 = worst. Repeat VAS assessments of pain, activity, and sleep were performed three times per week before each treatment session. In addition, the pain VAS was repeated 5–10 min after each treatment session. The daily oral analgesic requirements (pills per day) were recorded in the patient's diary during each phase of the study. The SF-36 questionnaire was repeated after completing all six treatment sessions with each of the four frequency modalities. Finally, each patient completed a global assessment questionnaire comparing the relative effectiveness of the sham and the three stimulation frequencies 72 h after the final treatment session.

The NCSS software package (version 6.0.1; NCSS, Kaysville, UT) was used for all statistical analyses. An *a priori* power analysis with $\alpha = 0.05$, $\beta = 0.10$ (power 90%) and SD of 2.0 determined that a group size of 60 should be adequate to demonstrate a difference of 25% among the pain VAS scores for the four frequencies

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studied. The changes in the VAS scores were analyzed using repeated-measures analysis of variance and Student's *t*-test, with a Bonferroni correction applied for multiple comparisons. Analysis of discrete data was performed by using the χ^2 test. Changes and differences in the SF-36 scores were analyzed by using paired sample *t*-tests. Data are presented as mean values ± SD, median values, and percentages. $P < 0.05$ was considered statistically significant.

Results

The prestudy SF-36 evaluation suggested that this LBP patient population (age 46 ± 21 yr) reported significantly lower health-related quality of life scores compared with the general population. The median prestudy scores were 29.8 and 41.4 for the PCS and MCS, respectively, compared with general population norms of 50 for these two variables. The posttreatment SF-36 test results revealed that the 4-Hz, 15/30-Hz, and 100-Hz frequencies produced significant improvements over the prestudy scores for both the PCS and the MCS components ($P < 0.01$). Moreover, the absolute (mean) magnitude of the changes in PCS and MCS components at the end of each treatment period were similar with 4 Hz (7.0 and 2.8, respectively), 15/30 Hz (7.3 and 3.2, respectively), and 100 Hz (7.1 and 3.1, respectively). In contrast, the sham treatments did not show any significant improvement in posttreatment functionality.

All three frequencies of electrical stimulation produced significant decreases in the pain scores immediately after each treatment (Table 1). Compared with the sham treatments, the 4-Hz, 15/30-Hz, and 100-Hz frequencies of PENS therapy also produced statistically greater decreases in the degree of pain and improved physical activity and sleep quality at the end of the 2-wk treatment period (Fig. 2). However, the overall percent changes in pain, physical activity, and quality of sleep scores were significantly greater after electrical stimulation at 15/30 Hz compared with 4 Hz or 100 Hz.

The daily requirements for nonopioid analgesic medications are summarized in Figure 3. Compared with baseline values 24 h before starting each frequency modality, the need for oral analgesic medications was significantly decreased over the course of the 2-wk treatment period with 4 Hz, 15/30 Hz, and 100 Hz, but not with the sham treatments. Moreover, the overall percent decrease in the oral analgesic requirements was greater with 15/30 Hz (48%) than with 4 Hz (35%) or 100 Hz (33%).

Finally, the global assessment of the four modalities indicated that 15/30 Hz was the therapy preferred by 40% of the patients, whereas 28%, 30%, and 2% favored the 4 Hz, 100 Hz, and sham treatments, respectively (Table 2). In addition, the 15/30-Hz treatments were significantly more effective in improving the patient's physical activity and sense of well-being compared with the 4-Hz, 100-Hz, and sham treatments. Given a hypothetical situation, patients indicated that they would be more willing to pay out-of-pocket for the PENS treatment when it was administered at a frequency of 15/30 Hz (versus the sham treatment).

Table 1. Comparison of the Effects of the Four Frequency (F) Modalities on the VAS Pain Scores

Treatment	Sham	F 4	F 15/30	F 100
1				
Pre	5.8 ± 1.5	6.4 ± 1.6	6.0 ± 1.7	5.7 ± 1.6
Post	5.6 ± 1.8	2.3 ± 1.2*	2.5 ± 1.3*	2.7 ± 1.5*
2				
Pre	5.9 ± 1.8	6.1 ± 1.7	5.4 ± 1.7	5.4 ± 1.8
Post	5.5 ± 1.6	2.1 ± 1.4*	2.3 ± 1.3*	2.5 ± 1.3*
3				
Pre	5.8 ± 1.7	5.9 ± 1.8	5.1 ± 2.0	5.1 ± 1.9
Post	5.7 ± 1.8	2.5 ± 1.2*	2.5 ± 1.4*	2.2 ± 1.5*
4				
Pre	5.6 ± 1.6	5.1 ± 1.5	4.9 ± 1.6	5.0 ± 1.7
Post	5.5 ± 1.9	1.8 ± 1.2*	1.7 ± 1.3*	1.7 ± 1.5*
5				
Pre	5.9 ± 1.7	4.9 ± 1.8	4.5 ± 1.9	4.7 ± 1.8
Post	5.8 ± 1.9	1.4 ± 1.4*	1.3 ± 1.3*	1.6 ± 1.3*
6				
Pre	5.7 ± 1.7	4.7 ± 1.6	4.0 ± 1.4	4.5 ± 1.5
Post	5.5 ± 1.8	1.2 ± 1.2*	1.1 ± 1.4*	1.2 ± 1.5*

Values are mean ± SD.
VAS = visual analog scale, with 0 = no pain to 10 = worst pain imaginable.
* Significantly different from values before (pre) each treatment session ($P < 0.01$).

Discussion

Analogous to previously reported findings in animals with electroacupuncture (15), these data suggest that the frequency of electrical stimulation influences the analgesic response to PENS therapy in patients with chronic LBP. Compared with low- (4 Hz) and high- (100 Hz) frequency stimulation, a mixed pattern (15/30 Hz) of electrical stimulation produced the greatest decrease in pain and improvement in physical activity and quality of sleep at the end of a 2-wk treatment period.

Using a rat model for studying electroacupuncture, Chen et al. (15) reported that the dense-disperse mode of electrical stimulation (alternating 2 Hz and 15 Hz) was more effective than a fixed frequency of stimulation at either 2 Hz or 100 Hz in producing experimental analgesia. According to Sun and Han (16), the enhanced analgesia produced by alternating frequencies results from the differing effects of the frequency of stimulation on the pattern of neurotransmitter release within the central nervous system (CNS). At

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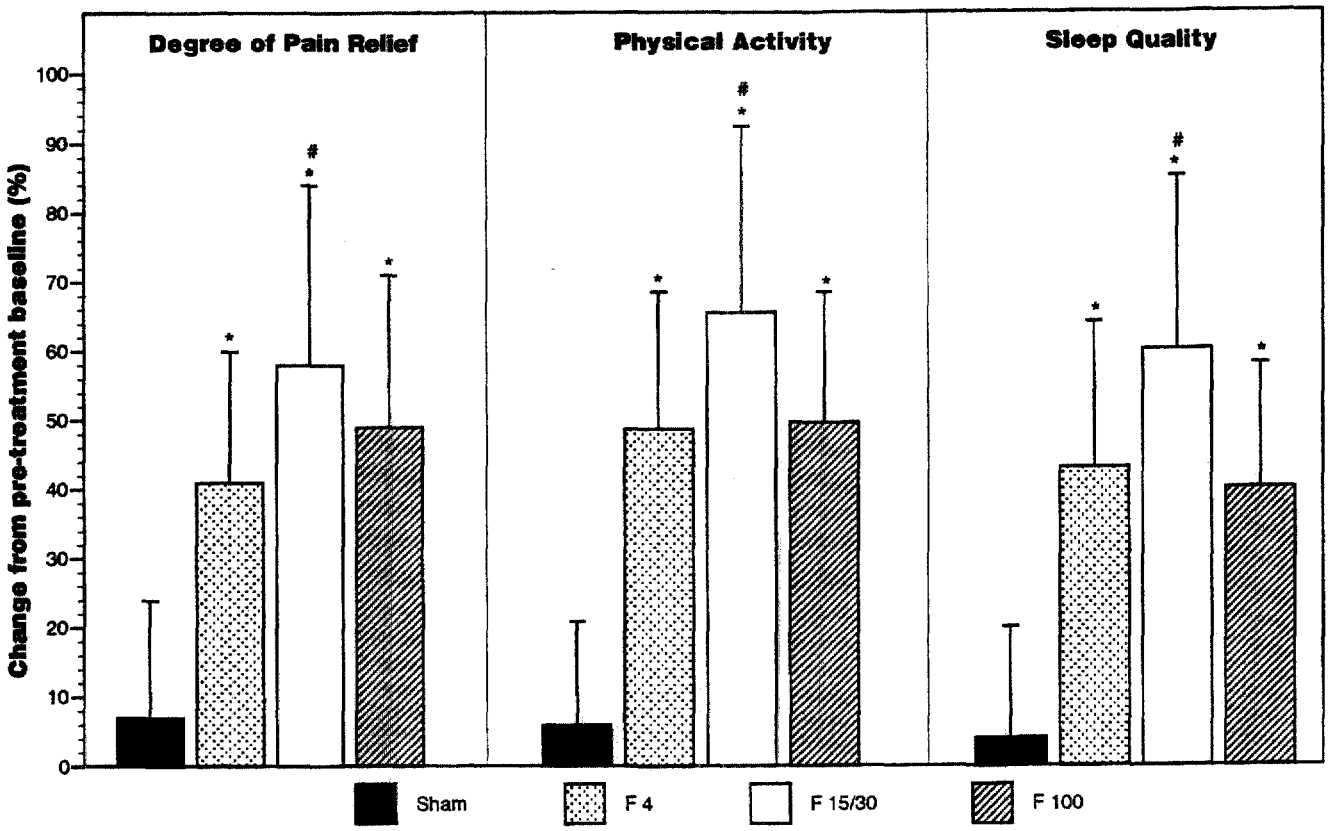


Figure 2. Comparison of the percent changes from baseline value (24 h before the first treatment session with each modality) in the degree of pain relief, physical activity, and sleep quality at the end of each 2-wk treatment period. Data are mean values ± SD. * $P < 0.05$ compared with the sham-percutaneous electrical nerve stimulation values. # $P < 0.05$ compared with F4 and F100 values.

2 Hz, analgesia was alleged to be mediated by stimulation of μ and δ opioid receptors, whereas, at 100 Hz, analgesia was reportedly mediated by activation of κ opioid receptors in the CNS (16).

In studying the effect of the frequency of electroacupuncture stimulation on the release of substance P in the spinal cord, Chen et al. (17) also found that 15 Hz was more effective than either lower (2, 4, or 8 Hz) or higher (30 or 100 Hz) frequencies of electrical stimulation. Analogous to the findings of Sun and Han (16), Goldstein and Naidu (18) also reported that high-frequency (100 Hz) electroacupuncture-induced analgesia was mediated by the activation of κ opioid receptors, whereas low-frequency stimulation (2 Hz) activated μ and δ opioid receptors. One might speculate that using a combination of intermediate frequencies (e.g., alternating 15 Hz and 30 Hz) would activate both subtypes of opioid receptors. However, opioid receptor binding studies would have to be performed to determine the pattern of opioid receptor activation that occur when mixed frequencies of electrical stimulation are used to produce electroanalgesia in humans.

Controversy still surrounds the optimal frequency of electrical stimulation for TENS therapy (19). For example, Walsh et al. (20) reported that a low frequency (4 Hz) of stimulation had a greater hypoalgesic effect than high-frequency (100 Hz) stimulation using an experimental pain model. However, Johnson et al. (21) reported that using high-frequency stimulation (20–80 Hz) produced greater analgesic effects than low-frequency stimulation (10 Hz). Consistent with our findings using PENS therapy, Hansson and Ekblom (22) reported significant pain relief at both high and low frequencies of electrical stimulation. In a recent TENS study, Hamza et al. (23) found that mixed-frequency electrical stimulation at 2 and 100 Hz produced greater postoperative analgesic-sparing effects than either 2 Hz or 100 Hz alone. Thus, it seems that both PENS and TENS therapies are most effective when administered using mixed frequencies of electrical stimulation.

The deficiencies in the current study design relate to an inability to effectively blind the patients, although a sham treatment was included because of the unique nature of the electrical sensation produced by the active PENS treatments. In an attempt to minimize investigator bias, all patient assessments were performed by one of the investigators not involved in actually administrating the PENS therapy. To avoid

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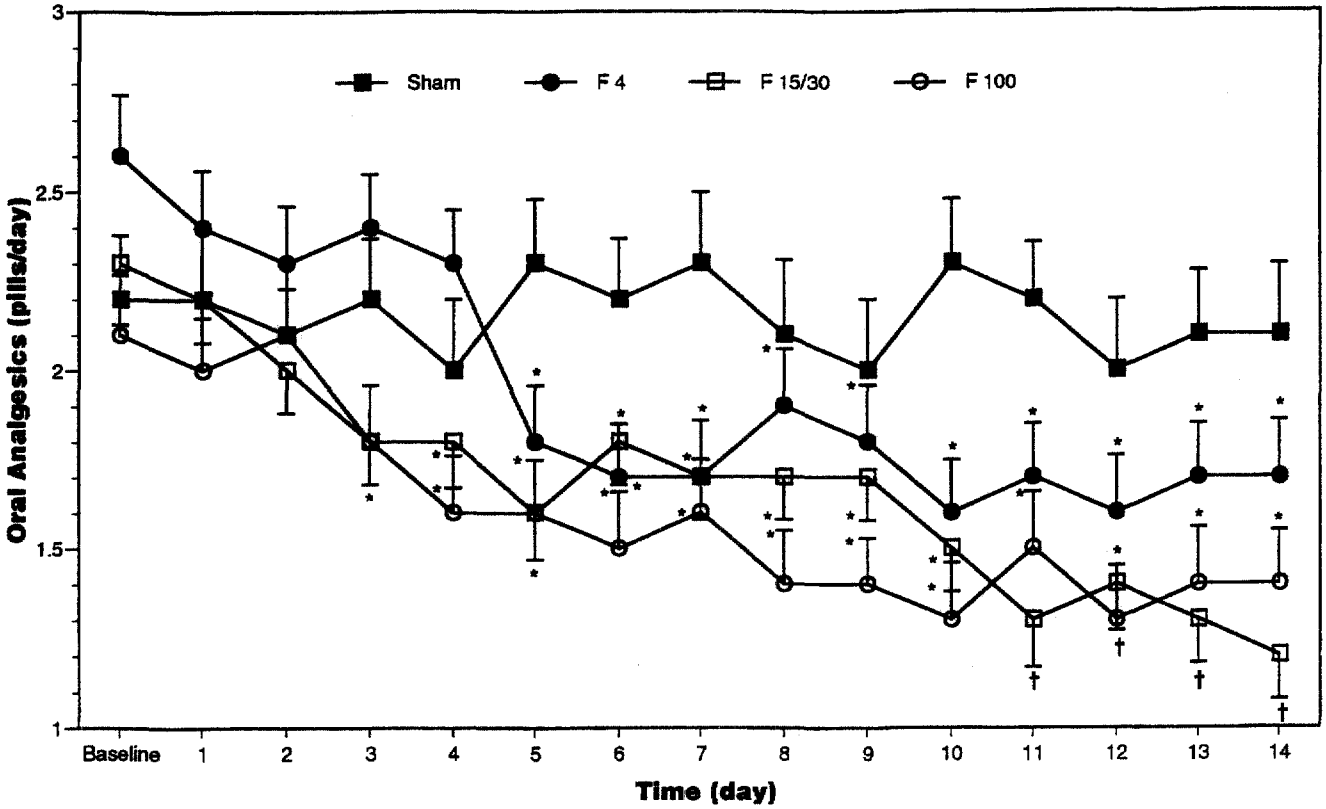


Figure 3. Changes in the daily oral intake of nonopioid analgesic medications (pills per day) during the 2-wk treatment period with each of the four frequency modalities. Data are mean values ± SEM. * $P < 0.05$ and † $P < 0.01$ compared with values 24 h before the first treatment (baseline).

Table 2. Overall Patient Evaluation of the Relative Effectiveness of the Three Different Frequencies (F) and Sham Therapies After All Six Treatment Sessions with Each Modality

	Sham	F 4	F 15/30	F 100
Most desirable modality	2	28*	40*†‡	30*
Improved physical activity	3	30*	38*†‡	29*
Improved sense of well-being	5	23*	44*†‡	28*
Preferred pain therapy	2	28*	40*†‡	30*
Willing to pay extra for therapy	3	25*	45*†‡	27*

Values are expressed as percentages.
* Significantly different from the sham treatments ($P < 0.05$).
† Significantly different from the F4 treatments ($P < 0.05$).
‡ Significantly different from the F100 treatments ($P < 0.05$).

prejudicing patients in favor of the active PENS treatments, the sham treatment was described to the patients as "acupuncture-like" therapy. Because the needles for the sham-PENS treatments were placed in the same dermatomal montage used for the PENS therapy, rather than at specific acupoints, it would be inappropriate to conclude that classic Chinese acupuncture is of no benefit based on these findings. In addition, the use of alternating 15-Hz and 30-Hz frequencies (rather than alternating 4 Hz and 100 Hz) may be a limitation because of the limitations of the electrical generator used in this study. The study was designed to cover the widest possible frequency range (4–100 Hz), but the stimulating device was not able to combine these frequencies when used in the alternating stimulation mode. In a future study, it would be of interest to compare 15-Hz and 30-Hz frequencies of electrical stimulation alone with an alternating 15/30-Hz pattern.

Given the interest of both patients and healthcare providers in unconventional (or so-called complementary) medical therapies (24,25), it is not surprising that nonpharmacologic electroanalgesic therapies (e.g., PENS, electroacupuncture) are increasing in popularity. Future studies in patients with LBP should focus on the effects of these nontraditional modalities on long-term outcome measures (e.g., chronic analgesic use, return to work) when used to supplement conventional analgesic medications and physical therapy as part of a multimodal treatment program (26).

In conclusion, using a mixed frequency (alternating 15 Hz and 30 Hz) of PENS was more effective than either low (4 Hz) or high (100 Hz) frequencies alone in improving short-term outcome measures in patients with LBP.

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Effect of the Duration of Electrical Stimulation on the Analgesic Response in Patients with Low Back Pain

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Background: **Electrical stimulation of peripheral nerves produces acute analgesic effects. This randomized, sham-controlled, crossover study was designed to evaluate the effect of differing durations of electrical stimulation on the analgesic response to percutaneous electrical nerve stimulation in 75 consenting patients with low back pain.**

Methods: **All patients received electrical stimulation for four different time intervals (0, 15, 30, and 45 min) in a random sequence over the course of an 11-week study period. All active percutaneous electrical nerve stimulation treatments were administered using alternating frequencies of 15 and 30 Hz three times per week for 2 consecutive weeks. The prestudy assessments included the health status survey short form questionnaire and 10-cm visual analog scale scores for pain, physical activity, and quality of sleep, with 0 being the best and 10 being the worst. The pain scoring was repeated 5–10 min after each 60-min study session and 24 h after the last treatment session with each of the four methods. The daily oral analgesic requirements were assessed during each of the four treatment blocks. At the end of each 2-week treatment block, the questionnaire was repeated.**

Results: **Electrical stimulation using percutaneously placed needles produced short-term improvements in the visual analog scale pain, physical activity, and quality of sleep scores, and a reduction in the oral analgesic requirements. The 30-min and 45-min durations of electrical stimulation produced similar hypoalgesic effects (48 ± 21% and 46 ± 19%, respectively) and were significantly more effective than either 15 min (21 ± 17%) or 0 min (10 ± 11%). The 30- and 45-min treatments were also more effective in improving physical activity and sleep scores over the course of the 2-week treatment period. In contrast to the sham treatment (0 min), the health status survey short form revealed that electrical stimulation for 15 to 45 min three times per week for 2 weeks improved patient function.**

Conclusion: **The recommended duration of electrical stimulation with percutaneous electrical nerve stimulation therapy is 30 min. (Key words: Electroanalgesia; lumbago; stimulation interval.)**

THERAPIES for low back pain (LBP) include physical therapy, epidural steroid injections, opioid and nonopioid analgesic medications, implantable spinal cord–stimulating devices, and various psychologic and behavioral modification programs. Although these therapeutic methods may be effective for patients with acute LBP,[1] they are unsatisfactory for many patients with chronic LBP. If pain symptoms persist, the use of pharmacologic therapy can interfere with physical activity and sleep patterns and produce unwanted side effects.[2] These concerns have increased interest in nonpharmacologic therapies for LBP, including transcutaneous electrical nerve stimulation (TENS),[3] acupuncture,[4] electroacupuncture,[5] and percutaneous electrical nerve stimulation (PENS).[6–8]

Percutaneous electrical nerve stimulation is a novel, nonpharmacologic analgesic therapy that combines the advantages of transcutaneous electrical nerve stimulation (*i.e.*, peripheral dermatomal-based electrical nerve stimulation) and electroacupuncture (*i.e.*, electrical stimulation at specific acupoints *via* percutaneously placed needles). This therapy involves the placement of acupuncture needle probes in the soft tissues or muscles to stimulate peripheral sensory nerves at the dermatomal (or sclerotomal) levels corresponding to the local dis-

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ease. The effect of the duration of the electrical stimulation on the short-term analgesic response to PENS therapy has not been studied previously.

Therefore, we designed a randomized, single-blind, crossover study to evaluate the analgesic effectiveness of different durations of electrical stimulation of PENS therapy in patients with LBP. In addition, the comparative effects of the different durations of stimulation on the patients' levels of physical activity and quality of sleep, as well as daily oral analgesic requirements, were assessed over each 2-week treatment interval.

Materials and Methods

After obtaining local institutional review board approval and written informed consent, 75 patients (34 men and 41 women, ranging between 21 and 76 yr of age) with LBP secondary to radiologically confirmed degenerative lumbar disk disease received electrical stimulation *via* acupuncture needle probes for periods of 0, 15, 30, and 45 min, according to a randomized, single-blind, crossover study design. Inclusion criteria included age older than 18 yr and a history of LBP related to degenerative lumbar disk disease with a pain level that remained unchanged over a period of at least 3 months before enrolling in the study. Forty-two percent of the study patients had undergone previous back surgery. Exclusion criteria included LBP with a radicular component (sciatica), a history of drug or alcohol abuse, previous experience with acupuncture, a change in the character or severity of the pain within the last 3 months, a recent change in analgesic medications (or current use of opioid-containing drugs), and the inability to reliably complete the health status survey short form (SF-36),[9] daily assessment tools, or the global assessment questionnaire.

All patients were told that each treatment session would last for 60 min, with varying periods of electrical stimulation (producing either no sensation or a light tapping sensation), three times per week (on Monday, Wednesday, and Friday afternoons) for 2 consecutive weeks, with 1 week "off" before each treatment modality. Patients were exposed to all four stimulation intervals in a random sequence over the course of the 11-week study period.

Treatment Methods

Ten 32-gauge stainless steel acupuncture needle probes (ITO, Tokyo, Japan) were placed into the soft tissue or muscle to a depth of 2–4 cm in the low back region according to the dermatomal (or sclerotomal) distribution of the pain for a period of 60 min, as shown in figure 1. The 10 probes were connected to five bipolar leads (with each lead connected to one positive and one negative probe) from an investigational low-output electrical generator and stimulated for a period of 0, 15, 30, or 45 min at an alternating frequency of 15 and 30 Hz.[10] The intensity of the electrical stimulation was adjusted to produce a tolerable tapping sensation without muscle contractions. The maximum amplitude of the electrical stimulation produced by the generator was 25 mA using a unipolar square-wave pattern and a pulse width of 0.5 ms. The electrical current was direct and the duty cycle was continuous.

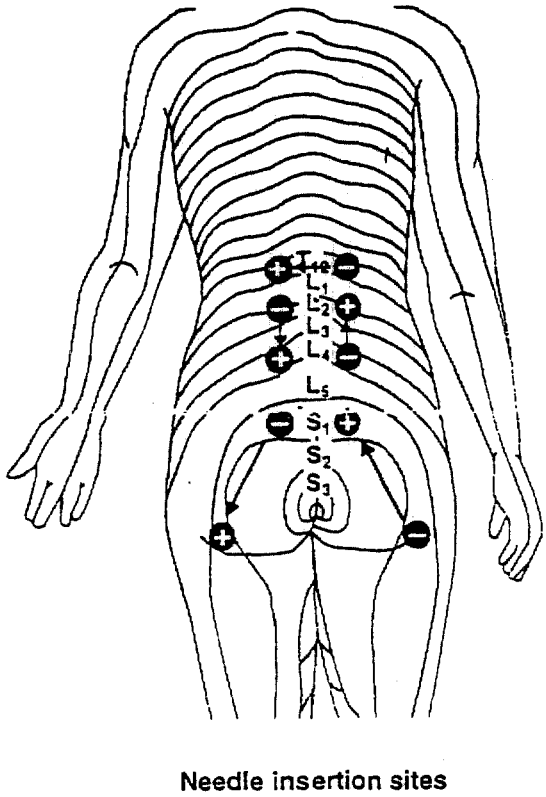


Fig. 1. The location of the needle probes for the percutaneous electrical nerve stimulation and nonelectrical ("sham") needle treatments. Each of the five bipolar leads are connected to a pair of needles, alternating the positive (+) and negative (-) connections as shown in the illustration.

Assessment Procedures

Before initiating any of the four treatments, patients were required to complete the SF-36 questionnaire.[9] The physical component summary and mental component summary scores of the SF-36 were used to assess patient

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response to each of the different stimulation intervals.[11] All patients were also asked to assess their level of LBP, physical activity, and quality of sleep during the 24-h interval before the first treatment and after the last (sixth) treatment for each of the four different timing intervals, using three separate 10-cm visual analog scales (VAS), with 0 being the best and 10 being the worst score. Subsequent VAS assessments of the degree of pain, physical activity, and quality of sleep were performed three times per week before each treatment session. In addition, the pain VAS assessment was repeated 5–10 min after completion of each treatment session to determine the acute analgesic response to the therapy. Patients were instructed to record in their diaries (which were checked by the investigators at each clinic visit) the number of oral nonopioid analgesic pills they used each day. The SF-36 questionnaire was again filled out after completing all six treatment sessions with each of the four stimulation intervals.

Data Analysis

The Number Cruncher Statistical System (NCSS) software package (NCSS 6.0.1 statistical system for Windows; NCSS, Kaysville, UT) was used for all statistical analysis. An *a priori* power analysis with $\alpha = 0.05$, $\beta = 0.10$ (power = 90%), and standard deviations of 2.0 and 1.5 determined that a group size of 75 should be adequate to show differences of 20 and 10% between the VAS scores and the daily oral analgesic requirements (pills per day), respectively, for the four treatment intervals studied. The changes in the VAS scores and daily oral analgesic medication usage were analyzed using repeated measures analysis of variance (ANOVA) and the Student *t* test. Changes and differences in the SF-36 scores were analyzed by paired *t* tests. Data are presented as mean values (± SD for tables and ± SEM for figures) and percentages, with $P < 0.05$ considered significant.

Results

Seventy-five patients with a mean age of 47 ± 18 yr, a mean baseline VAS pain score of 7.4 ± 2.2, and a mean duration of pain of 38 ± 13 months, were enrolled in this study. The prestudy SF-36 evaluation suggested that this LBP population reported significantly lower health-related "quality-of-life" scores compared with the general population. The mean prestudy scores were 32.7 ± 7.6 and 41.8 ± 5.9 for the physical and mental component summaries, respectively, compared with general population norms of 50 for these two variables. The post-treatment SF-36 test results revealed that electrical stimulation for 15 to 45 min produced significant improvements compared with the sham (0 min) treatments with respect to the physical and the mental components of the survey ($P < 0.01$ for 15 min and $P < 0.001$ for 30- and 45-min stimulation intervals). However, the absolute mean magnitude of the changes in physical and mental components with the 30-min (+7.4 and +3.1, respectively) and 45-min (+7.1 and +2.9, respectively) stimulation intervals were significantly greater than with the 15-min stimulation interval (+5.4 and +2.1, respectively; $P < 0.01$). Although the improvements after the 30-min interval were greater than those after the 45-min interval, the differences were not statistically significant.

Table 1. Comparison of the Acute Analgesic Effects of the Four Stimulation Intervals on the VAS Pain Scores Immediately before (Pre) and After (Post) Each Treatment Session

Treatment Number	0 min	15 min	30 min	45 min
1 Pre	6.2 ± 1.9	6.8 ± 1.7	6.4 ± 1.9	6.3 ± 1.9
Post	5.8 ± 1.7	5.9 ± 1.9	3.9 ± 1.8†	3.8 ± 1.8†
2 Pre	6.3 ± 1.7	6.2 ± 1.7	5.8 ± 1.8	5.9 ± 1.8
Post	5.8 ± 1.9	4.9 ± 1.8*	3.1 ± 1.7†	3.2 ± 1.7†
3 Pre	6.1 ± 1.8	5.5 ± 2.0	5.4 ± 1.9	5.4 ± 1.7
Post	5.7 ± 2.1	3.8 ± 1.8*	2.9 ± 1.7†	2.9 ± 2.0†
4 Pre	6.2 ± 1.9	4.9 ± 1.6	4.6 ± 2.2	4.9 ± 1.6
Post	5.6 ± 1.9	3.0 ± 2.0*	2.2 ± 1.8†	2.3 ± 1.9†
5 Pre	6.1 ± 2.2	4.3 ± 1.9	4.5 ± 1.8	4.2 ± 1.8
Post	5.5 ± 1.5	2.7 ± 1.7*	2.0 ± 1.7†	1.9 ± 1.6†
6 Pre	6.0 ± 1.6	3.8 ± 1.9	4.5 ± 2.1	4.6 ± 1.5
Post	5.4 ± 1.9	2.0 ± 1.7*	1.6 ± 1.8†	1.5 ± 1.4†

Values are mean ± SD.

VAS = Visual analog scale: 0 = the best to 10 = the worst.

* Significantly different from values before (pre) each treatment session ($P < 0.05$).

† Significantly different from values before (pre) each treatment session ($P < 0.01$).

Electrical stimulation produced significant decreases in pain scores immediately after each treatment, with $P < 0.05$ for the 15-min and $P < 0.01$ for the 30- and 45-min stimulation intervals (table 1). Compared with the values 24 h after the completion of the sixth treatment with each method, mean (overall) percentage changes in the degree of pain, physical activity, and quality of sleep from the baseline values 24 h before starting each treatment block were statistically significant for the 15-min interval ($P < 0.05$) and the 30- and 45-min stimulation

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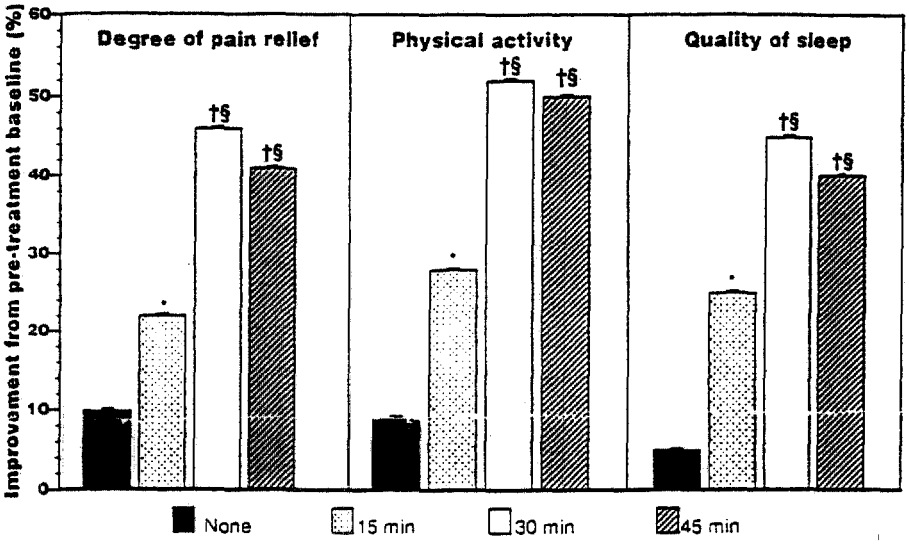


Fig. 2. Comparison of the percentage improvements from the baseline (24 h before and after the first treatment session with each method) in the degree of pain, physical activity, and sleep quality at the end of each 2-week treatment period. Data are mean values ± SEM. Significant differences compared with nonelectrical needle therapy values are designated as follows: *$P < 0.05$; †$P < 0.01$. Significant differences compared with 15-min values are designated by §$P < 0.05$.

intervals ($P < 0.01$) (fig. 2). In addition, there were significant differences between the 30- and 45-min treatment intervals compared with the 15-min treatment interval.

The daily requirements for oral nonopioid analgesic medications (pills per day) are summarized in figure 3. Compared with baseline values, the need for oral analgesic medications was decreased by an average of 8 ± 11%, 21 ± 13 %, 38 ± 16%, and 35 ± 17% over the course of the 2-week treatment period for the 0-, 15-, 30-, and 45-min stimulation intervals, respectively. Compared with no electrical stimulation, it was found that a 15-min stimulation interval ($P < 0.05$) and both the 30- and the 45-min stimulation intervals ($P < 0.01$) were more effective in decreasing the daily oral analgesic requirements. Moreover, the overall decrease in the daily oral analgesic requirements was greater with the 30- and 45-min (*vs.* 15-min) stimulation intervals ($P < 0.05$).

Discussion

Preliminary studies with PENS therapy showed that this therapy produces short-term benefits in patients with chronic LBP secondary to osteoarthritis[6] and degenerative disk disease,[8] and acute herpes zoster pain.[7] This crossover study showed that the duration of electrical stimulation with PENS therapy influences the degree of

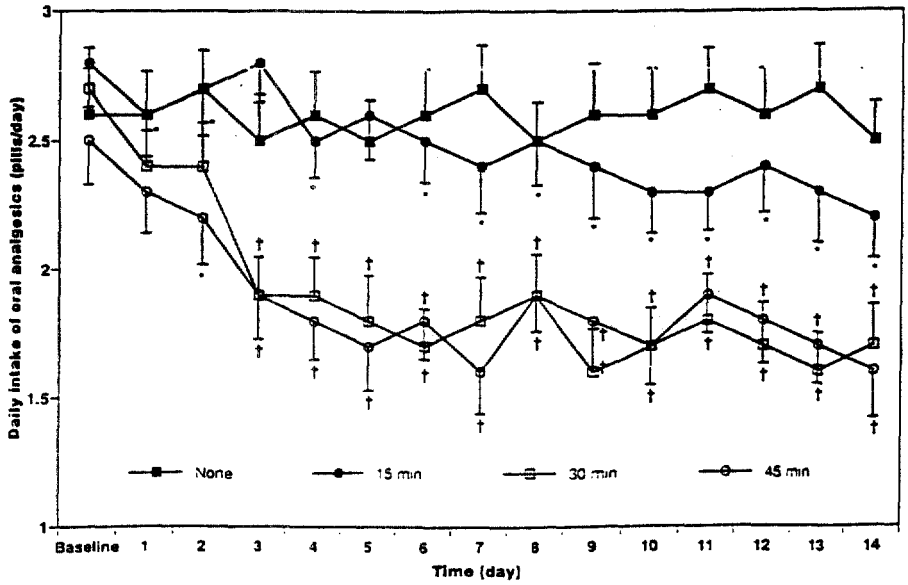


Fig. 3. Changes in the daily oral intake of nonopioid analgesic medications (pills per day) during the 2-week treatment period with each of the four methods. Data are mean values ± SEM. Significant changes from the values 24 h before the first treatment (baseline) are indicated as follows: *$P < 0.05$; †$P < 0.01$.

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acute pain relief and the improvement in function over a 2-week treatment period. Although there were no significant differences between the 30- and 45-min durations of electrical stimulation, both intervals were more effective than the 15-min interval and the no-electrical-stimulation ("sham") treatments. These data suggest that the recommended duration of electrical stimulation for PENS therapy should be 30 min because no additional benefit was achieved with a longer stimulation interval.

These findings are consistent with a study by Romita *et al.*[12] in rodents. Using a rat model to study electroacupuncture-induced analgesia, these investigators found that electrical stimulation for a period of 20 min elicited a greater and longer lasting antinociceptive effect than 10- or 40-min intervals of stimulation. Moreover, a study by Chung *et al.*[13] showed that a 5-min train of electrical stimulation elicited a poststimulation inhibition of spinothalamic tract cells lasting less than 2 min. If the same stimulus was maintained for 15 min, these investigators reported, the inhibition persisted for up to 30 min.[14] These data suggest that more prolonged stimulation may allow summation of central mechanisms, thereby producing a more persistent analgesic effect. However, with continuous electroacupuncture the evoked antinociceptive effect appears to gradually decrease as a function of the time of stimulation.[15] Although short-term electroacupuncture stimulation produces marked analgesic effects, prolonged electroacupuncture stimulation appears to result in the development of tolerance.[16] Other investigators also have reported that prolonged periods of electrical stimulation are associated with the development of tolerance to the electroanalgesic effect.[17]

It has been proposed that the accumulation of antiopioid substances within the central nervous system may account for the development of tolerance to electroacupuncture.[18,19] During prolonged electroacupuncture stimulation, release of endogenous opioids activates the cholecyctokinin octapeptide system, which can counteract the analgesia produced by endogenous opioid substances. Moreover, electroacupuncture appears to enhance the release of endogenous orphanin FQ[20] in the brain, which can also antagonize electroacupuncture-induced analgesia. Therefore, orphanin FQ may play an important role in the development of tolerance to the analgesic effects of electrical stimulation.

In electroacupuncture studies, the effects of the duration of electrical stimulation on the analgesic response also have been reported to be highly variable. For example, it was found that 30 min of stimulation produced hypoalgesic effects lasting several hours,[21-23] whereas a 40-min period of stimulation produced analgesia lasting for only 30 min.[24] If the electrical stimulation was applied for 75 min, the duration of analgesia lasted for only 15 min[24,25] Consistent with these electroacupuncture studies, our data suggest that 30 min is the optimal stimulation interval for PENS therapy. The results of the SF-36 assessment further support this clinical finding by providing an additional outcome measure that shows the superiority of the 30-min electrical stimulation interval (*vs.* intervals ≤ 15 min). These data revealed that if PENS therapy was administered for 30 min at each treatment session, it was more effective in improving the physical (*e.g.*, fewer limitations in self-care, less severe body pains) and mental (*e.g.*, less psychologic distress, less disability resulting from emotional problems) health and well-being of patients with chronic LBP compared with shorter stimulation intervals.

The major limitations in the study design include (1) potential bias because of inability to "blind" the patient to the electrical stimulus, (2) the "placebo effect," resulting from placement of the needles, and (3) the failure to show a sustained analgesic effect after the PENS treatments, with the pain levels returning to baseline values within 1 week after discontinuing each method. Although the investigator collecting these data was blinded to the duration of the electrical stimulation, it was not possible to blind the patients. However, the patients were told that they "may or may not actually feel the stimulus" and they were not informed as to the duration of the electrical stimulation they received at each session. All treatment sessions lasted for 60 min. The placebo (analgesic) effect of the needles alone appeared to be very limited, consistent with previous studies involving PENS therapy.[8,10] Finally, the short-term analgesic effects of PENS are consistent with previous studies in this patient population.[8,10] Future studies need to evaluate the long-term effect of PENS therapy.

In conclusion, this study shows that the duration of electrical stimulation influences the short-term outcome with PENS therapy. Of the different durations of electrical stimulation studied, the 30-min interval appears to be the most suitable for this LBP patient population.

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The Effect of Montage on the Analgesic Response to Percutaneous Neuromodulation Therapy

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The analgesic response to percutaneous neuromodulation therapy (PNT) is influenced by the location, frequency, and duration of electrical stimulation. We evaluated the effect of different patterns of stimulation (montages) on the acute analgesic response to PNT when applied at the same dermatomal levels in 72 consenting patients with low back pain. All of the patients received a standardized montage (I) and three alternative montage (II–IV) patterns according to a randomized, single-blinded, crossover study design. All of the PNT treatments were administered at identical alternating stimulation frequencies of 15 and 30 Hz for a period of 30 min, three times per week for two consecutive weeks, with 1 wk "off" between each modality. Pretreatment assessments included the health status survey short form (SF-36) questionnaire, as well as visual analog scale scores for pain, physical activity, and quality of sleep (with 0 = the best to 10 = the worst). The pain visual analog scale was repeated 5–10 min after each treatment session. The daily oral analgesic usage was recorded in a patient diary. All four montages produced significant improvements in pain (42%–64%), physical activity (35%–51%), and quality of sleep (28%–46%), as well as 23% to 47% reductions in the daily oral analgesic usage. However, Montage II was significantly more effective than the standard (Montage I) and the other two montages studied. These data suggest that the pattern of stimulation (i.e., montage) can influence the acute analgesic response to PNT.

(Anesth Analg 2001;92:483–7)

Recent studies involving percutaneous neuromodulation therapy (PNT), formerly referred to as percutaneous electrical nerve stimulation, have demonstrated the analgesic efficacy of this therapy in the short-term management of low back pain (LBP), sciatica, headaches, and diabetic neuropathic pain (1–4). The response to PNT is influenced by the frequency of the electrical stimulus (5), as well as the duration (6) and location (7) of the percutaneously applied electrical stimulation. For example, the use of mixed stimulating frequencies alternating at 15 and 30 Hz (15/30) is more effective than either low- or high-frequency electrical stimulation alone (5), and the optimal duration of the electrical stimulation is determined to be 30–45 min (6). Furthermore, stimulation of the dermatomal levels corresponding to the patients' pain symptoms was more effective than stimulating nonrelated (remote) dermatomes (7). The effect of the specific pattern of electrical stimulation (i.e., montage) when administered at the same dermatomal levels has not been studied.

Therefore, we designed a randomized, single-blinded, cross-over study to test the hypothesis that the pattern of electrical stimulation influences the acute analgesic response to PNT when applied at the same dermatomal levels in patients with LBP. The short-term analgesic efficacy of three different PNT montages was compared with the standard montage used in previous studies (1,5,6). In addition, the comparative effects of the four different montages on the patients' physical activity, quality of sleep, and need for supplemental oral analgesic medication were assessed over the 11-wk study period.

Methods

After obtaining local IRB approval and written informed consent, 72 patients (31 men and 41 women ranging between 21 and 76 yr of age) with LBP of >6-mo duration, were treated with four different PNT montages according to a randomized, single-blinded, crossover study design. Inclusion criteria included age over 18 yr and radiologically confirmed degenerative lumbar spine disease, with a "stable" level of LBP and

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analgesic usage for at least 3 mo before entering the study. Exclusion criteria included LBP with a radicular component (sciatica), history of drug or alcohol abuse, change in the character or severity of the pain within the last 3 mo, recent change in analgesic medications, and inability to reliably complete the health status survey Short-Form (SF-36), or the daily assessment tools.

Each PNT treatment was administered for 30 min, three times per week (on Monday, Wednesday, and Friday afternoons) for 2 consecutive wk, with a 1 wk "washout" period between each treatment modality. All of the patients received the four different montages over the course of the 11-wk study period. Any missed treatment sessions were completed before switching to the next montage. Montage I (Fig. 1A) was used in our preliminary PNT studies, and this standard montage was compared with three other montages (II–IV) when applied at the same dermatomal levels (Fig. 1B–D). The basic PNT procedure consists of the placement of 10 32-gauge stainless steel acupuncture needles into the soft tissue and/or muscle in the low back region to a depth of 2–4 cm. The 10 needles used with all 4 montages were connected to 5 bipolar leads (with each lead connected to one positive and one negative probe) by using a low-output battery-powered generator. The maximal amplitude of the electrical stimulation produced by the generator was 37 mA with an asymmetric biphasic waveform pattern, a pulse width of 0.7 ms, and a continuous duty cycle. The intensity of the electrical stimulation was adjusted to produce the maximal tolerable "tapping" sensation without eliciting muscle contractions.

Before initiating any of the treatment modalities, the patients were required to complete the SF-36 (8). The physical component summary (PCS) and mental component summary (MCS) scores were used to assess the patient's psychological response to each of the different montages (9). All of the patients were asked to assess their level of LBP, physical activity, and quality of sleep during the 24-h interval before the first treatment session by using three separate 10-cm visual analog scales (VAS), with a response of 0 = the best to 10 = the worst. The VAS assessments of pain, physical activity, and quality of sleep were performed three times per week before each treatment session. In addition, the pain VAS was repeated 5–10 min after completion of each individual treatment to assess the acute analgesic response. The daily oral analgesic requirements were recorded in a patient diary. Finally, the SF-36 was repeated 24 h after completing all six treatment sessions with each of the four montages.

The Number Cruncher Statistical System software package (NCSS 6.0.1 Statistical System for Windows; NCSS Statistical Software, Kaysville, UT) was used for all statistical analyses. An *a priori* power analysis with $\alpha = 0.05$, $\beta = 0.10$ (power = 90%), and standard deviation of 2 cm, suggested that a group size of 72 should be adequate to demonstrate a 17% difference among the pain VAS scores. The changes in the VAS scores over time were analyzed with repeated measures analysis of variance and Student's *t*-test, with a Bonferroni test applied for multiple comparisons. Analysis of discrete data was performed using the χ^2 test. Changes and differences in the SF-36 scores were analyzed by paired *t*-tests. Data were presented as mean values ± SD or SEM and percentages, with *P* values <0.05 considered statistically significant.

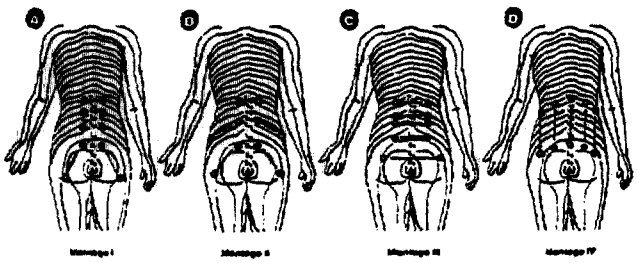


Figure 1. The needle insertion positions and electrode pairing patterns used for the four different PNT montages. Montage I (A) was the standard montage used in all of the earlier PNT studies involving patients with low back pain (1,5,6).

Results

The prestudy SF-36 evaluation suggested that this LBP population reported significantly lower health-related "quality-of-life" scores compared with an age-matched general population without chronic diseases. The prestudy baseline scores were 32.7 and 41.8 for the PCS and MCS, respectively, compared with general population norms of 50 for these two health status survey scores. A comparison of the posttreatment SF-36 test results revealed that all four PNT montages produced significant improvements compared with the baseline scores for both the PCS and the MCS components of the survey ($P < 0.01$). However, the mean magnitude of the changes in the PCS and MCS components with the standard Montage I (+7.1 and +2.9, respectively) and Montage II (+7.6 and +3.2, respectively) were significantly greater than with Montages III (+5.9 and +1.9, respectively) and IV (+5.7 and +1.8, respectively) ($P < 0.05$).

All four montages produced similar 25% to 68% decreases in pain VAS scores immediately after each treatment session (Table 1). However, the cumulative effects over the course of the 2-wk treatment period indicated a better efficacy with Montage II compared with the other three montages (Table 1). Furthermore, the overall percentage changes at the end of the 2-wk treatment period in the VAS pain, physical activity, and quality-of-sleep scores with Montage II (64%,

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Table 1. Comparison of the Effects of the Four Montages of Electrical Stimulation on the Pain VAS Scores Before and After Each of the Six Consecutive Treatment Sessions

Treatment no.	Montage I	Montage II	Montage III	Montage IV
1				
Pretreatment	6.0 ± 1.6	6.1 ± 1.7	5.5 ± 1.9	5.5 ± 1.9
Posttreatment	3.8 ± 1.7*	3.2 ± 1.5†	3.9 ± 1.8*	4.1 ± 1.8*
2				
Pretreatment	5.9 ± 1.7	5.3 ± 1.7‡	5.8 ± 1.8	5.9 ± 1.8
Posttreatment	3.2 ± 1.9†	2.9 ± 1.8†	3.7 ± 1.7*	3.9 ± 1.7*
3				
Pretreatment	5.3 ± 1.8‡	5.1 ± 2.0‡	5.4 ± 1.9	5.4 ± 1.7
Posttreatment	2.8 ± 1.9†	2.5 ± 1.8†	2.9 ± 1.7†	3.6 ± 2.0*
4				
Pretreatment	5.1 ± 1.5‡	4.9 ± 1.6‡	5.2 ± 1.7	5.3 ± 1.6
Posttreatment	2.8 ± 1.9†	1.9 ± 1.6†	2.2 ± 1.8†	2.5 ± 1.9†
5				
Pretreatment	4.7 ± 1.8‡	4.3 ± 1.9‡	4.8 ± 1.8‡	5.0 ± 1.8
Posttreatment	1.9 ± 1.5†	1.6 ± 1.5†	2.0 ± 1.7†	1.9 ± 1.6†
6				
Pretreatment	4.4 ± 1.6‡	3.8 ± 1.4‡	4.5 ± 1.5‡	4.6 ± 1.5‡
Posttreatment	1.4 ± 1.3†	1.2 ± 1.7†	1.6 ± 1.5†	1.5 ± 1.4†

Pretreatment = VAS score 5–10 min before the start of each treatment session.
Posttreatment = VAS score 5–10 min after the end of each treatment session.
VAS = visual analog scale. Mean (±SD) VAS scores, with 0 = the best to 10 = the worst.
* Significantly different from the pretreatment score, $P < 0.05$.
† Significantly different from the pretreatment score, $P < 0.01$.
‡ Significantly different from values before treatment session 1, $P < 0.05$.

51%, and 46%, respectively) were significantly greater compared with the standard (Montage I) (47%, 42%, and 30%, respectively), as well as Montages III (43%, 37%, and 28%, respectively) and IV (42%, 35%, and 29%, respectively) (Table 2). Although the need for oral analgesic medications was decreased over the course of the 2-wk treatment period with all four PNT montages (Fig. 2), the percentage of decrease over the course of the 2-wk treatment period with Montages I (43% ± 23%) and II (47% ± 21%) were significantly greater than with Montages III (27% ± 23%) and IV (23% ± 23%) ($P < 0.05$).

Discussion

Consistent with the previous PNT studies in patients with chronic LBP (1,5,6), Montage I produced both acute and cumulative analgesic effects over the course of the two-week treatment period. This "standard" montage also produced comparable improvements in physical activity and quality of sleep, as well as a reduction in the need for supplemental oral (nonopioid) analgesic medication, as reported in the previous studies involving a similar patient population. These data also support the hypothesis that electrical stimulation of myotomes and sclerotomes at dermatomal levels corresponding to the local pathology is an important factor in the analgesic response to PNT.

In contrast to the previous study (7), in which we evaluated the effect of local-versus-remote dermatomal stimulation, we evaluated the acute analgesic response to PNT when it was administered using different patterns of electrical stimulation at the *same* dermatomal levels. These data suggest that the pattern of stimulation or montage (as determined by electrode placement) influences the acute analgesic response even when the same electrical current is applied at identical dermatomal levels.

Of interest, stimulating along the involved nerve roots at the dermatomal levels corresponding to the patients' pain symptoms (Montage II) was found to be more effective for the acute and short-term pain-reducing effects of PNT, as well as in improving the patients' perceived levels of physical activity and quality of sleep. Although the precise mechanism of PNT-induced analgesia is not known, we speculate that the stimulation pattern used with Montage II produces more effective electrical stimulation of the involved myotomes and/or sclerotomes. On the basis of the PNT studies performed to date, it is recommended to start the therapy using Montage II. If this montage fails to achieve the expected benefits, the patient should be switched to Montage I or one of the other two montages studied.

The failure to conduct the study in a double-blinded manner is a valid criticism of the study. However, all of the evaluations were performed by an independent observer who was unaware of the montage. Another concern relates to the potential residual ("carryover")

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Table 2. Comparison of the Average VAS Scores, as Well as the Percentage Changes, for the Degree of Pain, Level of Activity, and Quality of Sleep During the 24-Hr Period Before Receiving the First Treatment (Before) and 24 Hr After the Last Treatment (After) With Each of the Four Montages

	Montage I	Montage II	Montage III	Montage IV
Degree of pain				
Before (cm)	6.0 ± 1.6	6.1 ± 1.7	6.1 ± 1.6	6.2 ± 1.7
After (cm)	3.2 ± 1.2*	2.2 ± 1.3*	3.5 ± 1.5*	3.6 ± 1.5*
Change (%)	47 ± 2	64 ± 2†	43 ± 2	42 ± 2
Level of activity				
Before	6.2 ± 1.6	6.1 ± 1.7	6.3 ± 1.8	6.3 ± 1.7
After (cm)	3.6 ± 1.4*	3.0 ± 1.3*	4.0 ± 1.3*	4.1 ± 1.5*
Change (%)	42 ± 2	51 ± 2‡	37 ± 2	35 ± 2
Quality of sleep				
Before (cm)	5.4 ± 1.8	5.2 ± 1.7	5.3 ± 1.9	5.5 ± 1.7
After (cm)	3.8 ± 1.2*	2.8 ± 1.4*	3.8 ± 1.5*	3.9 ± 1.5*
Change (cm)	30 ± 2	46 ± 2§	28 ± 2	29 ± 2

Mean (± SD) VAS scores, with 0 = the best to 10 = the worst.
VAS = visual analog scale.
* Significantly different from the 24-h period before the first treatment, $P < 0.05$.
† Significantly different from the 24-hr period before the first treatment, $P < 0.01$.
‡ Significantly different from Montages III and IV, $P < 0.05$.
§ Significantly different from Montages I, III, and IV, $P < 0.05$.

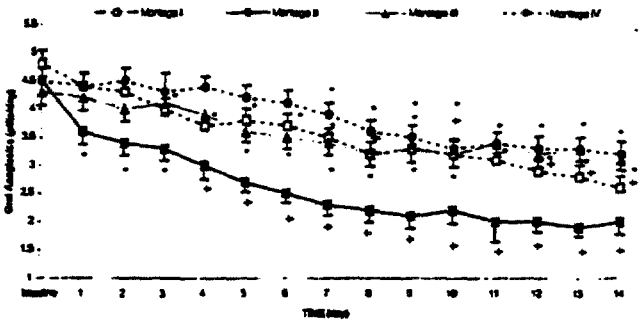


Figure 2. The daily nonopioid analgesic usage (pills per day) during the 2-wk treatment period with each of the four different montages. Baseline refers to the average number of pills consumed per day before entering the study. Values are means ± SEM. *Significantly different from the baseline, $P < 0.05$. +Significantly different from Montages III and IV, $P < 0.05$.

effect of the previous montages. To minimize this effect, the montages were evaluated in random order, and a one-week washout period was allowed between the different montages. Finally, the failure to distinguish between the different types of nonopioid analgesic drugs used by the patients may have confounded the interpretation of the effects of the montages on the patient's oral analgesic requirement.

In future studies involving this chronic pain population, the long-term effects of PNT should be evaluated by using the treatment variables that have been established in the preliminary studies (1,5,6). These studies should not only assess pain, physical activity, sleep, and oral analgesic requirements, but also more important outcome measures such as resumption of normal activities and patient satisfaction. Another important area for future investigation relates to the

beneficial effects of using PNT as a complementary therapy in a multimodal rehabilitation program (10). Finally, the availability of a simple, inexpensive, disposable electrode system would facilitate the use of PNT in the management of both acute and chronic pain disorders.

We conclude that the pattern of electrical stimulation can influence the effects of PNT even when applied at the same dermatomal levels. Peripheral stimulation along the involved nerve roots appears to be the most effective approach in patients with LBP.

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4110-03

TITLE 21--FOOD AND DRUGS

CHAPTER I--FOOD AND DRUG ADMINISTRATION,
DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

EFFECTIVE
10.4.79

9.4.79
44FR51775

SUBCHAPTER H--MEDICAL DEVICES

[DOCKET NO. 78N-1100]

PART 882--NEUROLOGICAL DEVICES

CLASSIFICATION OF TRANSCUTANEOUS ELECTRICAL NERVE STIMULATORS FOR PAIN RELIEF

AGENCY: Food and Drug Administration.

ACTION: Final Rule.

SUMMARY: The Food and Drug Administration (FDA) is issuing a final rule classifying transcutaneous electrical nerve stimulators for pain relief into class II (performance standards). The effect of classifying a device into class II is to provide for the future development of one or more performance standards to assure the safety and effectiveness of the device. This action is being taken under the Medical Device Amendments of 1976.

EFFECTIVE DATE: (Insert date 30 days after date of publication in the FEDERAL REGISTER.)

79-1100

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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FOR FURTHER INFORMATION CONTACT:

James R. Veale,
Bureau of Medical Devices (HFK-430),
Food and Drug Administration,
Department of Health, Education, and Welfare,
8757 Georgia Ave.,
Silver Spring, MD 20910,
301-427-7226.

SUPPLEMENTARY INFORMATION: FDA published in the FEDERAL REGISTER of November 28, 1978 (43 FR 55640) a proposed regulation explaining the development of the proposed regulations classifying neurological devices, the medical device classification procedures, and the activities of the Neurological Device Classification Panel. FDA also published in that issue of the FEDERAL REGISTER (43 FR 55726) a proposed regulation to classify transcutaneous electrical nerve stimulators for pain relief into class II (performance standards). A period of 60 days was provided for interested persons to submit written comments to FDA.

No written comments have been received regarding the proposed regulation to classify this device. Accordingly, the proposed regulation is being adopted without change.

Therefore, under the Federal Food, Drug, and Cosmetic Act (secs. 513, 701(a), 52 Stat. 1055, 90 Stat. 540-546 (21

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U.S.C. 360c, 371(a))) and under authority delegated to him (21 CFR 5.1), the Commissioner of Food and Drugs is amending Part 882 in Supart F by adding new § 882.5890, to read as follows:

§ 882.5890 Transcutaneous electrical nerve stimulator for pain relief.

(a) Identification. A transcutaneous electrical nerve stimulator for pain relief is a device used to apply an electrical current to electrodes on a patient's skin to treat pain.

(b) Classification. Class II (performance standards).

Effective date. This regulation shall be effective (insert date 30 days after date of publication in the FEDERAL REGISTER).

(Secs. 513, 701(a), 52 Sat. 1055, 90 Stat. 540-546 (21 U.S.C. 360c, 371(a)).)

Dated: August 17, 1979.

AUG 17 1979

William F. Randolph

William F. Randolph
Acting Associate Commissioner for
Regulatory Affairs

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Gola L Batson

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DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

FOOD AND DRUG ADMINISTRATION

[21 CFR PART 882]

[DOCKET NO. 78N-1100]

11-29-78
43FR55726

MEDICAL DEVICES

CLASSIFICATION OF TRANSCUTANEOUS ELECTRICAL NERVE STIMULATORS FOR PAIN RELIEF

AGENCY: Food and Drug Administration.

ACTION: Proposed Rule.

SUMMARY: The Food and Drug Administration (FDA) is issuing for public comment a proposed regulation classifying transcutaneous electrical nerve stimulators for pain relief into class II (performance standards). The FDA is also publishing the recommendation of the Neurological Device Classification Panel that the device be classified into class II. The effect of classifying a device into class II is to provide for the future development of one or more performance standards to assure the safety and effectiveness of the device. After considering public comments, FDA will issue a final regulation classifying the device. These actions are being taken under the Medical Device Amendments of 1976.

DATES: Comments by (insert date 60 days after date of publication in the FEDERAL REGISTER). The Commissioner of Food and Drugs proposes that the final regulation based on this proposal become

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effective 30 days after the date of its publication in the FEDERAL REGISTER.

ADDRESS: Written comments to the Hearing Clerk (HFA-305), Food and Drug Administration, Rm. 4-65, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT:

James R. Veale,
Bureau of Medical Devices (HFK-430),
Food and Drug Administration,
Department of Health, Education, and Welfare,
8757 Georgia Ave.,
Silver Spring, MD 20910,
301-427-7226.

SUPPLEMENTARY INFORMATION:

PANEL RECOMMENDATION

A proposal elsewhere in this issue of the FEDERAL REGISTER provides background information concerning the development of the proposed regulation. The Neurological Device Classification Panel, an FDA advisory committee, made the following recommendation with respect to the classification of transcutaneous electrical nerve stimulators for pain relief:

1. Identification: A transcutaneous electrical nerve stimulator for pain relief is a device used to apply an electrical

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current to electrodes on a patient's skin to treat pain.

2. Recommended classification: Class II (performance standards). The Panel recommends that establishing a performance standard for this device be a high priority.

3. Summary of reasons for recommendation: The Panel recommends that transcutaneous electrical nerve stimulators for pain relief be classified into class II (performance standards) because the patient may be injured if the device is used incorrectly or if the output current is excessive. The Panel believes that general controls will not provide sufficient control over these characteristics. The Panel believes that a standard will provide reasonable assurance of the safety and effectiveness of the device and that there is sufficient information to establish a standard to provide such assurance.

4. Summary of data on which the recommendation is based: The Panel members based their recommendation on their extensive

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personal clinical experience with this device, data presented by experts in the use of the device, and a review of the relevant literature on the device. A summary of the literature reviewed was prepared by the Panel (Ref. 1). Users of transcutaneous electrical nerve stimulator devices have reported that long-term (1 year or more) effectiveness of this device in treating pain is about 25 to 30 percent for selected patients who have intractable chronic pain. The best results were obtained on patients who had chronic low back pain, phantom limb pain, and pain of osteoarthritis. The literature contains no reports of mortalities caused by this device.

5. Risks to health: (a) Burns. The patient's skin may be burned if the output current levels are excessive or if the electrodes are too small. (b) Skin reactions. The conductive cream or gel used with the electrodes or the presence of the electrodes on the skin may cause adverse skin reactions.

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PROPOSED CLASSIFICATION

The Commissioner agrees with the Panel's recommendation and is proposing that the transcutaneous electrical nerve stimulator for pain relief be classified into class II (performance standards). The Commissioner believes that a performance standard is necessary for this device because general controls by themselves are insufficient to control the risks to health. A performance standard would provide reasonable assurance of the safety and effectiveness of the device. The Commissioner also believes that there is sufficient information to establish a standard to provide reasonable assurance of the safety and effectiveness of the device.

REFERENCES

The following information has been placed in the office of the Hearing Clerk (HFA-305), Food and Drug Administration, Rm. 4-65, 5600 Fishers Lane, Rockville, MD 20857, and may be seen by interested persons, from 9 a.m. to 4 p.m., Monday through Friday.

1. "Report on the Findings and Recommendations on Transcutaneous Electrical Nerve Stimulation for Pain Relief," prepared by the Panel on Review of Neurological Devices, Food and Drug Administration, February 1976.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Therefore, under the Federal Food, Drug, and Cosmetic Act (secs. 513, 701(a), 52 Stat. 1055, 90 Stat. 540-546 (21 U.S.C. 360c, 371(a))) and under authority delegated to him (21 CFR 5.1), the Commissioner proposes to amend Part 882 in Subpart F by adding new § 882.5890 as follows:

§ 882.5890 Transcutaneous electrical nerve stimulator for pain relief.

(a) Identification. A transcutaneous electrical nerve stimulator for pain relief is a device used to apply an electrical current to electrodes on a patient's skin to treat pain.

(b) Classification. Class II (performance standards).

Interested persons may, on or before (insert date 60 days after date of publication in the FEDERAL REGISTER) submit to the Hearing Clerk (HFA-305), Food and Drug Administration, Rm. 4-65, 5600 Fishers Lane, Rockville, MD 20857, written comments regarding this proposal. Four copies of all comments shall be submitted, except that individuals may submit single copies of comments, and shall be identified with the Hearing Clerk docket number found in brackets in the heading of this document. Received comments may be seen in the above office between the hours of 9 a.m. and 4 p.m., Monday through Friday.

Dated: Nov. 15, 1978.

NOV 15 1978

William F. Randolph

William F. Randolph
Acting Associate Commissioner for Regulatory Affairs

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1. "Report on the Findings and Recommendations on Transcutaneous Electrical Nerve Stimulation for Pain Relief," prepared by the Panel on Review of Neurological Devices, Food and Drug Administration, February 1976.

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DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
ROCKVILLE, MARYLAND 20852

The attached report was prepared by the Food and Drug Administration's Advisory Panel on Review of Neurological Devices to document its initial recommendations to the agency on Transcutaneous Electrical Nerve Stimulators. The report represents only the opinion of the panel and is not to be considered the opinion or the policy of the Food and Drug Administration.

James R. Veale
Executive Secretary
Panel on Review of Neurological Devices
Bureau of Medical Devices &
Diagnostic Products (HFK-450)
Food and Drug Administration
8757 Georgia Avenue
Silver Spring, Maryland 20910

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Report on the Findings and Recommendations on Transcutaneous Electrical Nerve Stimulation for Pain Relief

by the

Panel on Review of Neurological Devices
Food and Drug Administration

February, 1976

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Abstract

Electrical stimulation is being used more frequently for therapeutic purposes. This paper discusses the use of electrical stimulation for pain relief including such topics as: historical background, theory, devices, placebo effect, applications and results. The available information does not allow a complete evaluation of this method at this time and several of the commercial devices used to develop the method lack engineering sophistication but there is sufficient evidence to indicate that this is an effective method for the treatment of certain types of pain disorders. No harmful side effects have been demonstrated to date but scientific information is not available to ascertain safety and therefore caution is advised on the use of TENS during pregnancy, in patients with cardiac pacemakers, and over the carotid sinuses.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Report on Transcutaneous Electrical Nerve Stimulation for Pain Relief

Panel on Review of Neurological Devices

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1. Purpose

It is the purpose of this report to review the background, devices, applications and results of TENS (Transcutaneous Electrical Nerve Stimulation) and to make certain recommendations in order that the FDA may have scientific guidance in the preparation of guidelines for classification of TENS devices based on the best knowledge available as of this date.

2. Historical Background

The concept of Transcutaneous Electrical Nerve Stimulation (TENS) for the purpose of relieving pain is one of the oldest in health care, first reported in 50 A.D. by Scribonius Largus. It is a concept that has sporatically held great interest for the medical community. Interest in this subject was evidenced a century ago with the publication of numerous articles and textbooks on this method of pain relief therapy. One text by Beard and Rockwell, initially published in 1875, continued for ten successive editions. Interest in TENS therapy waned at the turn of the century because of limited clinical efficiency (probably due to a lack of suitable instrumentation) and the apparent conclusion that the clinical results did not justify the effort expended. For this reason, the TENS devices which remained in use were typically in the hands of peri-medical (e.g., chiropractic and naturopathic) practitioners rather than physicians.

A case in point is the "Electreat" device, a battery operated TENS device based on the inductorium principle. This "mechanical heart" originally introduced in 1918 was touted as a treatment for "any known disease." It was said by the manufacturer in the manual supplied with the device to function by alleviating the "congestion of the electrolyte forces of

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attraction and repulsion by balancing 'protectones' and 'irritones'." This device was the subject of regulatory action by the FDA and was also referred to in hearings of the Senate Health Subcommittee of the Committee on Labor & Public Welfare in January 1975. Although crude in design and manufacture, this device (which is still being sold) demonstrates limited efficacy in the treatment of pain.

In 1965, the publication in Science of "Pain Mechanisms: A New Theory" by R. Melzack and P. Wall produced a resurgence of medical interest in electrical nerve stimulation (ENS) as a non-drug, non-destructive method for the treatment of pain. The possibility of using electrical modulation of the nervous system for pain relief led to the development by J. T. Mortimer and C. N. Shealy of the Dorsal Column Stimulator in 1967. This surgically implanted electrical system was designed to block pain by stimulating the myelinated dorsal column nerve fibers of the spinal cord. Battery operated TENS devices (developed for use in testing muscle activation) were used as a non-invasive means of testing a patient's response to electrical stimulation to determine the suitability of implanting a stimulator for the relief of pain in that particular patient. It was soon recognized that, in some cases, the pain relief afforded by the TENS device was adequate and the TENS device could be used as the preferred mode of therapy.

The ease of application, efficacy and lack of undesirable side effects make TENS an attractive mode of therapy. As a consequence, physicians have rapidly accepted TENS as a mode of therapy in the treatment of pain and at least fifteen manufacturers are currently offering TENS stimulators.

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In addition dozens of custom made devices have been developed for the delivery of pulsatile electric currents. These stimulators range in design from relatively sophisticated devices that deliver uniform pulses to overly simplified devices lacking in stability.

3. Theory

The development of a cohesive, integrated theory to describe the effects of TENS has been difficult because of several factors: The incomplete knowledge of neural tissue electrical properties; the incomplete knowledge as to current pathways and local current densities during TENS; the lack of completeness of scientific data in most papers describing TENS with respect to electrode locations, waveshapes, current levels and concurrent drug therapy; the fact that many TENS stimulators used to gather data do not deliver consistant current levels or waveshapes.

The major difficulty in determining the mechanism by which TENS acts on the nervous system to produce pain relief relates to a lack of scientific understanding of the functioning of the highly complex human nervous system. The "Gate Control Theory", of Melzack and Wall, relates the ability of TENS currents to block pain by maintaining a "quantitative superiority at Neurologic gates" where only the more intense stimulus (in this case non-pain) is passed to the brain and perceived. The original theory, which held that a single gate was present at the spinal substancia gelatinosa, has been modified to include multiple gates at higher spinal cord and brain levels.

M. Zimmerman has advanced a number of theories which describe electrical stimulation pain relief thru reference to more classic neurophysiological principles. He advances the following factors as having significance:

1. Suppression of on-going discharges which are initiated in peripheral endings of regenerating nociceptive afferents.

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2. Pre or postsynaptic inhibition of spinal neurons which are involved in the processing of noxious stimuli.

3. Repression of denervation supersensitivity of neurons in the central nervous system.

4. Long lasting hyper-polarization by postexcitatory active ion transport.

The above theories are appealing because they allow an arrangement of known physiological evidence into logical order to clarify the mechanisms by which TENS augments large fiber activity to afford pain relief.

Many other theories have been advanced, some of which imply TENS efficacy by direct inhibition rather than by direct stimulation. As an example, a recent theory of Mayer and Hayes even suggests that the mechanism of TENS pain relief may be the result of inducing some neurons to produce enkephaline, an endogenous opiate, which interacts with receptors to produce analgesia in the same way as morphine and other opiates.

An understanding of current pathways and local current densities in the brain would greatly help in the development of a theory to understand the mechanisms of TENS mediated pain relief. Classical field theory is quite useful in developing plots of current pathways and local current densities when the geometry is simple and the media are homogeneous and isotropic. Driscoll has developed such a mathematical model for the human head that is quite useful to show the results of applying currents at an interior location and plotting the resultant potentials that appear on the

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surface. Unfortunately, due to the complexity of the human brain and the fact that neural tissue is neither homogeneous nor isotropic, it is impossible to develop models to show the local current densities developed within the brain due to externally applied currents.

Methods have been developed for the measurement of current densities and impedance within the brain during the application of electrical currents but to date no one has used these methods to map the current pathways during the application of TENS.

4. Devices

TENS devices currently in use comprise an electrical pulse generator, typically battery operated, connected by wire (or cable) to two or more electrodes. Most of the commercial devices are intended for use by physicians and are so labeled. Prices for pulse generators range from less than $300 to over $500 and the pulse generators are typically sold directly to the physician.

Commercial pulse generators are available with a variety of waveshapes and other electrical characteristics. The most common waveshapes are the unidirectional rectangular pulse with a duty cycle of less than 10% and a bidirectional rectangular pulse with a similar duty cycle (ratio of on time to off time). Current pulses vary in repetition rate from less than ten per second to over 1,000 per second with duty cycles ranging from 1% to 20%. Peak current amplitudes vary from less than 1 milliampere to over

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100 milliamperes. Average currents (peak current x duty cycle) are correspondingly smaller. Some pulse generators are able to supply a constant current and waveshape to various electrodes while many fall short of this goal.

Electrodes supplied by various manufacturers vary from simple saline soaked pads to stainless steel wire mesh, conducting elastomeric pads and conducting adhesive tape. All of the above electrode types are inherently capable of passing the required amounts of current. However, some of the pulse generators are not capable of supplying constant currents with certain of the electrodes. This is due to the electrode-electrolyte-skin interface impedance which is a function of the size and kind of electrode, electrolyte used, and the skin of the particular patient in the location chosen for stimulation.

5. Methods

The therapeutic use of TENS for the relief of pain involves placement of electrodes on the body at locations selected by the physician and application of electrical impulses to the patient thru the electrodes. Electrodes may be placed directly over the painful site although better results are often obtained thru more distal electrode locations. Electrode placement is based on a knowledge of neuroanatomy, previous experience and corrections are based on experience with the particular patient. At present, this process seems to be a combination of art and science.

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6. Results

In testimony before the FDA Advisory Panel on Neurological Devices, June 25, 1975, Dr. Donlin Long, Professor and Chairman of the Department of Neurosurgery, Johns Hopkins School of Medicine, discussed his clinical experience and studies of TENS for pain relief. He reviewed a study of 200 unselected chronic pain patients, all of whom were unable to obtain relief with other modes of pain therapy. Of this group, 150 were given placebo treatment whereby 50 patients received stimulation at the threshold of sensation, 50 received subliminal stimulation and 50 were given stimulation with no power applied. The placebo response was so small that the trial was soon abandoned and normal treatment commenced.

Initial results (3-6 days) indicated that 78 patients (39%) received excellent relief, 54 (27%) received good relief and 65 (33%) received little or no relief. At the end of a year the 78 patients who initially reported excellent pain relief were surveyed. Of 75 patients contacted, 10 still were able to report excellent results, 33 (44%) reported good relief and 32 (43%) reported fair relief. Of the 75 patients 66 (88%) were able to reduce medication and 48 (64%) reported increased functional abilities.

Dr. Long also reported a survey of several other centers where TENS had been used for the relief of pain. Of 2000 patients, TENS alone provided adequate long term relief in 500 (25%) patients.

Dr. Long noted that pain of psychogenic origin was rarely helped by TENS. The best results were reported for patients with chronic low back

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pain, phantom limb pain and osteoarthritis. Poorest results were obtained in treating cancer pain, central pain states and neuropathies. It was his opinion that one of the most significant factors in achieving success with TENS was adequate patient education in proper use of the device. Dr. Long stated that TENS was an important adjunct in the management of pain and should provide adequate long term therapy for 25%-30% of patients.

The panel also conducted a survey of the scientific literature on TENS and reviewed the long term results reported by various other investigators. These reports substantiated the reports of Dr. Long. A recent study by R. Melzack (to be published in Pain) of the ability of TENS to relieve severe pathological pain on a short term basis indicated that TENS "was a powerful method of control". Success was achieved in 75% of the trials for pain due to peripheral nerve injury and 66% of the trials for low back pain. Melzack also found that the duration of relief frequently outlasted the period of stimulation by several hours and "occasionally for days or weeks". "Control experiments, which included two forms of placebo stimulation, showed that brief intense electrical stimulation is significantly more effective than placebo effects."

Although patient responses are variable, a successful TENS response not only blocks local pain but also produces sustained pain relief lasting from minutes to hours or even days following cessation of stimulation.

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No deaths or complications of existing diseases have been reported following or during the use of TENS. The reported morbidity has involved only slight skin reactions at electrode sites. Clinical indications to date suggest that the incidence of adverse skin reaction is quite low.

Participants of the December, 1973 international seminar on Electrical Stimulation of the Human Nervous System for the Control of Pain concluded that TENS is "an innocuous, noninvasive means of pain relief with broad application for acute and chronic pain. It may be sufficient in many cases as the only therapeutic method required. It is also valuable but not definitive as a screening test for implanted devices. Effective results have been seen during and/or consequent to stimulation over effected body parts, adjacent skin areas and/or areas removed from those in pain".

7. Placebo Effect

The degree of placebo effect inherent in the use of TENS devices has been the subject of concern by many investigators. Although studies such as those of Dr's. Long and R. Melzack indicate that this effect is minimal in this situation, the placebo effect appears to be present, to some degree, with the clinical use of all electronic devices. Pertinent to this observation is a commentary published in the June 23, 1975 issue of the Journal of the American Medical Association by H. Benson and M. Epstein entitled "The Placebo Effect: A Neglected Asset in the Care of Patients".

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The authors point out that the physiology of the placebo effect remains relatively unexplored although there are known physiological changes associated with it. It is their conclusion that the placebo effect "must be allowed to survive if medicine is to provide optimal care for patients".

8. Discussion and Recommendations

TENS, unlike accupuncture, is progressing in technical sophistication. Long term trials in this country have documented a degree of efficacy which is reasonable and acceptable, particularly in view of the very low potential risk to the patient and the absence of alternate low risk therapy. There is good reason to believe that efficacy can be significantly improved by patient education, improved device labeling and improved pulse generators.

There is concern by the panel that too many physicians, as well as patients, tend to initially, and erroneously, consider TENS as a panacea. This highly receptive environment could lead to a widespread misuse of TENS with dubious results. It could also lead to a proliferation of "Saturday Night Specials" manufactured without adequate engineering design and/or manufacturing controls. It would be unfortunate if such usage were to destroy confidence in TENS for the applications where it is effective in relieving pain.

For these reasons, it is strongly recommended that stringent prescription and labeling criteria be required. These devices should be restricted to sale by or on the order of a licensed physician, dentist or

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veterinarian. If information regarding clinical efficacy, contraindications and possible risks are mandatory, the use of the devices will be more realistic.

TENS devices appear to be simple, safe and reasonably effective when produced by reputable manufacturers. Inherently, any simple, safe, effective mode of therapy is valuable to the public when properly used. This reason is sufficient justification for intensive investigation of TENS to better understand the physiological effects and improve its clinical application. This should include basic research to determine the mechanism of operation, electrical properties of tissues involved, current pathways and local current densities, the effect of various waveshapes and the relationship between minimum current density to relieve pain and electrode location in relation to known neuroanatomy. Resus and macaque monkeys have been shown to be reasonably acceptable models for electrical stimulation studies in the past. These animals can provide a vast amount of new information relative to TENS if recently developed methods of impedance and current density measurements are used.

Even though the efficacy varies from study to study, clinic to clinic and patient to patient, TENS is being accepted by many members of the health care community as a relatively safe, simple therapeutic means for alleviation of pain. However, an effective analysis of the clinical variations is difficult because the scientific papers describing TENS rarely furnish the important electronic variables, e.g., actual current density, waveshape, stability of the TENS pulse generator, etc. In addition, the available evidence indicates that the characteristics of certain stimulators allow

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the waveshape and current level to vary during treatment without the knowledge of the clinician.

Additional studies should, therefore, include an evaluation of the effect that stimulus parameter variation has on efficacy. These studies should include a study of waveshape, pulse generator output impedance and pulse generator compliance (maximum delivered potential). Regardless of the outcome of these studies, labeling requirements should inlcude these parameters.

No deaths have been reported following use of TENS. Reported morbidity has involved skin reactions at electrode sites. Incidence of skin reaction appears to be slightly higher than the 1.6% incidence of adverse reactions to cosmetics reported by the FDA (Drug Bulletin, July-August 1975).

Although no documentation of adverse effect exists, it appears reasonable to assume that legitimate contraindications would include use in a patient with a cardiac pacemaker (particularly a demand pacemaker) and use over the carotid sinuses where a vagal-vagal reflex might produce cardiac arrest. Effect on pregnancy is unknown but care should also be recommended in this situation.

The following recommendations are made in the interest of conveying to standards writing groups certain concerns of the Neurological Device Panel and outside specialists who have communicated their suggestions to the panel members.

A. The manufacturer of a specific device should clearly specify the device waveshape parameters. In the event that controls are provided to modify the waveshape, each control should be clearly described as to the effect that it has on the waveshape.

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B. Constant current generators (stimulators) should provide a constant waveshape and current regardless of the electrode and patient impedance within reasonable limits. Said limits may well be a part of the specification. Whereas it is a simple task for a competent design engineer to provide a stimulator circuit with output impedances in excess of a megohm, such limit is not unreasonable.

C. Constant potential stimulators should maintain a constant stimulus potential and other pulse parameters regardless of the patient load within certain limits that may well be determined by the standards writing group. It may well be that constant potential stimulators may be deemed too dangerous for clinical use.

D. The standards should define terms for all stimulation work and include terms to differentiate between units with multiple outputs as to the relative isolation and phase relationship between the multiple outputs.

E. Attention should be given to the problem of safety as regards current limiting in the event of device failure. This may be addressed through the use of overpotential and overcurrent testing, stressful environmental testing and the use of redundant circuitry.

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F. Attention should be given to the problem of AC power vs. battery power. The standards should not preclude the use of AC line operated devices but these devices should be carefully designed to preclude excessive power to the patient when used by inexperienced medical practioners.

G. The subject of TENS damage during defibrillation may seem remote but the effect on a particular TENS unit of excessive voltages from an outside source should be considered. This is not a difficult problem for a competent designer so should pose no burden on the manufacturer that he should not willingly accept. It would be nothing other than good practice for a professional.

In summary, TENS appears to represent a worthwhile means of therapy for pain relief when used by a person with adequate medical knowledge and training in this method. It should be available only by prescription and each device should be properly labeled with appropriate efficacy, contraindications and device parameters.

There is evidence that clinical efficacy can be improved by better scientific understanding of the technique, improved devices, patient and physician education and by the knowledge that will come with experience. Careful labeling and product information are essential to avoid unwarranted commercial claims. If good engineering design, good manufacturing practices and appropriate standards are combined with the studies suggested above, the public will be provided with a realistic idea as to potential efficacy. TENS does provide a meaningful alternative to other types of pain therapy which are known to have a higher degree of risk.

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Outcome Measures for Low Back Pain Research

A Proposal for Standardized Use

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Study Design. An international group of back pain researchers considered recommendations for standardized measures in clinical outcomes research in patients with back pain.

Objectives. To promote more standardization of outcome measurement in clinical trials and other types of outcomes research, including meta-analyses, cost-effectiveness analyses, and multicenter studies.

Summary of Background Data. Better standardization of outcome measurement would facilitate comparison of results among studies, and more complete reporting of relevant outcomes. Because back pain is rarely fatal or completely cured, outcome assessment is complex and involves multiple dimensions. These include symptoms, function, general well-being, work disability, and satisfaction with care.

Methods. The panel considered several factors in recommending a standard battery of outcome measures. These included reliability, validity, responsiveness, and practicality of the measures. In addition, compatibility with widely used and promoted batteries such as the American Academy of Orthopaedic Surgeons Lumbar Cluster were considered to minimize the need for changes when these instruments are used.

Results. First, a six-item set was proposed, which is sufficiently brief that it could be used in routine care settings for quality improvement and for research purposes. An expanded outcome set, which would provide more precise measurement for research purposes, includes measures of severity and frequency of symptoms, either the Roland or the Oswestry Disability Scale, either the SF-12 or the EuroQol measure of general health status, a question about satisfaction with symptoms, three types of "disability days," and an optional single item on overall satisfaction with medical care.

Conclusion. Standardized measurement of outcomes would facilitate scientific advances in clinical care. A short, 6-item questionnaire and a somewhat expanded, more precise battery of questionnaires can be recommended. Although many considerations support such recommendations, more data on responsiveness and the minimally important change in scores are needed for most of the instruments. [Key words: back pain, clinical research, disability, health status, outcomes] **Spine 1998;23:2003–2013**

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The measurement of patient outcomes in clinical studies of low back pain has been vexing for many investigators. Traditionally, in an effort to achieve objectivity, physiologic measures such as range of motion and muscle strength were widely used. However, in many cases, such measures are only weakly associated with outcomes that are more relevant to patients and to society, such as symptom relief, daily functioning, and work status.[7] In recent years, social science methods and clinical expertise have been fused in the creation of a series of questionnaire measures that seek to capture this broader range of relevant outcomes.[7,8] However, there is little standardization of use of these instruments, and comparisons among studies are therefore difficult or impossible. New questionnaires seem constantly to emerge. As a result, there is little shared understanding of what certain results mean, what their clinical relevance may be, or how

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Table 1. Advantages of a Standardized Set of Outcome Measures

Improve comparability of results among clinical studies
Improve comparability of baseline patient characteristics among clinical studies
Facilitate meta-analysis (pooling of results from multiple studies)
Facilitate cost-effectiveness analysis by creating an accepted metric for effectiveness (would also facilitate comparison of cost-effectiveness with treatments for other medical conditions)
Encourage more complete reporting of relevant outcomes
Facilitate conduct of multicenter studies
Facilitate design and review of manuscripts, publications, research proposals
Avoid "reinventing the wheel"

the patient populations and results of different studies may compare.

A multinational group of investigators met as part of an international program on primary care research on back pain held in The Hague, The Netherlands, in May 1997. The group considered the question of whether a relatively standardized set of outcome measures could be recommended, based on published studies and the group's assessment of the important domains. This report summarizes the discussion and provides initial recommendations for investigators in this field.

A standardized "core" set of questions and questionnaires would have many advantages for clinicians and investigators. Such a core would facilitate many types of comparison and pooling of data, while leaving investigators free to augment the core with a wide variety of measures of their own choice. Thus, the effort to develop a standardized set of instruments is not intended to force investigators into a straitjacket, but to provide a common yardstick that is appropriate for use in many types of studies. For individual investigations, it may be important to augment this core with measures of specific clinical effects or to experiment with new measures of the constructs included in the standardized core. Thus, it should be anticipated that the "core" measures may change somewhat with time but that change may be gradual enough to maintain some standardization within the field.

It seems clear that the traditional surgical outcome measure of a single rating scale (excellent, good, fair, and poor) is no longer sufficient. Howe and Frymoyer[13] demonstrated that different definitions of these terms could result in widely differing conclusions about the success of a given surgical procedure. Furthermore, such a rating scale fails to indicate, for example, how many patients are employed at the beginning of a study and how many are employed at the end of a study. It also combines multiple dimensions of outcome, such as symptoms, function, and work disability, which may be relatively unrelated in their clinical trajectory after a treatment intervention. For example, it has been shown that among patients undergoing discectomy for sciatica, surgery offers substantial advantages in symptom and functional outcomes at 1 year, but that return to work is equivalent for surgical and nonsurgical treatments.[1] Thus, a standardized set of instruments should measure various outcomes in different dimensions and keep them relatively distinct.

■ Advantages of Standardized Outcome Measurement

A standardized set of clinical outcome measures would make it easier to compare the results of clinical studies of similar treatments. Presently, this is almost impossible, even when outcome ratings are superficially similar (such as the excellent–good–fair–poor scale). Even when studies are concordant in demonstrating benefit for a given treatment, differences in outcome measures may make it difficult to assess the relative magnitude of treatment effects among various studies. This may make it difficult or impossible to pool the results of multiple studies in the form of a meta-analysis. Such pooling of results may be important when there are multiple small studies in which results show a treatment benefit, but the individual studies are too small to show statistical significance; when clinical subgroup analyses may be important, but studies must be combined to achieve adequate numbers of patients; and when a single assessment of the magnitude of treatment effects is sought for purposes of cost-effectiveness analyses. Because cost-effectiveness analysis is always a ratio of cost to treatment effectiveness, the denominator must be a valid estimate of the magnitude of treatment effects, along with confidence intervals. If the outcome measures can be integrated with an assessment of patient preferences or weighting of the outcomes (utilities) the effectiveness and cost-effectiveness measures can be transferred into a standardized metric that permits comparison with many other treatments for other medical conditions. This may be important for resource allocation purposes.

The availability of a standardized outcome measurement set should also improve the quality of the medical literature. It would encourage more complete reporting of relevant outcomes, so that investigators do not simply report a single dimension of outcome while ignoring others. Having a common set of measures that are widely used would also encourage development of cooperative multicenter studies, which offers the prospect of large,

Table 2. Factors to Consider in Choosing "Standardized" Outcome Measures

Breadth of coverage
Demonstrated validity and reproducibility
Demonstrated responsiveness
Practicality (brevity and low cost)
Compatibility with widely promoted instruments or batteries (e.g., SF-36, AAOS, NASS)
Importance to patient
Importance to society

AAOS = American Academy of Orthopaedic Surgeons; NASS = North American Spine Society; SF-36 = Short Form, 36 items (from Medical Outcomes Study[16]).

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Table 3. A Proposed "Core Set" of Six Questions, Practical for Routine Clinical Use, Quality Improvement, and as a Component of More Formal Research*

Domain	Specific Question	Source, References	Where Used
Pain symptoms	During the past week, how bothersome have the following symptoms been? a) low back pain b) leg pain (sciatica) or Conventional visual analog pain scales	From back pain PORT; Patrick et al,[14] Atlas et al[1]	MLSS AAOS NASS TyPE
Function	During the past week, how much did pain interfere with your normal work (including both work outside the home and housework?	SF-36 and SF-12[16,17]	AAOS MLSS TyPE
Well-being	If you had to spend the rest of your life with the symptoms you have right now, how would you feel about it?	From back Pain PORT; Cherkin et al[4]	AAOS MLSS
Disability	During the past 4 weeks, about how many days did you cut down on the things you usually do for more than half of the day because of back pain or leg pain (sciatica)?	Adapted from Questions in NHIS; Patrick et al[14]	MLSS TyPE
Disability (social role)	During the past 4 weeks, how many days did low back pain or leg pain (sciatica) keep you from going to work or school?		
Satisfaction with care	Over the course of treatment for your low back pain or leg pain (sciatica), how would you rate your overall medical care? (optional)		TyPE

* The exact questions and response options are listed in Appendix I.
PORT = patient outcome research team; MLSS = Maine Lumbar Spine Study; AAOS = American Academy of Orthopaedic Surgeons; NASS = North American Spine Society; NHIS = National Health Interview Survey; TyPE = typology of patient experience; SF = Short Form.

rapid, and generalizable efficacy and effectiveness studies. If various centers were familiar with a core set of measures, had the instruments readily available, and were familiar with their administration and manipulation, the design and conduct of such cooperative studies would be facilitated. Finally, having some standardized measures of outcome would simplify the process of designing and reviewing research proposals, manuscripts, and published studies.

■ Dimensions of Outcome

Some have previously argued for measuring the outcomes of low back pain in terms of symptoms, functional status, overall well-being, and work disability.[14] Valid measures of all of these constructs are available, and such dimensions have been incorporated into the outcome instruments of the American Academy of Orthopaedic Surgeons (AAOS) and the North American Spine Society (NASS). Thus, there seems to be a growing consensus that these are appropriate dimensions of outcome for patients with back pain.

There is substantial evidence that symptoms and functional status change fairly readily among patients with acute low back pain and that these aspects of outcome can be influenced by various treatments. In contrast, results in some studies show that affecting work disability or employment status may be very difficult.[1] Although work status has the advantage that it is easily assessed, objective, and highly relevant, it is usually a function of many factors, among which medical intervention may be only minor. For example, physical job demands, job satisfaction, relationships with fellow employees, supervisor ratings, income, regional job availability, closeness to retirement age, or the availability of another breadwinner in the family all influence the likelihood of return to work. Thus, although return to work is an outcome of great social and personal importance, it may also be one that is less responsive to clinical treatment than symptoms or daily functioning. In considering a core set of outcome measures, it seems appropriate to consider outcomes that are highly responsive to treatment and those that are of major social importance, even though some outcome measures do not have both traits.

For many purposes, physiologic outcomes such as neurologic function, range of motion, or muscle strength are important outcomes to measure as well. However, the wide range of methods for measuring such physiologic functions and the extensive literature on the reliability and validity of such measures is beyond the scope of this article. Furthermore, there are many examples in which measures such as electromyogram activity, spine mobility, or straight leg raising results were poorly associated with pain relief, functional status, or use of health care resources.[7] Thus, the current group chose to focus on questionnaire measures that could be easily administered in multiple settings and by a wide variety of personnel.

Finally, health care use may be considered an important outcome domain, because hospitalization, use of imaging, surgery, and health care costs are important considerations in studying therapy. However, these are measures of the process of care, rather than outcomes.

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Table 4. A Proposed "Core Set" of Instruments for Clinical Researchers

Domain	Specific Instrument	Source References
Pain symptoms	Bothersomeness or severity and frequency of low back pain and leg pain (sciatica)	From LBP TyPE, used in AAOS and NASS instruments. Patrick et al,[14] Atlas et al,[1] Daltroy et al[5]
Back-related function	Roland and Morris Disability Scale (or adaptations)	Roland et al,[15] Fairbank et al,[11] Daltroy et al,[5] Patrick et al,[14] Modified Oswestry used in NASS and AAOS
or		
	Oswestry Disability questionnaire (or adaptations)	
Generic well-being	SF-12 or EuroQoL; also, "If you had to spend the rest of your life with the symptoms you have right now, how would you feel about it?"	From SF-36,[16] Ware et al,[17] Patrick et al,[14] Used in AAOS, EuroQoL Group
Disability (social role)	Days of work absenteeism, cut down activities, bed rest	"Cut down days" from NHIS, Patrick et al[14]
Satisfaction with care	Single question on overall satisfaction (optional)	TyPE

NHIS = National Health Interview Survey; TyPE = typology of patient experience. LBP = low back pain; AAOS = American Academy of Orthopaedic Surgeons; NASS = North American Spine Society; SF-36 = Short Form, 36 items.

They do not necessarily reflect health status and are not easily measured with a brief, uniform set of items. Again, measures of cost or health care use could easily be added by individual investigators, depending on the goals of their research.

■ Factors to Consider in Recommending a Standard Battery of Outcome Measures

Many factors could be considered in selecting questions or questionnaires for standardized use. The recommendations made here were drawn up primarily in consideration of the demonstrated validity of instruments, their responsiveness to change with time, and their practicality. For validity, the major concern was whether the items selected had evidence of construct validity—that is, associations with different but related measures in a predictable direction and of moderate magnitude. Construct validation is necessary, because for symptoms, function, and well-being, there is no widely accepted gold standard for measurement.

Responsiveness refers to the ability to detect true changes in patient status beyond the random variability that is expected on repeat measurement of any sort. All measures of responsiveness are in some way measures of "signal" to "noise:" The signal is the true change in patient status and the noise is the random variability of measures. Several indicators of responsiveness have been proposed, including effect size, the standardized response mean, and variations of these statistics. Some investigators have also examined score changes as they relate to other external measures of improvement or deterioration, using either correlation analysis or receiver operating characteristic (ROC) curves.[9] For an instrument designed to measure change in longitudinal studies, such measures of responsiveness may be more important than cross-sectional reliability, in which the signal-to-noise ratio represents differences between patients (rather than longitudinal change for a single patient) related to cross-sectional score variability.

The major concern regarding practicality was the length of the questionnaires. To be practical, they should be as brief as possible, minimizing response burden and the costs of data collection and management. Furthermore, the core data set should be brief if investigators are to feel free to add other measures to the battery.

A final consideration was the compatibility of questions with widely promoted instruments or batteries, such as the Lumbar Cluster developed by the AAOS, the NASS Lumbar Spine Outcome Assessment Instrument, or the typology of patient experience (TyPE) originally developed by InterStudy (later reverting to the Health Outcomes Institute, Bloomington, Minnesota, now a part of Stratis Health, Bloomington). Thus, it would be desirable for the core items to be included in commonly used instruments so that practitioners or health care systems that have already implemented one of these batteries would not have to make changes (or could make minor changes) to include the core battery.

■ A Very Parsimonious Six-Item Core Set

A proposed core set of just six questions was developed (Table 3 and Appendix I) that would be practical for use in a wide variety of settings, including routine clinical care, quality improvement efforts, and more formal research. It is so brief that even lengthy supplemental measures (*e.g.*, physiologic measures, detailed questionnaires) could be added and still be practical, retaining a core set of multidimensional measures that would assure comparability with results in a wide variety of other studies. Most investigators would want to collect other demographic and clinical information for baseline description, and this set focuses strictly on outcomes of care. However, many investigators would also want to measure each of these constructs at a baseline time, or before some intervention. This set has the advantage of measuring several dimensions of outcome, each with a single item. Even this short set of measures would be a

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substantial improvement compared with simply measuring pain severity, or excellent–good–fair–poor outcomes.

Each of the questions in this short set has been studied and validated elsewhere and is already incorporated into other widely promulgated questionnaires. For example, the questions on bothersomeness of back and leg pain, function, and well-being are all included in the Lumbar Cluster of the AAOS and the NASS outcome questionnaire.[5] However, some of the questions (*e.g.*, those concerning the "bother" of symptoms) have not been translated into languages other than English or tested outside the United States.

The first item in this core set is a measure of pain symptoms that have been divided into low back symptoms and leg symptoms. For this purpose, the current suggestion is that pain severity be measured in one of two ways at the discretion of the investigator. First, a set of questions could be used to determine how bothersome pain symptoms have been, as was reported in the Maine Lumbar Spine Study and is incorporated in the AAOS, NASS, and TyPE instruments. This question is shown in Appendix I. A 1-week time frame for these symptoms is suggested because it allows the patient to integrate recent experience of a long enough interval to be meaningful, but short enough that memory is not likely to be a problem and short-term improvements are apparent.[5] The severity of low back and leg pain could also be measured using conventional visual analog scales, a type of measure more familiar to some investigators. Guyatt et al[12] demonstrated nearly identical statistical measures of responsiveness for 7-point Likert Scales and Visual Analog Scales. However, they found that the Likert format with verbal descriptors (such as the "bothersome" question) was easier to understand for patients and required less instruction. This is likely to be especially important with elderly patients, such as those with spinal stenosis.

Although some investigators may wish to ask much more extensive pain questions, such as the most severe pain, the duration of pain, or other aspects of pain symptomatology, the current investigators recommend these items on pain severity for the past week as a minimum set of core questions. The questions on "bothersomeness" of pain symptoms have been validated in patients with sciatica by demonstrating highly significant associations with measures of functional status, absence from work, reflex changes, straight leg raising, and use of opioid analgesics.[1,14] Similarly, visual analog pain scales have enjoyed wide use, and similar evidence of construct validity has accrued.

Regarding function, the parsimonious set includes a single question about how much pain interfered with normal work. This question is derived from the widely used Short Form 36 (SF-36)[16] and its derivative shorter version, the SF-12, developed by Ware and colleagues.[17] It is also incorporated into the Lumbar Cluster of the AAOS and was a part of the Maine Lumbar Spine Study.[1]

The current proposal is that a single item be used to measure overall well-being by asking, "If you had to spend the rest of your life with the symptoms you have right now, how would you feel about it?" This item was used by the low back pain Patient Outcome Research Team at the University of Washington, and was also used by the initial Patient Outcome Research Teams for studies in coronary heart disease, prostate disease, and cataract disease that were funded by the Agency for Health Care Policy and Research. This item was also adopted as part of the Lumbar Cluster of the AAOS and was incorporated into the Maine Lumbar Spine Study. The performance of this particular question has been studied in relation to Roland Disability Scores, symptom bothersomeness, and the presence of symptoms and depression.[4] In the Maine Lumbar Spine Study, it was highly responsive to differences in treatment outcomes.[14]

Two items on disability related to social role are included in the core set. Both are derived from the U. S. National Health Interview Survey, and have been validated by identifying significant associations with compensation status, use of opioid analgesics, abnormal lower extremity strength, symptom frequency and severity, and changes in symptoms.[14] The first item asks on how many days patients have had to cut down on their normal activities, an item that is applicable even for retired or nonworking people. The second question asks about days lost from usual work or school because of leg or back pain. Although this item is not as responsive to changes occurring after therapy as direct measures of symptoms or functional status, it reflects significant differences in treatment outcomes for surgical *versus* nonsurgical patients in the Maine Lumbar Spine Study.[1,14] For the working-age population, specific time of absence from work was thought to be a key outcome measure. This question is also a part of the Low Back Pain TyPE questionnaire.

Finally, the parsimonious core set includes an optional question regarding patient satisfaction with care. Although this is not a measure of health outcome, it is an important concern in many types of interventions and in quality improvement applications. As ineffective treatments are used less frequently and as efforts are made to reduce unnecessary imaging, it may be important to measure and maintain patient satisfaction with care.

■ Proposed Core Instruments for Clinical Researchers

For many clinical research purposes, greater precision in measurement than is achievable with a single question is desirable. Thus, a somewhat expanded set of core instruments is recommended for investigators who have sufficient resources to collect and analyze such data. It is still a brief set of instruments, designed with the intent that other specific measures could be added at an investigator's discretion. This modestly expanded set of outcome

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measures is listed in Table 4. Some of the actual instruments are included as Appendices II—IV.

The same dimensions of outcome used in the parsimonious six-item set are preserved. The same measures of pain severity or bothersomeness are recommended as are used in the parsimonious core set. This includes separate measures of back pain severity and leg pain severity. In this expanded set, however, the determination of symptom frequency is also recommended.

With regard to functional status, the use of either the Roland and Morris Disability Scale[15] (or its adaptations[14]) or the Oswestry Disability Questionnaire[11] (and its adaptations) is recommended. These are among the most widely used and well validated of functional status questionnaires, and both would be highly acceptable. The Roland and Morris Scale, which was derived from the longer Sickness Impact Profile,[6,15] is well suited to administration by telephone, which may be important when seeking high follow-up rates at low cost. The Oswestry Scale would be tedious at best to administer by telephone. The Roland and Morris Disability Scale may be most useful in primary care settings, or in any situation in which the anticipated level of dysfunction at the end of a trial is small. The Oswestry Disability Questionnaire may be most useful in specialty care settings or in situations in which the disability level is likely to remain relatively high throughout a trial (*e.g.*, chronic severe low back pain).[2] A modest adaptation of the Roland and Morris Disability Scale has been studied and validated with the intent of producing a more responsive instrument, although head-to-head comparisons are unavailable.[14] The original version is reproduced in Appendix II. This instrument is now available in eight non-English languages (French, Dutch, Flemish, Spanish, Romanian, Italian, Portuguese, Polish, and Czech). These translations are available from Dr. Sandra Sinclair (e-mail address: ssinclair@wh,on.ca) or from the MAPI Research Institute (27 Rue de la Villette, 69003 Lyon, France). In addition, a modest adaptation of the Oswestry Disability Questionnaire has been developed and validated for use in the AAOS and NASS outcome questionnaires[5] (Appendix III).

With regard to generic well-being, inclusion of either the SF-12 (adapted from the SF-36[16]) or the EuroQoL (Appendix IV) is tentatively recommended.[10,17] Both are measures of general health that are not disease specific and that provide an assessment of a patient's overall health status. The SF-12 has been incorporated into the Lumbar Cluster of the AAOS and is widely used in a variety of settings within the United States. Translations are available in several languages. The EuroQoL instrument has the advantage that it produces a preference-weighted score that is necessary for use in formal decision analysis and cost-effectiveness analysis. That is, it measures a patient's "utility" for various health states in the manner that is theoretically necessary for these forms of analysis. Unfortunately, there is little evidence regarding the responsiveness of either the SF-12 or the EuroQoL instrument, although the larger SF-36 has been found to be responsive.[3,14] In general, such generic measures have proved to be less responsive than disease-specific questionnaires. In addition, the use of the single item from the parsimonious set that asks "if you had to spend the rest of your life with the symptoms you have right now, how would you feel about it?" is recommended.

Regarding disability from social role, the questions about days of work absenteeism and days in which the patient had to cut down on normal activities are recommended, but days spent in bed for at least half a day should also be determined. Again, these questions have been adapted from the National Health Interview Survey, validated for use in patients with back problems, and shown to discriminate between surgical and nonsurgical outcomes in the Maine Lumbar Spine Study.[1,14] Finally, the optional inclusion of a single item on overall patient satisfaction with care is again recommended.

The SF-12 includes questions related to mental health and depression, but the battery proposed here does not include a more extensive or formal measure of depression or mental health. Depending on the goal of a particular study, such measures might be added to this battery, but in many studies of back problems, measures of mental health are not as responsive to treatment effects as measures of physical health.[1]

■ Interpreting Changes or Differences in Outcome Measures

In some cases there are sufficient data to make recommendations for the smallest clinically relevant change or difference in outcome measures. For example, data from the Maine Lumbar Spine Study show that the minimum change that is of clinical importance in Roland Scale Score is between 2 and 3 points and in the SF-36 Physical Function subscale, it is approximately 7 points.[14] Effect sizes for many of the outcome measures listed here have been published among a cohort of patients with sciatica who demonstrated general improvements in 3 months.[14] These effect sizes could be used for purposes of calculating sample sizes for clinical trials. Nonetheless, there is a general need for more data on the responsiveness and the minimal changes of clinical importance in these outcome measures.

In summary, there are several scientific advantages to the use of a standardized set of measures for most clinical trials of treatment for low back pain. There are well-validated measures available that capture the many dimensions of outcome that are important for most patients with back pain, including symptoms, daily functioning, well-being, work disability, and satisfaction. The current group of investigators has prepared a core set of six items for extensive use and a modestly larger set of instruments that could be widely used by investigators with sufficient resources. There can be no

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illusion that either of these standardized sets will be sufficient for all research studies, and it is anticipated that most investigators will want to add specific and more detailed measures of outcomes that are particularly important for their individual settings or particular forms of treatment. In addition, it is hoped that the battery of questionnaires proposed here will undergo further evaluation, and it is anticipated that it will be continually refined and updated. To the extent that research on back pain incorporates this standardized set, however, it will facilitate comparability among studies, formal pooling of data, and an increase in large, multicenter studies.

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Appendix I: Proposed Core Outcome Measures

PATIENT OUTCOMES (note: most of these items are included in the AAOS Lumbar Cluster, the Low Back Pain TyPE, and the NASS low back outcome instrument.)

1. During the past week, how bothersome have each of the following symptoms been? (circle one number in each row)

		Not at all bothersome	Slightly bothersome	Moderately bothersome	Very bothersome	Extremely bothersome
a.	Low back pain	1	2	3	4	5
b.	Leg pain (sciatica)	1	2	3	4	5

2. During the past week, how much did pain interfere with your normal work (including both work outside the home and housework)?

☐ Not at all ☐ A little bit ☐ Moderately ☐ Quite a bit ☐ Extremely

3. If you had to spend the rest of your life with the symptoms you have right now, how would you feel about it?

☐ Very dissatisfied ☐ Somewhat dissatisfied ☐ Neither satisfied nor dissatisfied ☐ Somewhat satisfied ☐ Very satisfied

4. During the past 4 weeks, about how many days did you cut down on the things you usually do for more than half the day because of back pain or leg pain (sciatica)? _____ Number of days

5. During the past four weeks, how many days did low back pain or leg pain (sciatica) keep you from going to work or school? _____ Number of days

6. Over the course of treatment for your low back pain or leg pain (sciatica), how satisfied were you with your overall medical care?

☐ Very dissatisfied ☐ Somewhat dissatisfied ☐ Neither satisfied nor dissatisfied ☐ Somewhat satisfied ☐ Very satisfied

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Appendix II: Roland and Morris Disability Questionnaire (with instructions)

When your back hurts, you may find it difficult to do some of the things you normally do.

This list contains some sentences that people have used to describe themselves when they have back pain. When you read them, you may find that some stand out because they describe you *today*. As you read the list, think of yourself today. When you read a sentence that describes you today, put a tick against it. If the sentence does not describe you, then leave the space blank and go on to the next one. Remember, only tick the sentence if you are sure that it describes you today.

Because of my back or leg pain (sciatica) *today:*

YES	NO	
		1. I stay at home most of the time because of my back.
		2. I change position frequently to try to get my back comfortable.
		3. I walk more slowly than usual because of my back.
		4. Because of my back I am not doing any of the jobs that I usually do around the house.
		5. Because of my back, I use a handrail to get upstairs.
		6. Because of my back, I lie down to rest more often.
		7. Because of my back, I have to hold on to something to get out of an easy chair.
		8. Because of my back, I try to get other people to do things for me.
		9. I get dressed more slowly than usual because of my back.
		10. I only stand up for short periods of time because of my back.
		11. Because of my back, I try not to bend or kneel down.
		12. I find it difficult to get out of a chair because of my back.
		13. My back is painful almost all the time.
		14. I find it difficult to turn over in bed because of my back.
		15. My appetite is not very good because of my back pain.
		16. I have trouble putting on my socks (or stockings) because of the pain in my back.
		17. I only walk short distances because of my back pain.
		18. I sleep less well because of my back.
		19. Because of my back pain, I get dressed with help from someone else.
		20. I sit down for most of the day because of my back.
		21. I avoid heavy jobs around the house because of my back.
		22. Because of my back pain, I am more irritable and bad tempered with people than usual.
		23. Because of my back, I go upstairs more slowly than usual.
		24. I stay in bed most of the time because of my back.

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Appendix III: Modified version of the Oswestry Disability Questionnaire used in the AAOS Lumbar Cluster

In the past week, please tell us how pain has affected your ability to perform the following activities. (Circle the ONE statement that best describes your average ability.)

	I can dress myself without pain	I can dress myself without increasing pain	I can dress myself but pain increases	I can dress myself but with significant pain	I can dress myself but with very severe pain	I cannot dress myself
808. Getting dressed (In the past week).	1	2	3	4	5	6

	I can lift heavy objects without pain	I can lift heavy objects but it is painful	Pain prevents me from lifting heavy object off the floor, but I can lift heavy object if they are on a table	Pain prevents me from lifting heavy objects, but I can lift light to medium objects if they are on a table	I can only lift light objects	I cannot lift anything
809. Lifting (in the past week).	1	2	3	4	5	6

	I can run or walk without pain	I can walk comfortably, but running is painful	Pain prevents me from walking more than 1 hour	Pain prevents me from walking more than 30 minutes.	Pain prevents me from walking more than 10 minutes	I am unable to walk or can walk only a few steps at at time
810. Walking and Running (in the past week).	1	2	3	4	5	6

	I can sit in any chair as long as I like	I can only sit in a special chair for as long as I like	Pain prevents me from sitting more than 1 hour	Pain prevents me from sitting more than 30 minutes	Pain prevents me from sitting more than 10 minutes	Pain prevents me from sitting at all
811. Sitting (in the past week).	1	2	3	4	5	6

	I can stand as long as I want	I can stand as long as I want but it gives me pain	Pain prevents me from standing more than 1 hour	Pain prevents me from standing for more than 30 minutes	Pain prevents me from standing for more than 10 minutes	Pain prevents me from standing at all
812. Standing (in the past week).	1	2	3	4	5	6

	I sleep well	Pain occasionally interrupts my sleep	Pain interrupts my sleep half of the time	Pain often interrupts my sleep	Pain always interrupts my sleep	I never sleep well
813. Sleeping (in the past week).	1	2	3	4	5	6

	My social and recreational life is unchanged	My social and recreational life is unchanged but it increases pain	My social and recreational life is unchanged but it severely increases pain	Pain has restricted my social and recreational life	Pain has severely restricted my social and recreational life	I have essentially no social and recreational life because of pain
814. Social and Recreational Life (in the past week).	1	2	3	4	5	6

	I can travel anywhere	I can travel anywhere but it gives me pain	Pain is bad but I can manage to travel over two hours	Pain restricts me to trips of less than one hour	Pain restricts me to trips of less than 30 minutes	Pain prevents me from traveling
815. Traveling (in the past week).	1	2	3	4	5	6

	My sex life is unchanged	My sex life is unchanged but causes some pain	My sex life is nearly unchanged but it is very painful	My sex life is severely restricted by pain	My sex life is nearly absent because of pain	Pain prevents any sex life at all
816. Sex life.	1	2	3	4	5	6

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Appendix IV: The EuroQoL instrument for utility-weighted health status (useful for cost-effectiveness analysis)

Questionnaire for EuroQol Instrument Revised Classification

We are trying to find out what people think about health. We are going to describe a few health states that people can be in. We want you to indicate how good or bad each of these states would be for a person like you. There are no right or wrong answers. Here we are interested only in your personal view.

But first of all, we would like you to indicate (on the next page) the state of your own health today.

By placing a tick (thus ☑) in one box in each group below, please indicate which statements best describe your own health state today.

Mobility

- I have no problems in walking about
- I have some problems in walking about
- I am confined to bed

Self-Care

- I have no problems with self-care
- I have some problems washing or dressing myself
- I am unable to wash or dress myself

Usual Activities

- I have no problems with performing my usual activities (e.g., work, study, housework, family or leisure activities)
- I have some problems with performing my usual activities
- I am unable to perform my usual activities

Pain/Discomfort

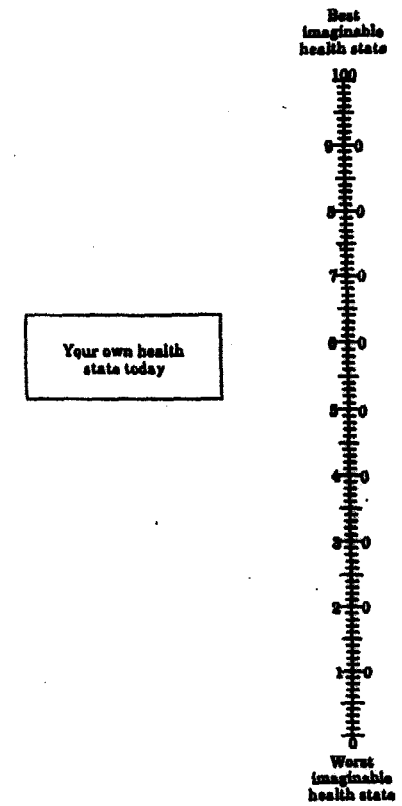
- I have no pain or discomfort
- I have moderate pain or discomfort
- I have extreme pain or discomfort

Anxiety/Depression

- I am not anxious or depressed
- I am moderately anxious or depressed
- I am extremely anxious or depressed

Compared with my general level of health over the past 12 months, my health state today is: (Please tick one box)

- Better
- Much the same
- Worse



To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked by 100 and the worst state you can imagine is marked by 0. We would like you to indicate on this scale how good or bad is your own health today, in your opinion. Please do this by drawing a line from the box above to whichever point on the scale indicates how good or bad your current health state is.

Reference: EuroQoL Group. EuroQoL – a new facility for the measurement of health-related quality of life. Health Policy 1990; 16:199-208

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Research Report

The Effects of Selected Stimulus Waveforms on Pulse and Phase Characteristics at Sensory and Motor Thresholds

Gideon Kantor
Gad Alon
Henry S Ho

Background and Purpose. *The purposes of this investigation were to determine the effect of five commonly used voltage waveforms (four pulsed and one sinusoidal) on excitation of sensory and motor nerves and to characterize variables associated with reaching threshold.* ***Subjects.*** *Eighteen healthy subjects were stimulated during one session via surface electrodes placed over the forearm and leg.* ***Methods.*** *Stimulation amplitude was increased at a constant rate, and the threshold of sensory and motor excitation was determined. Measured variables included peak voltage, peak current, phase charge, and total pulse charge.* ***Results.*** *Three-factorial, repeated-measures analysis of variance and Newman-Keuls tests revealed that phase charge varied the least during excitation induced by the five waveforms. Total pulse charge markedly increased when bursts of 10 symmetrical pulses, 25 symmetrical pulses, or amplitude-modulated waveforms were used. Monophasic and symmetrical biphasic waveforms required the least amount of total pulse charge. All measurements were higher during motor threshold than during sensory threshold, and the measurements were higher in the leg than in the forearm.* ***Conclusion and Discussion.*** *The authors concluded that all five studied waveforms were effective at threshold excitation of peripheral sensory and motor nerves. Of the five waveforms, the symmetrical biphasic waveform, having a low total pulse charge, may be the preferred waveform, and the 25 symmetrical pulses and amplitude-modulated waveforms may be considered the least preferred due to high total pulse charge. [Kantor G, Alon G, Ho HS. The effects of selected stimulus waveforms on pulse and phase characteristics at sensory and motor thresholds. Phys Ther. 1994;74:951–962.]*

Key Words: *Electrotherapy, electrical stimulation; Motor activity; Neurophysiology/neuroanatomy; Peripheral nerves; Sensory thresholds.*

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This study was approved by the Institutional Review Board of the University of Maryland and the Research Involving Human Subjects Committee of the Food and Drug Administration.

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Clinical use of transcutaneous electrical stimulation is frequently associated with the excitation of sensory and motor nerves. Commercial stimulators provide many different waveforms and a variety of pulse settings. These stimulators are used for treatment of numerous clinical conditions that require stimulation of various body sites.[1,2] Researchers have attempted to identify a preferred waveform during neuromuscular excitation.[3–9] Most of these researchers tested the comfort

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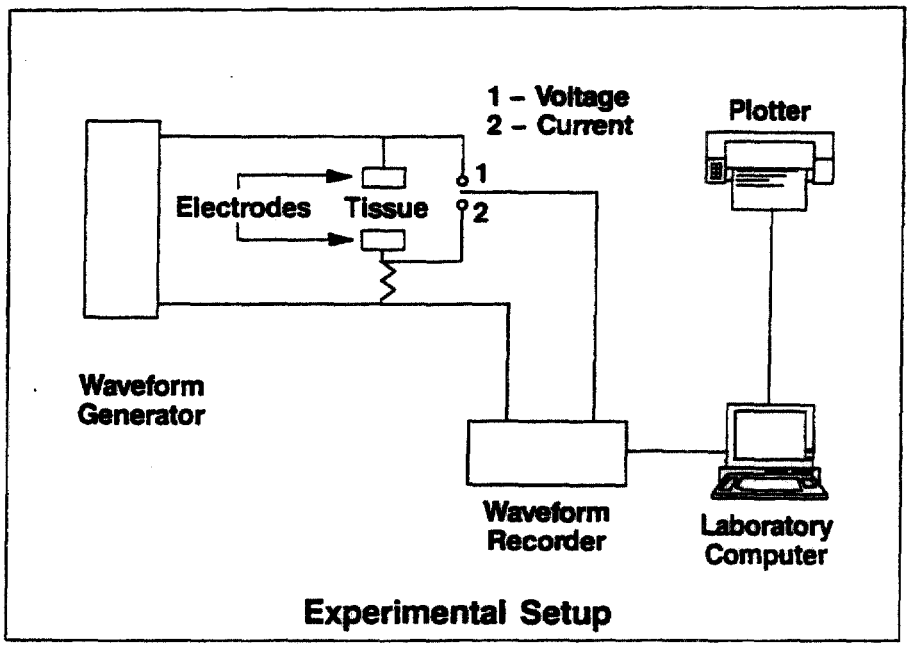


Figure 1. *A schematic representation of the Center for Devices and Radiological Health electrical stimulation system.*

perception to different waveforms either at the highest tolerable intensity[3,5] or at fixed levels of muscle torque production.[4,6–9] Wong[3] stimulated the forearm of healthy subjects and reported that a monophasic waveform was more comfortable and generated more torque than an asymmetric biphasic waveform. Bowman and Baker[6] found that most subjects preferred a symmetric biphasic waveform over a monophasic or asymmetric biphasic waveform for stimulation of the quadriceps femoris muscle. The upper and lower extremities, therefore, may respond differently and may require different waveforms to optimize comfort.[7–9]

Determining whether waveforms differently affect nerve excitation in the upper and lower limbs, or whether waveforms affect sensory and motor nerves differently, can be studied through testing of the minimum, threshold excitation values of the various waveforms. Use of invasive electrodes with animal models[10,11] or mathematical modeling[12,13] suggests that the depolarization and action potential propagation patterns are independent of waveform. Stimulus characteristics, however, vary appreciably with waveforms when human subjects are stimulated via surface electrodes at threshold levels. Kantor and colleagues[14,15] collected preliminary data from healthy subjects and reported that peak voltage, peak current, and total pulse charge all vary significantly between different waveforms. In contrast, they found that phase charge values were the same at threshold excitation irrespective of waveform.

Minimum levels of sensory and motor nerve stimulation are common in clinical practice. Thus, establishing minimum values of stimulus characteristics, at thresholds that excite peripheral nerves of both the upper and lower extremities, may help clinicians in setting these waveform levels. The data may also help to identify potential advantages and disadvantages of each waveform and may indicate whether there is a preferred waveform for excitation. In addition, the safety of stimulation may depend in part on stimulus waveform.[2]

The purpose of our investigation was to document the effect of five waveforms on four variables: peak current, peak voltage, phase charge, and total pulse charge during threshold excitation of peripheral nerves in the forearm and leg. The data were used to establish minimum values for nerve excitation and to compare (1) sensory and motor nerves and (2) upper- and lower-extremity nerves.

Method

Subjects

Sixteen female and two male subjects, all healthy volunteers with a mean age of 26.9 years (SD=7.5, range=19–45), participated in the study. All subjects stated they had no neuromuscular abnormality and that they had normal tactile and pressure perception.

Instrumentation

A stimulation and recording system was developed at the Center for Devices and Radiological Health (Rockville, Md) to generate, control, and record various waveforms (four pulsed and one sinusoidal) currently used in the clinic.[1,2] The system consisted of two constant-voltage signal generators (Wavetek model 175* and HP model 3314A†) controlled by an HP model 5000 microcomputer† and an HP model 5180A waveform recorder† (Fig. 1). The accuracy of the waveform recorder was reported by the manufacturer to be ±3% over the range of the voltages of the signal. Using a software program written by one of us (HSH), the system generated five different waveforms: monophasic (MP); symmetric biphasic (SBP); bursts of 10 or 25 symmetrical pulses (10 SP and 25 SP); and amplitude modulated (AM), also known as premodulated interferential current.[2] Figures 2 through 5 show typical plots for four of the five voltage waveforms and associated current waveforms. The phase duration and pulse repetition rate of all five waveforms were

*Wavetek Corp, 9045 Balboa Ave, San Diego, CA 92123.
†Hewlett-Packard, 2 Choke Cherry Rd, Rockville, MD 20850.

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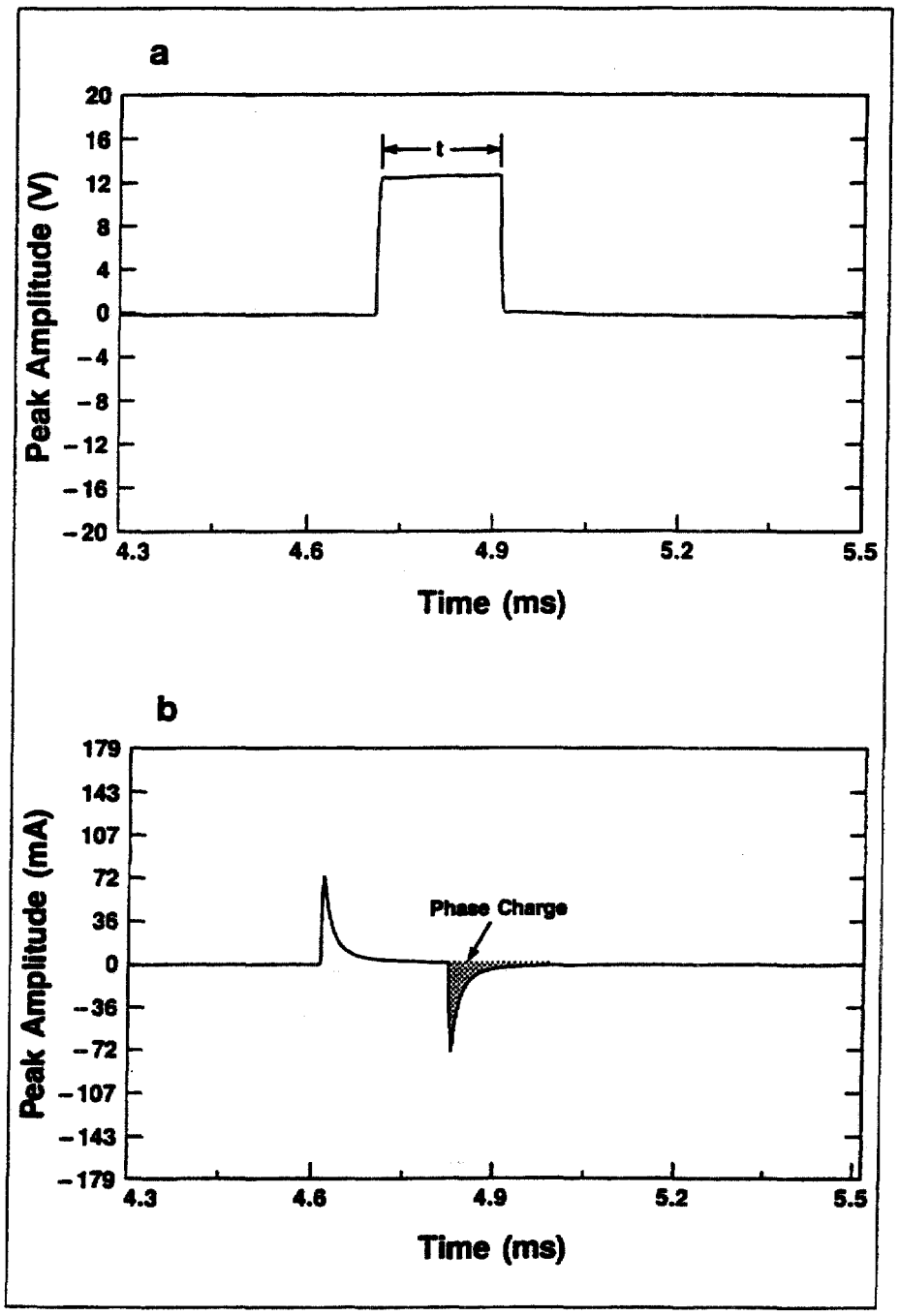


Figure 2. *A single pulse of the monophasic voltage waveform (Fig. 2a) and associated current waveform (Fig. 2b) recorded during motor nerve threshold excitation of the forearm. Phase duration (t) of the voltage waveform was 200 microseconds. The phase duration of the current waveform was much shorter due to the use of a constant-voltage stimulator. Pulse rate (not illustrated) was set at 50 pulses per second. The shaded area of the largest phase represents phase charge measured in microcoulombs.*

200 microseconds and 50 pulses per second (pps), respectively. The 25-SP waveform is not shown as it was almost identical to the 10-SP waveform.

During stimulation, the stimulus voltage and current waveforms were recorded and peak voltage, peak current, phase charge, and total pulse charge were determined by use of the computer. Phase charge (current integrated over phase duration, namely between two zero crossings) was calculated by the computer through digital integration using the formula $Q_P = It$, where Q_P represents the phase charge, I is the peak current, and t is the phase duration. The algorithm to calculate phase charge included (1) threshold detection of peak current at 0.3% of the peak, (2) 20 consecutive counts of peak current above threshold, and (3) summation of peak current over time until the signal dropped below threshold for 20 consecutive counts of peak current. Sampling of the signal was done every 2 microseconds. Total pulse charge was calculated as the sum of all phase charges contained in the pulse, irrespective of polarity (absolute values).

Procedure

Each subject signed a consent form, after which he or she assumed a sitting position, resting the right lower extremity on a chair with the knee in full extension and the foot supported in 0 degrees of dorsiflexion. The right upper extremity was positioned on an armrest with the shoulder in the anatomical position, the elbow at 90 degrees of flexion, the forearm in full pronation, and the hand and fingers fully supported yet relaxed on the armrest.

Two conductive polymer, self-adhesive surface electrodes (model 651-1842[‡]), each 8.8 cm long and 3.8 cm wide, were used in the study. The right forearm of each subject was cleansed with water, and the proximal electrode was placed perpendicular to the segment on the dorsal surface over the extensor muscle group, 4 cm distal to the lateral epicondyle. The second electrode was placed 8 cm distal to the first electrode. During stimulation of the lower extremity, the same electrode application procedure was repeated over the dorsiflexor muscle group, but the placement of the proximal electrode was 10 cm distal to the tibial plateau.

[‡]ConMed Corp, 310 Broad St, Utica, NY 13501.

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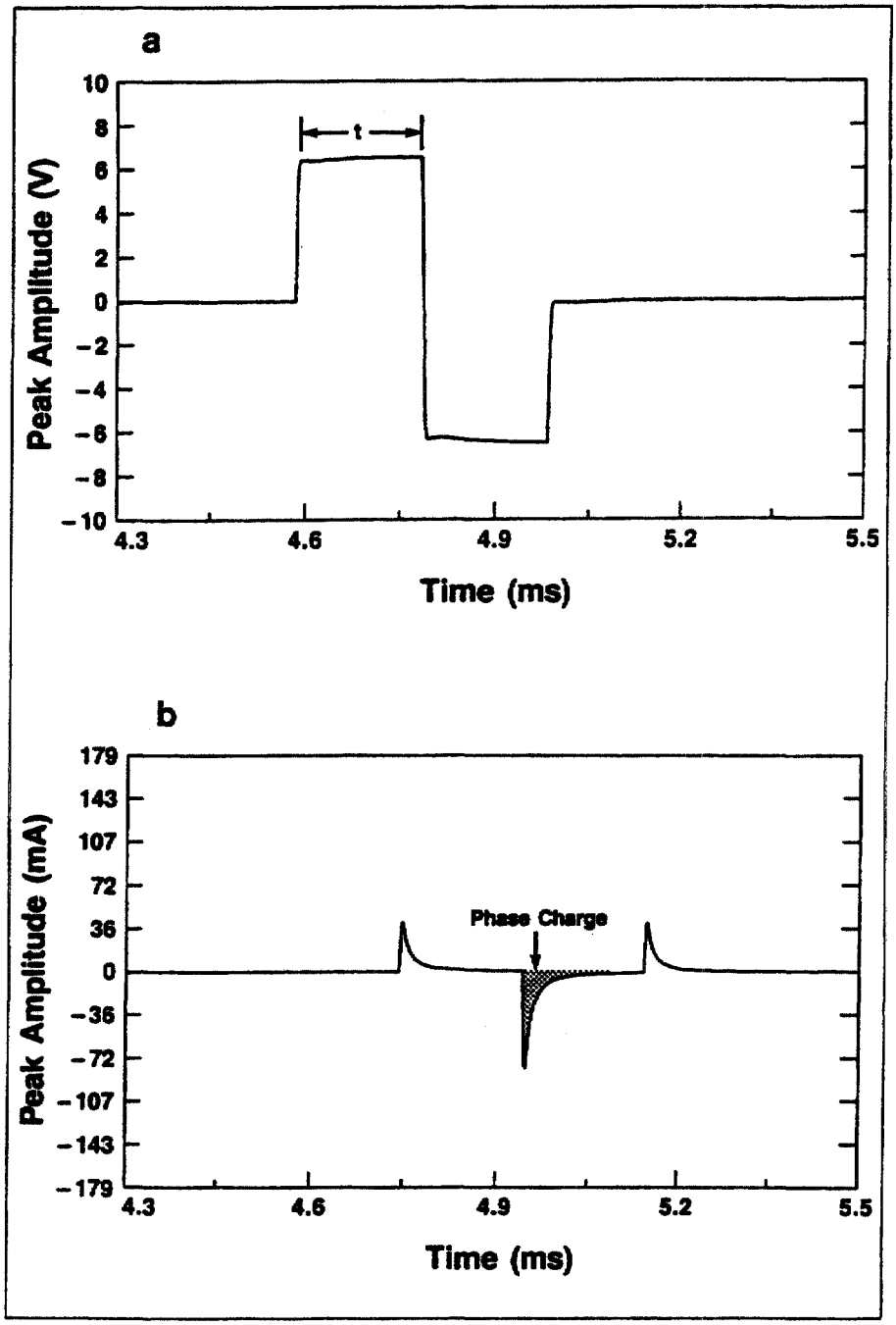


Figure 3. *A single pulse of the symmetrical biphasic voltage waveform (Fig. 3a) and associated current waveform (Fig. 3b) recorded during motor nerve threshold excitation of the forearm. Phase duration (t) of the voltage waveform was 200 microseconds. The phase duration of the current waveform was much shorter due to the use of a constant-voltage stimulator. Pulse rate (not illustrated) was set at 50 pulses per second. The shaded area of the largest phase represents phase charge measured in microcoulombs.*

Determination of sensory nerve threshold excitation was achieved by gradual increase of stimulus amplitude at a rate of 0.2 V/s. At the instant the subject began to perceive tingling, the amplitude was held constant for a 30-second "on" period, then switched "off" for 15 seconds and then switched on again. If the subject perceived the stimulation throughout the two on periods, the peak voltage, peak current, phase charge, and total pulse charge were recorded. Peak current and phase charge were measured for the highest phase component of each waveform. The same procedure was repeated for motor threshold excitation by observing and/or palpating the initiation of minimal muscle contraction beneath the electrodes. Motor threshold was determined by the investigator, not the subject.

The sequence of testing the five waveforms was ordered as follows. Waveform presentation to subject 1 was selected at random and followed the order AM, MP, SBP, 10 SP, and 25 SP. Subject 2 started with MP followed by SBP, 10 SP, 25 SP, and AM, and so on. This sequential ordering ensured that each waveform was introduced as first, second, third, forth, or fifth the same number of tests and minimized the effect of novelty on threshold determination. The time between presentation of each waveform was 2 minutes.

Data Analysis

Three main factors were considered in this study: the five waveforms, the sensory and motor excitation thresholds, and the forearm and leg segments. The four measured variables were peak voltage, peak current, phase charge, and total pulse charge. Each of the four variables was subjected to a separate analysis of variance (ANOVA) for repeated measures on all three factors. Significant F ratios (α=.05) were further analyzed by Newman-Keuls *post hoc* tests (α=.05) to identify significant differences among means. We examined all three factors to permit comparison of pulse characteristics at different excitation thresholds, and between the upper and lower extremities.

Results

All four ANOVAs indicated significant interaction among the three factors in each of the four measured variables (Table). The *post hoc* analysis of the interaction of 20 means of peak voltage showed that the peak voltage of the MP and AM waveforms was higher than that of the SBP, 10-SP, and 25-SP

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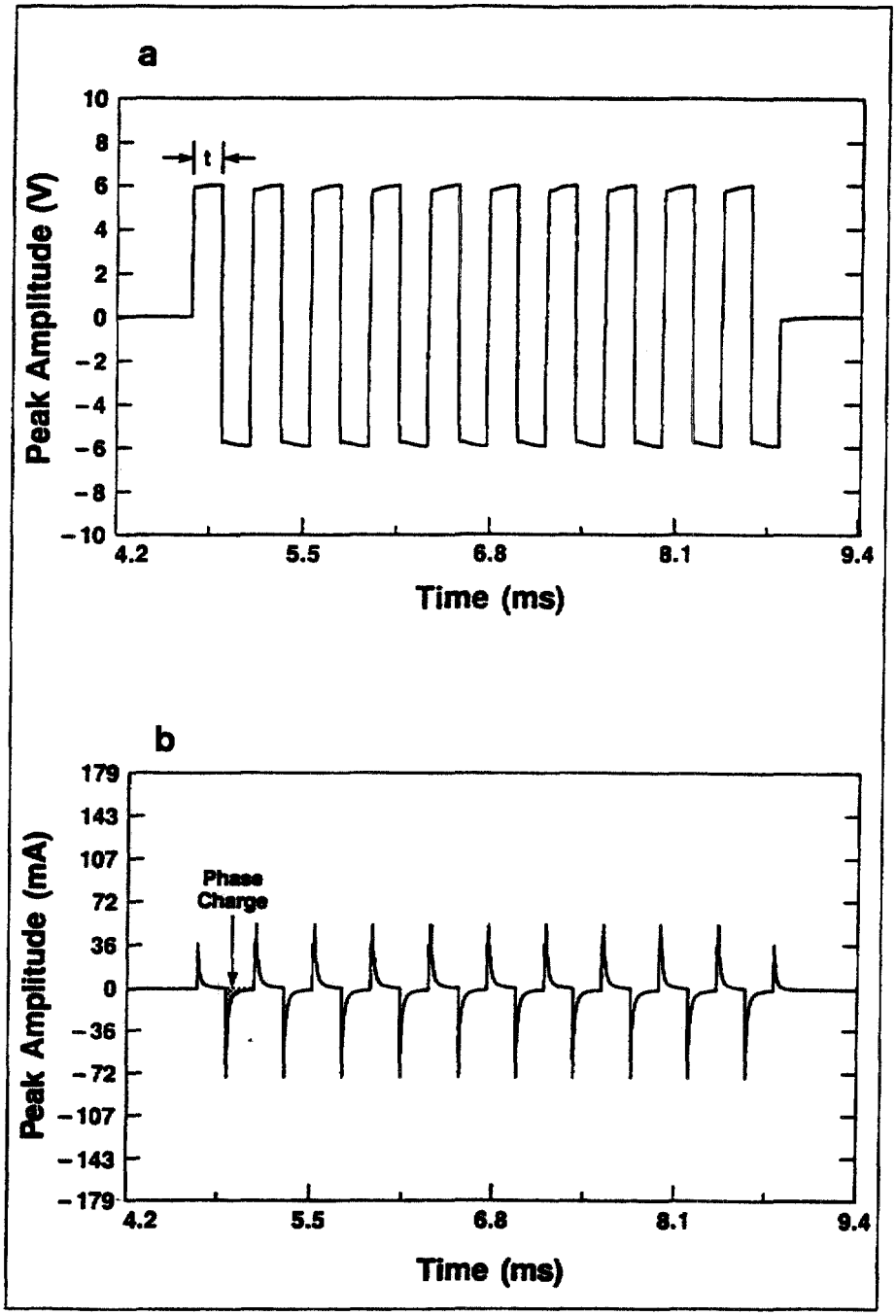


Figure 4. *A single burst of the 10-symmetrical pulse (10-SP) voltage waveform (Fig. 4a) and associated current waveform (Fig. 4b) recorded during motor nerve threshold excitation of the forearm. Phase duration (t) of the voltage waveform was 200 microseconds. The phase duration of the current waveform was much shorter due to the use of a constant-voltage stimulator. Repetition rate (not illustrated) was set at 50 bursts per second. The shaded area of the largest phase represents phase charge measured in microcoulombs. (The waveform with bursts of 25 symmetrical pulses used in this study is not shown as it was almost identical to the 10-SP waveform.)*

waveforms during motor excitation of either the forearm or the leg. In contrast, the peak current of the AM waveform was lower than that of the other four waveforms in all test conditions. The peak currents of the SBP, MP, 10-SP, and 25-SP waveforms were not different.

The five different waveforms had little effect on the amount of phase charge required to excite the sensory nerves of the forearm. Likewise, the waveform did not affect the phase charge during sensory excitation of the leg or motor nerve excitation in the forearm or leg. Unlike the absence of a discernible change in phase charge, there was a marked increase in total pulse charge associated with the AM and 25-SP waveforms compared with the MP, SBP, and 10-SP waveforms. The differences were particularly noticeable during forearm and leg motor nerve excitation. The total pulse charge of the 10-SP waveform was higher than that of the SBP and MP waveforms, which did not differ from each other. The means and standard deviations of the four measured stimulus characteristics are presented in Figures 6 through 9.

Discussion

In general and irrespective of waveforms, sensory nerve excitation required less stimulus magnitude of peak voltage, peak current, phase charge, and total pulse charge than did motor stimulation. Likewise, forearm stimulation required less magnitude of all four stimulus characteristics than did leg stimulation. In contrast, the sensory threshold in the forearm was elicited with an average of 18.4% (SD=4.0%) less stimulus peak voltage, peak current, phase charge, and total pulse charge compared with the sensory threshold in the leg. The mean difference for motor threshold was more pronounced, averaging 41.4% (SD=2.3%) more output for the measured variables in the leg than in the forearm.

Our data verified the clinical observation that many different waveforms can be used to excite peripheral nerves.[1,16–19] The results are in agreement with those of Johnston and Kasper,[10] who stimulated a frog nerve-muscle preparation and reported that all five studied waveforms induced very similar compound action potentials. Our data, however, demonstrate that the five waveforms had diverse effects on stimulus peak voltage, peak

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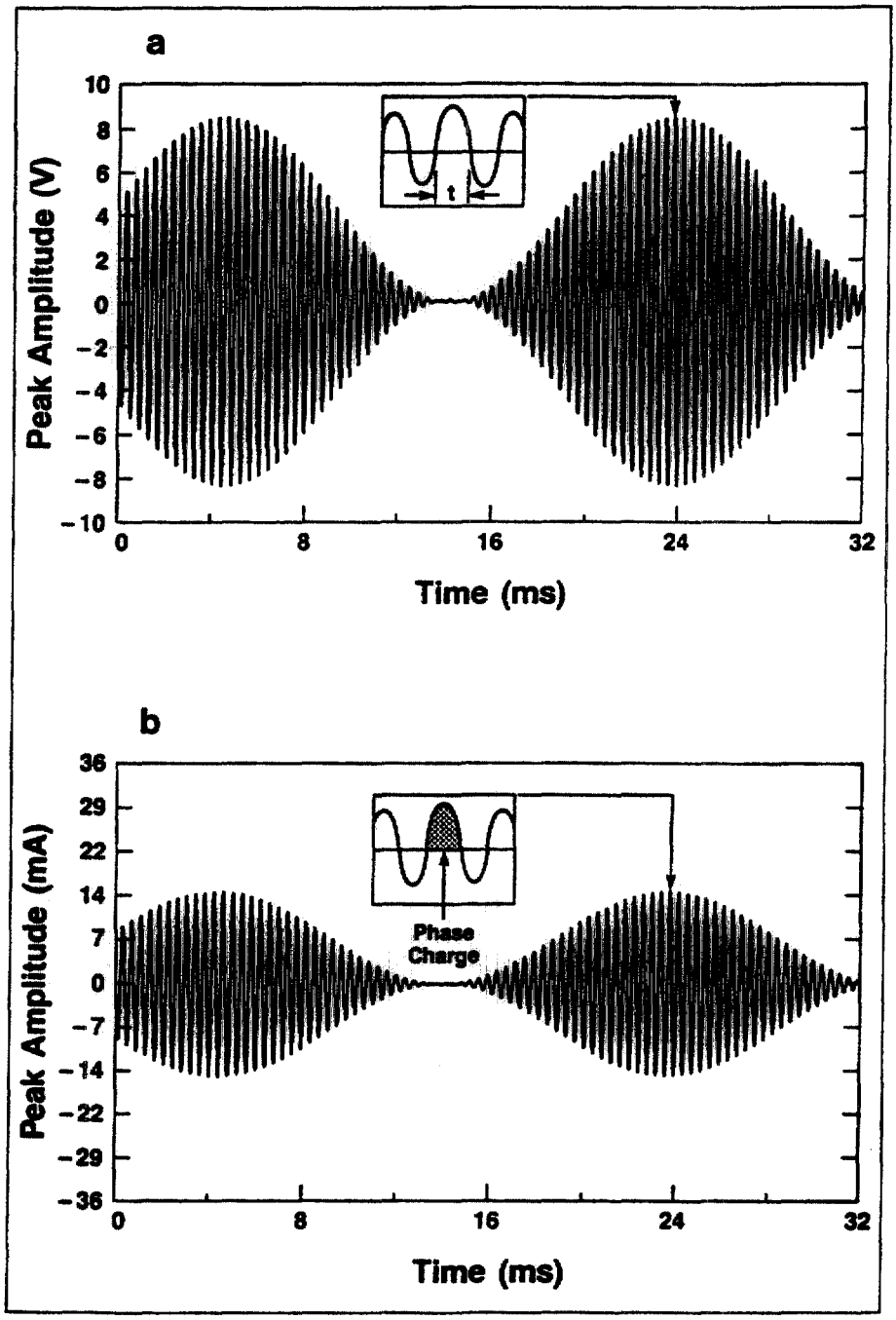


Figure 5. *Two multiphasic pulses of the amplitude-modulated (AM) voltage waveform (Fig. 5a) and associated current waveform (Fig. 5b) recorded during motor nerve threshold excitation of the forearm. As shown in the insert, phase duration (t) was 200 microseconds and the shaded area of the largest phase represents phase charge measured in microcoulombs. Pulse rate (not illustrated) was set at 50 pulses per second.*

current, phase charge, and total pulse charge.

Peak Voltage and Current

Peak voltage and peak current were less variable than total pulse charge but more variable than phase charge. We could find neither published references nor reasonable explanations for peak voltages of the MP and AM waveforms being significantly higher than those of the SBP, 10-SP, and 25-SP waveforms during motor excitation. Conceivably, the MP and AM waveforms require higher voltages to generate the appropriate phase charges when a regulated voltage stimulator is used.

The peak current of the AM stimulus was significantly lower than the peaks of the other waveforms because it was the only one in which the phase duration of the current waveform was the same (200 microseconds) as that of the voltage waveform. This finding was due to the sinusoidal shape of the AM waveform. In the other four waveforms, the phase duration of the current waveform was much shorter (Figs. 2–4). The human body exhibits nonlinear, resistive-capacitive, frequency-dependent conduction characteristics.[12,20] The four square waveforms contained multiple frequencies, whereas the sinusoidal waveform had only one frequency (2,500 Hz). Consequently, the square waveforms exhibited a very fast discharge of the current, which resulted in a much shorter effective phase duration.[1] In accordance with the excitatory rule, which states that a shorter phase duration requires a higher peak current, our results are consistent with the expected relationship between phase duration and peak current amplitude.[12,21]

Comparing peak current between the MP and SBP waveforms showed that they are not different. Gorman and Mortimer[11] observed that the peak current of the SBP waveform was higher than that of a monophasic pulse, and they concluded that the biphasic waveform is less desired for nerve excitation. Our results did not support this conclusion. Gorman and Mortimer studied anesthetized cats, using surgically implanted electrodes, and they did not test the statistical significance of the reported differences. Their results should therefore be limited to the studied model.

Further examination of the differences in peak current indicated that the 10-SP and 25-SP waveforms required somewhat lower peak current than the SBP waveform. This result was also observed by Reilly and associ-

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Table. *Summary of Analysis of Variance Tests on the Measured Variables*

Source	df	MS	F Ratio[a]
Peak voltage			
Forearm/leg (FL)	1	622.9	57.5
Sensory/motor (SM)	1	2025.1	224.5
FL×SM	1	302.1	55.7
Waveform (W)	4	311.7	412.9
FL×W	4	16.4	20.1
SM×W	4	74.2	147.7
FL×SM×W	4	11.9	21.0
Error	68	0.5	
Peak current			
FL	1	55136.0	82.6
SM	1	144413.9	242.6
FL×SM	1	22920.4	87.5
W	4	31770.3	203.6
FL×W	4	1541.0	18.6
SM×W	4	4081.9	67.6
FL×SM×W	4	684.1	17.2
Error	68	39.7	
Phase charge			
FL	1	57.99	74.9
SM	1	199.70	232.3
FL×SM	1	30.63	82.5
W	4	4.67	74.8
FL×W	4	0.46	7.8
SM×W	4	1.06	21.6
FL×SM×W	4	0.14	4.1
Error	68	0.03	
Total pulse charge			
FL	1	39469.1	85.0
SM	1	120078.1	220.0
FL×SM	1	19486.7	89.9
W	4	175526.6	729.2
FL×W	4	8786.1	72.4
SM×W	4	25701.9	168.4
FL×SM×W	4	4175.9	66.6
Error	68	62.6	

[a]Significant at $P>.0001$.

ates,[12] who reported a decreased threshold of excitation with increased number of sinusoidal cycles. Theoretically, the addition of more phases to the SBP waveform may facilitate the depolarization of the nerve membrane through temporal summation. But how many additional phases are needed to minimize the peak current? Mathematical modeling by Buetikoffer and Lawrence[13] suggested that three symmetrical pulses would be the optimal number in what they termed "quantal stimulation." Clinical verification of this modeling is currently not available.

Phase Charge

When evoking sensory and motor responses, phase charge was less variable than the other stimulus characteristics. Whereas there were differences between sensory and motor thresholds and between forearm and leg stimulation, there were no differences in phase charge between the five waveforms. These results are not in accord with the findings of Bowman and Baker,[6] who found dissimilar values of phase charge during motor stimulation using SBP and asymmetric biphasic waveforms. Unfortunately, Bowman and Baker did not test the statistical significance of those differences. Furthermore, we tested threshold excitation levels of the wrist and ankle extensors, whereas Bowman and Baker studied the quadriceps femoris muscles at moderately strong contraction levels. Whether our results are specific to the test conditions and muscles under investigation, or whether they can be extended to higher levels of excitation and different body regions, cannot be determined at present.

There are indications that phase charge is the least affected variable of the waveform during excitation of peripheral nerves at various levels of intensity. This conclusion was implied by Laquicque and Weiss, according to a review by Geddes.[20] We believe this is because phase charge is represented by the area under the curve of the phase.[2,4,6,7] The phase charge, therefore, reflects the attributes of phase duration, current amplitude, and stimulus shape. We suggest monitoring and reporting phase charge values as part of any research. Doing so will permit comparisons among studies that used different waveforms to stimulate peripheral nerves.

We believe that considering and reporting only peak current (or peak voltage) and phase duration (as is usually done) may not allow comparison of data concerning excitation of peripheral nerves. Not knowing the shape of the waveform and whether the stimulus is generated as constant voltage or constant current may pro-

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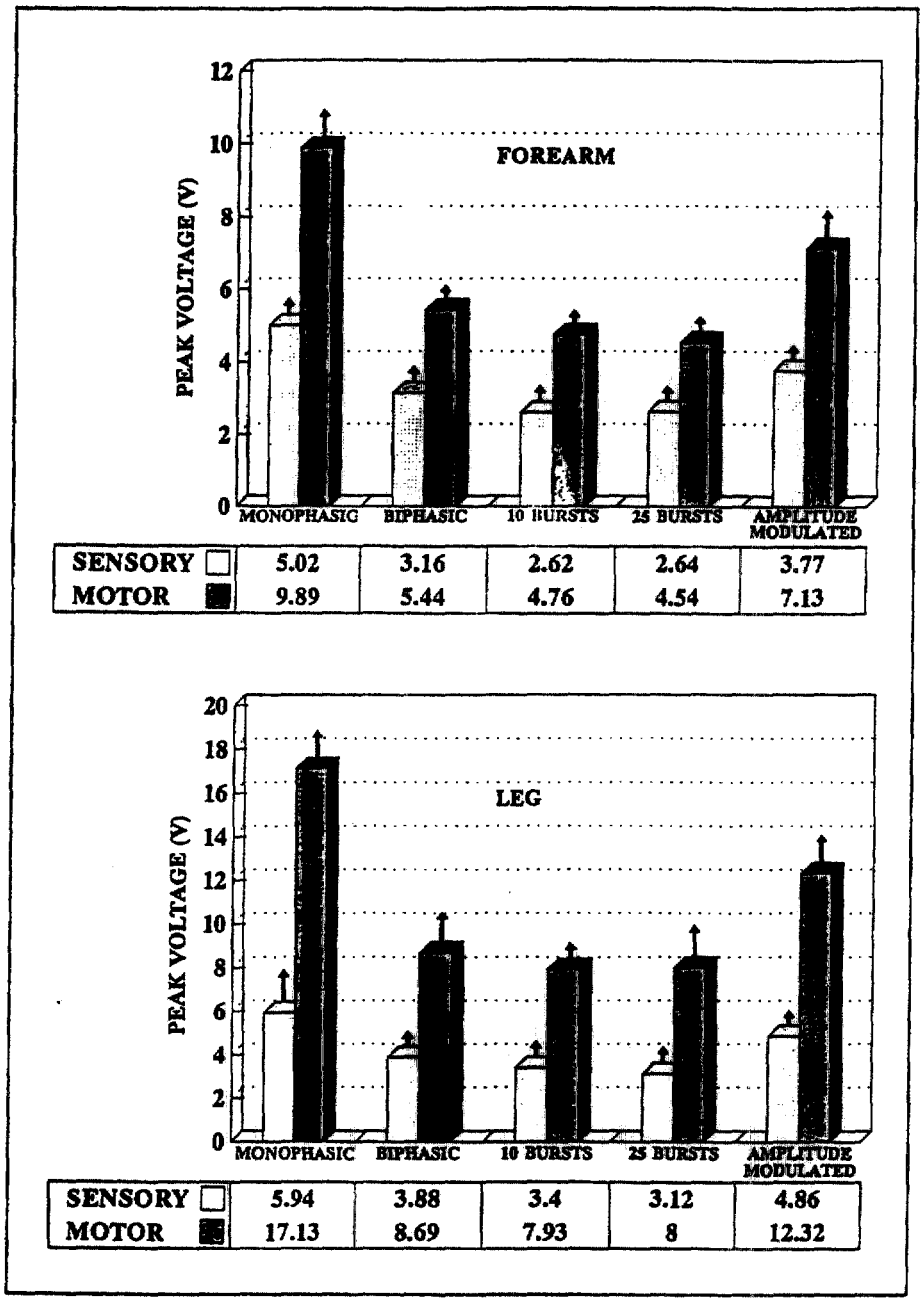


Figure 6. *Means of peak voltages recorded during threshold excitation of sensory and motor nerves in the forearm and leg. Arrows represent the standard deviations.*

vide for high variability of peak current and peak voltage. Because phase charge reflects not only phase duration and current amplitude but also stimulus shape, it is likely to be the most consistent and thus reproducible stimulus characteristic of the different waveforms. Furthermore, the repeatability of phase charge values has been demonstrated to be independent of three electrodes of significantly different conductivity,[22] and this repeatability held true whether constant-current or constant-voltage stimulators were used.[23] Hayden et al[24] added the dimension of time to phase charge reproducibility. They concluded that the phase charge quantities recorded during maximally tolerated stimulation of the lumbar erector spinae muscle were very consistent over 4 weeks of weekly stimulation.

There are limitations to our hypothesis on phase charge reproducibility. Our data show that the amount of phase charge varies between sensory and motor excitation, averaging 44.3% and 60.6% higher values during motor stimulation of the forearm and leg, respectively. Likewise, stimulation of the sensory and motor nerves in the forearm required a 34% lower average phase charge than for the leg nerves.

Alon et al[21] presented data on healthy subjects where the amount of phase charge necessary to excite sensory and motor nerves declined as phase duration became shorter. The amount of charge necessary to generate 1 N·m of elbow extension torque was fairly uniform between 20 and 200 microseconds and sharply increased with phase durations longer than 300 microseconds. We infer from these findings that the stability and reproducibility of phase charge can be expected as long as phase duration is approximately in the range of 20 to 300 microseconds.

Total Pulse Charge

The most dramatic differences were observed in total pulse charge. The threshold excitation with the SBP waveform was statistically no different than with the MP waveform. Furthermore, the mean differences of 18% to 21% were smaller than what could be extrapolated from the mathematical modeling of excitation thresholds published by Reilly et al.[12] The fact that total pulse charge did not differ statistically between the MP and SBP waveforms suggests that current mathematical models may not adequately address and thus may not accurately predict a multifactorial, in vivo human response. An improved model may require the consideration of a number of variables including electrode size, electrode location relative to the nerves, and method of threshold determination, all of which are inherently much less controlled when testing human subjects. Furthermore, the difference in total pulse charge between the MP and SBP waveforms

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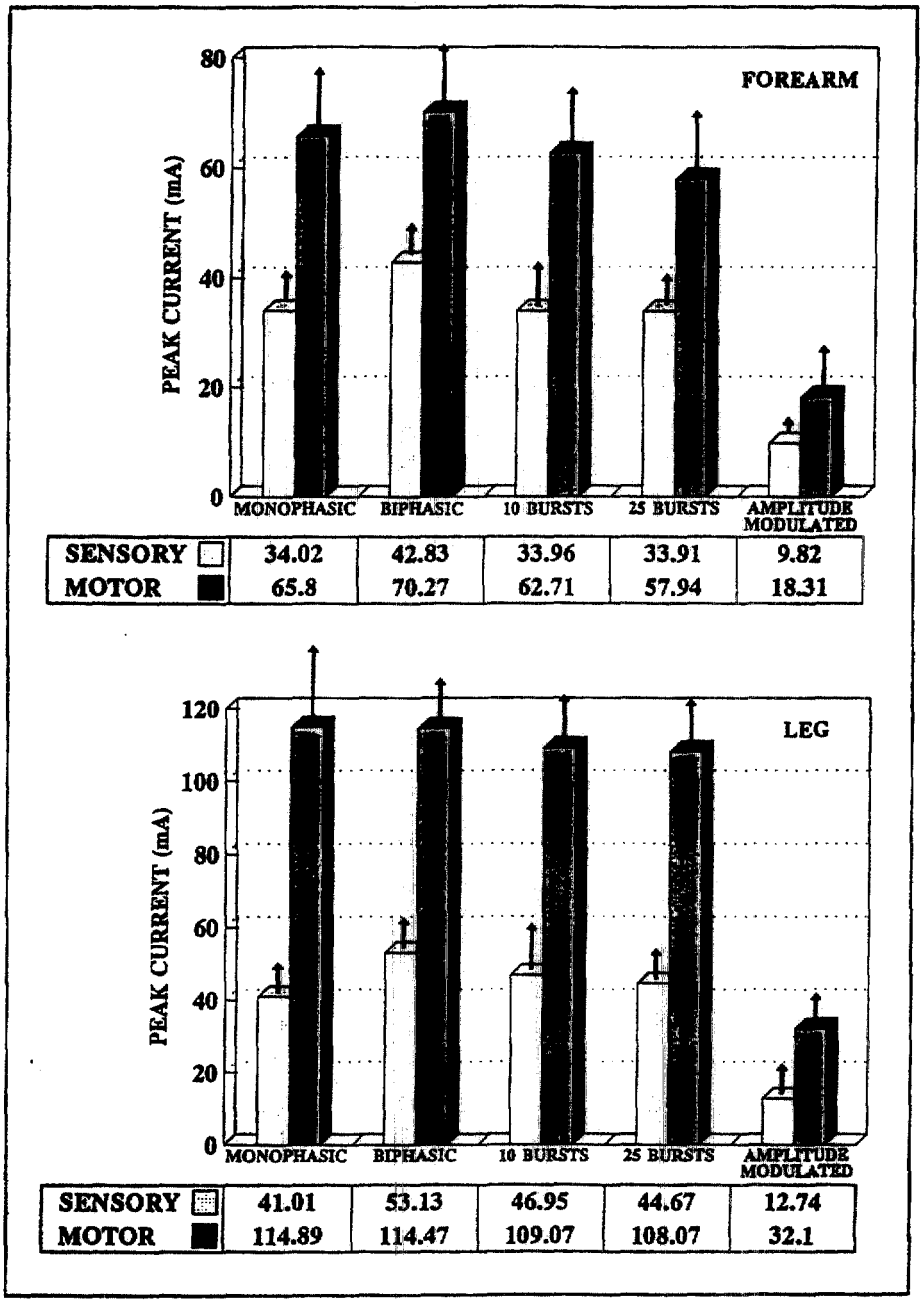


Figure 7. *Means of peak currents recorded during threshold excitation of sensory and motor nerves in the forearm and leg. Arrows represent the standard deviations.*

might have been even smaller if the SBP waveform had an interphase interval.[2] Adding an interval of 75 to 100 microseconds was advocated by several investigators[6,11,12] but was not included in our study due to technical difficulty.

The 10-SP waveform's total pulse charge was only 8.6 to 9.5 times greater than that of the SBP waveform, whereas theoretically a tenfold increase would have been anticipated. The 25-SP waveform's total pulse charge was approximately 21 to 24 times greater and the AM waveform's total pulse charge was 25 to 31 times greater than that associated with the SBP waveform. These differences may be related in part to inaccuracy in determining the exact instant of sensory or motor threshold excitation. Our method is probably less sensitive and accurate than those that used direct measurements of nerve excitation.[10,12] Our approach, however, is practical and applicable to clinical settings, in which therapists usually resort to palpation and patient report rather than invasive techniques of recording directly from the nerves. Furthermore, our results are in agreement with those of Snyder-Mackler et al,[16] who noted, without measuring, a similar contractile response comparing the SBP waveform with 25-SP and AM waveforms. The authors reported that the SBP waveform required much less total pulse charge to induce such contraction.

We believe our data support the hypothesis that greater total pulse charge does not necessarily add to a greater perception of stimulation or stronger muscle contraction. Further support for this view can be extrapolated from the study by Tracy et al,[25] in which the SBP and 25-SP waveforms equally augmented peripheral blood flow in the lower extremity. Once a nerve membrane is depolarized, most likely by the first few phases of the pulse,[11–13] additional charges that fall within the absolute or relative refractory period will not affect the excitation. The 10-SP, 25-SP, and AM waveforms, therefore, may deposit electrical energy that does not add to the excitation. Because total pulse charge multiplied by pulse frequency equals total current (in coulombs per second), the potential exists for the 25-SP and AM waveforms to reach total current levels, which may result in an adverse skin reaction, particularly when used with very small electrodes.[2]

Effects on Sensory and Motor Nerves

We demonstrated that sensory and motor nerves respond in a seemingly identical way to transcutaneous stimulation and that varying the waveform has no meaningful influence on the responses. Sensory excitation always preceded motor excitation irrespective of waveform or stimulated sites, a finding that is in accord with the well-documented fact that motor nerve thresholds are higher.[1,21] We

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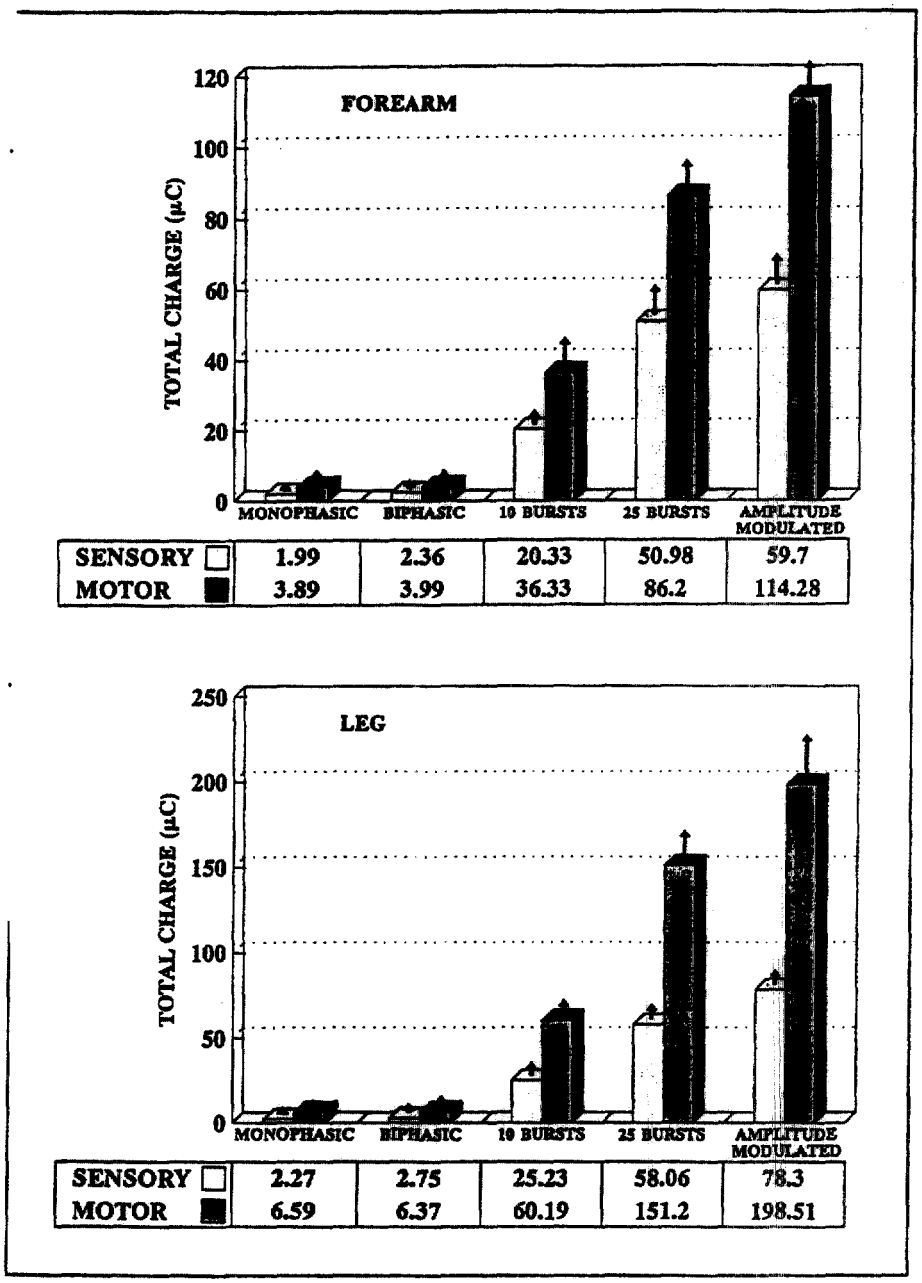


Figure 8. *Means of total pulse charge calculations during threshold excitation of sensory and motor nerves in the forearm and leg. Arrows represent the standard deviations.*

believe the reason for these higher thresholds is not necessarily related to a unique excitatory characteristic of the motor nerves. Rather, it seems to be associated with the fact that motor nerves are often situated deeper in the tissue than sensory nerves and therefore more stimulus intensity (phase charge) is required to cause their discharge.[12]

One practical implication of our findings is a need to reexamine the classification of stimulators into transcutaneous electrical nerve stimulators and neuromuscular electrical stimulators. Both types of devices excite the peripheral nerves in the same way; the only difference is that a higher phase charge is required for neuromuscular electrical stimulation than for transcutaneous electrical nerve stimulation.

Clinical Implications

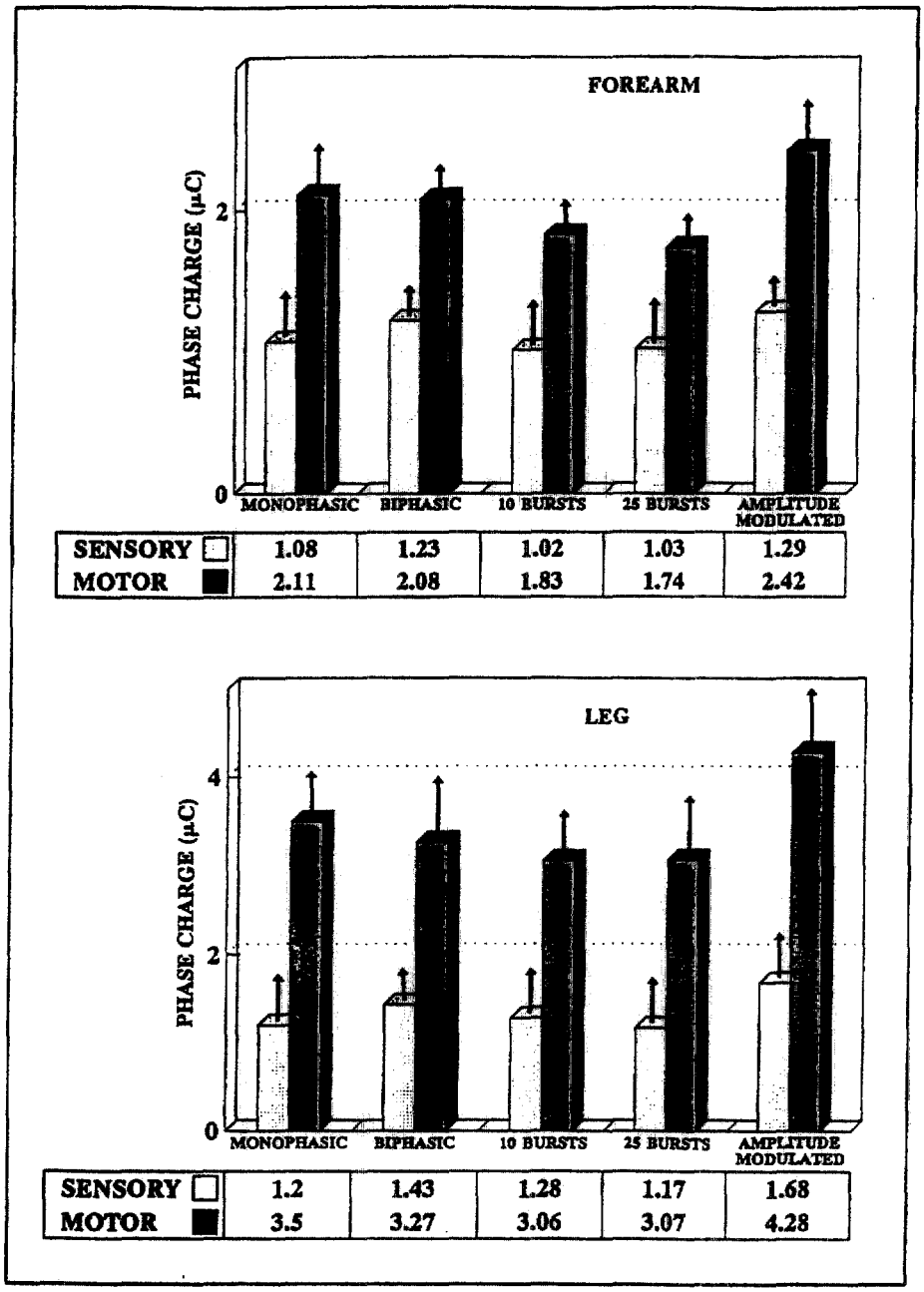
From a clinical perspective, the selection of a waveform should be based in part on criteria that include the ability to excite the target nerves with minimum electrical energy. All five waveforms were effective in exciting both sensory and motor nerves. The SBP waveform's peak current, peak voltage, and phase charge, with one exception, were equal to or lower than those of the MP, 10-SP, 25-SP, and AM waveforms. Yet, the total pulse charge of the SBP waveform was much smaller than that of the 10-SP, 25-SP, and AM waveforms. Based on these findings, we believe that the SBP waveform may be the preferred waveform for peripheral nerve stimulation. Not only does the SBP waveform minimize the total pulse charge, and thus the electrical energy involved in the stimulation, but it eliminates the potential skin irritation associated with monophasic pulses[1,2] and minimizes the discomfort of stimulation.[6,16]

The current Association for Advancement of Medical Instrumentation (AAMI) standard for transcutaneous electrical nerve stimulation has a safety requirement that maximum charge per pulse should not exceed 70 μC.[26] In our threshold study, the 25-SP and AM waveforms reached respective means of 151.2 and 198.5 μC of total pulse charge during motor stimulation. Because we used only very low levels of stimulation, we are unable to explain the limits advocated in the AAMI standard. We may speculate that the discrepancy is in terminology and the standard refers to phase rather than total pulse charge. Alternatively, the AAMI standard values are restricted to MP or biphasic waveforms and do not include pulses with multiple phases. As more and more waveforms are available in the clinic today, it seems that reevaluation of the AAMI standard is warranted.

Our results may also indicate that there is no need for multiple-waveform stimulators in the clinic. It seems that if the physiological objective of stimulation is to excite periph-

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SENSORY	1.08	1.23	1.02	1.03	1.29
MOTOR	2.11	2.08	1.83	1.74	2.42

SENSORY	1.2	1.43	1.28	1.17	1.68
MOTOR	3.5	3.27	3.06	3.07	4.28

Figure 9. *Means of phase charge calculations during threshold excitation of sensory and motor nerves in the forearm and leg. Arrows represent the standard deviations.*

eral nerves, then one waveform should be enough to achieve the desired effect. The presence of redundant waveforms only complicates the decision-making process of the clinician and probably adds unnecessarily to the cost of the stimulator. Redundant waveforms also do not appear to have an advantage in the elicitation of strong muscle contractions.[12,19]

Conclusion

Within the limits of this study, we conclude that all five studied waveforms excited both sensory and motor nerve fibers in the forearm and leg. Phase charge was the most repeatable of the studied variables and should be reported if the objective of stimulation is to excite peripheral nerves. Adding phases to the SBP pulse by creating 10-SP, 25-SP, or AM waveforms does not enhance the excitation, although it increases the total pulse charge dramatically. We thus conclude that the SBP waveform may be the preferred waveform for excitation of peripheral nerves. We likewise conclude that irrespective of waveform, the motor threshold requires higher stimulus characteristics than the sensory threshold and the leg thresholds are higher than those of the forearm. The sources of these differences are not clear at the present time and deserve further study.

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