DermaPort

510(k) Summary

Company Name: DermaPort, Inc.
25102 Rye Canyon Loop
Suite 110
Santa Clarita, CSA 91355

NOV 30 2007

Contact: Buzz Moran, President
Phone: (661) 362-7900
Fax: (661) 362-7902
Email: bmoran@dermaport.com

Summary Date: April 30, 2007

Trade Name: DermaPort Percutaneous Vascular Access System (PVAS)

Common Name: Hemodialysis Catheter, Implanted

Classification Name: 21 CFR 876.5540 Blood Access Device and Accessories, Class III, Product Code: MSD

Predicate Device(s):

510(k) Number: K994105
Manufacture: MEDCOMP®
Trade Name: Medcomp Hemo-Flow Catheter

510(k) Number: K062901
Manufacture: Med-Conduit Inc.
Trade Name: HemoCath II

1.0 Description of Device

The DermaPort Percutaneous Vascular Access System (PVAS) is designed to facilitate catheter placement, reposition, and exchange procedures while maintaining the catheter attachment, bacterial barrier, and fixation functions of the predicate catheter fibrous cuff. The main component of the PVAS is a metal port which is implanted into the subcutaneous tunnel at the catheter exit site on the chest wall. The hemodialysis catheter passes through the metal port which acts as a percutaneous conduit, into the subcutaneous tunnel, and then into the central venous system in the usual fashion. The metal surface of the PVAS port has a porous, tissue integrating coating which allows ingrowth of tissue to anchor the PVAS port. The PVAS port holds the hemodialysis catheter in place.

The DermaPort Percutaneous Vascular Access System (PVAS) consists of the following types of components:

1. Implanted Hemodialysis 14.5 F Catheter (24 cm, 28 cm or 32 cm lengths)
2. Guidewire; 0.038 inch (70 cm or 100 cm lengths)
3. 16F Tcaraway Set Griplock Hub
4. 12F Polyethylene Dilator
5. 14F Polyethylene Dilator
6. Clear Female Dust Cover
7. Injection Caps
8. 18 GA x 2.7" Cyrolite Introducer Needle
9. Tunneler with Tri ball tip
10. Tunneler Sleeve
11. DermaPort Blade
12. Commercially available alcohol pad
13. Commercially available adhesive wound dressing
14. Peel-away Sheath
15. DermaPort Percutaneous Vascular Access System (PVAS) Port

The catheter is identical to the HemoFlow catheter, with the exception that the fabric cuff on the HemoFlow catheter is omitted. The HemoFlow catheter is cleared to market by the FDA via 510(k) number K994105.

The Percutaneous Vascular Access System (PVAS^{TM}) has been developed to support central vascular access for hemodialysis and apheresis. The PVAS port consists of a percutaneous tubular conduit, through which a standard 14.5F polyurethane hemodialysis catheter enters the subcutaneous tunnel. An integral seal surrounds the catheter and prevents microbial migration along the catheter. The PVAS port is enclosed by a silicone anchor that braces the assembly to the skin, and an associated brake holds the catheter in place within the port. A tissue integrating biomaterial surrounds the port, providing anatomical fixation and prevention of microbial migration in a manner analogous to the fabric cuff of a tunneled catheter.

2.0 Intended Use of Device

The indication for use of the PVAS is consistent with the classification of 21 CFR 876.5540 Blood Access Device and Accessories, and the predicate Medcomp Hemo-Flow Catheter. The indication for use is:

> The DermaPort Percutaneous Vascular Access System (PVAS™) is indicated for long-term (greater than 30 days) vascular access for hemodialysis and apheresis. The system is inserted percutaneously and the catheter is typically placed in the internal jugular vein of an adult patient. The subclavian vein is an alternate catheter insertion site.

3.0 Technological Characteristics

The PVAS technical characteristics and construction are substantially equivalent to the predicate device. The difference in construction was qualified with bench and animal testing.

4.0 Conclusions

The DermaPort, Inc. PVAS is substantially equivalent to the predicate device. No new questions of safety or effectiveness are raised.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

NOV 3 0 2007

Mr. Buzz Moran
President
DermaPort, Inc.
25102 Rye Canyon Loop, Suite 110
SANTA CLARITA CA 91355

Re: K071202
Trade/Device Name: DermaPort Percutaneous Vascular Access System (PVAS™)
Regulation Number: 21 CFR §876.5540
Regulation Name: Blood access device and accessories
Regulatory Class: III
Product Code: MSD
Dated: November 14, 2007
Received: November 15, 2007

Dear Mr. Moran:

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 (the Act). You may, therefore, market the device, subject to the general controls provisions of Act. However, you are responsible to determine that the medical devices you use as components in the kit have either been determined as substantially equivalent under the premarket notification process (Section 510(k) of the act), or were on the market prior to May 28, 1976, the enactment date of the Medical Device Amendments. *Please note*: If you purchase your device components in bulk (i.e., unfinished) and further process (e.g., sterilize) you must submit a new 510(k) before including these components in your kit. 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 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 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.

In addition, we have determined that your device kit contains an alcohol pad which is subject to regulation as a drug.

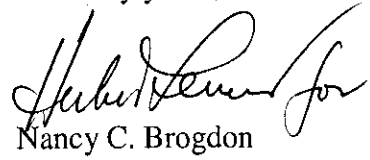
Our substantially equivalent determination does not apply to the drug component of your device. We recommend you first contact the Center for Drug Evaluation and Research before marketing your device with the drug component. For information on applicable Agency requirements for marketing this drug, we suggest you contact:

Director, Division of Drug Labeling Compliance (HFD-310)
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857
(301) 594-0101

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, please contact the Office of Compliance at (240) 276-0115. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll free number (800) 638-2041 or (240) 276-3150, or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,



Nancy C. Brogdon
Director, Division of Reproductive, Abdominal,
and Radiological Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): K071202

Device Name: DermaPort Percutaneous Vascular Access System (PVAS)

Indications for Use:

The DermaPort Percutaneous Vascular Access System (PVAS™) is indicated for long-term (greater than 30 days) vascular access for hemodialysis and apheresis. The system is inserted percutaneously and the catheter is typically placed in the internal jugular vein of an adult patient. The subclavian vein is an alternate catheter insertion site.

Prescription Use ___X___ (Part 21 CFR 801 Subpart D) AND/OR Over-The-Counter Use _____ (21 CFR 807 Subpart C)

(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 Reproductive, Abdominal and Radiological Devices
510(k) Number K071202

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

April 28, 2009

DERMAPORT, INC
800 LEVANGER LANE
STOUGHTON WISCONSIN 53589

Re: Premarket Notification Number: K071202

Dear Manufacturer:

The Food and Drug Administration (FDA) is currently in the process of evaluating the classification of class III devices that are currently marketed through clearance of a premarket notification (510(k)) submission. These devices were found to be substantially equivalent to a preamendments class III device type for which no date has yet been established for requiring the submission of a premarket approval application (PMA). (A class III preamendments device type is a device type that was legally on the market before May 28, 1976, and that was subsequently classified into class III.) FDA premarket notification (510(k)) records indicate that you received clearance to market a device belonging to one of the class III device types being evaluated. Accordingly, FDA is requesting that you submit specific information, discussed below, to support these classification efforts. These classification efforts will culminate in a decision either to call for a PMA for these class III devices, or to reclassify these devices into Class II (special controls) or Class I (general controls). FDA will reach this decision based on all available and reviewed information pertaining to each device type. For certain device types, classification panel hearings may be held to assist in these efforts. Any future proposed decisions will apply to the device type as a whole, not solely to your individual device.

As stated, FDA, in accordance with Section 515(i) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. § 360e(i)), is requiring manufacturers who were marketing, or have clearance to market through a 510(k) substantial equivalence decision, the class III device types referenced above as of April 9, 2009, to submit certain information. The enclosed Federal Register notice details the specific device types, the requested information, and the submission instructions. You are required to submit this information by August 7, 2009, to:

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD, 20852.

Please note that items posted to this docket will be redacted in accordance with the Freedom of Information Act (FOIA) (5 U.S.C. § 552), and posted to the docket. To ensure your posted documents are redacted, prior to posting, please denote submissions uploaded to the docket as such by typing the following words in the top of the *"General Comments"* box: *"CONFIDENTIAL MATERIAL DO NOT POST TO THE WEB AS REQUESTED BY SUBMITTER. STATUS SHOULD BE CONFIDENTIAL."*

If you have information showing that you have received this letter in error, or that our records supporting this letter are inaccurate, such that you are relieved of the obligation to submit the requested information, please send an explanation of the error, noting your 510(k) number, to:

Attn.: 510(k) Staff, 515(i) Submission
Document Mail Center, HFZ-401
Center for Devices and Radiological Health
9200 Corporate Boulevard
Rockville, MD, 20850

Please note that in lieu of submitting the above requested information, you may also petition FDA to reclassify the device type in accordance with Section 513(e) of the act (21 U.S.C. 360c(e)) and our regulations found in 21 CFR Part 860. In general, FDA's review of reclassification petitions can be completed more efficiently when manufacturers collaborate and submit a single reclassification petition that includes all relevant and accurate information for the given device type. This collaboration can be organized by contacting other manufacturers of the pertinent device through either a professional association or other affiliation.

Additional information or inquiries relevant to this classification mandate can be obtained by referencing the FDA Class III website at: http://www.fda.gov/cdrh/classiii.html, or by contacting Sarah K. Morabito at (240) 276-3975.

Sincerely yours,

Donna-Bea Tillman, Ph.D.
Director
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

NOV 3 0 2007

Mr. Buzz Moran
President
DermaPort, Inc.
25102 Rye Canyon Loop, Suite 110
SANTA CLARITA CA 91355

Re: K071202
Trade/Device Name: DermaPort Percutaneous Vascular Access System (PVAS™)
Regulation Number: 21 CFR §876.5540
Regulation Name: Blood access device and accessories
Regulatory Class: III
Product Code: MSD
Dated: November 14, 2007
Received: November 15, 2007

Dear Mr. Moran:

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 (the Act). You may, therefore, market the device, subject to the general controls provisions of Act. However, you are responsible to determine that the medical devices you use as components in the kit have either been determined as substantially equivalent under the premarket notification process (Section 510(k) of the act), or were on the market prior to May 28, 1976, the enactment date of the Medical Device Amendments. *Please note*: If you purchase your device components in bulk (i.e., unfinished) and further process (e.g., sterilize) you must submit a new 510(k) before including these components in your kit. 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.

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In addition, we have determined that your device kit contains an alcohol pad which is subject to regulation as a drug.

Our substantially equivalent determination does not apply to the drug component of your device. We recommend you first contact the Center for Drug Evaluation and Research before marketing your device with the drug component. For information on applicable Agency requirements for marketing this drug, we suggest you contact:

Director, Division of Drug Labeling Compliance (HFD-310)
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857
(301) 594-0101

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, please contact the Office of Compliance at (240) 276-0115. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll free number (800) 638-2041 or (240) 276-3150, or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Nancy C. Brogdon
Director, Division of Reproductive, Abdominal,
and Radiological Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): K071202

Device Name: DermaPort Percutaneous Vascular Access System (PVAS)

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Prescription Use X (Part 21 CFR 801 Subpart D) AND/OR Over-The-Counter Use _____ (21 CFR 807 Subpart C)

(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 Reproductive, Abdominal and Radiological Devices
510(k) Number K071202

Mr. Buzz Moran
President
DermaPort, Inc.
25102 Rye Canyon Loop, Suite 110
SANTA CLARITA CA 91355

NOV 3 0 2007

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Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857
(301) 594-0101

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Sincerely yours,

Nancy C. Brogdon
Director, Division of Reproductive, Abdominal,
and Radiological Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure
cc: HFZ-401 DMC
HFZ-404 510(k) Staff
HFZ-470 Division
D.O.

HFZ470:JeffCooper:lrm:11.30.2007

FILE COPY

OFFICE	SURNAME	DATE	OFFICE	SURNAME	DATE	OFFICE	SURNAME	DATE
HFZ470	Cooper	11/30/07						
HFZ-401								

U.S. GPO 1986-169-089

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

July 31, 2007

DERMAPORT, INC
C/O QUALITY & REGULATORY ASSOCIATES
800 LEVANGER LANE
STOUGHTON, WI 53589
ATTN: GARY SYRING

510(k) Number: K071202
Device: DERMAPORT PERCUTANEOUS VASCULAR ACCESS SYSTEM (PVAS)

Extended Until: 19-NOV-2007

Based on your recent request, an extension of time has been granted for you to submit the additional information we requested.

If the additional information (AI) is not received by the "Extended Until" date shown above, your premarket notification will be considered withdrawn (21 CFR 807.87(l)). If the submitter does submit a written request for an extension, FDA will permit the 510(k) to remain on hold for up to a maximum of 180 days from the date of the AI request.

If you have procedural questions, please contact the Division of Small Manufacturers International and Consumer Assistance (DSMICA) at (240)276-3150 or at their toll-free number (800) 638-2041, or contact the 510k staff at (240)276-4040.

Sincerely yours,

Marjorie Shulman
Supervisory Consumer Safety Officer
Premarket Notification Section
Office of Device Evaluation
Center for Devices and
Radiological Health

DermaPort

July 30, 2007

K071202

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

Re: 510(k) K071202, DermaPort Percutaneous Vascular Access System (PVAS™),

DermaPort, Inc. is requesting an extension of time to respond to the 510(k) reviewer questions. It is the intention of DermaPort, Inc. to respond to the request for additional information no later than November 19, 2007.

Please contact me with any questions.

Regards,

Buzz Moran, President
DermaPort, Inc.
Phone: (661) 362-7901
Fax: (661) 362-7902
Email: bmoran@dermaport.com

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

July 16, 2007

DERMAPORT, INC
C/O QUALITY & REGULATORY ASSOCIATES
800 LEVANGER LANE
STOUGHTON, WI 53589
ATTN: GARY SYRING

510(k) Number: K071202
Product: DERMAPORT PERCUTANEOUS VASCULAR ACCESS SYSTEM (PVAS)

We are holding your above-referenced Premarket Notification (510(k)) for 30 days pending receipt of the additional information that was requested by the Office of Device Evaluation. Please remember that all correspondence concerning your submission MUST cite your 510(k) number and be sent in duplicate 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. Also, please note the new Blue Book Memorandum regarding Fax and E-mail Policy entitled, "Fax and E-Mail Communication with Industry about Premarket Files Under Review. Please refer to this guidance for information on current fax and e-mail practices at www.fda.gov/cdrh/ode/a02-01.html.

The deficiencies identified 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.

If after 30 days the additional information (AI), or a request for an extension of time, is not received, we will discontinue review of your submission and proceed to delete your file from our review system (21 CFR 807.87(l)). Please note our guidance document entitled, "Guidance for Industry and FDA Staff, FDA and Industry Actions on Premarket Notification (510(k)) Submissions: Effect on FDA Review Clock and Performance Assessment". If the submitter does submit a written request for an extension, FDA will permit the 510(k) to remain on hold for up to a maximum of 180 days from the date of the AI request. The purpose of this document is to assist agency staff and the device industry in understanding how various FDA and industry actions that may be taken on 510(k)s should affect the review clock for purposes of meeting the Medical Device User Fee and Modernization Act. You may review this document at http://www.fda.gov/cdrh/mdufma/guidance/1219.html. Pursuant to 21 CFR 20.29, a copy of your 510(k) submission will remain in the Office of Device Evaluation. If you then wish to resubmit this 510(k) notification, a new number will be assigned and your submission will be considered a new premarket notification submission. Please remember that the Safe Medical Devices Act of 1990 states that you may not place this device into commercial distribution until you receive a decision letter from FDA allowing you to do so.

If you have procedural questions, please contact the Division of Small Manufacturers International and Consumer Assistance (DSMICA) at (240)276-3150 or at their toll-free number (800) 638-2041, or contact the 510k staff at (240)276-4040.

Sincerely yours,

Marjorie Shulman
Supervisor Consumer Safety Officer
Premarket Notification Section
Office of Device Evaluation
Center for Devices and
Radiological Health

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

May 01, 2007

DERMAPORT, INC
C/O QUALITY & REGULATORY ASSOCIATES
800 LEVANGER LANE
STOUGHTON, WI 53589
ATTN: GARY SYRING

510(k) Number: K071202
Received: 01-MAY-2007
Product: DERMAPORT PERCUTANEOUS VASCULAR ACCESS SYSTEM (PVAS)

The Food and Drug Administration (FDA), Center for Devices and Radiological Health (CDRH), has received the Premarket Notification, (510(k)), you submitted in accordance with Section 510(k) of the Federal Food, Drug, and Cosmetic Act(Act) for the above referenced product and for the above referenced 510(k) submitter. Please note, if the 510(k) submitter is incorrect, please notify the 510(k) Staff immediately. We have assigned your submission a unique 510(k) number that is cited above. Please refer prominently to this 510(k) number in all future correspondence that relates to this submission. We will notify you when the processing of your 510(k) 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.

Please remember that all correspondence concerning your submission MUST be sent to the Document Mail Center (DMC)(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 510(k) submission.

Please note the following documents as they relate to 510(k) review: 1)Guidance for Industry and FDA Staff entitled, "FDA and Industry Actions on Premarket Notification (510(k))Submissions: Effect on FDA Review Clock and Performance Assessment". The purpose of this document is to assist agency staff and the device industry in understanding how various FDA and industry actions that may be taken on 510(k)s should affect the review clock for purposes of meeting the Medical Device User Fee and Modernization Act (MDUFMA). Please review this document at www.fda.gov/cdrh/mdufma/guidance/1219.html. 2)Guidance for Industry and FDA Staff entitled, "Format for Traditional and Abbreviated 510(k)s". This guidance can be found at www.fda.gov/cdrh/ode/guidance/1567.html. Please refer to this guidance for assistance on how to format an original submission for a Traditional or Abbreviated 510(k). 3)Blue Book Memorandum regarding Fax and E-mail Policy entitled, "Fax and E-Mail Communication with Industry about Premarket Files Under Review". Please refer to this guidance for information on current fax and e-mail practices at www.fda.gov/cdrh/ode/a02-01.html.

In all future premarket submissions, we encourage you to provide an electronic copy of your submission. By doing so, you will save FDA resources and may help reviewers navigate through longer documents more easily. Under CDRH's e-Copy Program, you may replace one paper copy of any premarket submission (e.g., 510(k), IDE, PMA, HDE) with an electronic copy. For more information about the program, including the formatting requirements, please visit our web site at www.fda.gov/cdrh/elecsub.html.

Lastly, you should be familiar with the regulatory requirements for medical devices available at Device Advice www.fda.gov/cdrh/devadvice/". If you have questions on the status of your submission, please contact DSMICA at (240) 276-3150 or the toll-free number (800) 638-2041, or at their Internet address http://www.fda.gov/cdrh/dsma/dsmastaf.html. If you have procedural questions, please contact the 510(k) Staff at (240)276-4040.

Sincerely yours,

Marjorie Shulman
Supervisory Consumer Safety Officer
Office of Device Evaluation
Center for Devices and Radiological Health

K071202

DermaPort, Inc.

DermaPort Percutaneous Vascular Access System (PVAS)

Abbreviated 510(k) Pre-Market Notification

Copy 1 of 2

K24

510(k) Table of Contents

Form Approved: OMB No. 0910-XXX Expiration Date: January 31, 2010. See Instructions for OMB Statement

DEPARTMENT OF HEALTH AND HUMAN SERVICES FOOD AND DRUG ADMINISTRATION **MEDICAL DEVICE USER FEE COVER SHEET**	PAYMENT IDENTIFICATION NUMBER (b) (4) Write the Payment Identification number

A completed Cover Sheet must accompany each original application or supplement subject to fees. The following actions must be taken to properly submit your application and fee payment:

1. Electronically submits the completed Cover Sheet to the Food and Drug Administration (FDA) before payment is sent.
2. Include printed copy of this completed Cover Sheet with a check made payable to the Food and Drug Administration. Remember that the Payment Identification Number must be written on the check.
3. Mail Check and Cover Sheet to the US Bank Lock Box, FDA Account, P.O. Box 956733, St. Louis, MO 63195-6733. (*Note: In no case should payment be submitted with the application.*)
4. If you prefer to send a check by a courier, the courier may deliver the check and Cover Sheet to: US Bank, Attn: Government Lockbox 956733, 1005 Convention Plaza, St. Louis, MO 63101. (Note: This address is for courier delivery only. Contact the US Bank at 314-418-4821 if you have any questions concerning courier delivery.)
5. For Wire Transfer Payment Procedures, please refer to the MDUFMA Fee Payment Instructions at the following URL: http://www.fda.gov/cdrh/mdufma/faqs.html#3a. You are responsible for paying all fees associated with wire transfer.
6. Include a copy of the complete Cover Sheet in volume one of the application when submitting to the FDA at either the CBER or CDRH Document Mail Center.

1. COMPANY NAME AND ADDRESS (include name, street address, city state, country, and post office code)	2. CONTACT NAME
DERMAPORT INC 25102 RYE CANYON LOOP SUITE 110 Santa Clara CA 91355 US	Buzz Moran 2.1 E-MAIL ADDRESS bmoran@dermaport.com 2.2 TELEPHONE NUMBER (include Area code) 661-3627901
1.1 EMPLOYER IDENTIFICATION NUMBER (EIN) 201986561	2.3 FACSIMILE (FAX) NUMBER (Include Area code) null-null

3. TYPE OF PREMARKET APPLICATION (Select one of the following in each column; if you are unsure, please refer to the application descriptions at the following web site: http://www.fda.gov/dc/mdufma

Select an application type:	3.1 Select one of the types below
[X] Premarket notification(510(k)); except for third party	[X] Original Application
[ ] Biologics License Application (BLA)	Supplement Types:
[ ] Premarket Approval Application (PMA)	[ ] Efficacy (BLA)
[ ] Modular PMA	[ ] Panel Track (PMA, PMR, PDP)
[ ] Product Development Protocol (PDP)	[ ] Real-Time (PMA, PMR, PDP)
[ ] Premarket Report (PMR)	[ ] 180-day (PMA, PMR, PDP)

4. ARE YOU A SMALL BUSINESS? (See the instructions for more information on determining this status)

[ ] YES, I meet the small business criteria and have submitted the required qualifying documents to FDA

[X] NO, I am not a small business

4.1 If Yes, please enter your Small Business Decision Number.

5. IS THIS PREMARKET APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCEPTIONS? IF SO, CHECK THE APPLICABLE EXCEPTION.

[ ] This application is the first PMA submitted by a qualified small business, including any affiliates, parents, and partner firms

[ ] The sole purpose of the application is to support conditions of use for a pediatric population

[ ] This biologics application is submitted under secion 351 of the Public Health Service Act for a product licensed for further manufacturing use only

[ ] The application is submitted by a state or federal government entity for a device that is not to be distributed commercially

6. IS THIS A SUPPLEMENT TO A PREMARKET APPLICATION FOR WHICH FEES WERE WAIVED DUE TO SOLE USE IN A PEDIATRIC POPULATION THAT NOW PROPOSES CONDITION OF USE FOR ANY ADULT POPULATION? (If so, the application is subject to the fee that applies for an original premarket approval application (PMA).)

[ ] YES [X] NO

7. USER FEE PAYMENT AMOUNT SUBMITTED FOR THIS PREMARKET APPLICATION

(b) (4)

16-Apr-2007

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

CDRH PREMARKET REVIEW SUBMISSION COVER SHEET

Form Approval
OMB No. 9010-0120
Expiration Date: May 31, 2007.
See OMB Statement on page 5.

Date of Submission	User Fee Payment ID Number	FDA Submission Document Number (if known)
April 30, 2007	(b) (4)	

SECTION A TYPE OF SUBMISSION

PMA	PMA & HDE Supplement	PDP	510(k)	Meeting
☐ Original Submission	☐ Regular (180 day)	☐ Original PDP	X Original Submission:	☐ Pre-510(K) Meeting
☐ Premarket Report	☐ Special	☐ Notice of Completion	☐ Traditional	☐ Pre-IDE Meeting
☐ Modular Submission	☐ Panel Track (PMA Only)	☐ Amendment to PDP	☐ Special	☐ Pre-PMA Meeting
☐ Amendment	☐ 30-day Supplement		X Abbreviated (Complete section I, Page 5)	☐ Pre-PDP Meeting
☐ Report	☐ 30-day Notice		☐ Additional Information	☐ Day 100 Meeting
☐ Report Amendment	☐ 135-day Supplement		☐ Third Party	☐ Agreement Meeting
☐ Licensing Agreement	☐ Real-time Review			☐ Determination Meeting
	☐ Amendment to PMA &HDE Supplement			☐ Other *(specify):*
	☐ Other			

IDE	Humanitarian Device Exemption (HDE)	Class II Exemption Petition	Evaluation of Automatic Class III Designation (De Novo)	Other Submission
☐ Original Submission	☐ Original Submission	☐ Original Submission	☐ Original Submission	☐ 513(g)
☐ Amendment	☐ Amendment	☐ Additional Information	☐ Additional Information	☐ Other
☐ Supplement	☐ Supplement			*(describe submission):*
	☐ Report			
	☐ Report Amendment			

Have you used or cited Standards in your submission? ☐ Yes ☐ No *(If Yes, please complete Section I, Page 5)*

SECTION B SUBMITTER, APPLICANT OR SPONSOR

Company / Institution Name DermaPort, Inc.	Establishment Registration Number *(if known)* Not assigned at this time		
Division Name *(if applicable)*	Phone Number *(including area code)* (661) 362-7901		
Street Address 25102 Rye Canyon Loop, Suite 110	FAX Number *(including area code)* (661) 362-7902		
City Santa Clarita	State / Province CA	ZIP/Postal Code 91355	Country USA
Contact Name Mr. Buzz Moran			
Contact Title President	Contact E-mail Address bmoran@dermaport.com		

SECTION C APPLICATION CORRESPONDENT (e.g., consultant, if different from above)

Company / Institution Name Quality & Regulatory Associates, LLC			
Division Name *(if applicable)*	Phone Number *(including area code)* (608) 877-2635		
Street Address 800 Levanger Lane	FAX Number *(including area code)* (608) 873-7382		
City Stoughton	State / Province WI	ZIP/Postal Code 53589	Country USA
Contact Name Gary Syring			
Contact Title Principal Consultant	Contact E-mail Address QRASupport@AOL.com		

SECTION D1 REASON FOR APPLICATION - PMA, PDP, OR HDE

- ☐ Withdrawal
- ☐ Additional or Expanded Indications
- ☐ Request for Extension
- ☐ Post-approval Study Protocol
- ☐ Request for Applicant Hold
- ☐ Request for Removal of Applicant Hold
- ☐ Request to Remove or Add Manufacturing Site

- ☐ Change in design, component, or specification:
  - ☐ Software / Hardware
  - ☐ Color Additive
  - ☐ Material
  - ☐ Specifications
  - ☐ Other *(specify below)*

- ☐ Location change:
  - ☐ Manufacturer
  - ☐ Sterilizer
  - ☐ Packager

- ☐ Process change:
  - ☐ Manufacturing
  - ☐ Sterilization
  - ☐ Packaging
  - ☐ Other *(specify below)*

- ☐ Labeling change:
  - ☐ Indications
  - ☐ Instructions
  - ☐ Performance
  - ☐ Shelf Life
  - ☐ Trade Name
  - ☐ Other *(specify below)*

- ☐ Report Submission:
  - ☐ Annual or Periodic
  - ☐ Post-approval Study
  - ☐ Adverse Reaction
  - ☐ Device Defect
  - ☐ Amendment

- ☐ Response to FDA correspondence:

- ☐ Change in Ownership
- ☐ Change in Correspondent
- ☐ Change of Applicant Address

- ☐ Other Reason *(specify)*:

SECTION D2 REASON FOR APPLICATION - IDE

- ☐ New Device
- ☐ New Indication
- ☐ Addition of Institution
- ☐ Expansion / Extension of Study
- ☐ IRB Certification
- ☐ Termination of Study
- ☐ Withdrawal of Application
- ☐ Unanticipated Adverse Effect
- ☐ Notification of Emergency Use
- ☐ Compassionate Use Request
- ☐ Treatment IDE
- ☐ Continued Access

- ☐ Change in:
  - ☐ Correspondent / Applicant
  - ☐ Design / Device
  - ☐ Informed Consent
  - ☐ Manufacturer
  - ☐ Manufacturing Process
  - ☐ Protocol - Feasibility
  - ☐ Protocol - Other
  - ☐ Sponsor

- ☐ Report submission:
  - ☐ Current Investigator
  - ☐ Annual Progress Report
  - ☐ Site Waiver Report
  - ☐ Final

- ☐ Repose 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
  - ☐ Request Hearing

- ☐ Other Reason *(specify)*:

SECTION D3 REASON FOR SUBMISSION - 510(k)

- X New Device
- ☐ Additional or Expanded Indications
- ☐ Change in Technology

- ☐ Other Reason *(specify)*:

SECTION E ADDITIONAL INFORMATION ON 510(K) SUBMISSIONS

Product codes of devices to which substantial equivalence is claimed

1	MSD	2		3		4	
5		6		7		8	

Summary of, or statement concerning, safety and effectiveness information

X 510 (k) summary attached

☐ 510 (k) statement

Information on devices to which substantial equivalence is claimed *(if known)*

	510(k) Number		*Trade or Proprietary or Model Name*		*Manufacturer*
1	K994105	1	Medcomp Hemo-Flow Catheter	1	MEDCOMP
2	K062901	2	HemoCath II	2	Med-Conduit, Inc.
3		3		3	
4		4		4	
5		5		5	
6		6		6	

SECTION F PRODUCT INFORMATION - APPLICATION TO ALL APPLICATIONS

Common or usual name or classification

Hemodialysis Catheter, Implanted

	Trade or Proprietary or Model Name for This Device		Model Number
1	DermaPort Percutaneous Vascular Access System (PVAS™)	1	
2		2	
3		3	
4		4	
5		5	

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

1	2	3	4	5	6
7	8	9	10	11	12

Data Included in Submission

X Laboratory Testing X Animal Trials ☐ Human Trials

SECTION G PRODUCT CLASSIFICATION - APPLICATION TO ALL APPLICATIONS

Product Code	C.F.R. Section *(if applicable)*	Device Class
MSD	21 CFR 876.5540	☐ Class I ☐ Class II
Classification Panel		X Class III ☐ Unclassified
Gastroenterology – Urology		

Indications *(from labeling)*

The DermaPort Percutaneous Vascular Access System (PVAS™) is indicated for long-term (greater than 30 days) vascular access for hemodialysis and apheresis. The system is inserted percutaneously and the catheter is typically placed in the internal jugular vein of an adult patient. The subclavian vein is an alternate catheter insertion site.

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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 *(if known)*

SECTION H MANUFACTURING / PACKAGING / STERILIZATION SITES RELATING TO A SUBMISSION

☐ Original ☑ Add ☐ Delete	FDA Establishment Registration Number Not assigned at this time	X Manufacturer ☐ Contract Manufacturer	☐ Contract Sterilizer ☐ Repackager / Relabeler
Company / Institution Name DermaPort, Inc.		Establishment Registration Number Not assigned at this time	
Division Name *(if applicable)*		Phone Number *(including area code)* (661) 362-7901	
Street Address 25102 Rye Canyon Loop, Suite 110		FAX Number *(including area code)* (661) 362-7902	
City Santa Clarita		State / Province CA	ZIP/Postal Code 91355 / Country USA
Contact Name Buzz Moran	Contact Title President	Contact E-mail Address bmoran@dermaport.com	

X Original ☐ Add ☐ Delete	FDA Establishment Registration Number (b)(4)	☐ Manufacturer X Contract Manufacturer	☐ Contract Sterilizer ☐ Repackager / Relabeler

(b) (4)

☐ Original ☐ Add ☐ Delete	FDA Establishment Registration Number	☐ Manufacturer ☐ Contract Manufacturer	X Contract Sterilizer ☐ Repackager / Relabeler

(b) (4)

SECTION I	UTILIZATION OF STANDARDS				
Note: Complete this section if your application or submission cites standards or includes a *"Declaration of Conformity to a Recognized Standard"* statement.					
	Standards No.	Standards Organization	Standards Title	Version	Date
1	F1980-02	ASTM	ASTM F1980-02 Standard Guide for Accelerated Aging of Sterile Medical Device Packages	2002	2002
	Standards No.	Standards Organization	Standards Title	Version	Date
2	F2503-05	ASTM	ASTM F2503-05 Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment	2005	2005
	Standards No.	Standards Organization	Standards Title	Version	Date
3	10555-1	ISO	ISO 10555-1:1995 Sterile, Single-use Intravascular Catheters – Part 1: General Requirements	1995	1995
	Standards No.	Standards Organization	Standards Title	Version	Date
4	10555-3	ISO	ISO 10555-3:1996 Sterile, Single-use Intravascular Catheters – Part 3: Central Venous Catheters	1996	1996
	Standards No.	Standards Organization	Standards Title	Version	Date
5	10993-1:2003	ISO	ISO 10993-1:2003 Biological evaluation of medical devices-Part 1: Evaluation and Testing	2003	2003
	Standards No.	Standards Organization	Standards Title	Version	Date
6	10993-3:2003	ISO	ISO 10993-3:2003 Biological evaluation of medical devices-Part 3: Tests for Genotoxicity, Carcinogenicity and Reproductive Toxicity	2003	2003
	Standards No.	Standards Organization	Standards Title	Version	Date
7	10993-5:1999	ISO	ISO 10993-5:1999 Biological evaluation of medical devices-Part 5: Tests for in vitro cytotoxicity	1999	1999

Please include any additional standards to be cited on a separate page.

Public reporting burden for this collection of information is estimated to average 0.5 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Food and Drug Administration
CDRH (HFZ-342)
9200 Corporate Blvd.
Rockville, MD 20850

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control

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	Standards No.	Standards Organization	Standards Title	Version	Date
8	10993-6:1999	ISO	ISO 10993-6:1999 Biological evaluation of medical devices-Part 6: Tests for implantation	1999	1999
	Standards No.	Standards Organization	Standards Title	Version	Date
9	10993-10:2002	ISO	ISO 10993-10:2002 Biological evaluation of medical devices-Part 10: Tests for Irritation and Sensitization	2002	2002
	Standards No.	Standards Organization	Standards Title	Version	Date
10	10993-11:1993	ISO	ISO 10993-11:1993 Biological evaluation of medical devices-Part 11: Tests for systemic toxicity	1993	1993
	Standards No.	Standards Organization	Standards Title	Version	Date
11	11135:1999	ISO	ISO 11135:1999 Medical devices—Validation and routine control of ethylene oxide sterilization	1999	1999
	Standards No.	Standards Organization	Standards Title	Version	Date
12	11607-1:2006	ISO	ISO 11607-1:2006 Packaging for terminally sterilized medical devices – Part 1: Requirements for materials, sterile barrier systems and packaging systems	2006	2006
	Standards No.	Standards Organization	Standards Title	Version	Date
13	11607-2:2006	ISO	ISO 11607-2:2006 Packaging for terminally sterilized medical devices – Part 2: Validation requirements for forming, sealing and assembly processes	2006	2006

510(k) Elements	Submission Location
Cover letter, containing elements listed on page 3-2 of the Premarket Notification 510(k) Manual.	Cover Letter
Table of Contents	Table of Contents
Truthful and Accurate Statement	Section 2.0
Device Trade Name, Device Classification Name and Establishment Registration Number	Cover Letter - Items 3, 4, 5, 6
Device Classification Regulation Number and Regulatory Status (Class I, Class II, Class III or Unclassified).	Cover Letter - Item 6
Proposed Labeling including material listed on page 3-4 of the Premarket Notification 510(k) Manual.	Attachment B
Statement of Indications for Use	Attachment H
Substantial Equivalence Comparison, comparisons of the new device with the predicate.	Section 4.0
510(k) summary	Attachment I
Description of the device (or modification of the device). Identification of legally marketed predicate device.	Section 1.0 Cover Letter - Item 8
Compliance with performance standards.	Cover Letter - Item 10
Class III certification and Summary.	Attachment G
Financial Certification or Disclosure Statement for 510(k) notifications with a clinical study.	NA - No sponsored clinical study.
510(k) Kit Certification	Section 1.3
Abbreviated 510(k) Elements	
Biocompatibility data for all patient-contacting materials, OR certification of identical material/formulation.	Section 7.0
Sterilization and expiration dating information	Section 8.0.
Software Documentation	NA - No software.
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.	Sections 7.0, 8.0, 9.0
For a submission, which relies on a recognized standard, a declaration of conformity.	Sections 7.0, 8.0, 9.0
For a submission, which relies on a recognized standard without a declaration of conformity, a statement that the manufacturer intends to conform to a recognized standard and that supporting data will be available before marketing the device.	NA. Recognized Standard conformance declared.
For a submission, which relies on a non-recognized standard that has been historically accepted by FDA, a statement that the manufacturer intends to conform to a recognized standard and that supporting data will be available before marketing the device.	NA. Recognized Standard conformance declared.
For a submission, which relies on a non-recognized standard that has not been historically accepted by FDA, a statement that the manufacturer intends to conform to a recognized standard and that supporting data will be available before marketing the device and any additional information requested by the reviewer in order to determine substantial equivalence.	NA. Recognized Standard conformance declared.
Any additional information, which is not covered by the guidance document, special control, recognized standard and/or non-recognized standard, in order to determine substantial equivalence.	NA. Recognized Standard conformance declared.

DermaPort

April 30, 2007

Food and Drug Administration
Center for Devices and Radiological Health
510(k) Document Mail Center (HFZ-401)
9200 Corporate Boulevard
Rockville, MD 20850

Re: DermaPort Percutaneous Vascular Access System (PVAS™),
Abbreviated 510(k) Application

The enclosed Abbreviated 510(k) Application is submitted in compliance with 21 CFR 807. This Abbreviated 510(k) Application supports commercial introduction of a DermaPort Percutaneous Vascular Access System (PVAS™). The PVAS is classified by 21 CFR 876.5540 Blood Access Device and Accessories, Product Code MSD. For reference, applicable parts of the classification regulation follow:

(a) *Identification.*

A blood access device and accessories is a device intended to provide access to a patient's blood for hemodialysis or other chronic uses. When used in hemodialysis, it is part of an artificial kidney system for the treatment of patients with renal failure or toxemic conditions and provides access to a patient's blood for hemodialysis. The device includes implanted blood access devices, nonimplanted blood access devices, and accessories for both the implanted and nonimplanted blood access devices.

(1) The implanted blood access device consists of various flexible or rigid tubes, which are surgically implanted in appropriate blood vessels, may come through the skin, and are intended to remain in the body for 30 days or more. This generic type of device includes various shunts and connectors specifically designed to provide access to blood, such as the arteriovenous (A-V) shunt cannula and vessel tip.

(2) The nonimplanted blood access device ... *device under review is implanted.*

The PVAS under review in this 510(k) is intended to be implanted for longer than 30 days. By classification, the PVAS is a Class III device. These devices are reviewed and cleared to market by the 510(k) premarket notification process.

The PVAS consists of a kit of medical device components. The components in the PVAS kit are all intended to be single patient use devices and are not intended to be reprocessed.

The following 510(k) submission information is provided for reference.

1. Applicant Name: DermaPort, Inc.
   25102 Rye Canyon Loop
   Suite 110
   Santa Clarita, CA 91355
   Contact: Buzz Moran, President, DermaPort, Inc.
   Phone: (661) 362-7901
   Fax: (661) 362-7902
   Email: bmoran@dermaport.com

2. Submission Correspondent: On behalf of DermaPort, Inc., the following consultant may be contacted with regard to the 510(k) submission:
   Gary Syring, Principal Consultant
   Quality & Regulatory Associates, LLC
   800 Levanger Lane
   Stoughton, WI 53589
   Phone: (608) 877-2635
   Fax: (608) 873-7382
   Email: QRASupport@AOL.com

3. Trade Name: DermaPort Percutaneous Vascular Access System (PVAS™)

4. Common Name: Hemodialysis Catheter, Implanted

5. Manufacturing Site Address: These devices are manufactured by DermaPort, Inc. at:
   DermaPort, Inc.
   25102 Rye Canyon Loop
   Suite 110
   Santa Clarita, CA 91355

   DermaPort, Inc. will submit a FDA Establishment Registration application prior to commercial introduction of this device.

   The following contract manufacturer will perform supporting manufacturing operations:

   (b) (4) [redacted]

   (b) (4) [redacted]

   Contract sterilization is performed by:

   (b) (4) [redacted]

6. Classification Name: Predicate implanted hemodialysis catheters have been found substantially equivalent to 21 CFR 876.5540 Blood Access Device and Accessories, Class III, Product Code: MSD.

7. Reason for Abbreviated 510(k): Commercial introduction of a new device by DermaPort, Inc.

8. Predicate Device(s):

510(k) Number:	K994105
Manufacturer:	MEDCOMP®
Trade Name:	Medcomp Hemo-Flow Catheter
Product Code:	MSD
Classification:	21 CFR 876.5540

510(k) Number:	K062901
Manufacturer:	Med-Conduit, Inc.
Trade Name:	HemoCath II
Product Code:	MSD
Classification:	21 CFR 876.5540

9. Performance Standards:

No performance standards are established for this classification of device.

The following Recognized Consensus Standards are applicable and were applied to the device under review:

ASTM F1980-02 Standard Guide for Accelerated Aging of Sterile Medical Device Packages

ASTM F2503-05 Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment

ISO 10555-1:1995 Sterile, Single-use Intravascular Catheters – Part 1: General Requirements

ISO 10555-3:1996 Sterile, Single-use Intravascular Catheters – Part 3: Central Venous Catheters

ISO 10993-1:2000 Biological evaluation of medical devices-Part 1: Evaluation and Testing

ISO 10993-3:2003 Biological evaluation of medical devices-Part 3: Tests for Genotoxicity, Carcinogenicity and Reproductive Toxicity

ISO 10993-5:1999 Biological evaluation of medical devices-Part 5: Tests for in vitro cytotoxicity

ISO 10993-6:1999 Biological evaluation of medical devices-Part 6: Tests for implantation

ISO 10993-10:2002 Biological evaluation of medical devices-Part 10: Tests for Irritation and Sensitization

ISO 10993-11:1993 Biological evaluation of medical devices-Part 11: Tests for systemic toxicity

ISO 11135:1999 Medical devices—Validation and routine control of ethylene oxide sterilization

ISO 11607-1:2006 Packaging for terminally sterilized medical devices – Part 1: Requirements for materials, sterile barrier systems and packaging systems

ISO 11607-2:2006 Packaging for terminally sterilized medical devices – Part 2: Validation requirements for forming, sealing and assembly processes

10. FDA Guidance Documents Applied:
Updated 510(k) Sterility Review Guidance K90-1; Final Guidance for Industry and FDA; Document Issued on: August 30, 2002

Contact me or the following regulatory consultant with any 510(k) Submission questions:

Gary Syring, Principal Consultant
Quality & Regulatory Associates, LLC
800 Levanger Lane
Stoughton, WI 53589
Phone: (608) 877-2635
Fax: (608) 873-7382
Email: QRASupport@AOL.com

Sincerely,

Buzz Moran, President
DermaPort, Inc.
Phone: (661) 362-7901
Fax: (661) 362-7902
Email: bmoran@dermaport.com

Enclosure

1.0 Description of Device, Drawings, Photographs

1.1 Background

Central venous catheters are ubiquitous in many medical environments. Health care professionals have become increasingly reliant upon these devices for the care of hospitalized patients and for an expanding list of outpatient therapeutic applications. For this reason, an increasing number of clinicians are inserting and utilizing central venous catheters.

Central venous catheters which are intended for long-term (greater than 30 days) use are typically inserted into the internal jugular vein and then tunneled through the subcutaneous tissue of the anterior chest wall. The *sine qua non* of a long-term, tunneled catheter is the fibrous cuff. The cuff is a band of fibrous material which encircles the external diameter of the catheter. The purpose of the fibrous cuff is two-fold: 1) to serve as a site for the ingrowth of tissue to firmly anchor the catheter within the subcutaneous tunnel, and 2) to provide a barrier to the migration of microorganisms along the external surface of the catheter and thereby decrease the incidence of catheter-related infections. For these reasons it is advantageous for the fibrous cuff to become firmly attached to the subcutaneous tunnel. The disadvantage of the fibrous cuff is the difficulty of catheter removal or exchange. The firm attachment of the cuff to the surrounding tissue prevents easy removal or replacement of the attached catheter. Typically, the physician uses traction or blunt dissection to separate the cuff from the surrounding tissue during catheter removal or exchange.

Recent scientific reports have demonstrated that catheter replacement, through the same subcutaneous tunnel, is advantageous when treating hemodialysis patients with a catheter-related infection[1,2,3]. This is commonly referred to as a catheter exchange procedure. The traditional management of a catheter-related infection requires removal of the catheter device. However, many hemodialysis patients are critically dependent upon their tunneled catheter to provide vascular access for hemodialysis treatment. Removing an infected catheter and inserting a new catheter at a new site can lead to thrombosis or venous stenosis, and eventually to depletion of the patient's central veins. Preservation of central veins is a

[1] Robinson D, Suhocki P, Schwab SJ. Treatment of infected tunneled venous access hemodialysis catheters with guidewire exchange. *Kidney International,* 53: 1792-1794 (1998).

[2] Tanriover B, Carlton D, Saddekni S, Hamrick K, Oser R, Westfall A, Allon M. Bacteremia associated with tunneled dialysis catheters: comparison of two treatment strategies. *Kidney International,* 57: 2151-2155 (2000).

[3] d'Othee B, Tham J, Sheiman R. Restoration of patency in failing tunneled hemodialysis catheters: a comparison of catheter exchange, exchange and balloon disruption of the fibrin sheath, and femoral stripping. *J Vasc Interv Radiol,* 17: 1001-1015 (2006).

fundamental tenet for management of chronic hemodialysis patients[4]. When performed in the appropriate clinical situation, the catheter exchange procedure has proven beneficial for treatment of catheter-related infections, eliminating the need for a new catheter access site, thereby preserving the patient's central venous anatomy.

The firm attachment of the fibrous cuff to the subcutaneous tunnel often prevents easy removal of a hemodialysis catheter during a catheter exchange procedure. As intended, the fibrous cuff becomes incorporated into the subcutaneous tissue, frequently requiring a minor surgical procedure to remove the cuff. While the optimal placement of the cuff is 2-3 cm subcutaneous to the exit site, the choice of cuff location is often superseded by the positioning of the catheter tip[5], which is of greater clinical concern.

1.2 Description of Device

The DermaPort Percutaneous Vascular Access System (PVAS) was designed to facilitate the catheter placement, repositioning, and exchange procedures while maintaining the catheter attachment, bacterial barrier and fixation functions of the fibrous cuff. The PVAS includes a port which acts as a percutaneous conduit enabling the catheter to enter into the body.

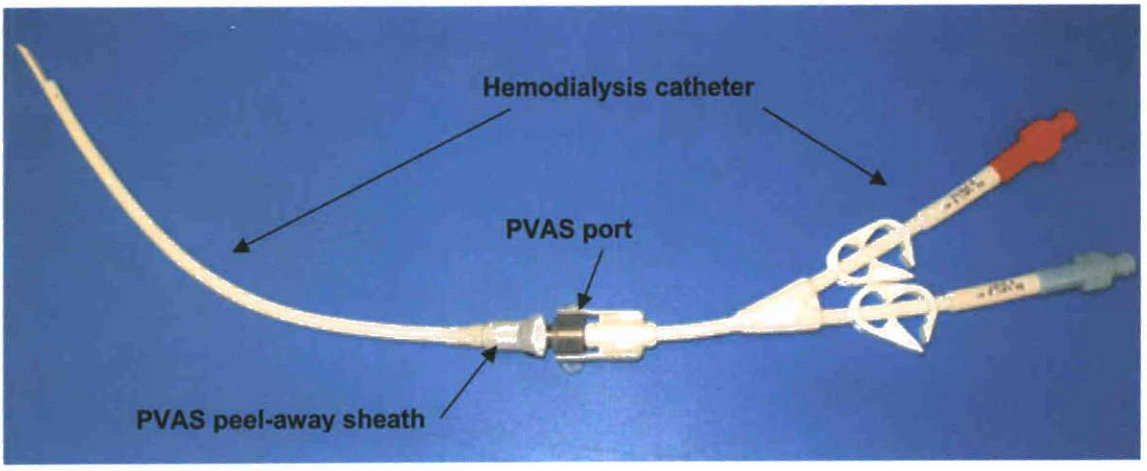
The main component of the PVAS is a metal port, which provides a percutaneous conduit and is implanted into the subcutaneous tunnel at the catheter exit site on the chest wall. The hemodialysis catheter passes through the metal port, into the subcutaneous tunnel, and then into the central venous system in the usual fashion. The metal surface of the port has a porous, tissue integrating coating which allows ingrowth of tissue to anchor the PVAS device. The PVAS device also holds the hemodialysis catheter in place.

The PVAS device contains an internal three (3) wiper seal, which provides a barrier to the migration of bacteria along the external surface of the catheter. The hemodialysis catheter is attached to the implanted metal PVAS conduit with a removable locking mechanism (brake) which encircles the catheter, allows optimal placement of the catheter tip, and maintains its position. The unique design of the PVAS provides cutaneous fixation of the hemodialysis

[4] Saad TF & Vesely TM. Venous access for patients with chronic kidney disease. *J Vasc Interv Radiol* 15:1041-1045 (2004).
[5] Trerotola S. Hemodialysis catheter placement and management. *Radiology* 215: 651-658 (2000).

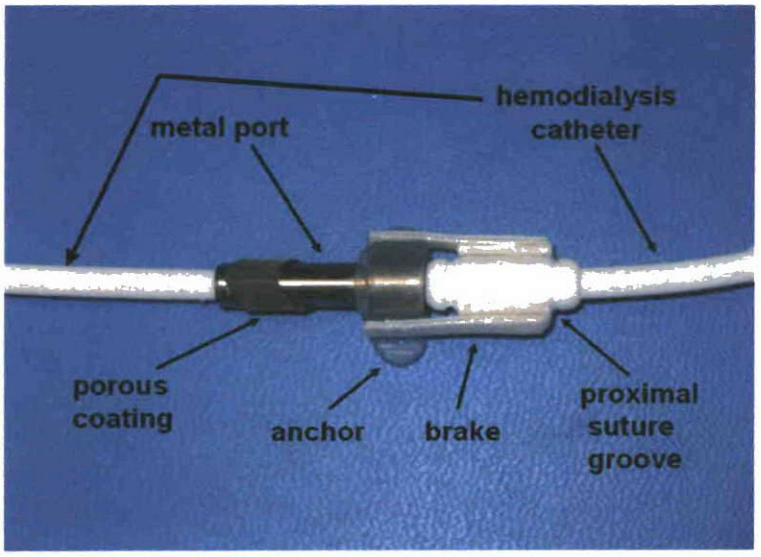
catheter while allowing easy repositioning, replacement and removal of the catheter as well as removal of the PVAS device itself.

The Percutaneous Vascular Access System consists of several components, including a surgical blade for incision at the exit site, a 14.5F long-term catheter surrounded by the PVAS metal port with peel-away sheath, and various accessories associated with the insertion of tunneled catheter systems. Picture 1.2-1 provides an overview of the PVAS.



Picture 1.2-1: The DermaPort Percutaneous Vascular Access System

A short section (1 cm) of the metal surface of the PVAS port is treated with a porous, tissue-integrating coating that promotes tissue ingrowth and fixation of the device. During the insertion procedure, this porous coated surface is covered by a removable peel-away sheath that eases placement and prevents contamination as the port is implanted into the subcutaneous tunnel. After appropriate positioning of the PVAS conduit, the peel-away sheath is manually split and removed from the subcutaneous tunnel. Picture 1.2-2 provides an image of the PVAS with the peel-away sheath removed.

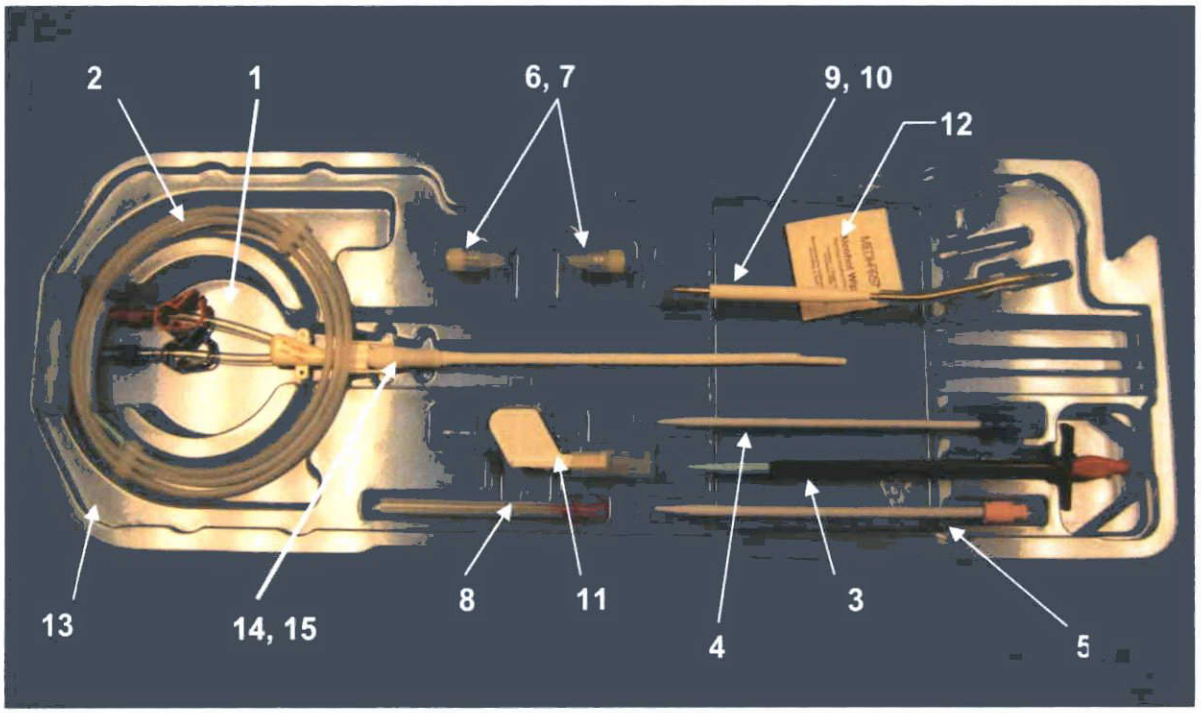


Picture 1.2-2: PVAS and Catheter Interface Detail, PVAS peel-away sheath removed

The metal port contains an internal three (3) wiper seal which serves as a physical barrier to minimize bacterial contamination of the subcutaneous tunnel during subsequent catheter reposition or exchange procedures.

The proximal portion of the PVAS port is encased by a silicone anchor which has two lateral suture wings for securing the device to the chest wall.

The hemodialysis catheter is secured to the inserted PVAS port conduit using a locking attachment (brake) mechanism. This attachment brake component consists of a moveable cylindrical silicone collar, which is attached to the anchor of the PVAS port by two lateral braces. After appropriately positioning the hemodialysis catheter, the cylindrical brake collar is placed around the catheter and secured using one encircling suture in the proximal groove. Picture 1.2-3 provides an image of the packaged PVAS.



Picture 1.2-3: Packaged PVAS and Catheter

The DermaPort Percutaneous Vascular Access System (PVAS) consists of the following components:

1. Implanted Hemodialysis 14.5 F Catheter (24 cm, 28 cm or 32 cm lengths)
2. Guidewire; 0.038 inch (70 cm or 100 cm lengths)
3. 16F Tearaway Set Griplock Hub
4. 12F Polyethylene Dilator
5. 14F Polyethylene Dilator
6. Clear Female Dust Cover
7. Injection Caps
8. 18 GA x 2.7" Cyrolite Introducer Needle
9. Tunneler with Tri ball tip
10. Tunneler Sleeve
11. DermaPort Blade
12. Commercially available alcohol pad
13. Commercially available adhesive wound dressing (not shown)
14. Peel-away sheath
15. DermaPort Percutaneous Vascular Access System (PVAS) Port

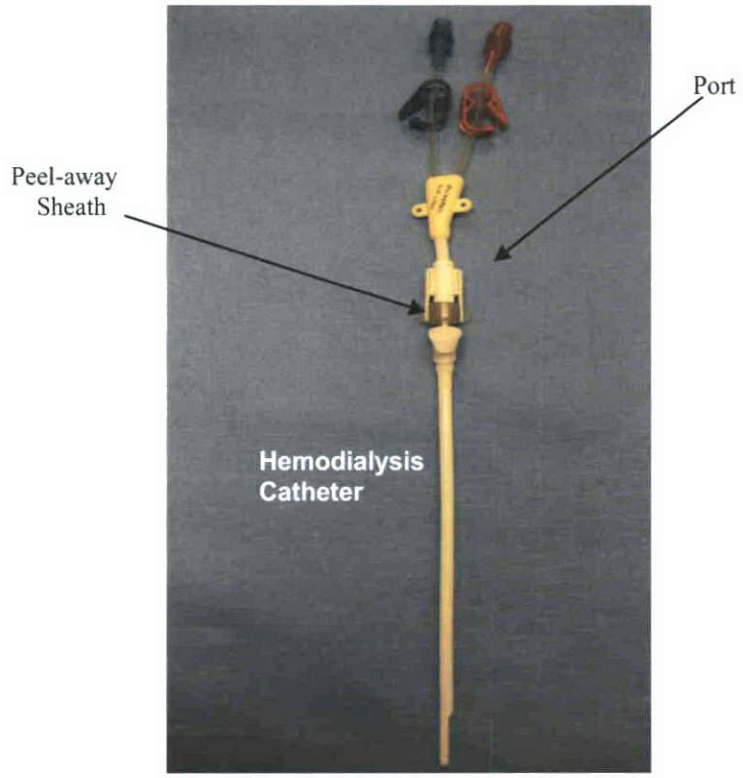
Note: The PVAS is provided with 1 of 3 catheter lengths, with an appropriately sized guidewire.

Attachment A contains drawings for the PVAS port, peel-away sheath, catheter and DermaPort blade. The PVAS port, peel-away sheath, catheter and DermaPort blade are the only components that are not commercially available. The catheter is identical to the Hemoflow, with the exception of the fibrous cuff, cleared to market by the FDA via 510(k) number K994105. The following sections provide details on the significant components of the DermaPort PVAS.

1.2.1 Implanted Hemodialysis Catheter

The PVAS kit contains a 14.5F dual lumen polyurethane hemodialysis catheter. This catheter is identical to the HemoFlow catheter, with the exception that the fibrous cuff on the HemoFlow catheter is omitted. The HemoFlow catheter is cleared to market by the FDA via 510(k) number K994105. Materials and manufacturing processing equivalence are defined in Section 7.0.

The catheter is manufactured for DermaPort by Martech, Inc. Harleysville, PA, USA, an FDA registered establishment medical device manufacturer that supplies catheters to the medical device industry. The catheter is certified to comply with ISO 10555-1 and ISO 10555-3, recognized standards for central venous catheters. A certification of compliance to the ISO 10555 standard is included in Section 9.0.



Picture 1.2.1: Hemodialysis Catheter with PVAS

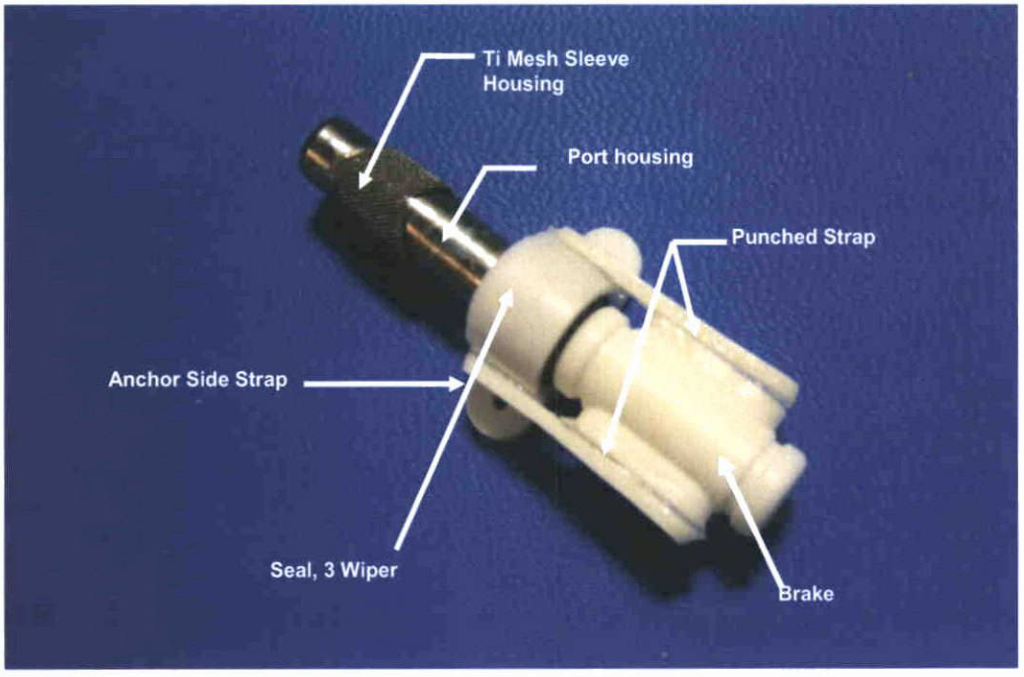
As stated previously, the predicate Medcomp hemodialysis catheter is manufactured by Martech. MedComp (Harleysville, PA, USA) performs kitting and distribution. Martech and MedComp are affiliated companies. MedComp holds the 510(k)s for the components and catheters manufactured by Martech.

The predicate MedComp hemodialysis catheter applies a fixed polyester cuff to allow tissue ingrowth for long term transcutaneous placement. The DermaPort hemodialysis catheter is passed through a PVAS port. This port takes the place of the fixed polyester cuff and supports tissue ingrowth for long term placement. Evaluation of tissue ingrowth on the PVAS port is addressed by evaluation *in vivo*, reference Section 6.0

1.2.2. DermaPort Percutaneous Vascular Access System (PVAS) Port

The PVAS port is an accessory to the implanted hemodialysis catheter, replacing the fixed fibrous cuff. The PVAS port has been developed to support central venous access for hemodialysis. The PVAS port consists of a percutaneous tubular conduit, through which a

standard 14.5F polyurethane hemodialysis catheter enters the subcutaneous tunnel. An integral three (3) wiper seal surrounds the catheter and prevents microbial migration along the catheter. The port is enclosed by a silicone anchor that braces the assembly to the skin, and an associated brake holds the catheter in place within the port. A tissue integrating, titanium mesh biomaterial surrounds the port, providing anatomical fixation and prevention of microbial migration through tissue integration, in a manner analogous to the fabric cuff of a tunneled catheter, reference Picture 1.2.2-1.



Picture 1.2.2-1: PVAS Port

The PVAS includes the port with associated peel-away sheath, brake, anchor, seal, three (3) wiper and tissue integrating biomaterial, a custom DermaPort blade, and a 14.5F polyurethane catheter with accessories necessary for tunneled catheter placement using the Seldinger technique. The PVAS port offers an advantage over tunneled cuffed catheters: by decoupling the tissue integrating biomaterial from the catheter, the PVAS port enables catheter repositioning and exchange procedures in a repeatable and safe manner while preventing the passage of microbes along the catheter.

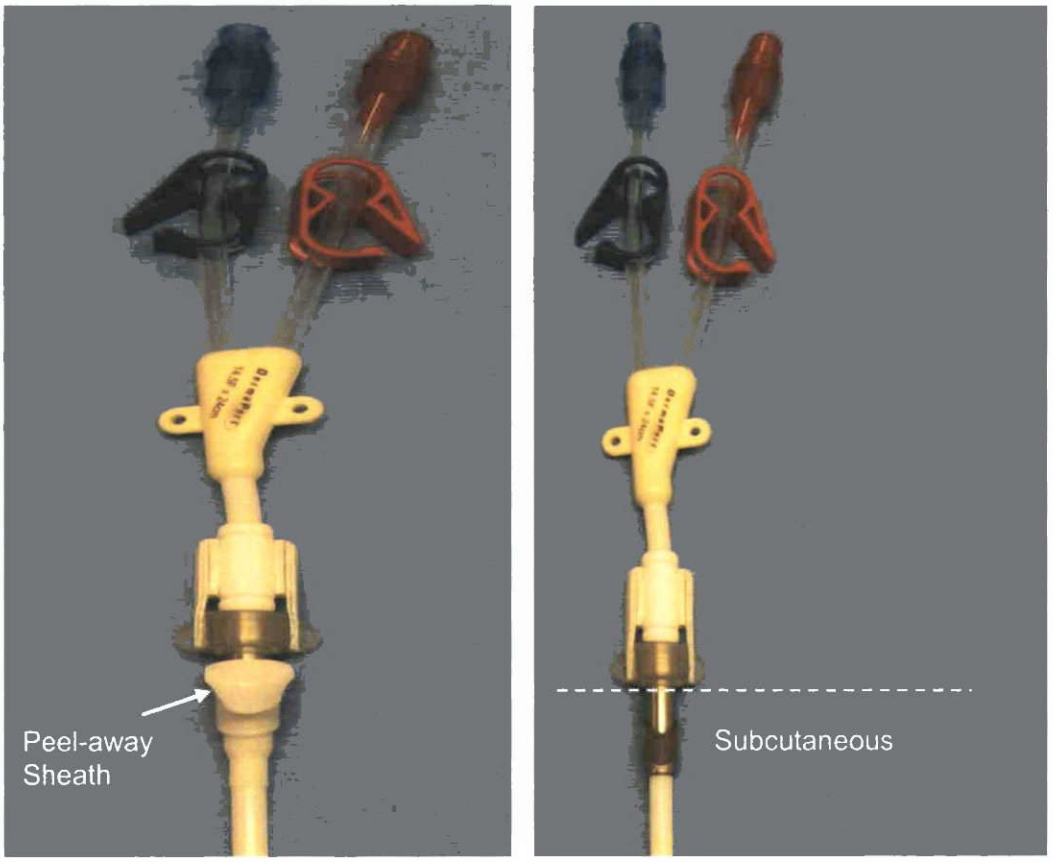
Central venous catheters often cease to function due to the catheter tip location. Correction requires reversal of the flow direction in the two catheter lumens, which can lead to greater

recirculation. Tunneled cuffed catheters with integrated cuffs require blunt dissection in order to reposition the catheter tip and reestablish flow. The PVAS port allows the repositioning of the catheter tip, both through rotation and retraction of the catheter. This is performed without disruption of the tissue integrating biomaterial and the exit site epidermal seal is preserved.

Central venous catheters can also cease to function due to thrombosis or infection. Removing an infected catheter and inserting a new catheter at a new site can lead to thrombosis or venous stenosis, and, eventually, to depletion of the patient's central veins. Preservation of central veins is a fundamental tenet for management of chronic hemodialysis patients. The preferred site for long term hemodialysis access through a tunneled catheter is the right internal jugular vein (NKF/DOQI 2006 Update, Clinical Practice Guidelines for Vascular Access). Additional access sites, such as the left internal jugular or the subclavian veins, may be available, but have higher complication rates and may interfere with future arteriovenous fistula success due to venous stenosis. Removal of an infected or thrombosed tunneled cuffed catheter often requires the subsequent use of less desirable vascular access sites with higher complication and failure rates.

When performed in the appropriate clinical situation, the catheter exchange procedure has proven beneficial for treatment of catheter-related infections, eliminating the need for a new venous entry site and thereby preserving the patient's central venous anatomy. The removal of tunneled cuffed catheters during catheter exchange requires that the integrated biomaterial fibrous cuff also be removed. As intended, the fibrous cuff becomes incorporated into the subcutaneous tissue, frequently requiring a minor surgical procedure to separate the cuff. This requires blunt dissection and may prevent the use of the same exit site for catheter replacement. While the ideal placement of the cuff is 2-3 cm subcutaneous to the exit site, the choice of cuff location is often superseded by the positioning of the catheter tip, which is of greater clinical concern. The PVAS port allows the rapid and safe exchange of a malfunctioning catheter through the integrated biomaterial port without dissection, with preservation of the existing percutaneous exit site and venous entry site. In addition, by decoupling the tissue integrating biomaterial port from the catheter, the PVAS port allows independent positioning of the catheter tip.

PVAS port removal is similar to the removal of a tunneled cuffed catheter, but may be easier. The cuffed catheter biomaterial is located subcutaneously, while the PVAS port tissue integrating biomaterial is located just below the incision, reference Picture 1.2.2-2. At the time of removal, the tissue integrating biomaterial is exposed through retraction of the PVAS port housing. The biomaterial is removed from the surrounding tissue with minor dissection.



Picture 1.2.2-2: DermaPort Percutaneous Vascular Access System (PVAS)

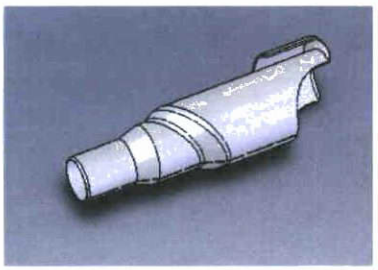
The PVAS port is a percutaneous device, part of which is implanted into the body. The port is supplied installed onto the proximal end of the catheter assembly. The port enables the heath care professional to move the catheter while maintaining tissue integration at the exit site.

The PVAS port assembly contains two major sub-assemblies which have been joined together into one part. The first subassembly is the implanted section. It is made from titanium. The second subassembly, which is joined to the first implanted section, is composed

of medical grade silicone parts that contact the skin, but are not implanted. Section 7.0 addresses material biocompatibility.

1.2.3 Peel-away Sheath

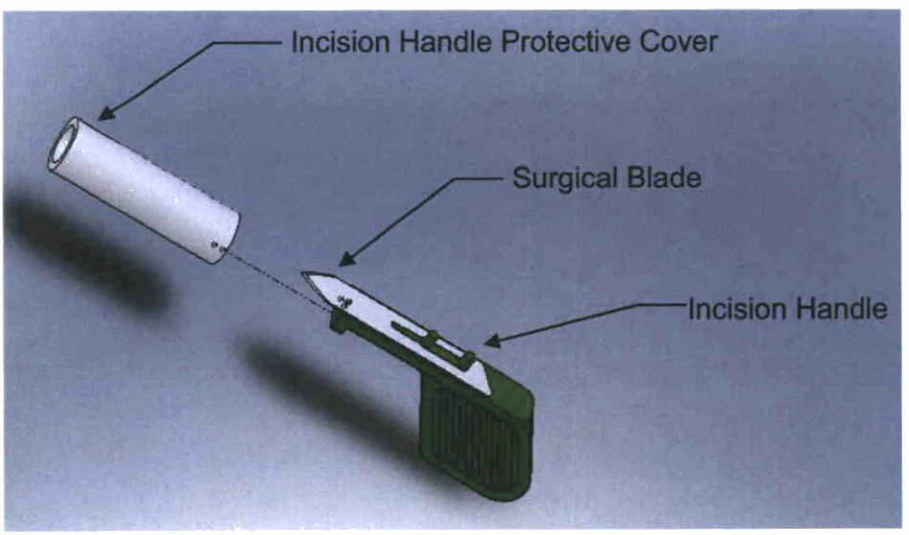
A temporary splittable peel-away sheath is supplied that covers the PVAS port assembly to aid in its placement, reference picture 1.2.3. The peel-away sheath is made from Teflon. The peel-away sheath resides over the PVAS port and is removed during and discarded immediately after the initial operative procedure.



Picture 1.2.3: Peel-away sheath

1.2.4 DermaPort Blade

The PVAS kit contains a surgical blade (DermaPort blade). This DermaPort blade is designed to control the width and depth of the initial incision in the surgical procedure in support of PVAS port placement. The DermaPort blade is made from surgical stainless steel. The handle of the blade is made from injection molded medical grade ABS plastic. The blade is provided with a protective cover made from medical grade silicone rubber.



Picture 1.2.3-2: PVAS DermaPort Blade with Protective Cover

Picture 1.2.3-2: PVAS DermaPort Blade

The DermaPort Blade complies with the device classification defined in 21 CFR 878.4800 Manual Surgical Instrument for General Use and is a Class I, 510(k) exempt device.

1.3 Kit Certification

As described, the PVAS is a kit. The kit components include Class III and Class I FDA regulated components. Table 1.3 defines the FDA regulatory basis for the kit components that are currently cleared to market devices.

Table 1.3: Regulatory Status of Components

Description	Martech Part Number	FDA Regulatory Basis	FDA Class
Implanted Hemodialysis Catheter	AC5108D	K994105 (Hemoflow)	III
Guidewire 70 cm	AC6100WL	K040318 (SPLIT CATH III)	III
Guidewire 100 cm	AC6106WL	K022678 (SPLIT STREAM)	III
16F Tearaway Set Griplock Hub	AC4613GL	K040318 (SPLIT CATH III)	III
12F, 14F Polyethylene Dilator	AC4328, AC4330	K040318 (SPLIT CATH III)	III
Clear Female Dust Cover	PPM1063	K040318 (SPLIT CATH III)	III
Injection Cap	PPO1034	K040318 (SPLIT CATH III)	III
18 GA x 2.7" Cryolite Introducer Needle	AC1830-1	K040318 (SPLIT CATH III)	III
Tunneler with Tri ball tip	PPO1246	K994105 (Hemoflow)	III
Tunneler Sleeve	PPO1885	K994105 (Hemoflow) & K020465 (SPLIT CATH II)	III
DermaPort Blade	Not Applicable	878.4800 Manual surgical instrument for general use; 510(k) exempt	I

All of the noted components are used for the indication for use cleared to market by the noted 510(k) or are 510(k) exempt in compliance with the noted regulation. The components are manufactured by Martech Medical Products. These same parts are commercialized by MedComp Components Inc. (MEDCOMP). Martech Medical Products is affiliated by common ownership with MEDCOMP. The following Kit Certification is provided to support the FDA regulation status of all components.

DermaPort

Kit Certification

DermaPort Percutaneous Vascular Access System (PVAS)

I certify that the following components of the DermaPort Percutaneous Vascular Access System (PVAS) kit are either:

(1) legally marketed pre-Amendments devices,

(2) exempt from premarket notification consistent with the exemption criteria described in the classification regulation(s) and the limitation of exemptions for Section 510(k) of the act (e.g., 878.9), or

(3) have been found to be substantially equivalent through the premarket notification process for the use(s) for which the kit is to be intended (i.e., I am not claiming or causing a new use for the component(s)).

I further certify that these components are consistent with their pre-Amendments, exemption, or premarket notification criteria and status.

B. M

(Signature)

Buzz Moran, President

(Printed Name, Title)

30 APRIL 2007

Date

1.4 Variations

Variations of the PVAS kit are available. The variations consist of different catheter lengths and different PVAS kit components based upon whether the kit is a "Standard" kit or an "Exchange" kit. The Catheter variations are:

1) 14.5F, 24 cm long
2) 14.5F, 28 cm long
3) 14.5F, 32 cm long.

The Catheter is supplied with the PVAS port in place.

The PVAS kits are available in the variations noted in Table 1.4-1.

Table 1.4-1: Kit Variations

Kit Number	Description
HD-100-24	PVAS 24 cm Standard Kit
HD-100-28	PVAS 28 cm Standard Kit
HD-100-32	PVAS 32 cm Standard Kit
HD-100-24E	PVAS 24 cm Exchange Kit
HD-100-28E	PVAS 28 cm Exchange Kit
HD-100-32E	PVAS 32 cm Exchange Kit

The Standard PVAS kits are used during initial catheter insertion. The three Standard Kits are identical, except for the length of the catheter and guidewire, as itemized in Table 1.4-2.

Table 1.4-2: PVAS Standard Kits

DermaPort Standard Kit Number	Component	Description
HD-100-24	Catheter 14.5 F, 24 cm with PVAS port	14.5 F dual lumen hemodialysis catheter, 24 cm long, with PVAS port and protective peel-away sheath pre-installed
HD-100-28	Catheter 14.5 F, 28 cm with PVAS port	14.5 F dual lumen hemodialysis catheter, 28 cm long, with PVAS port and protective peel-away sheath pre-installed
HD-100-32	Catheter 14.5 F, 32 cm with PVAS port	14.5 F dual lumen hemodialysis catheter, 32 cm long, with PVAS port and protective peel-away sheath pre-installed
HD-100-24	Guidewire 70 cm	0.038" Guidewire, 70 cm long
HD-100-28	Guidewire 70 cm	0.038" Guidewire, 70 cm long

Table 1.4-2: PVAS Standard Kits, continued		
DermaPort Standard Kit Number	**Component**	**Description**
HD-100-32	Guidewire 100 cm	0.038" Guidewire, 100 cm long
HD-100-all	Tunneler with sleeve	
HD-100-all	18 GA x 2.7" Cyrolite Introducer Needle	
HD-100-all	16F Tearaway Set Griplock Hub	16F Valved Sheath/Dilator
HD-100-all	12F Dilator	
HD-100-all	14F Dilator	
HD-100-all	Injection Caps/Female dust covers	
HD-100-all	DermaPort blade	Scalpel blade with handle for initial insertion
HD-100-all	Adhesive wound dressing	Pre-packaged off-the-shelf component
HD-100-all	Alcohol pad	Pre-packaged off-the-shelf component

The Exchange Kits are used during catheter exchange. The three Exchange Kits are identical, except for the length of the catheter and guidewire as defined in Table 1.4-3.

Table 1.4-2: PVAS Exchange Kits		
DermaPort Exchange Kit Number	**Component**	**Description**
HD-100-24E	Catheter 14.5 F, 24 cm	14.5 F dual lumen hemodialysis catheter, 24 cm long
HD-100-28E	Catheter 14.5 F, 28 cm	14.5 F dual lumen hemodialysis catheter, 28 cm long
HD-100-32E	Catheter 14.5 F, 32 cm	14.5 F dual lumen hemodialysis catheter, 32 cm long
HD-100-32E	Guidewire 70 cm	0.038" Guidewire, 70 cm long
HD-100-28E	Guidewire 70 cm	0.038" Guidewire, 70 cm long
HD-100-32E	Guidewire 100 cm	0.038" Guidewire, 100 cm long
HD-100-all	Injection Caps/Female dust covers	
HD-100-all	Adhesive wound dressing	Pre-packaged off-the-shelf component
HD-100-all	Alcohol pad	Pre-packaged off-the-shelf component

1.5 Technology

The catheter technology supporting hemodialysis and apheresis is unchanged from the predicate Hemodialysis Catheter cleared to market by 510(k) K994105. The hemodialysis catheter is implanted for more than 30 days of single patient use. The flowing blood contacting materials of the catheter remain unchanged.

The method of retaining the catheter is modified to a PVAS port device. Evaluation of the PVAS port and performance with the catheter is provided in Section 6.0. Material and skin contact material biocompatibility is addressed in Section 7.0.

The only implanted component, other than the standard and cleared to market hemodialysis catheter itself, is the metal section of the PVAS port. The PVAS port is made from biocompatible, implant grade titanium. Descriptions of the tests performed to qualify the PVAS port are contained in Section 6.0 and 7.0.

1.6 Application

The clinical application of the DermaPort Percutaneous Vascular Access System (PVAS) and catheter is consistent with clinical applications of the predicate Hemodialysis Catheter cleared to market by 510(k) K994105.

1.7 Indications for Use

The indication for use of the DermaPort Percutaneous Vascular Access System (PVAS) is consistent with the classification of 21 CFR 876.5540 Blood Access Device and Accessories. The indication for use is:

> The DermaPort Percutaneous Vascular Access System (PVAS™) is indicated for long-term (greater than 30 days) vascular access for hemodialysis and apheresis. The system is inserted percutaneously and the catheter is typically placed in the internal jugular vein of an adult patient. The subclavian vein is an alternate catheter insertion site.

The FDA Indications For Use Form is provided as Attachment H.

DermaPort

2.0 Truthful and Accurate Statement

PREMARKET NOTIFICATION

TRUTHFUL AND ACCURATE STATEMENT

(As Required by 21 CFR 807.87 (j))

DermaPort Percutaneous Vascular Access System (PVAS)

I certify that, in my capacity as President of DermaPort, 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.

M. Moran

(Signature)

Buzz Moran, President

(Printed Name, Title)

30 APRIL 2007

Date

[Premarket Notification (510(k)) Number]

3.0 Labeling

Enclosed as Attachment B is proposed DRAFT labeling for the PVAS.

Enclosed as Attachment C are examples of predicate device labeling.

4.0 Specifications/Comparison to Predicates

Table 4.0 compares features and specifications of the PVAS with Catheter device under review to the predicate devices.

Table 4.0: Comparison of Features

Feature	PVAS Under Review	Medcomp Hemo-Flow Catheter K994105 Predicate Device	Med-Conduit HemoCath II K062901 Predicate Device	Comments on Comparison
1. Intended Use	(b) (4) [redacted]	The Medcomp Hemo-Flow Catheter is indicated for use in attaining long-term vascular access for hemodialysis and apheresis. It may be inserted percutaneously and is ideally placed in the internal jugular vein of an adult patient. Alternate insertion site includes the subclavian vein.	The HemoCath Hemodialysis/Aphersis Catheter is indicated for use in attaining long term vascular access for hemodialysis or aphersis therapy via the jugular or subclavian vein. The catheter is intended for implantation dwell time of greater than 30 days.	Equivalent
2. Indication for Use		Adult	Believed to be Adult	Same
3. Contraindications		These catheters are intended for long-term vascular access only and should not be used for any other purpose other than indicated in these instructions for use.	Not known	Same
4. Insertion Method		Percutaneous	Percutaneous	Same

Table 4.0: Comparison of Features, continued

Feature	PVAS Under Review	Medcomp Hemo-Flow Catheter K994105 Predicate Device	Med-Conduit HemoCath II K062901 Predicate Device	Comments on Comparison
5. Catheter Insertion Sites	(b) (4)	Internal jugular vein or subclavian vein	Internal jugular vein or subclavian vein	Same
6. Sterile		Yes	Yes	Same
7. Sterilization Method		Ethylene Oxide	Assumed to be Ethylene Oxide	Same
8. Sterility Assurance Level		Assumed to be SAL 10^{-6}	Assumed to be SAL 10^{-6}	Equivalent
9. Labeled Pyrogen Free		Yes	Assumed yes	Same
10. Method of Pyrogen Evaluation		Assumed to be LAL	Unknown	Equivalent Details are provided in Section 8.0.
11. Reusable		No	No	Same
12. Reprocessed		No	Unknown	Same
13. Patient Contacting Material		Catheter: Polyurethane Fibrous cuff: Polyester	Catheter: Silicone Port: Polyurethane Cuff: Polyester	Catheter: Same PVAS Port material biocompatibility is addressed in Section 7.0
14. Environment of Use		Hospital, Clinics, Out Patient Facilities	Believed to be Hospital, Clinics, Out Patient Facilities	Same

Table 4.0: Comparison of Features, continued				
Feature	**PVAS Under Review**	**Medcomp Hemo-Flow Catheter K994105 Predicate Device**	**Med-Conduit HemoCath II K062901 Predicate Device**	**Comments on Comparison**
15. Packaging	(b) (4) [redacted]	Thermoplastic pouch with TYVEK header	Not known	Equivalent Packaging evaluation is addressed in Section 8.0.
16. Shelf Life		5 years	Not known	Equivalent
17. Dual Lumen Catheter		Yes	Yes	Same
18. Catheter Length Variations		Five (5): 14.5F, 24 cm long 14.5F, 28 cm long 14.5F, 32 cm long 14.5F, 36 cm long 14.5F, 40 cm long	Believed to be in the range of 28 to 36 cm range to support jugular and subclavian insertion sites.	Equivalent
19. Sold as a kit		Yes	Not known	Equivalent
20. Catheter Retention		Polyester Cuff	Port through which the catheter enters the skin	The PVAS Port and Catheter functions are evaluated by testing described in Section 6.0.

4.1 Comparison Summary

The features and functions of the PVAS under review are equivalent to those of the predicate device. Differences are qualified as defined in Sections 6.0 through Section 9.0.

5.0 Risk/Hazard Analysis

The PVAS is used to insert a tunneled central venous catheter percutaneously to support hemodialysis or apheresis. There are known, well-established risks associated with hemodialysis using a central venous catheter. Many of these risks are the same for the PVAS as for the predicate polyester cuffed catheter.

A summary of known safety and effectiveness concerns for hemodialysis catheters and blood access devices is provided in the Class III Summary, reference Attachment G. A risk assessment and mitigation analysis was performed addressing issues unique to the PVAS. The risks associated with central hemodialysis with a cuffed catheter are well known.

The individuals who conducted the risk analyses are identified below:

(b) (4), (b) (6)

[redacted]

The Risk Analysis is provided in Attachment E.

5.1 Risk/Hazard Analysis Conclusions

The risks of the PVAS are mitigated to acceptable levels by application of labeling, selection of materials, controlled manufacturing processes, specification and verification. All resulting mitigated risks are found to be acceptable.

For reference, risk mitigation information is provided as follows:

- Instructions for Use (IFU) are in Attachment B.
- Verification of performance is in Section 6.0.
- Material biocompatibility is in Section 7.0
- Verification of sterility and sterile packaging is in Section 8.0.

In comparing the risks to the benefits of the PVAS, the benefits clearly outweigh the resulting mitigated risks. The greatest problem associated with central venous hemodialysis catheters is maintenance of access due to the loss of patency primarily as a result of thrombosis and fibrin sheath formation. The ability to reposition and exchange the catheter while maintaining tissue integration offers the clinician another tool to alleviate this major problem.

6.0 Performance Tests

The primary performance specifications of the PVAS include the following:

1. Meet the requirements of ISO 10555-3: Sterile, Single-use Intravascular Catheters – Part 3: Central Venous Catheters;
2. Allow repositioning and exchange of the catheter with the integrated percutaneous components *in situ;*
3. Maintain a flow rate through the catheter in the PVAS port that is sufficient for effective hemodialysis.
4. Patients may be exposed to Magnetic Resonance Imaging (MRI) clinical examinations. The metal PVAS Port must be tested and labeled in compliance with FDA standards for MRI compatibility.

The differences between the PVAS under review and the predicate catheter device with a polyester cuff can be summarized as:

1. The predicate Medcomp hemodialysis catheter applies a fixed polyester cuff to allow tissue ingrowth for long term transcutaneous placement. The DermaPort hemodialysis catheter is passed through [redacted (b) (4)]

[redacted (b) (4)]

3. The predicate Medcomp hemodialysis catheter is held in place by an ingrown polyester cuff bonded to the catheter. [redacted (b) (4)]

[redacted (b) (4)]

Table 6.0-1 summarizes evaluations performed to support performance specification verification and safety and effectiveness of the differences.

Table 6.0-1: Evaluations Performed to Establish Safety and Effectiveness of Differences		
Specification Verification, Difference Evaluation	**Evaluation Applied**	**Evaluation Summary**
(b) (4) [redacted]		

6.1 Microbial Barrier Properties between the Implanted Catheter and PVAS port

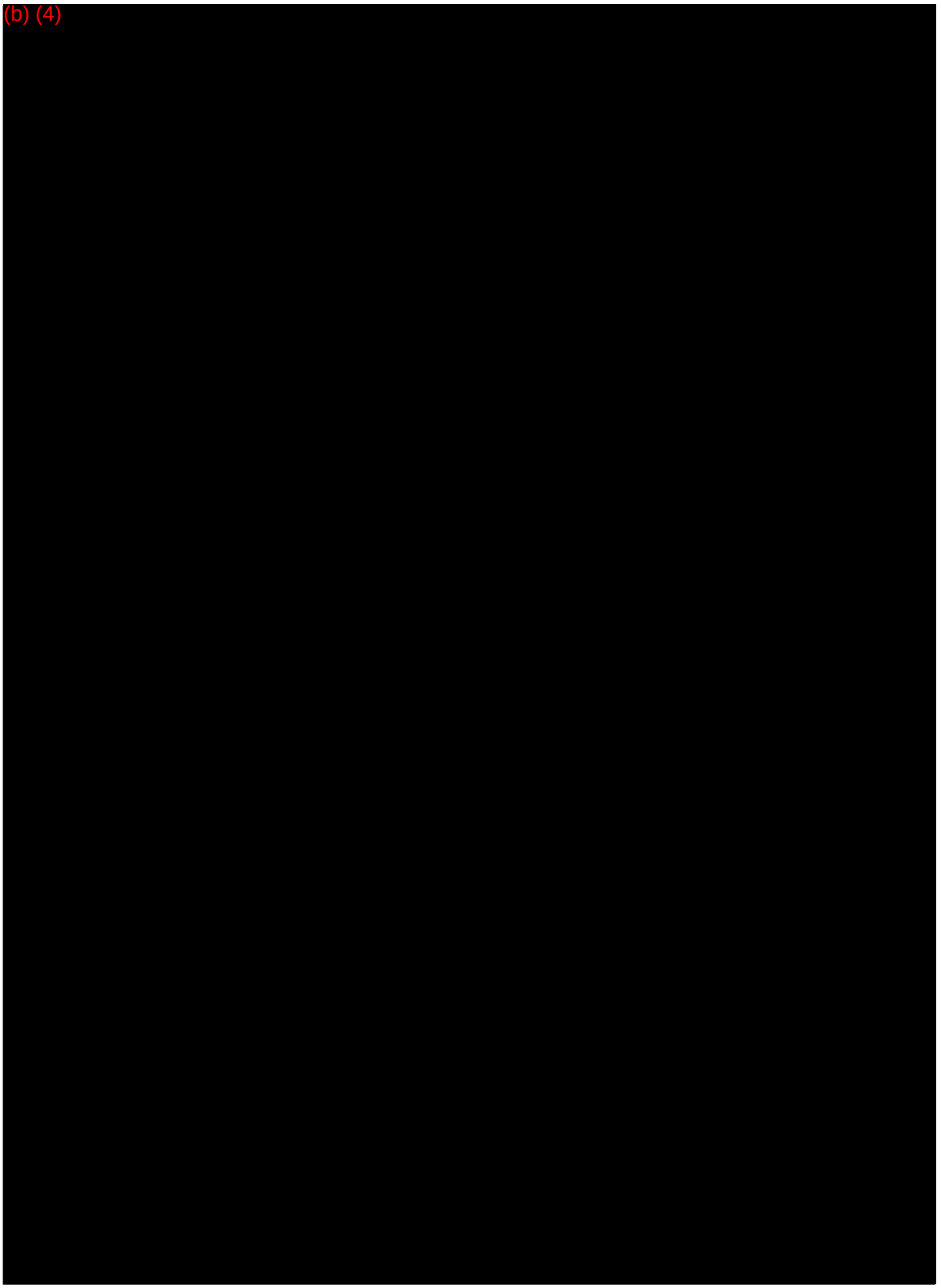
(b) (4) [redacted] The test report is provided in Attachment D.

6.2 PVAS port and Hemodialysis Catheter Flow

(b) (4) [redacted] The flow test report is provided in Attachment D.

6.3 Tissue Ingrowth Evaluation

(b) (4)



(b) (4)

[redacted]

6.4 MRI Evaluation

(b) (4)

[redacted]

Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment. The MRI test report is provided in Attachment D.

6.5 Catheter Retention in the PVAS Port

The retention tensile force of the catheter in the PVAS brake was evaluated (b) (4)

(b) (4)

Attachment D.

(b) (4), (b) (6)

(b) (4), (b) (6)

7.0 Biocompatibility

As described in Section 1.2, the PVAS device kit under review can be summarized as consisting of the following two groups of components:

(b) (4)

The following sections provide details with regard to the biocompatibility of the materials in these two components.

7.1 Catheter with Associated Components

(b) (4)

Third Party Testing Lab (b) (4)

Third Party Testing Lab (b) (4)

Third Party Testing Lab (b) (4)

Third Party Testing Lab (b) (4)

DermaPort

Declaration of Conformity

Catheter and Associated Components

Material Biocompatibility

The materials of the DermaPort Catheter, Guidewire, Tearaway Set griplock Hub, Dilator, Dust Cover, Injection Cap, Tunneler, Tunneler Sleeve, 18 GA Needle are the same materials in formulation, processing and no other chemicals have been added (e.g., plasticizers, fillers, cleaning agents, mold release agents, etc.) as cleared to market by 510(k) K994105 (cleared 10/03/2001)), K020465 (cleared 05/22/2002), K022678 (cleared 02/24/2003) and K040318 (cleared 02/03/2005).

(Signature)

Buzz Moran, President, DermaPort, Inc.

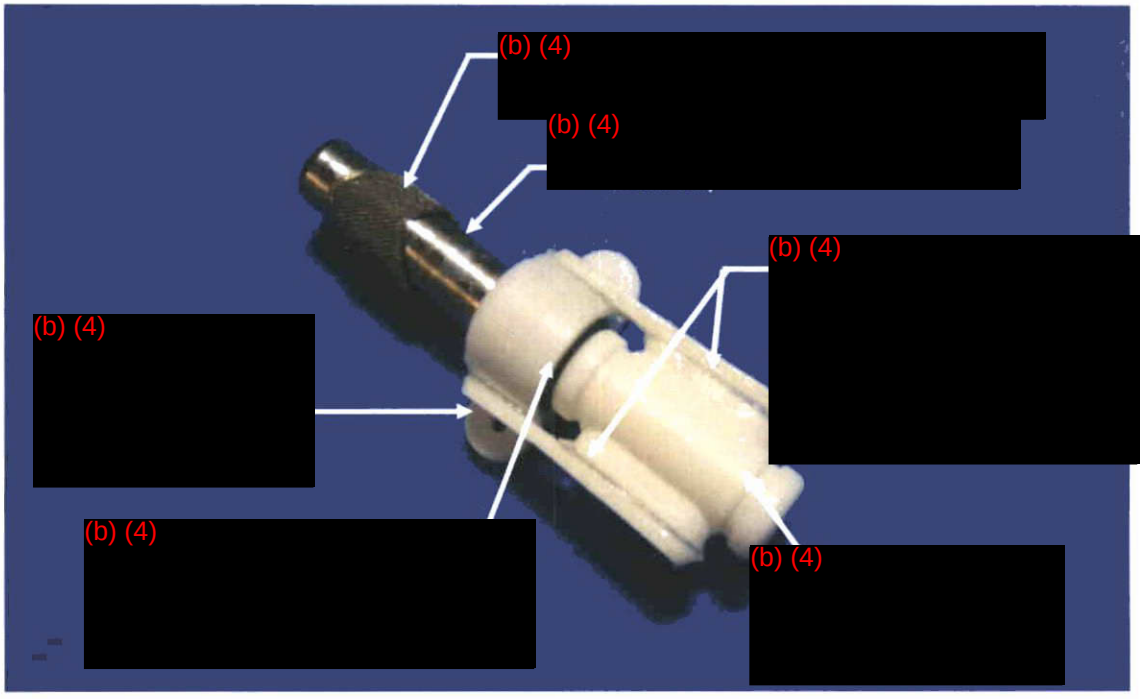
(Printed Name, Title)

30 APRIL 2009

(Date)

7.2 PVAS Port

Picture 7.2 provides guidance on the materials of the PVAS Port.



Picture 7.2: PVAS Port Material Detail

Table 7.2 summarizes the materials that construct the PVAS.

Table 7.2: PVAS Port Patient Contact Materials			
Supplier	Material	MAF #	Comments
(b) (4)			

Table 7.2: PVAS Port Patient Contact Materials, continued		
Supplier	**Material**	**Comments**
(b) (4) [redacted]		

7.2.1 PVAS Port Flexible Material Biocompatibility

The silicone materials of the PVAS reside outside of the body and contact the skin and are not implanted. The silicone materials are declared by the supplier (b) (4) [redacted]

A temporary, splittable PVAS peel-away sheath is supplied that covers the PVAS port assembly to aid in its placement. (b) (4) [redacted] away sheath is removed during and discarded immediately after the initial operative procedure (b) (4) [redacted]

To confirm the biocompatibility of the peel-away sheath (b) (4) [redacted] cytotoxicity testing was performed. The cytotoxicity testing was performed in compliance with ISO-10993-5:1999 Biological evaluation of medical devices-Part 5: Tests for in vitro cytotoxicity. The test was conducted in compliance with Good Laboratory Practices (GLP) and the test passed. Table 7.2.1-1 supports the Declaration of Conformity to this FDA Recognized Standard.

Table 7.2.1-1: Conformity to FDA Recognized Consensus Standards ISO-10993-5:1999 Biological Evaluation of Medical Devices-Part 5: Tests for in vitro cytotoxicity	
Required Elements for a Declaration of Conformity to a Recognized Standard:	**Compliance Statement:**
a. An identification of the applicable recognized consensus standards that were met.	ISO-10993-5:1999 Biological evaluation of medical devices-Part 5: Tests for in vitro cytotoxicity
b. A statement, for each consensus standard, that all requirements were met, except for inapplicable requirements or deviations noted below.	All applicable requirements are met.
c. An identification, for each consensus standard, of 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).	None.
d. An identification, for each consensus standard, of any requirements that were not applicable to the device.	None.
e. A specification of any deviations from each applicable standard that were applied.	No deviations to the standards were applied.
f. 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.	None.
g. The name and address of the testing laboratory and/or certification body involved in determining the conformance of the device with applicable consensus standards and a reference to any accreditations for those organizations.	Evaluation performed and documented by: (b) (4) [redacted]

The following Declaration of Conformity is provided.

DermaPort

Declaration of Conformity

DermaPort Percutaneous Vascular Access System (PVAS) Peel-away Sheath

Material Biocompatibility

The PVAS peel-away sheath material of the DermaPort Percutaneous Vascular Access System (PVAS) was evaluated for compliance with the FDA Recognized Standard ISO-10993-5:1999 Biological evaluation of medical devices-Part 5: Tests for in vitro cytotoxicity. All the requirements were met with a passing result.

(Signature)

Buzz Moran, President
(Printed Name, Title)

30 APRIL 2007
(Dated)

With a transient duration of use for contact with compromised tissues, the FDA recognized consensus standard ISO 10993-1:2003 indicates the following types of material biocompatibility tests should be performed on the (b) (4) Cytotoxicity (completed), Irritation and Sensitization (Intracutaneous Reactivity). The sensitivity and irritation tests will be completed prior to commercial introduction of the (b) (4) peel-away sheath. Table 7.2.1-2 supports the accompanying Declaration of Conformity confirming these tests will be performed prior to commercial introduction.

Table 7.2.1-2: PVAS Peel-away sheath Conformity to FDA Recognized Consensus Standards ISO-10993-10:2002 Biological Evaluation of Medical Devices-Part 10: Tests for in Irritation and Sensitization.

Required Elements for a Declaration of Conformity to a Recognized Standard:	**Compliance Statement:**
a. An identification of the applicable recognized consensus standards that were met.	ISO-10993-10:2002 Biological evaluation of medical devices-Part 10: Tests for Irritation and Sensitization;
b. A statement, for each consensus standard, that all requirements were met, except for inapplicable requirements or deviations noted below.	All applicable requirements will be met prior to commercial introduction.
c. An identification, for each consensus standard, of 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).	None.
d. An identification, for each consensus standard, of any requirements that were not applicable to the device.	None.
e. A specification of any deviations from each applicable standard that were applied.	No deviations to the standards will be applied.
f. 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.	None.
g. The name and address of the testing laboratory and/or certification body involved in determining the conformance of the device with applicable consensus standards and a reference to any accreditations for those organizations.	(b) (4)

The following Declaration of Conformity is provided.

DermaPort

Declaration of Conformity

DermaPort Percutaneous Vascular Access System (PVAS) Peel-away Sheath

Material Biocompatibility

The PVAS peel-away sheath material of the DermaPort Percutaneous Vascular Access System (PVAS) will be evaluated for compliance with the FDA Recognized Standards ISO-10993-10:2002 Biological evaluation of medical devices-Part 10: Tests for Irritation and Sensitization prior to commercial introduction. All the requirements will be met with a passing result.

(Signature)

Buzz Moran, President
(Printed Name, Title)

30 APRIL 2007
(Dated)

7.2.2 PVAS Port Metal Material Biocompatibility

The metal materials of the PVAS port are implanted long term(b) (4) has a long history of safe use as an implant material, and is used extensively in the pacemaker and other industries.

(b) (4)

In addition to a history of material safe use, testing of these materials was conducted as guided by the FDA Recognized Consensus Standard AAMI/ANSI/ISO 10993-1:2003, Biological Evaluation of Medical Devices – Part 1: Evaluation and Testing. For the PVAS port as an implanted device with tissue/bone contact, material biocompatibility testing was performed for permanent contact duration. Table 7.2.2-1 summarizes the material biocompatibility tests applied to the PVAS port metal materials and the FDA Recognized Consensus Standard applied to support the test process.

Table 7.2.2-1: PVAS Port Metal Material Biocompatibility Evaluation

Test	Test Method
Cytotoxicity	ISO 10993-5:1999 Biological evaluation of medical devices- Part 5: Tests for in vitro cytotoxicity
Sensitization	ISO 10993-10:2002 Biological evaluation of medical devices- Part 10: Tests for Irritation and Sensitization
Intracutaneous Reactivity	ISO 10993-10:2002 Biological evaluation of medical devices- Part 10: Tests for Irritation and Sensitization
Acute Systemic Toxicity	ISO 10993-11:1993 Biological evaluation of medical devices- Part 11: Tests for systemic toxicity
Subacute and Subchronic Toxicity	ISO 10993-11:1993 Biological evaluation of medical devices- Part 11: Tests for systemic toxicity
Genotoxicity	ISO 10993-3:2003 Biological evaluation of medical devices- Part 3: Tests for Genotoxicity, Carcinogenicity and Reproductive Toxicity
Implantation	ISO 10993-6:1995 Biological evaluation of medical devices - Part 6: Test for local effects after implantation

The material biocompatibility tests passed. Table 7.2.2-2 supports the Declaration of Conformity to these FDA Recognized Standards.

Table 7.2.2-2: Conformity to FDA Recognized Consensus Standards for Biocompatibility Evaluation	
Required Elements for a Declaration of Conformity to a Recognized Standard:	**Compliance Statement:**
a. An identification of the applicable recognized consensus standards that were met.	ISO-10993-3:2003 Biological evaluation of medical devices-Part 3: Tests for Genotoxicity, Carcinogenicity and Reproductive Toxicity ISO-10993-5:1999 Biological evaluation of medical devices-Part 5: Tests for in vitro cytotoxicity. ISO 10993-6:1995 Biological evaluation of medical devices - Part 6: Test for local effects after implantation ISO-10993-10:2002 Biological evaluation of medical devices-Part 10: Tests for Irritation and Sensitization. ISO-10993-11:1993 Biological evaluation of medical devices-Part 11: Tests for systemic toxicity
b. A statement, for each consensus standard, that all requirements were met, except for inapplicable requirements or deviations noted below.	All applicable requirements are met.
c. An identification, for each consensus standard, of 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).	None.
d. An identification, for each consensus standard, of any requirements that were not applicable to the device.	None.
e. A specification of any deviations from each applicable standard that were applied.	No deviations to the standards were applied.
f. 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.	None.
g. The name and address of the testing laboratory and/or certification body involved in determining the conformance of the device with applicable consensus standards and a reference to any accreditations for those organizations.	Evaluation performed and documented by: (b) (4) [redacted]

The following Declaration of Conformity is provided.

DermaPort

Declaration of Conformity

DermaPort Percutaneous Vascular Access System (PVAS)

Material Biocompatibility

The metal patient contact materials of the DermaPort Percutaneous Vascular Access System (PVAS) port were evaluated for compliance with the FDA Recognized Standards:

a. ISO 10993-3:2003 Biological evaluation of medical devices-Part 3: Tests for Genotoxicity, Carcinogenicity and Reproductive Toxicity,
b. ISO 10993-5:1999 Biological evaluation of medical devices-Part 5: Tests for in vitro cytotoxicity,
c. ISO 10993-6:1995 Biological evaluation of medical devices - Part 6: Test for local effects after implantation,
d. ISO 10993-10:2002 Biological evaluation of medical devices-Part 10: Tests for Irritation and Sensitization,
e. ISO 10993-11:1993 Biological evaluation of medical devices-Part 11: Tests for systemic toxicity.

All the requirements were met with a passing result.

(Signature)

Buzz Moran, President
(Printed Name, Title)

30 APRIL 2007
(Dated)

8.0 Sterility

The following sterility information is provided for the PVAS in compliance with the FDA Guidance document: Updated 510(k) Sterility Review Guidance K90-1; Final Guidance for Industry and FDA.

1. Sterilization method: Ethylene Oxide, 100% ethylene oxide gas.

2. Method used to validate the sterilization cycle: ANSI/AAMI/ISO 11135: 1994 Medical devices—Validation and routine control of ethylene oxide sterilization. A Declaration of Conformity to the ANSI/AAMI/ISO 11135 standard is provided in Section 8.2.

3 The packaging to maintain the device sterile: See Section 8.1.

4. Ethylene oxide residuals limit: Less than 250 ppm per device; Less than 0.1 mg per day Ethylene Chlorohydrin Residuals limit: Less than 2 mg per day.

5. The PVAS patient contact components are labeled pyrogen free. The method applied to determine the blood contact components are pyrogen free is the FDA recognized Limulus Amebocyte Lysate (LAL) method (b) (4) (b) (4)

LAL Results	
Device	Endotoxin
(b) (4)	

6. Sterility assurance level (SAL): SAL of 10^{-6}

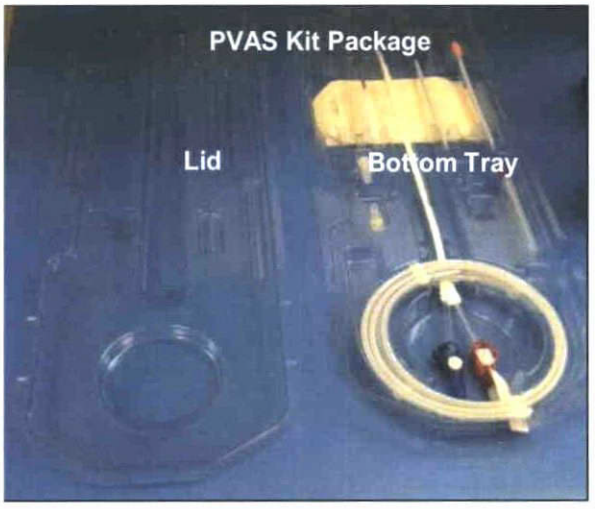
8.1 Packaging

The PVAS is packaged in a lidded tray and pouch system. Details of the packaging are as follows:

(b) (4)

[redacted]

The PVAS and accessories are inserted into the bottom tray and are secured in place with a snap-on lid. The tray and lid are inserted into the pouch and sealed using a validated pouch sealer. Photographs of the components (Picture 8.1-1) and packaged kit (Picture 8.1-2) are shown below.



Picture 8.1-1: Components in the Open Tray

Picture 8.1-2: Components in the Closed Tray

8.2 Sterilization Declaration of Conformity

The sterilization process for the PVAS applies the FDA Recognized Consensus Standards ANSI/AAMI/ISO 11135: 1994 Medical devices—Validation and routine control of ethylene oxide sterilization. Table 8.2-1 supports the Declaration of Conformity to the ANSI/AAMI/ISO 11135 standard, reference Section 8.4.

Table 8.2-1: Conformity to FDA Recognized Consensus Standards ANSI/AAMI/ISO 11135: 1994 Medical devices—Validation and routine control of ethylene oxide sterilization

Required Elements for a Declaration of Conformity to a Recognized Standard:	**Compliance Statement:**
a. An identification of the applicable recognized consensus standards that were met.	ANSI/AAMI/ISO 11135:1994 Medical devices—Validation and routine control of ethylene oxide sterilization
b. A statement, for each consensus standard, that all requirements were met, except for inapplicable requirements or deviations noted below.	All requirements were met.
c. An identification, for each consensus standard, of 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).	None.
d. An identification, for each consensus standard, of any requirements that were not applicable to the device.	None.
e. A specification of any deviations from each applicable standard that were applied.	No deviations to the standards were applied.
f. 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.	None.
g. The name and address of the testing laboratory and/or certification body involved in determining the conformance of the device with applicable consensus standards and a reference to any accreditations for those organizations.	Testing was performed and is documented by: (b) (4) [redacted]

8.3 Packaging

The packaging for the PVAS is a thermoplastic package with (b) (4) [redacted] sealed. A declaration of conformity to FDA Recognized Consensus Standards ANSI/AAMI/ISO 11607-1:2006 Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems and AAMI/ANSI/ISO 11607-2:2006, Packaging for terminally sterilized medical devices - Part 2: Validation requirements for forming, sealing and assembly processes, is provided in Section 8.4. Table 8.3-1 supports the Declaration of Conformity.

Table 8.3-1: Conformity to FDA Recognized Consensus Standards ANSI/AAMI/ISO 11607-1:2006 Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems and AAMI/ANSI/ISO 11607-2:2006, Packaging for terminally sterilized medical devices - Part 2: Validation requirements for forming, sealing and assembly processes

Required Elements for a Declaration of Conformity to a Recognized Standard:	**Compliance Statement:**
a. An identification of the applicable recognized consensus standards that were met.	ANSI/AAMI/ISO 11607-1:2006 Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems and AAMI/ANSI/ISO 11607-2:2006, Packaging for terminally sterilized medical devices - Part 2: Validation requirements for forming, sealing and assembly processes.
b. A statement, for each consensus standard, that all requirements were met, except for inapplicable requirements or deviations noted below.	All applicable requirements are met.
c. An identification, for each consensus standard, of 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).	None.
d. An identification, for each consensus standard, of any requirements that were not applicable to the device.	None.
e. A specification of any deviations from each applicable standard that were applied.	No deviations to the standards were applied.

Table 8.3-1: Conformity to FDA Recognized Consensus Standards ANSI/AAMI/ISO 11607-1:2006 Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems and AAMI/ANSI/ISO 11607-2:2006, Packaging for terminally sterilized medical devices - Part 2: Validation requirements for forming, sealing and assembly processes, Continued	
Required Elements for a Declaration of Conformity to a Recognized Standard:	**Compliance Statement:**
f. 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.	None.
g. The name and address of the testing laboratory and/or certification body involved in determining the conformance of the device with applicable consensus standards and a reference to any accreditations for those organizations.	Testing will be performed and documented by: (b) (4) [redacted]

8.4 Declaration of Conformity

The following Declaration of Conformity is provided in support of the sterilization and packaging standards compliance information in Sections 8.2 and 8.3.

DermaPort

Declaration of Conformity

DermaPort Percutaneous Vascular Access System (PVAS) with Catheter

Compliance to Sterilization and Packaging Standards

I certify that, in my capacity as President of DermaPort, Inc., the sterilization validation complies with the applicable requirements of Ethylene Oxide Sterilization per ANSI/AAMI/ISO 11135:1994 Medical devices—Validation and routine control of ethylene oxide sterilization; and the sterile barrier packaging of the DermaPort Percutaneous Vascular Access System (PVAS) AAMI/ANSI/ISO 11607-1:2006 Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems and AAMI/ANSI/ISO 11607-2:2006, Packaging for terminally sterilized medical devices - Part 2: Validation requirements for forming, sealing and assembly processes will be met prior to commercial introduction. .

M. Moran
(Signature)

Buzz Moran, President
(Printed Name, Title)

30 APRIL 2007
(Dated)

25102 Rye Canyon Loop, Suite 110, Santa Clarita, CA 91355, Telephone (661) 362-7900, Fax (661) 362-7902

8.5 Shelf Life

The protocol for evaluation of PVAS with Cather shelf life is presented in Attachment D. The initial shelf life of the PVAS with Catheter will be 6 months. As data are available to support a longer shelf life, the shelf life will be extended.

9.0 Standards Compliance

Compliance with FDA Recognized Consensus Standards for sterilization and sterile barrier packaging standards are noted in Section 8.0.

The catheter component of the PVAS will be contract manufactured (b) (4)
Products and are supplied to DermaPort Inc. (b) (4)
(b) (4)

a. ISO 10555-3:1996; Sterile, Single-use Intravascular Catheters – Part 3: Central Venous Catheters; Catheter lumen minimum flow rate,
b. ISO 10555-1:1995; Sterile, Single-use Intravascular Catheters – Part 1: General Requirements; Catheter function and Catheter and joint bond tensile strength,
c. ISO 594-1:1986, Conical fittings with a 6% (Luer) taper for syringes, needles and certain other medical equipment - Part 1: General requirements: Luer connections.

Table 9.0-1 documents catheter compliance with additional applicable FDA Recognized Consensus Standards. The removal of the polyester cuff does not affect catheter compliance to these standards.

Table 9.0-1: FDA Recognized Consensus Standard Compliance; Required Elements for a Declaration of Conformity to a Recognized Standard	
a. An identification of the applicable recognized consensus standards that were met.	ISO 10555-1 Sterile, Single-use Intravascular Catheters – Part 1: General Requirements ISO 10555-3 Sterile, Single-use Intravascular Catheters – Part 3: Central Venous Catheters ISO 594-1:1986, Conical fittings with a 6% (Luer) taper for syringes, needles and certain other medical equipment - Part 1: General requirements: Luer connections.
b. A statement, for each consensus standard, that all requirements were met, except for inapplicable requirements or deviations noted below.	All applicable requirements are met.
c. An identification, for each consensus standard, of 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).	None.
d. An identification, for each consensus standard, of any requirements that were not applicable to the device.	None.
e. A specification of any deviations from each applicable standard that were applied.	No deviations to the standards were applied.
f. 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.	None.
g. The name and address of the testing laboratory and/or certification body involved in determining the conformance of the device with applicable consensus standards and a reference to any accreditations for those organizations.	Testing was performed and documented by: (b) (4) [redacted]

The following letter from Medcomp is provided.

Third Party Testing Lab (b) (4)

Attachment A

Drawings

Diagrams (b) (4)

[redacted]

Diagrams (b) (4)

[redacted]

DermaPort

(b) (4) Hemo Flow Catheter Assembly (b) (4) REV: (b) (4) ECO#: (b) (4) Release Date (b) (4)

DP Part Number	Description	Mfg. P/N	Manufacturer	Supplier P/N	Suggested Supplier
(b) (4)					


Diagrams (b) (4)

Attachment B

DRAFT Directions for Use and Labeling

Labeling	Pages
Instructions for Use	Page B-2 through Page B-5
Package Labels	Page B-6 through Page B-16

(b) (4)

(b) (4)

(b)(4)

(b) (4)

(b) (4)

(b) (4)

(b) (4)

(b) (4)

(b) (4)

(b) (4)

(b) (4)

(b) (4)

(b) (4)

Attachment C

Predicate Labeling

Predicate	Pages
K932489 Medcomp Hemodialysis Catheter	Pages C-2 through C-5

medCOMP®

Hemo-Flow™
LONG-TERM HEMODIALYSIS CATHETER

INSTRUCTIONS FOR USE

INDICATIONS FOR USE:

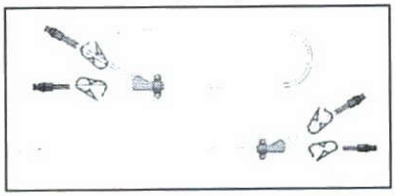
- The Hemo-Flow™ Dialysis Catheter is indicated for use in attaining Long-Term vascular access for Hemodialysis and Apheresis.
- It may be inserted percutaneously and is primarily placed in the internal jugular vein of an adult patient.
- Alternate insertion sites include subclavian vein as required.
- The curved Hemo-Flow™ Catheter is intended for internal jugular vein insertion.
- Catheters greater than 40cm are intended for femoral vein insertion.
- This catheter is indicated for a duration not to exceed (12) months.

CONTRAINDICATIONS:

- This catheter is intended for Long-Term vascular access only and should not be used for any purpose other than indicated in these instructions.

DESCRIPTION:

- The Hemo-Flow™ Dialysis Catheter is manufactured from soft radiopaque polyurethane material which provides increased patient comfort while providing excellent biocompatibility.



POTENTIAL COMPLICATIONS:

Air Embolus	Laceration of the Vessel
Bacteremia	Lumen Thrombosis
Brachial Plexus Injury	Mediastinal Injury
Cardiac Arrhythmia	Perforation of the Vessel
Cardiac Tamponade	Pleural Injury
Central Venous Thrombosis	Pneumothorax
Endocarditis	Retroperitoneal Bleed
Exit Site Infection	Right Atrial Puncture
Exsanguination	Septicemia
Femoral Artery Bleed	Subclavian Artery Puncture
Femoral Nerve Damage	Subcutaneous Hematoma
Hematoma	Superior Vena Cava Puncture
Hemorrhage	Thoracic Duct Laceration
Hemothorax	Tunnel Infection
Inferior Vena Cava Puncture	Vascular Thrombosis
	Venous Stenosis

- Before attempting the insertion, ensure that you are familiar with the above complications and their emergency treatment should any of them occur.

WARNINGS:

- In the rare event that a hub or connector separates from any component during insertion or use, take all necessary steps and precautions to prevent blood loss or air embolism and remove catheter.
- Do not advance the guidewire or catheter if unusual resistance is encountered.
- Do not insert or withdraw the guidewire forcibly from any component. The wire may break or unravel. If the guidewire becomes damaged, the introducer needle or Vascu-Sheath® introducer and guidewire must be removed together.
- Federal Law (USA) restricts the device to sale by or on the order of a physician.
- This catheter is for Single Use Only.

- Do not re-sterilize the catheter or accessories by any method.
- The manufacturer shall not be liable for any damages caused by reuse or re-sterilization of this catheter or accessories.
- Contents sterile and non-pyrogenic in unopened, undamaged package. STERILIZED BY ETHYLENE OXIDE

- Do not use catheter or accessories if package is opened or damaged.
- Do not use catheter or accessories if any sign of product damage is visible.

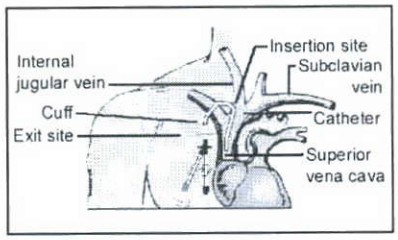
CATHETER PRECAUTIONS:

- There is a potential for product failure related to the use of ointments on catheters. Do not use ointments of any kind on this catheter.
- Do not use sharp instruments near the extension tubing or catheter lumen.
- Do not use scissors to remove dressing.
- Catheter will be damaged if clamps other than what is provided with this kit are used.
- Clamping of the tubing repeatedly in the same location may weaken tubing. Avoid clamping near the luers and hub of the catheter.
- Examine catheter lumen and extensions before and after each treatment for damage.
- To prevent accidents, assure the security of all caps and bloodline connections prior to and between treatments.
- Use only Luer Lock (threaded) Connectors with this catheter.
- Repeated over tightening of bloodlines, syringes, and caps will reduce connector life and could lead to potential connector failure.

INSERTION SITES:

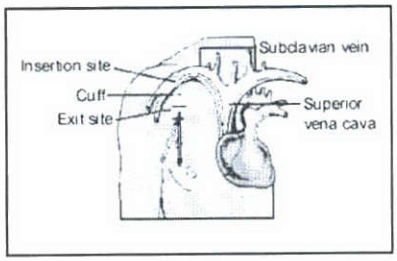
- The patient should be in a modified Trendelenburg position, with the upper chest exposed and the head turned slightly to the side opposite the insertion area. A small rolled towel may be inserted between the shoulder blades to facilitate the extension of the chest area.

Internal Jugular Vein



- Have patient lift his/her head from the bed to define the sternomastoid muscle. Catheterization will be performed at the apex of a triangle formed between the two heads of the sternomastoid muscle. The apex should be approximately three finger breadths above the clavicle. The carotid artery should be palpated medial to the point of catheter insertion.

Subclavian Vein

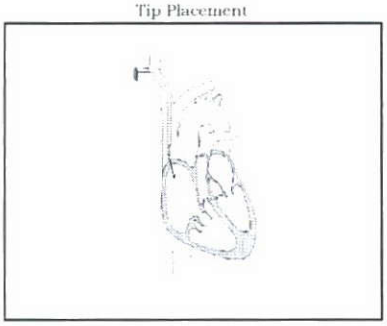


- Note the position of the subclavian vein, which is posterior to the clavicle, superior to the first rib, and anterior to the subclavian artery. (At a point just lateral to the angle made by the clavicle and the first rib.)

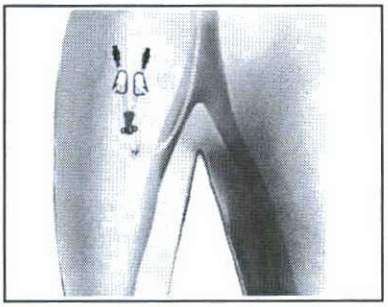
WARNING:

- Patients requiring ventilator support are at increased risk of pneumothorax during subclavian vein cannulation, which may cause complications.
- Extended use of the subclavian vein may be associated with subclavian vein stenosis.

Tip Placement



Femoral Vein



- The patient should lie completely on his/her back. Both femoral arteries should be palpated for site selection and consequence assessment. The knee on the same side of the insertion site should be flexed and the thigh abducted. Place the foot across the opposite leg. The femoral vein is then posterior/medial to the artery.

Caution: The incidence of infection may be increased with femoral vein insertion.

- Confirm final position of catheter with chest x-ray. Routine x-ray should always follow the initial insertion of this catheter to confirm proper tip placement prior to use.

- Femoral catheter tip placement is recommended at the junction of the iliac vein and the inferior vena cava.[1]

DIRECTIONS FOR SELDINGER INSERTION

- Read instructions carefully before using this device. The catheter should be inserted, manipulated, and removed by a qualified, licensed physician or other qualified health care professional under the direction of a physician.

- The medical techniques and procedures described in these instructions for use do not represent all medically acceptable protocols, nor are they intended as a substitute for the physician's experience and judgement in treating any specific patient.

- Use standard hospital protocols when applicable.

1. Strict aseptic technique must be used during insertion, maintenance, and catheter removal procedures. Provide a sterile operative field. The Operating Room is the preferred location for catheter placement. Use sterile drapes, instruments, and accessories. Shave the skin above and below the insertion site. Perform surgical scrub. Wear gown, cap, gloves, and mask. Have patient wear mask.

2. The selection of the appropriate catheter length is at the sole discretion of the physician. To achieve proper tip placement, proper catheter length selection is important. Routine x-ray should always follow the initial insertion of this catheter to confirm proper placement prior to use.

3. Administer sufficient local anesthetic to completely anesthetize the insertion site.

4. Make a small incision at the exit site on the chest wall approximately 8-10cm below the clavicle. Make a second incision above and parallel to the first, at the insertion site. Make the incision at the exit site wide enough to accommodate the cuff, approximately 1cm.

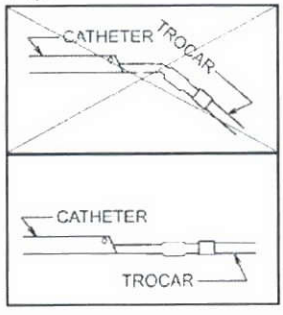
5. Use blunt dissection to create the subcutaneous tunnel opening. Attach the catheter to the trocar (a slight twisting motion may be helpful). Slide catheter tunneling sleeve over the catheter making certain that the sleeve covers the arterial holes of the catheter. Insert the trocar into the exit site and create a short subcutaneous tunnel. Do not tunnel through muscle. The tunnel should be made with care in order to prevent damage to surrounding vessels.

5a. For Femoral Vein Insertion: Create subcutaneous tunnel with the catheter exit site in the pelvic region.

Warning: Do not over-expand subcutaneous tissue during tunneling. Over-expansion may delay/prevent cuff in-growth.

6. Lead catheter into the tunnel gently. Do not pull or tug the catheter tubing. If resistance is encountered, further blunt dissection may facilitate insertion. Remove the catheter from the trocar with a slight twisting motion to avoid damage to the catheter.

Caution: Do not pull tunneler out at an angle. Keep tunneler straight to prevent damage to catheter tip.



Note: A tunnel with a wide gentle arc lessens the risk of kinking. The tunnel should be short enough to keep the Y-hub of the catheter from entering the exit site, yet long enough to keep the cuff 2cm (minimum) from the skin opening.

7. Irrigate catheter with saline, then clamp catheter extensions to assure that saline is not inadvertenly drained from lumens. Use clamps provided.

8. Insert the introducer needle with attached syringe, or *One-Step™ bulb needle*, into the target vein. Aspirate to insure proper placement. *When using the One-Step™, fill the bulb with saline. Once bulb is fully primed with no air present, squeeze bulb with thumb and forefinger. Continue to squeeze bulb until needle is under patient's skin. Once target vein is located, blood will flash back into flexible chamber.*

9. Remove the syringe, (*see 9a for One-Step™ Directions*), and place thumb over the end of the needle to prevent blood loss or air embolism. Draw flexible end of guidewire back into advancer so that only the end of the guidewire is visible. Insert advancer's distal end into the needle hub. Advance guidewire with forward motion into and past the needle hub into the target vein.

9a. One-Step™ Directions: Once blood has been aspirated into the flexible bulb, draw flexible end of guidewire back into advancer so that only the end of the guidewire is visible. Insert advancer's distal end into the One-Step™ bulb needle. Advance guidewire with a forward motion into and past the needle hub into the target vein.

Caution: The length of the wire inserted is determined by the size of the patient. Monitor patient for arrhythmia throughout this procedure. The patient should be placed on a cardiac monitor during this procedure. Cardiac arrhythmias may result if guidewire is allowed to pass into the right atrium. The guidewire should be held securely during this procedure.

10. Remove needle, leaving guidewire in the target vein. Enlarge cutaneous puncture site with scalpel.

11. Thread Vascu-Sheath® introducer over the proximal end of the guidewire. Once the Vascu-Sheath® introducer is in the target vein, remove the guidewire leaving the sheath and dilator in position.

Caution: DO NOT bend sheath/dilator during insertion as bending will cause the sheath to prematurely tear. Hold sheath/dilator close to the tip (approximately 3cm from tip) when initially inserting through the skin surface. To progress the sheath/dilator towards the vein, regrasp the sheath/dilator a few centimeters (approximately 5cm) above the original grasp location and push down on the sheath/dilator. Repeat procedure until sheath/dilator is fully inserted.

Note: For alternate sheath method, see Micro Puncture Insertion Method Section.

Caution: Never leave sheath in place as an indwelling catheter. Damage to the vein will occur.

12. Install injection cap over dilator opening to prevent blood loss or air embolism.

Caution: Do not clamp the dual lumen portion of the catheter. Clamp only the extensions. Do not use serrated forceps, use only the in-line clamps provided.

13. Remove dilator and injection cap from sheath.

14. Insert distal tip of catheter into and through the sheath until catheter tip is correctly positioned in the target vein.

15. Remove the tear-away sheath by slowly pulling it out of the vessel while simultaneously splitting the sheath by grasping the tabs and pulling them apart (a slight twisting motion may be helpful).

Caution: Do not pull apart the portion of the sheath that remains in the vessel. To avoid vessel damage, pull back the sheath as far as possible and tear the sheath only a few centimeters at a time.

16. Make any adjustments to catheter under fluoroscopy. The venous distal tip should be positioned at the level of the caval atrial junction or beyond into the right atrium to ensure optimal blood flow.

Note: Femoral catheter tip placement is recommended at the junction of the iliac vein and the inferior vena cava.[1]

17. Attach syringes to both extensions and open clamps. Blood should aspirate easily from both arterial and venous sides. If either side exhibits excessive resistance to blood aspiration, the catheter may need to be rotated or repositioned to obtain adequate blood flows.

18. Once adequate aspiration has been achieved, both lumens should be irrigated with saline filled syringes using quick bolus technique. Assure that extension clamps are open during irrigation procedure.

19. Close the extension clamps, remove the syringes, and place an injection cap on each luer lock connector. Avoid air embolism by keeping extension tubing clamped at all times when not in use and by aspirating then irrigating the catheter with saline prior to each use. With each change in tubing connections, purge air from the catheter and all connecting tubing and caps.

20. To maintain patency, a heparin lock must be created in both lumens. Refer to hospital heparinization guidelines.

Caution: Assure that all air has been aspirated from the catheter and extensions. Failure to do so may result in air embolism.

21. Once the catheter is locked with heparin, close the clamps and install injection caps onto the extensions' female luers.

22. Confirm proper tip placement with fluoroscopy. The distal venous tip should be positioned at the level of the caval atrial junction or into the right atrium to ensure optimal blood flow (as recommended in current NKF DOQI Guidelines).

Note: Femoral catheter tip placement is recommended at the junction of the iliac vein and the inferior vena cava.[1]

Caution: Failure to verify catheter placement may result in serious trauma or fatal complications.

CATHETER SECUREMENT AND WOUND DRESSING:

23. Suture insertion site closed. Suture the catheter to the skin using the suture wing. Do not suture the catheter tubing.

Caution: Care must be taken when using sharp objects or needles in close proximity to catheter lumen. Contact from sharp objects may cause catheter failure.

24. Cover the insertion and exit site with an occlusive dressing.

25. Catheter must be secured/sutured for entire duration of implantation.

26. Record catheter length and catheter lot number on patient's chart.

HEMODIALYSIS TREATMENT

- The heparin solution must be removed from each lumen prior to treatment to prevent systemic heparinization of patient. Aspiration should be based on dialysis unit protocol.
- Before dialysis begins all connections to catheter and extracorporeal circuits should be examined carefully.
- Frequent visual inspection should be conducted to detect leaks to prevent blood loss or air embolism.
- If a leak is found, the catheter should be clamped immediately.

Caution: Only clamp catheter with in-line clamps provided.

- Necessary remedial action must be taken prior to the continuation of the dialysis treatment.

Note: Excessive blood loss may lead to patient shock.

- Hemodialysis should be performed under physician's instructions.

HEPARINIZATION

- If the catheter is not to be used immediately for treatment, follow the suggested catheter patency guidelines.
- To maintain patency between treatments, a heparin lock must be created in each lumen of the catheter.
- Follow hospital protocol for heparin concentration.

1. Draw heparin into two syringes, corresponding to the amount designated on the arterial and venous extensions. Assure that the syringes are free of air.
2. Remove injection caps from the extensions.
3. Attach a syringe containing heparin solution to the female luer of each extension.
4. Open extension clamps.
5. Aspirate to insure that no air will be forced into the patient.
6. Inject heparin into each lumen using quick bolus technique.

Note: Each lumen should be completely filled with heparin to ensure effectiveness.

7. Close extension clamps.

Caution: Extension clamps should only be open for aspiration, flushing, and dialysis treatment.

8. Remove syringes.
9. Attach a sterile injection cap onto the female luers of the extensions.

- In most instances, no further heparin is necessary for 48-72 hours, provided the lumens have not been aspirated or flushed.

SITE CARE

Warning: DO NOT use ointments of any kind with this catheter.

- Clean skin around catheter. Chlorhexidine gluconate solutions are recommended; however, iodine-based solutions can also be used.
- Cover the exit site with occlusive dressing and leave extensions, clamps, and caps exposed for access by staff.
- Wound dressings must be kept clean and dry.

Caution: Patients must not swim, shower, or soak dressing while bathing.

- If profuse perspiration or accidental wetting compromises adhesion of dressing, the medical or nursing staff

must change the dressing under sterile conditions.

CATHETER PERFORMANCE

Caution: Always review hospital or unit protocol, potential complications and their treatment, warnings, and precautions prior to undertaking any type of mechanical or chemical intervention in response to catheter performance problems.

Warning: Only a physician familiar with the appropriate techniques should attempt the following procedures.

INSUFFICIENT FLOWS:

The following may cause insufficient blood flows:

- Occluded arterial holes due to clotting or fibrin sheath.
- Occlusion of the arterial side holes due to contact with vein wall.

Solutions include:

- Chemical intervention utilizing a thrombolytic agent.

MANAGEMENT OF ONE-WAY OBSTRUCTIONS:

One-way obstructions exist when a lumen can be flushed easily but blood cannot be aspirated. This is usually caused by tip malposition.

One of the following adjustments may resolve the obstruction:

- Reposition catheter.
- Reposition patient.
- Have patient cough.
- Provided there is no resistance, flush the catheter vigorously with sterile normal saline to try to move the tip away from the vessel wall.

INFECTION:

Caution: Due to the risk of exposure to HIV (Human Immunodeficiency Virus) or other blood borne pathogens, health care professionals should always use Universal Blood and Body Fluid Precautions in the care of all patients.

- Sterile technique should always be strictly adhered to.
- Clinically recognized infection at a catheter exit site should be treated promptly with the appropriate antibiotic therapy.
- If a fever occurs in a patient with a catheter in place, take a minimum of two blood cultures from a site distant from catheter exit site. If blood culture is positive, the catheter must be removed immediately and the appropriate antibiotic therapy initiated. Wait 48 hours before catheter replacement. Insertion should be made on opposite side of original catheter exit site, if possible.

MICRO PUNCTURE INSERTION METHOD

- Once an .018" guidewire has been introduced into the target vein, the 4F sheath dilator should be threaded over the proximal end of the wire and inserted into the target vein.
- When the 4F sheath dilator is located in the target vein, remove the guidewire and dilator one at a time.
- Insert an .038" guidewire into and through the sheath until it is located in the target vein.
- Remove the sheath and continue following directions starting at #11.

CATHETER REMOVAL

Warning: Only a physician familiar with the appropriate techniques should attempt the following procedures.

Caution: Always review hospital or unit protocol, potential complications and their treatment, warnings, and precautions prior to catheter removal.

1. Palpate the catheter exit tunnel to locate the cuff.
2. Administer sufficient local anesthetic to exit site and cuff location to completely anesthetize the area.
3. Cut sutures from suture wing. Follow hospital protocol for removal of skin sutures.
4. Make a 2cm incision over the cuff, parallel to the catheter.
5. Dissect down to the cuff using blunt and sharp dissection as indicated.
6. When visible, grasp cuff with clamp.
7. Clamp catheter between the cuff and the insertion site.
8. Cut catheter between cuff and exit site. Withdraw internal portion of catheter through the incision in the tunnel.
9. Remove remaining section of catheter (i.e. portion in tunnel) through the exit site.

Caution: Do not pull distal end of catheter through incision as contamination of wound may occur.

10. Apply pressure to proximal tunnel for approximately 10-15 minutes or until bleeding stops.
11. Suture incision and apply dressing in a manner to promote optimal healing.
12. Check catheter integrity for tears and measure catheter when removed. It must be equal to the length of catheter when it was inserted.

14.5F x 28cm PRESSURE

	200 ml/MIN	300 ml/MIN	400 ml/MIN
VENOUS	65 mmHg	90 mmHg	130 mmHg
ARTERIAL	-35 mmHg	-55 mmHg	-85 mmHg

FLOW RATE TESTING REPRESENTS OPTIMUM LABORATORY CONDITIONS.

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Because of continuing product improvement, prices, specifications, and model availability are subject to change without notice. Medcomp® reserves the right to modify its products or contents without notice.

References:

1. Zaleski GX, Funaki B, Lorenz JM, Garofalo RS, Moscatel MA, Rosenblum JD, Leef JA. Experience with tunneled femoral hemodialysis catheters. *Am J Roentgenol.* 1999 Feb; 172(2):493-6.

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Borngasse 20
35619 Braunfels
Germany

PN 4937 Rev. 7/03F

Attachment D

Test Reports

Report	Report Summary	Pages
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Engineering Report

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Preclinical Study Final Report

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Engineering Report

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Preclinical Study Pathology Report

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Engineering Report

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1.0 INTRODUCTION

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Engineering Report

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SPONSOR

DermaPort
25102 Rye Canyon Loop, Suite 110
Santa Clarita, CA 91355

TESTING SITE

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SUMMARY

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MATERIALS & METHODS:

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RESULTS

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DISCUSSION

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CONCLUSION

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TABLE I: RESULTS

TEST ARTICLES

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CONTROLS

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REFERENCES

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APPENDIX 1

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Third Party Testing Materials, Methods and Results (b) (4)

APPENDIX 2

Third Party Testing Materials, Methods and Results (b) (4)

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Third Party Testing Materials, Methods and Results (b) (4)

Third Party Testing Materials, Methods and Results (b) (4)

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Third Party Testing Materials, Methods and Results (b) (4)

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Engineering Report

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1.0 Purpose

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2.0 Background

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5.0 Test Procedure:

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6.0 Acceptance Criteria

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7.0 Results and Conclusions:

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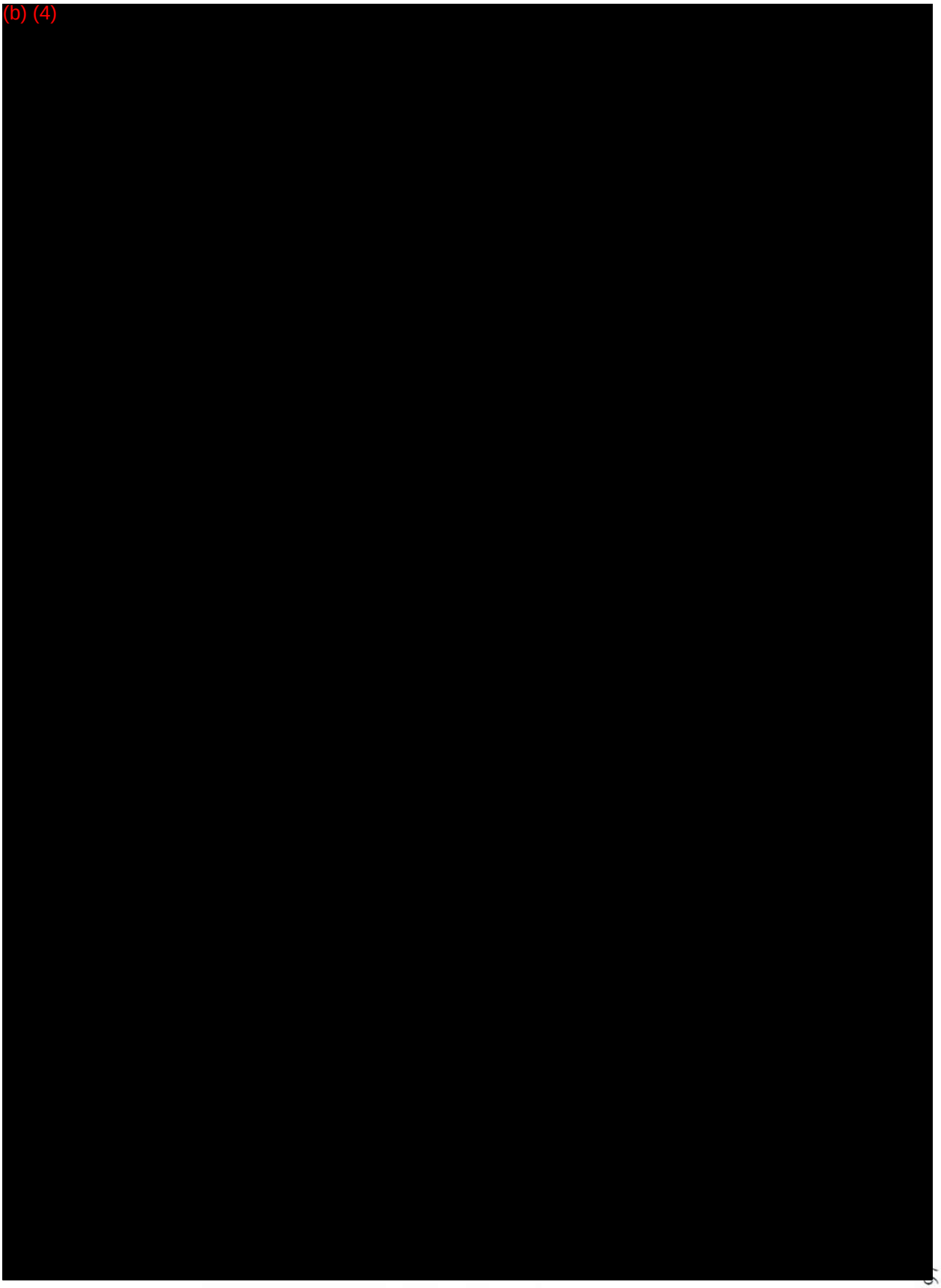

ATTACHMENT 1: Flow Test Fixture

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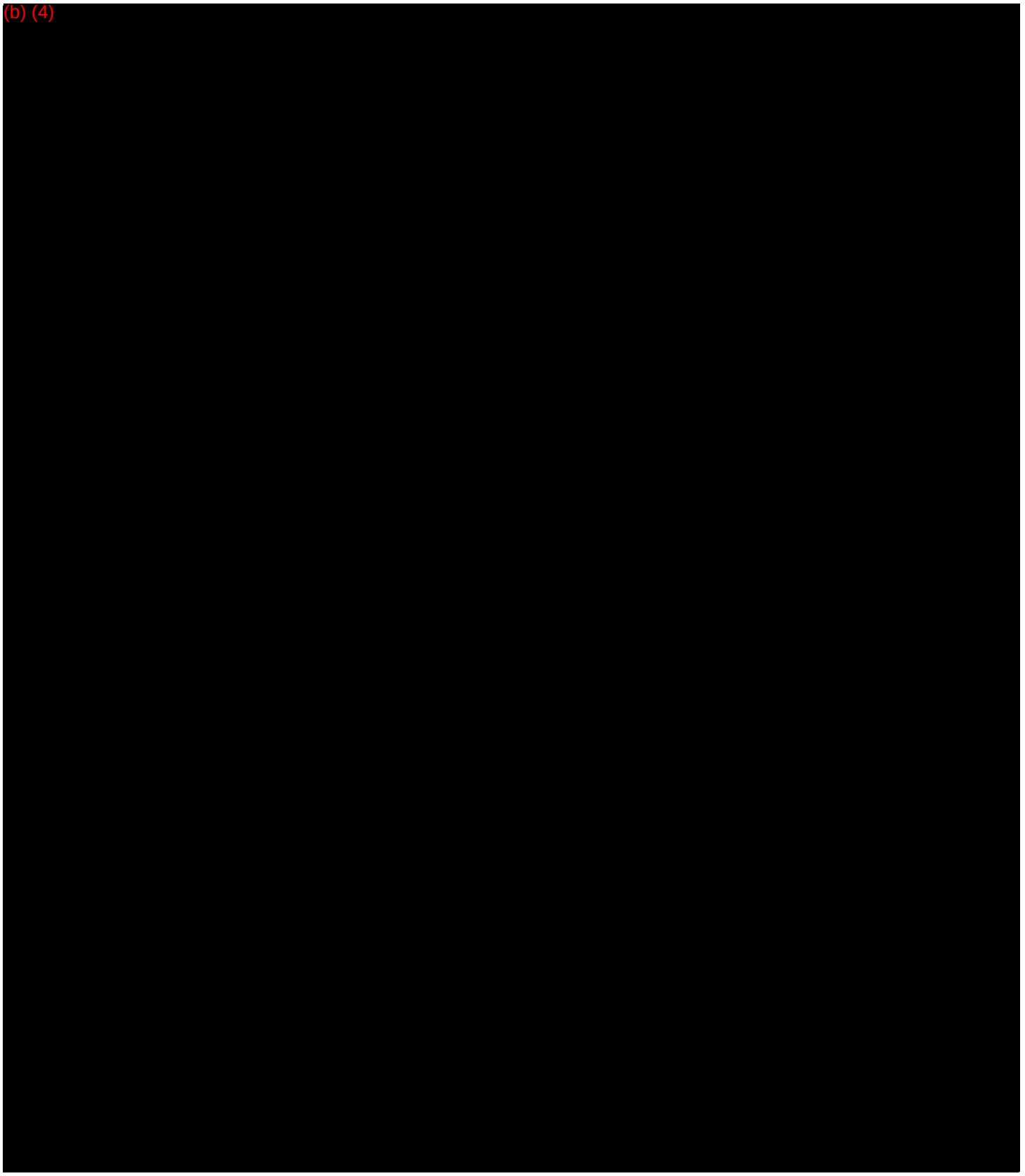

ATTACHMENT 2: Viscometer

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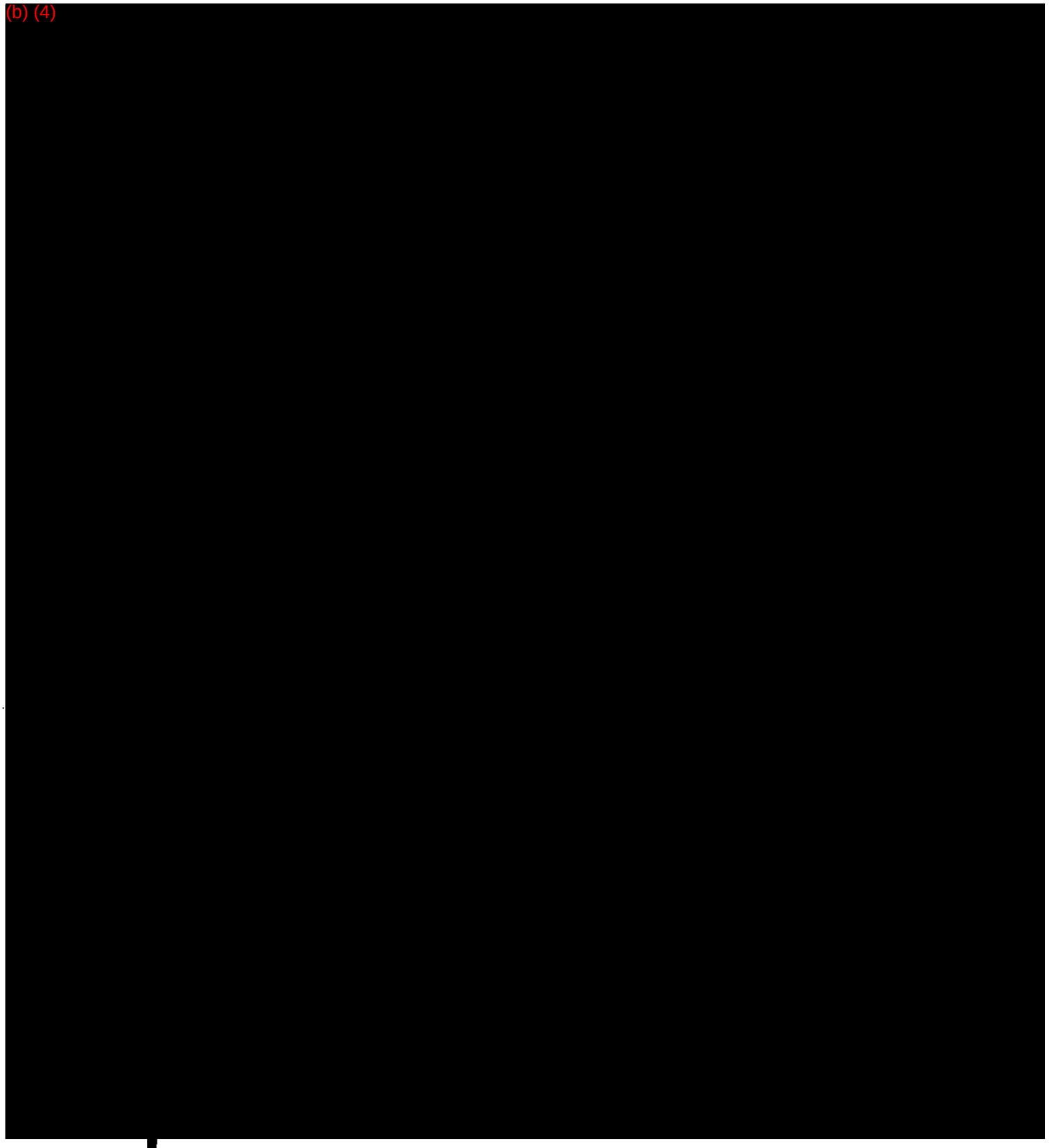

ATTACHMENT 2 (continued): Viscometer

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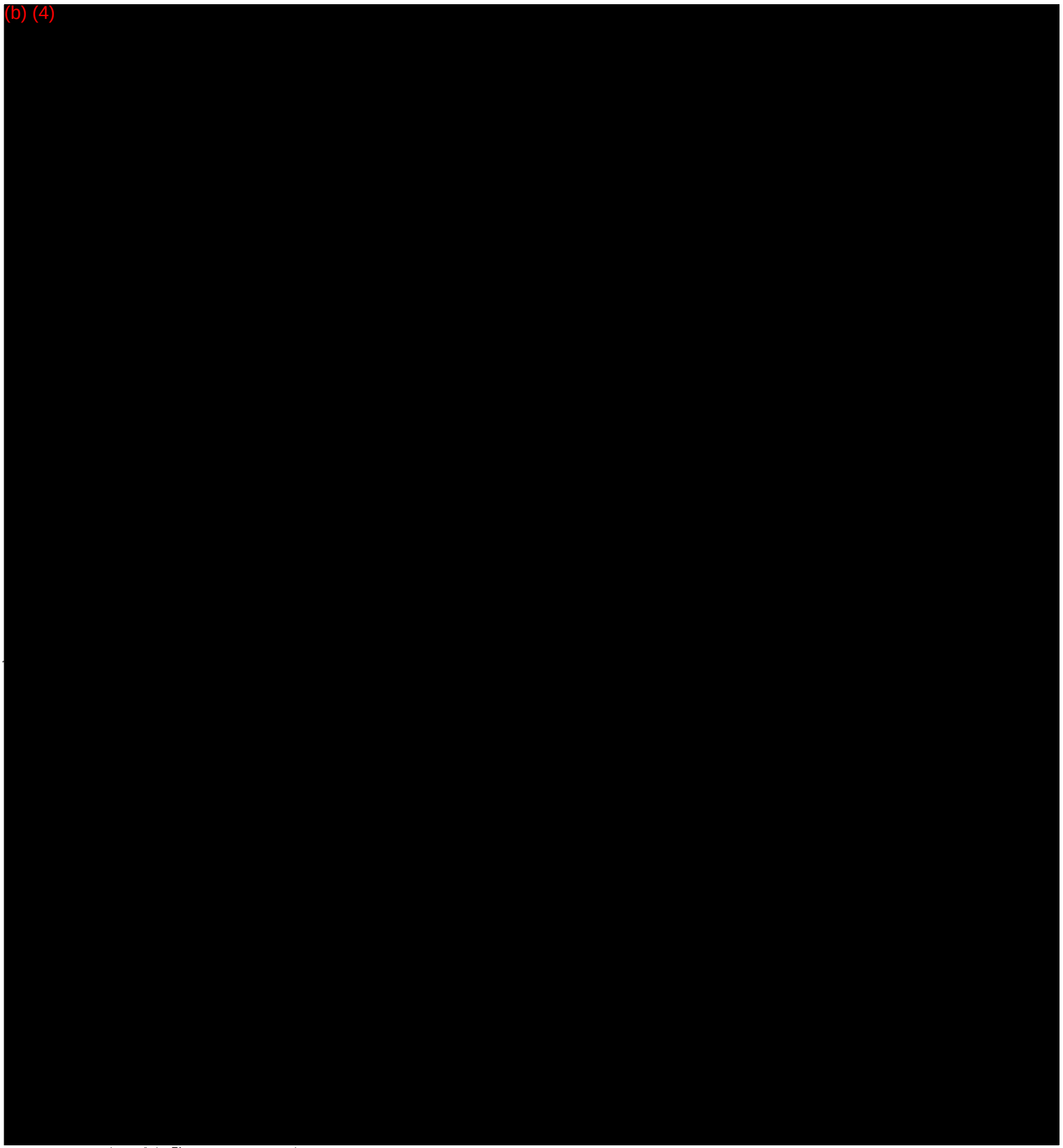

ATTACHMENT 3 (continued): Blood Simulant Preparation & Viscosity Calculations

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ATTACHMENT 3: Viscometer Calibration

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ATTACHMENT 3: Recalculation

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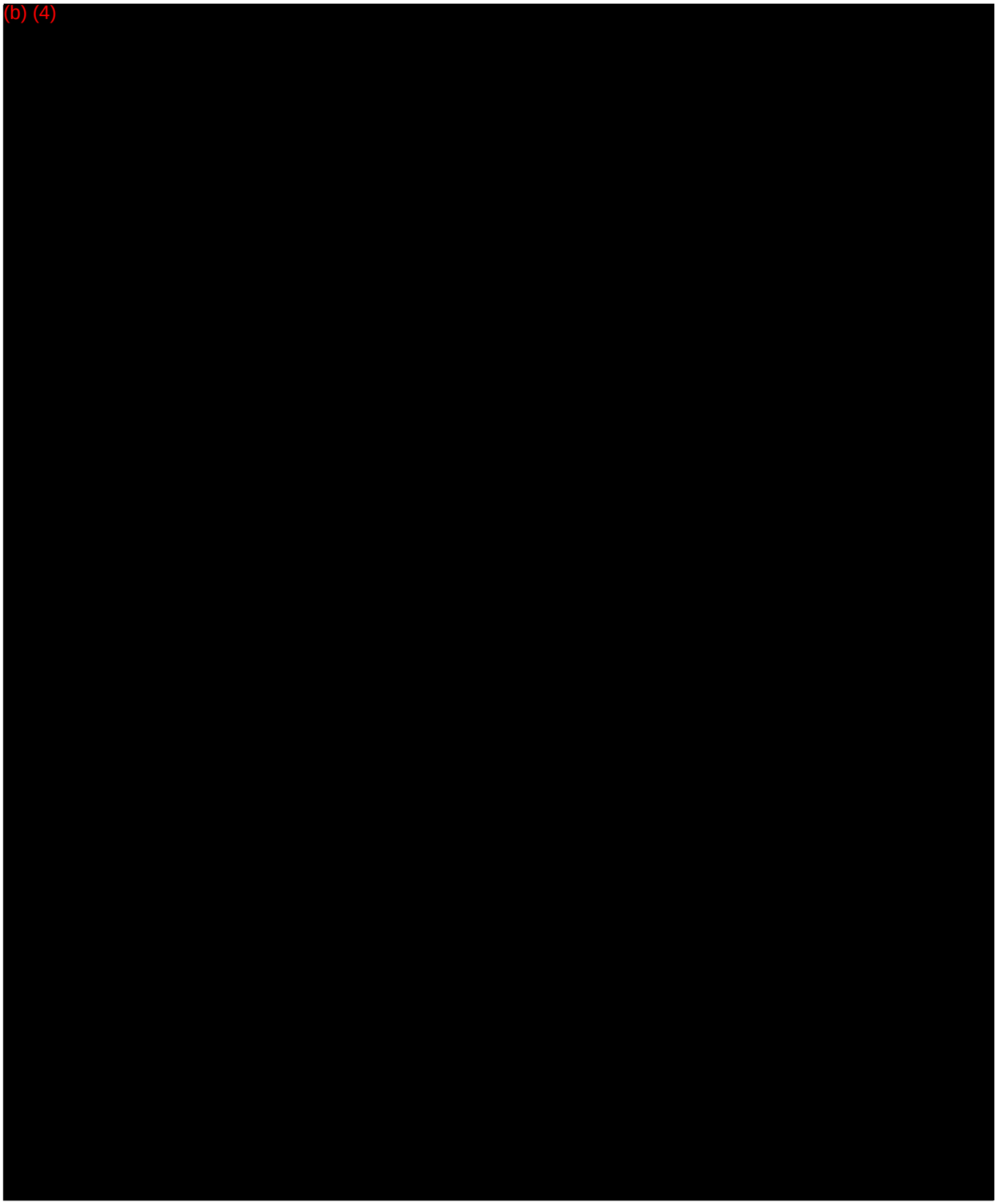

ATTACHMENT 4: Flow Tester Calibration Chart

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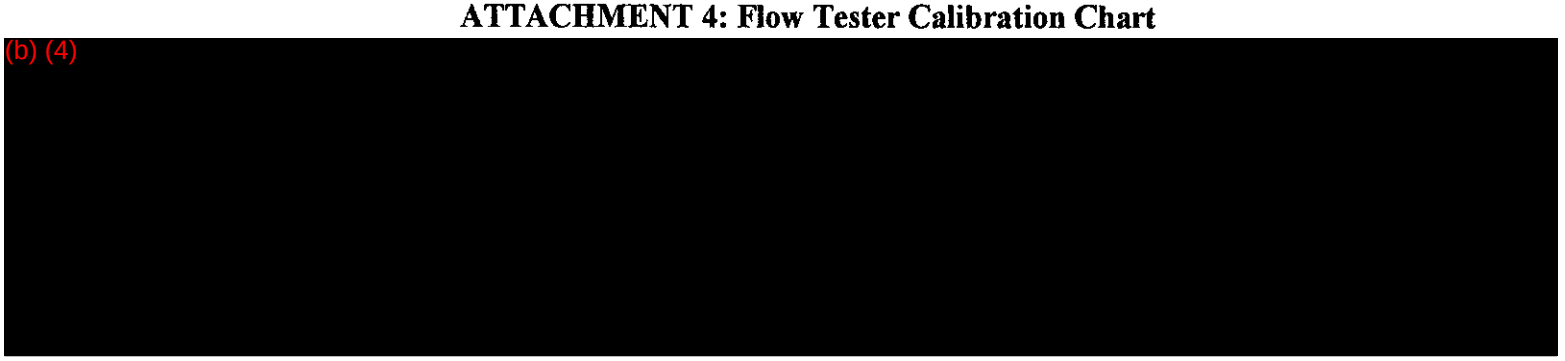

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Engineering Protocol

PVAS Shelf Life Testing

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ATTACHMENT 1: Table of Tests and Quantity per Test

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ENGINEERING REPORT

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Attachment E

Risk Analysis

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Attachment F

(b) (4) Material Device Master File References

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Third Party Materials Supplier (b) (4)

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Third Party Materials Supplier (b) (4)

Attachment G

Class III Summary and Certification

Class III Summary for the DermaPort Percutaneous Vascular Access System (PVAS)

The types and causes of safety and effectiveness concerns with the DermaPort Percutaneous Vascular Access System (PVAS) device are described in the 510(k) submission Risk Analysis, reference 510(k) submission Section 5.0. A summary of available literature and publications with regard to safety and effectiveness with these types of devices follows.

The current literature, including published case reports, clinical trials, meta-analyses, reviews, and clinical practice guidelines for central venous catheters and vascular access was reviewed to identify problems with efficacy, safety concerns and complications. Instructions for Use (IFUs) for currently marketed tunneled central venous catheters were also referenced. In addition, PubMed and MAUDE databases were reviewed. Findings with references are listed in the table below.

PROBLEM WITH EFFICACY, SAFETY CONCERN, OR COMPLICATION	REFERENCES
Air embolism	1, 2, 23, 27, 32, 47-49, 54, 62
Allergic reaction	2, 27, 29
Arterial puncture	1, 54
Arteriovenous fistula	27
Bacteremia	1, 4, 9, 10-12, 14, 15, 17, 19-22, 24, 25, 54, 56-60
Bilateral ophthalmoplegia	38
Bleeding (hemorrhage)	2, 27, 54, 64
Bleeding of esophageal varices	40, 67
Bloodstream infection	28, 41, 42, 60
Brachial plexus injury	1, 2, 23
Cardiac arrhythmia	1, 2, 23, 27, 50
Cardiac perforation	23, 27, 50
Cardiac tamponade	1, 2, 23
Catheter colonization	41
Catheter embolism	2, 23
Catheter exchange	55-57, 60
Catheter fragmentation	27, 60, 62
Catheter kinking	14, 26, 27, 31, 60
Catheter misplacement	23, 26, 31, 60
Catheter occlusion, damage or breakage due to compression between the clavicle and first rib	2

PROBLEM WITH EFFICACY, SAFETY CONCERN, OR COMPLICATION	REFERENCES
Catheter or cuff erosion through skin	2
Catheter or cuff occlusion	2, 23, 26, 27, 60
Catheter port/hub connection failure	27
Catheter related infection	2, 4, 10, 11, 15, 16, 19, 20-24, 26, 27, 29, 30, 31, 43, 44, 46, 53, 57-61
Catheter related sepsis	2, 4, 10, 11, 15, 16, 19, 20-24, 26, 27, 29, 30, 54, 58, 62, 64
Catheter removal	4, 10, 11, 15, 16, 19, 20-24, 26, 27, 29-31, 43, 44, 55, 56
Catheter thrombosis	1, 4, 6, 7, 8, 11-17, 19, 22, 31, 44, 46, 47, 53, 55, 57, 58, 60
Catheter tip migration	27, 31, 46, 50, 60
Cellulitis	59
Central venous thrombosis	1, 11, 13, 19, 23, 31
Chylothorax	23
Contrast reaction	27
Coronary sinus thrombosis	23
Cuff retention	52
Dementia	59
Endocarditis	1, 2, 36
Erosion of port/catheter through skin	27
Exit site infection	1, 2, 10, 12, 14, 15, 17, 20, 21, 24, 29, 30, 41, 54, 58, 60, 64
Exit site necrosis	2
Exophthalmos	38
Extravasation	2, 46
Extremity swelling	27
Exsanguination	1, 3
Fibrin sheath formation	2, 11, 27, 31, 53, 55, 57, 60, 61
Hematoma	1, 2, 23, 27, 47, 54, 58
Hemodynamic instability	65
Hemolysis	45
Hemomediastinum	54
Hemopericardium	33
Hemothorax	1, 2, 23, 27, 32, 47, 54

PROBLEM WITH EFFICACY, SAFETY CONCERN, OR COMPLICATION	REFERENCES
Hepatic vein thrombosis	23
Hydrothorax	2
Inability to access vascular access device	27
Inadvertent catheter removal	27
Infusate infiltration around access device	27
Infusate-related bloodstream infection	29
Intimal injury	27
Intolerance reaction to implanted device	2
Insufficient tissue ingrowth into cuff	3
Laceration of the vessel, or viscus	1, 2, 23, 27, 46, 47
Luminal thrombosis	1, 11, 12, 14, 16
Lymphatic disruption	66
Lymphatic fistula	23
Medastinal injury	1, 23
Meningitis	63
Myocardial erosion	2
Perforation of the vessel or viscus (subclavian vein puncture)	1, 2, 27, 32, 47
Pericatheter bleeding	48
Peripheral neuropathy	59
Persistent hiccups	61
Persistent pain at catheter site	27
Phlebitis	29, 41, 46, 47
Phrenic nerve injury	23, 34
Pleural injury	1
Pneumonia	59
Pneumothorax	1, 2, 23, 32, 47, 54
Pocket infection	29, 41, 60
Procedure-induced sepsis	47
Pseudoaneurysm	23, 35
Pulmonary absess	37
Recirculation	51, 60
Recurrent laryngeal nerve injury	23, 54
Retroperitoneal bleed	1

PROBLEM WITH EFFICACY, SAFETY CONCERN, OR COMPLICATION	REFERENCES
Right atrial puncture	1
Right atrial thrombus	65
Risks normally associated with local and general anesthesia, surgery, and post-operative recovery	2, 27
Septicemia	1, 10, 15, 19-22, 23, 24, 29, 63
Septic thrombosis	23
Soft tissue swelling	27
Spontaneous catheter tip malposition or retraction	2
Stroke	59
Subcutaneous hematoma	1, 23
Suboptimal blood flow	4, 5, 13, 26, 50, 54, 60
Subcutaneous emphysema	23
Superior vena cava puncture	1
Superior vena cava syndrome	46
Suppurative thrombophlebitis	23
Tension pneumothorax	23
Thoracic duct laceration or injury	1, 2, 23
Thromboembolism	2, 46
Tunnel infection	1, 10, 31, 41, 54, 58, 60, 64
Unilateral breast enlargement	39
Vagus nerve injury	23
Vascular thrombosis	1, 2, 4, 6-8, 13, 16, 27, 54, 58
Vasovagal reaction	27
Venous stenosis	4, 7, 8, 13, 15, 16, 18, 27, 39, 53, 54, 64
Ventricular thrombosis	2
Vessel erosion	2, 27,
Wound dehiscence	27, 47

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DermaPort

Class III Certification

DermaPort Percutaneous Vascular Access System (PVAS) with Catheter

I certify, in my capacity as President of DermaPort, Inc., that I have conducted a reasonable search of all information known or otherwise available about the types and causes of safety or effectiveness problems that have been reported for blood access catheters supporting hemodialysis and apheresis support. I further certify that I am aware of the types of problems to which the DermaPort Percutaneous Vascular Access System (PVAS) with Catheter device is susceptible and that, to the best of my knowledge, the summary of the types and causes of safety or effectiveness problems about the DermaPort Percutaneous Vascular Access System (PVAS) type of devices is complete and accurate.

B. Moran

(Signature)

Buzz Moran, President

(Printed Name, Title)

30 APRIL 2007

(Dated)

Attachment H

FDA Indications for Use Form

Indications for Use

510(k) Number (if known): _____

Device Name: DermaPort Percutaneous Vascular Access System (PVAS)

Indications for Use:

The DermaPort Percutaneous Vascular Access System (PVAS™) is indicated for long-term (greater than 30 days) vascular access for hemodialysis and apheresis. The system is inserted percutaneously and the catheter is typically placed in the internal jugular vein of an adult patient. The subclavian vein is an alternate catheter insertion site.

Prescription Use __X__ (Part 21 CFR 801 Subpart D) AND/OR Over-The-Counter Use _____ (21 CFR 807 Subpart C)

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

Attachment I

510(k) Summary

DermaPort

510(k) Summary

Company Name: DermaPort, Inc.
25102 Rye Canyon Loop
Suite 110
Santa Clarita, CSA 91355

Contact: Buzz Moran, President
Phone: (661) 362-7900
Fax: (661) 362-7902
Email: bmoran@dermaport.com

Summary Date: April 30, 2007

Trade Name: DermaPort Percutaneous Vascular Access System (PVAS)

Common Name: Hemodialysis Catheter, Implanted

Classification Name: 21 CFR 876.5540 Blood Access Device and Accessories, Class III, Product Code: MSD

Predicate Device(s):

510(k) Number: K994105
Manufacture: MEDCOMP®
Trade Name: Medcomp Hemo-Flow Catheter

510(k) Number: K062901
Manufacture: Med-Conduit Inc.
Trade Name: HemoCath II

1.0 Description of Device

The DermaPort Percutaneous Vascular Access System (PVAS) is designed to facilitate catheter placement, reposition, and exchange procedures while maintaining the catheter attachment, bacterial barrier, and fixation functions of the predicate catheter fibrous cuff. The main component of the PVAS is a metal port which is implanted into the subcutaneous tunnel at the catheter exit site on the chest wall. The hemodialysis catheter passes through the metal port which acts as a percutaneous conduit, into the subcutaneous tunnel, and then into the central venous system in the usual fashion. The metal surface of the PVAS port has a porous, tissue integrating coating which allows ingrowth of tissue to anchor the PVAS port. The PVAS port holds the hemodialysis catheter in place.

The DermaPort Percutaneous Vascular Access System (PVAS) consists of the following types of components:

1. Implanted Hemodialysis 14.5 F Catheter (24 cm, 28 cm or 32 cm lengths)
2. Guidewire; 0.038 inch (70 cm or 100 cm lengths)
3. 16F Tearaway Set Griplock Hub
4. 12F Polyethylene Dilator
5. 14F Polyethylene Dilator
6. Clear Female Dust Cover
7. Injection Caps
8. 18 GA x 2.7" Cyrolite Introducer Needle
9. Tunneler with Tri ball tip
10. Tunneler Sleeve
11. DermaPort Blade
12. Commercially available alcohol pad
13. Commercially available adhesive wound dressing
14. Peel-away Sheath
15. DermaPort Percutaneous Vascular Access System (PVAS) Port

The catheter is identical to the HemoFlow catheter, with the exception that the fabric cuff on the HemoFlow catheter is omitted. The HemoFlow catheter is cleared to market by the FDA via 510(k) number K994105.

The Percutaneous Vascular Access System (PVAS^{TM}) has been developed to support central vascular access for hemodialysis and apheresis. The PVAS port consists of a percutaneous tubular conduit, through which a standard 14.5F polyurethane hemodialysis catheter enters the subcutaneous tunnel. An integral seal surrounds the catheter and prevents microbial migration along the catheter. The PVAS port is enclosed by a silicone anchor that braces the assembly to the skin, and an associated brake holds the catheter in place within the port. A tissue integrating biomaterial surrounds the port, providing anatomical fixation and prevention of microbial migration in a manner analogous to the fabric cuff of a tunneled catheter.

2.0 Intended Use of Device

The indication for use of the PVAS is consistent with the classification of 21 CFR 876.5540 Blood Access Device and Accessories, and the predicate Medcomp Hemo-Flow Catheter. The indication for use is:

> The DermaPort Percutaneous Vascular Access System (PVAS™) is indicated for long-term (greater than 30 days) vascular access for hemodialysis and apheresis. The system is inserted percutaneously and the catheter is typically placed in the internal jugular vein of an adult patient. The subclavian vein is an alternate catheter insertion site.

3.0 Technological Characteristics

The PVAS technical characteristics and construction are substantially equivalent to the predicate device. The difference in construction was qualified with bench and animal testing.

4.0 Conclusions

The DermaPort, Inc. PVAS is substantially equivalent to the predicate device. No new questions of safety or effectiveness are raised.

Food and Drug Administration
Office of Device Evaluation &
Office of In Vitro Diagnostics

COVER SHEET MEMORANDUM

From: Reviewer Name Jeffrey Cooper, DDS

Subject: 510(k) Number K071202/S1

To: The Record

Please list CTS decision code SK

☐ Refused to accept (Note: this is considered the first review cycle, See Screening Checklist http://eroom.fda.gov/eRoomReg/Files/CDRH3/CDRHPremarketNotification510kProgram/ Screening Checklist)

☐ Hold (Additional Information or Telephone Hold).

☑ Final Decision (SE, SE with Limitations, NSE, Withdrawn, etc.).

Please complete the following for a final clearance decision (i.e., SE, SE with Limitations, etc.):		YES	NO
Indications for Use Page	*Attach IFU*	✓	
510(k) Summary /510(k) Statement	*Attach Summary*	✓	
Truthful and Accurate Statement.	*Must be present for a Final Decision*	✓	
Is the device Class III?		✓	
If yes, does firm include Class III Summary?	*Must be present for a Final Decision*	✓	
Does firm reference standards? (If yes, please attach form from http://eroom.fda.gov/eRoomReg/Files/CDRH3/CDRHPremarketNotification510kProgram/0_4136/ABBREVIATED STANDARDS DATA FORM.DOC)			✓
Is this a combination product? (Please specify category _____, see http://eroom.fda.gov/eRoomReg/Files/CDRH3/CDRHPremarketNotification510kProgram/0_413b/COMBINATION%20PRODUCT%20ALGORITHM%20(REVISED%203-12-03).DOC			
Is this a reprocessed single use device? (Guidance for Industry and FDA Staff – MDUFMA - Validation Data in 510(k)s for Reprocessed Single-Use Medical Devices, http://www.fda.gov/cdrh/ode/guidance/1216.html)			✓
Is this device intended for pediatric use only?			✓
Is this a prescription device? (If both prescription & OTC, check both boxes.)		✓	
Is clinical data necessary to support the review of this 510(k)?			✓
Does this device include an Animal Tissue Source?			✓
Is this device subject to Section 522 Postmarket Surveillance? (Postmarket Surveillance Guidance, http://www.fda.gov/cdrh/osb/guidance/316.html)	*Contact OSB.*		✓
Is this device subject to the Tracking Regulation? (Medical Device Tracking Guidance, http://www.fda.gov/cdrh/comp/guidance/169.html)	*Contact OC.*		✓

Regulation Number	Class*	Product Code
872.5540	II	MSD

(*If unclassified, see 510(k) Staff)

Additional Product Codes: _____

Review: [signature] (Branch Chief) (Branch Code) 11/30/07 (Date)

Final Review: [signature] (Division Director) 11/30/07 (Date)

K071202

"SUBSTANTIAL EQUIVALENCE" (SE) DECISION-MAKING DOCUMENTATION

Reviewer: Jeffrey Cooper, D.V.M. **Division/Branch:** DRARD/GRDB, HFZ-470

Device Trade Name: Dermaport Percutaneous Vascular Access System (PVAS) for Long-Term Hemodialysis
510(k) Number: K071202
Common Name: Implanted Dialysis Catheter

Regulation/Classification: The device is in 21 CFR §876.5540, Hemodialysis Catheter, Implanted (Long Term), Class III, ProCode 78 MSD.

Product to Which Compared: Medcomp Hemo-Flow (K994105) and Med-Conduit, Inc. HemoCath II (K062901).

Company: Dermaport, Inc.

Contact: Buzz Moran, President
Dermaport, Inc.
25102 Rye Canyon Loop, Suite 110
Santa Clarita, CA 91365

Phone: (661) 362-7901

	YES	NO*	
1. IS PRODUCT A DEVICE?	√	—	IF NO STOP
2. 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 YES STOP → SE IF NO GO TO 10
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?	√	—	IF YES STOP → SE

* "yes" responses to 4, 6, 8, and 11, and every "no" response requires an explanation below

Explanations to the Preceding Checklist:

7. There are questions on biocompatibility, tensile strength, aging, flow rates, and biofilm or thrombus stripping.

11. Test results for these questions were adequate.

NARRATIVE DEVICE DESCRIPTION

1. INTENDED USE: The Dermaport Percutaneous Vascular Access System (PVAS™) is indicated for long-term (greater than 30days) vascular access for hemodialysis and apheresis. The system is inserted percutaneously and the catheter is typically placed in the internal jugular vein of an adult patient. The subclavian vein is an alternate catheter insertion site.

2. DEVICE DESCRIPTION: See review.

Labeling: See Review.

Regulatory Information:

In compliance with the SMDA of 1990, the sponsor has included a summary of safety and effectiveness information as required by 21 CFR §807.92. The firm has provided a Truthful and Accurate Statement as required by 21 CFR §807.87(j), a Class III summary, and the Indications for Use Statement.

As long as this product is manufactured under GMPs, it should be as safe and effective for its intended use as other similar legally marketed devices.

	YES	NO	
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 for OTC use?	_	✓	
Is the device for prescription use?	✓		
Does the device contain a drug or biological product as a component?	_	✓	
Is this device a kit?	✓		(kit certificate supplied)

Recommendation:

I recommend that the proposed device be found substantially equivalent to other legally marketed devices as described in 21 CFR §876.5540, Hemodialysis Catheter, Implanted (Long Term), Class III, ProCode 78 MSD.

Jeffrey Cooper, D.V.M.

11/30/07
Date

Concur:

Carolyn Y. Neuland, Ph. D.
Chief, Gastroenterology and Renal Devices Branch

MEMORANDUM

Food and Drug Administration
Center for Devices and Radiological Health
Office of Device Evaluation
DRARD/GRDB

Date: November 30, 2007

From: Jeffrey Cooper, M.S., D.V.M.
Gastroenterology and Renal Devices Branch, HFZ-470

Subject: **K071202-S1 – Dermaport, Inc. – Dermaport Percutaneous Vascular Access System (PVAS) for Long-Term Hemodialysis**

Contact: Buzz Moran, President
25102 Rye Canyon Loop, Suite 110
Santa Clarita, CA 91365

Phone: (661) 362-7901

To: The Record

Background:

Dermaport, Inc. submitted a 510(k) for a catheter with a new titanium and silicone cuff. The catheter was cleared by Medcomp as the Hemo-Flow. This is my second review after sending a telephone hold email on July 13, 2007.

Intended Use:

The Dermaport Percutaneous Vascular Access System (PVAS™) is indicated for long-term (greater than 30days) vascular access for hemodialysis and apheresis. The system is inserted percutaneously and the catheter is typically placed in the internal jugular vein of an adult patient. The subclavian vein is an alternate catheter insertion site.

This is the same indication as the predicate except for minor grammar changes.

Predicate Device:

Medcomp Hemo-Flow (K994105) and Med-Conduit, Inc. HemoCath II (K062901).

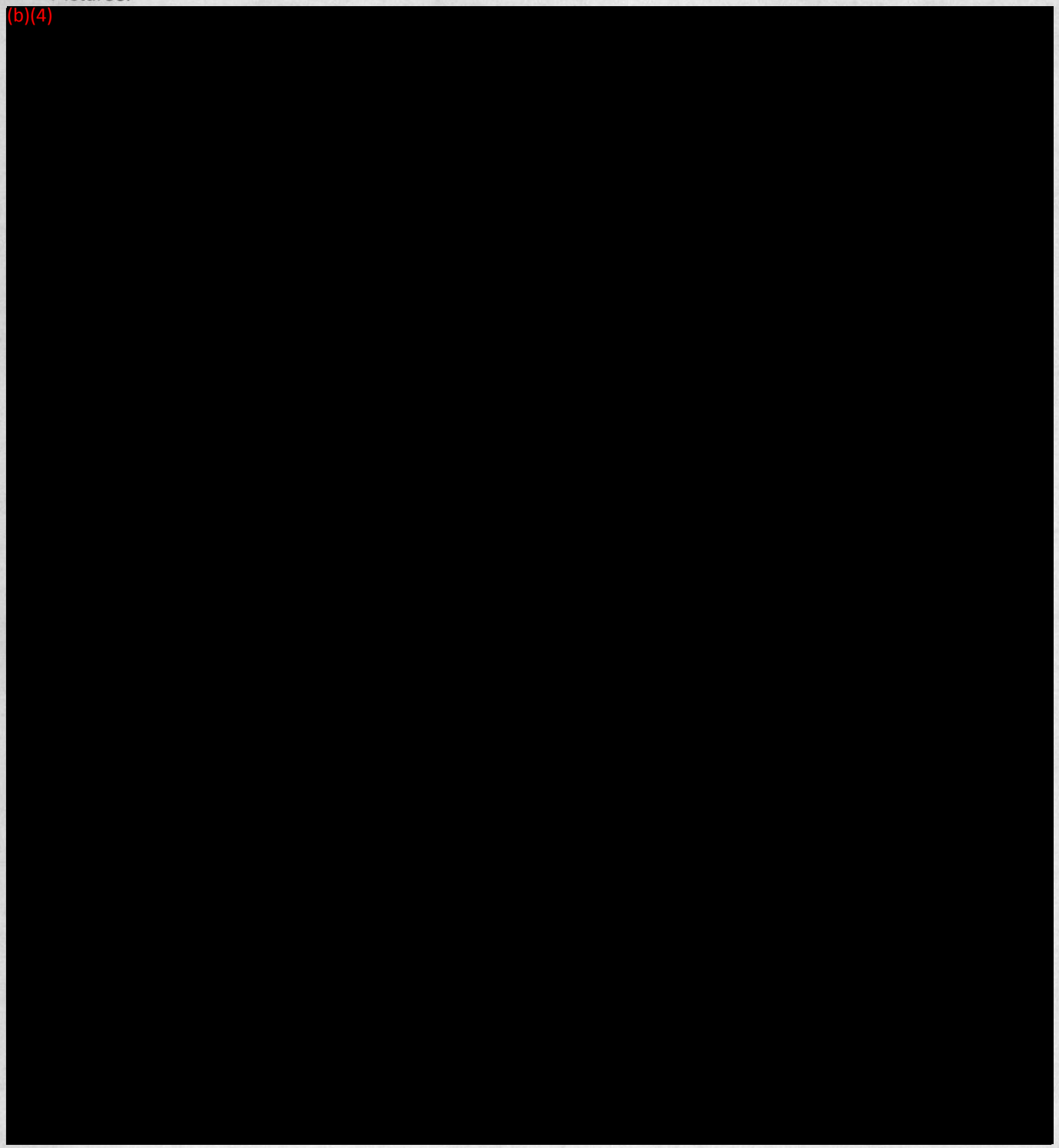
General Information Summary:

The Dermaport Percutaneous Vascular Access System is a 14.5 Fr HemoCath catheter with a different cuff. The new cuff is a roughened titanium surface that slides over the catheter. There is an internal 3 wiper seal to block bacterial migration along the external surface of the catheter. The catheter is anchored to the metal port with a removable silicone brake. The silcone brake collar grips the catheter by friction (2.5 lbs of force) and has two clips to hold the titanium port. The brake can be removed to allow optimum catheter tip positioning and optimum cuff placement.

A peel away sheath is just distal to the port to allow subcutaneous placement through a small incision to maintain a tight skin Juction and allow tissue ingrowth.

Pictures:

(b)(4)



(b)(4)

[redacted]

Biocompatibility is acceptable:

(b)(4)

[redacted]

Sterility is acceptable:

(b)(4)

[redacted]

Pyrogen Testing is acceptable:

(b)(4)

[redacted]

Labeling is adequate:

The labeling for the proposed device consists of instructions for use and package labels.

The device is labeled as sterile by EO, non-pyrogenic, for single use, for long-term use, with Dermaport's address and phone, kit contents, with a manufacturing date, an expiration date, and with a prescription statement. The instructions appear complete, and recommend the caval-atrial junction or right atrium for catheter tip placement. A caution states "Do not use ointments." The instructions have a pressure vs. flow summary and the priming volumes.

The instructions include clear pictures on how to use the new titanium cuff. A warning states, "Do not replace a catheter into a tunnel that is suspected to be infected.

MRI Testing is adequate:

(b)(4) [redacted]

Expiration Dating is acceptable:

(b)(4) [redacted]

Mechanical Hemolysis Testing:

(b)(4) [redacted]

Bench Testing is acceptable:

(b)(4)

Substantial Equivalence:

Intended Use:

The intended uses of the devices are equivalent

Device Design:

The device designs differ by the cuff design and the ability to rplace the catheter without removing the cuff.

Classification:

21 CFR §876.5540, Class III, Hemodialysis Catheter, Implanted, Product Code 78 MSD.

Deficiencies and responses from the Jul7 13, 2007, FDA email:

(b)(4)

(b)(4)

[redacted]

Recommendation:

I recommend that the proposed device be found substantially equivalent to other legally marketed devices as described in 21 CFR §876.5540, Hemodialysis Catheter, Implanted (Long Term), Class III, ProCode 78 MSD.

Jeffrey Cooper, M.S., D.V.M.

11/30/07
Date

Date: 09/24/2007	**Topic:** Discuss testing
Type: Email	**User:** Jeffrey Cooper
Summary:	

Date: 09/18/2007	**Topic:** Discuss testing
Type: Email	**User:** Jeffrey Cooper
Summary:	

Date: 07/19/2007	**Topic:** Clarify deficiencies
Type: Email	**User:** Jeffrey Cooper
Summary:	

Cooper, Jeffrey (CDRH)

From: Jennifer Hessel [jennifer.hessel@dermaport.com]
Sent: Friday, November 30, 2007 1:23 PM
To: Cooper, Jeffrey (CDRH); Buzz Moran
Subject: RE: K071202-S1

The predicate device used for the pressure vs. flow rate comparison was the MEDCOMP Hemo-Flow Catheter (510(k) Number K994105).

Jennifer Hessel

DermaPort
Manager Regulatory Affairs/Quality Assurance
25102 Rye Canyon Loop Suite 110
Santa Clarita, CA 91355
(661) 362-7904

From: Cooper, Jeffrey (CDRH) [mailto:jeffrey.cooper@fda.hhs.gov]
Sent: Friday, November 30, 2007 8:35 AM
To: Buzz Moran
Subject: RE: K071202-S1

I am finishing the review on your device and have a question. In your (b)(4) [redacted] you refer to the predicate device. Which catheter is the predicate device? You have two listed in the earlier submission.

Jeffrey Cooper, M.S., D.V.M.
Veterinary Medical Officer
Center for Devices & Radiological Health (CDRH)
Office of Device Evaluation (ODE)
Division of Reproductive, Abdominal and Radiological Devices (DRARD)
Gastroenterology and Renal Devices Branch (GRDB)
9200 Corporate Boulevard HFZ-470
Rockville, MD 20850
(240) 276-4151
jeffrey.cooper@fda.hhs.gov

Cooper, Jeffrey (CDRH)

From: Buzz Moran [bmoran@implantedacoustics.com]
Sent: Monday, September 24, 2007 1:10 PM
To: Cooper, Jeffrey (CDRH)
Cc: QRASupport@aol.com; jhessel@dermaport.com
Subject: RE: Re K071202

Jeff, thank you for the response to our questions. We will complete our test data and literature search, and will expand our CAUTION to a WARNING as you suggest.
Regards,
Buzz Moran
President
DermaPort

From: Cooper, Jeffrey (CDRH) [mailto:jeffrey.cooper@fda.hhs.gov]
Sent: Monday, September 24, 2007 9:29 AM
To: Buzz Moran
Subject: RE: Re K071202

Buzz-

The testing sounds adequate. We think the caution should be stronger. Most clinicians would not place a catheter back in the same tunnel if infection is suspected - they would create a second tunnel. (b)(4) [redacted] (b)(4) [redacted].

Jeffrey Cooper, M.S., D.V.M.
Veterinary Medical Officer
Center for Devices & Radiological Health (CDRH)
Office of Device Evaluation (ODE)
Division of Reproductive, Abdominal and Radiological Devices (DRARD)
Gastroenterology and Renal Devices Branch (GRDB)
9200 Corporate Boulevard HFZ-470
Rockville, MD 20850
(240) 276-4151
jeffrey.cooper@fda.hhs.gov

-----Original Message-----
From: Buzz Moran [mailto:bmoran@implantedacoustics.com]
Sent: Friday, August 24, 2007 2:10 AM
To: Cooper, Jeffrey (CDRH)
Subject: Re K071202

Re: K071202

(b)(4) [redacted]

(b)(4) [redacted]

(b)(4)

[redacted]

(b)(4)

[redacted]

I appreciate the opportunity for this dialog to insure that we are adequately addressing your concerns.

Best regards,

Buzz Moran

President

DermaPort

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Memorandum

From: Reviewer(s) - Name(s) Jeffrey Cooper DM

Subject: 510(k) Number K071202

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

- ☐ Refused to accept.
- ☒ Requires additional information (other than refuse to accept). Telephone hold
- ☐ Is substantially equivalent to marketed devices.
- ☐ NOT substantially equivalent to marketed devices.
- ☐ Other (e.g., exempt by regulation, not a device, duplicate, etc.)

Is this device subject to Section 522 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

Truthful and Accurate Statement ☐ Requested ☐ Enclosed

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

☐ The required certification and summary for class III devices

☐ The indication for use form

Combination Product Category (Please see algorithm on H drive 510k/Boilers) N

Animal Tissue Source ☐ YES ☐ NO 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: Carolyn Y Neuland (Branch Chief) GRDB (Branch Code) 7/13/07 (Date)

Final Review: (Division Director) (Date)

Revised:4/2/03

Internal Administrative Form

K071262

	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?	✓	
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.		

MEMORANDUM

Food and Drug Administration
Center for Devices and Radiological Health
Office of Device Evaluation
DRARD/GRDB

Date: July 6, 2007

From: Jeffrey Cooper, M.S., D.V.M.
Gastroenterology and Renal Devices Branch, HFZ-470

Subject: **K071202 – Dermaport, Inc. – Dermaport Percutaneous Vascular Access System**

Contact: Buzz Moran, President
25102 Rye Canyon Loop, Suite 110
Santa Clarita, CA 91365
Phone: (661) 362-7901

To: The Record

Background:

Dermaport, Inc. submitted a 510(k) for a catheter with a new titanium and silicone cuff. The catheter was cleared by Medcomp as the Hemo-Flow.

Intended Use:

The Dermaport Percutaneous Vascular Access System (PVAS™) is indicated for long-term (greater than 30days) vascular access for hemodialysis and apheresis. The system is inserted percutaneously and the catheter is typically placed in the internal jugular vein of an adult patient. The subclavian vein is an alternate catheter insertion site.

This is the same indication as the predicate except for minor grammar changes.

Predicate Device:

Medcomp Hemo-Flow (K994105) and Med-Conduit, Inc. HemoCath II (K062901).

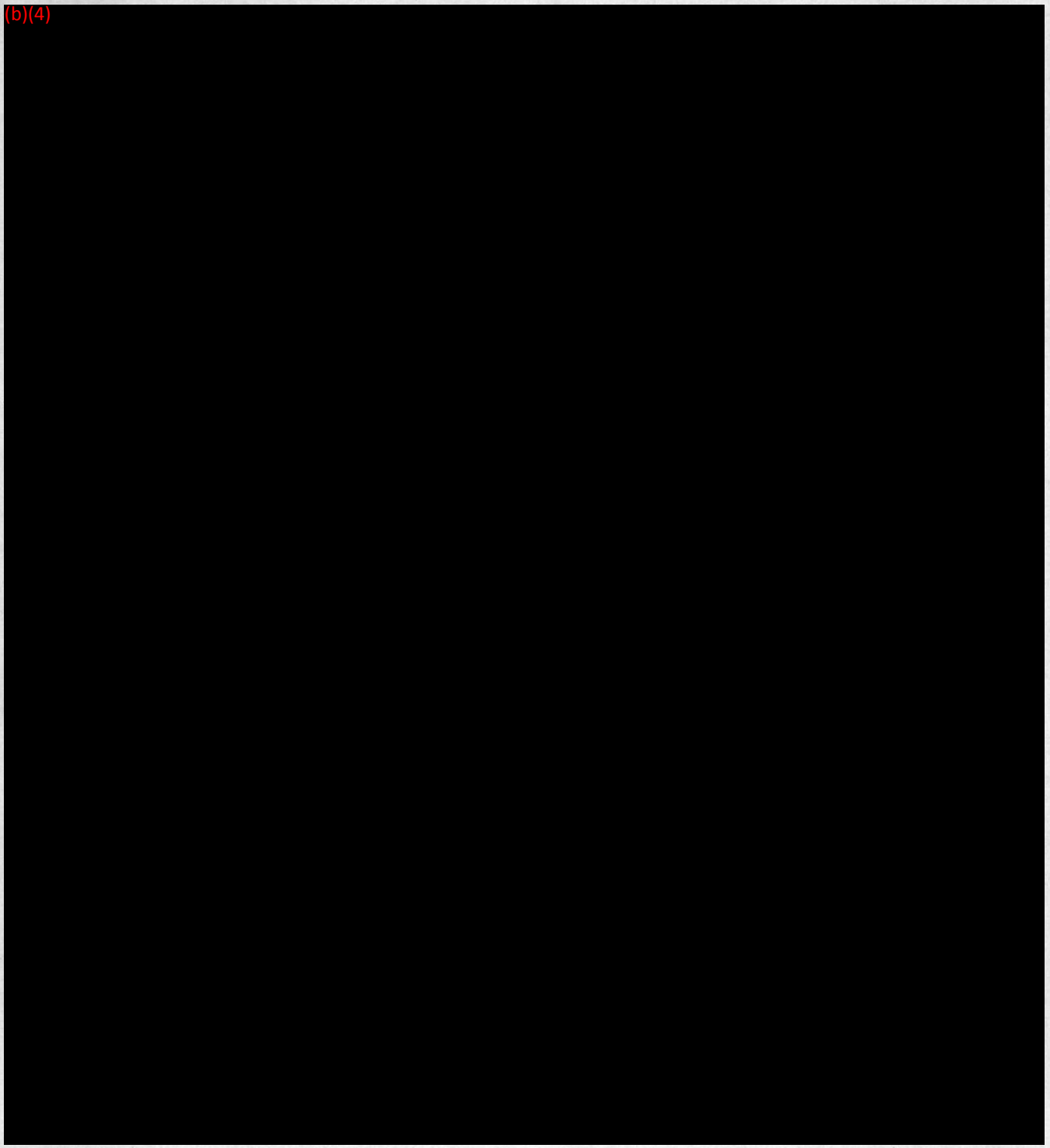
General Information Summary:

The Dermaport Percutaneous Vascular Access System is a 14.5 Fr HemoCath catheter with a different cuff. The new cuff is a roughened titanium surface that slides over the catheter. There is an internal 3 wiper seal to block bacterial migration along the external surface of the catheter. The catheter is anchored to the metal port with a removable silicone brake. The silcone brake collar grips the catheter by friction (2.5 lbs of force) and has two clips to hold the titanium port. The brake can be removed to allow optimum catheter tip positioning and optimum cuff placement.

A peel away sheath is just distal to the port to allow subcutaneous placement through a small incision to maintain a tight skin Juction and allow tissue ingrowth.

Pictures:

(b)(4)



(b)(4)

[redacted]

Biocompatibility:

(b)(4)

[redacted]

Sterility:

(b)(4)

[redacted]

Pyrogen Testing:

(b)(4)

[redacted]

Labeling:

The labeling for the proposed device consists of instructions for use and package labels.

The device is labeled as sterile by EO, non-pyrogenic, for single use, for long-term use, with Dermaport's address and phone, kit contents, with a manufacturing date, an expiration date, and with a prescription statement. The instructions appear complete, and recommend the caval-atrial junction or right atrium for catheter tip placement. A precaution recommends not to use ointments on the catheter. The predicate states "Do not use ointments." The proposed instructions should be modified to the same caution.

The instructions need a pressure vs. flow summary.

MRI Testing:

(b)(4) [redacted]

Expiration Dating:

(b)(4) [redacted]

Mechanical Hemolysis Testing:

(b)(4) [redacted]

Bench Testing:

(b)(4) [redacted]

(b)(4)

[redacted]

Substantial Equivalence:

Intended Use:

The intended uses of the devices are similar

Device Design:

The device designs differ by the cuff design.

Proposed Classification:

21 CFR §876.5540, Class III, Hemodialysis Catheter, Implanted, Product Code 78 MSD.

Deficiencies:

(b)(4)

[redacted]

(b)(4)

Recommendation:

Hold for additional information.

Jeffrey Cooper, M.S., D.V.M. Date 7/13/07

C. Neuland
7/13/07

Consulting Review Memo

K071202

Sterility consulting review

(b)(4)

[redacted]

Michelle P. Law, PhD
Microbiologist, GRDB
9/17/2007

Cooper, Jeffrey (CDRH)

From: Cooper, Jeffrey (CDRH)
Sent: Friday, July 13, 2007 5:05 PM
To: 'bmoran@dermaport.com'
Subject: K071202 Dermaport PVAS
Attachments: K071202 Deficiencies.doc

JN 7/13/07

Mr. Moran –

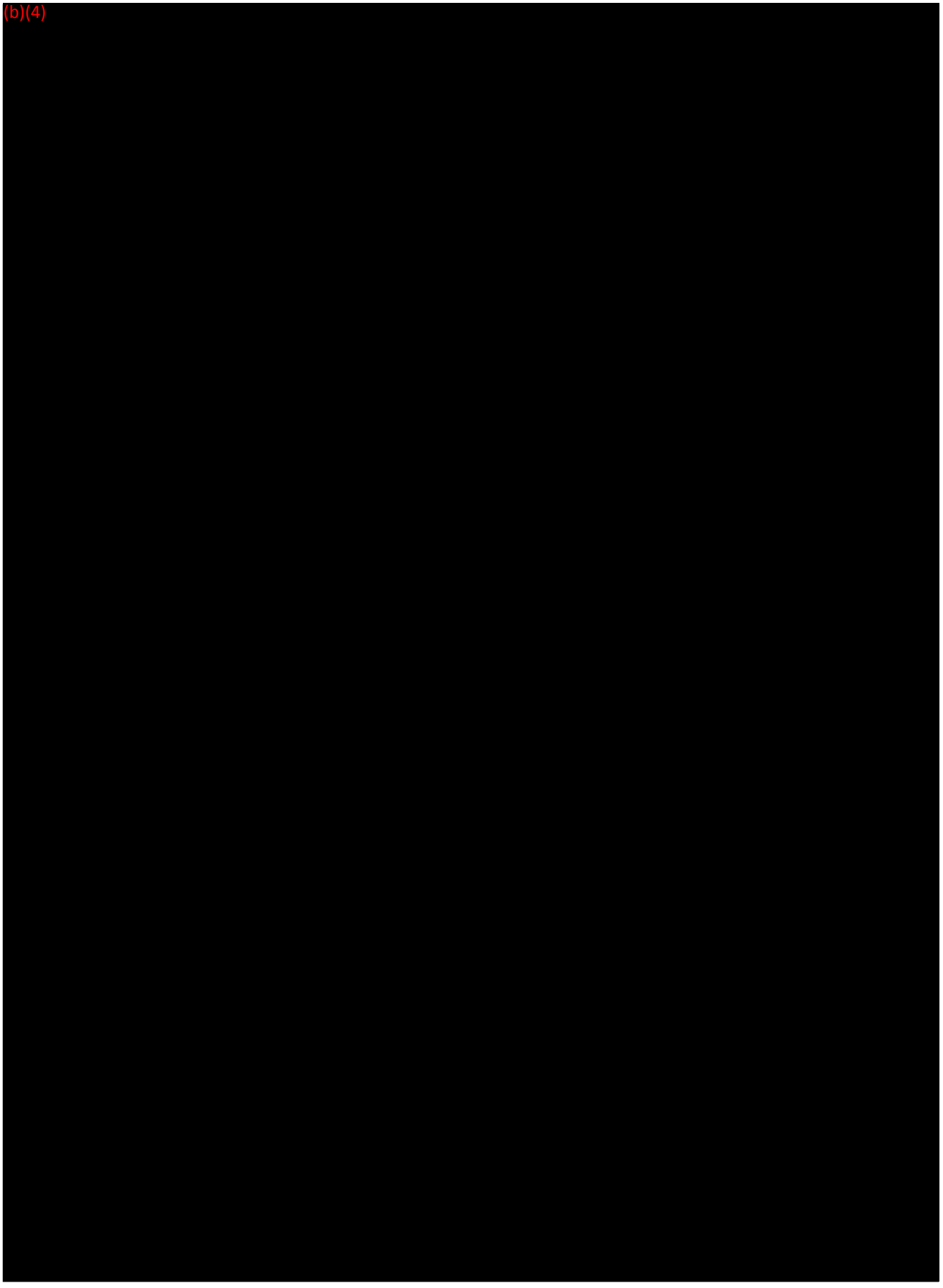
FDA has reviewed your 510(k) submission. We have some concerns about the device. Please respond to the attached deficiencies within 45 days. Your submission is now on telephone hold while we wait for your responses. If you have any questions, please email or call me.

Sincerely,

Jeffrey Cooper, M.S., D.V.M.
Veterinary Medical Officer
Center for Devices & Radiological Health (CDRH)
Office of Device Evaluation (ODE)
Division of Reproductive, Abdominal and Radiological Devices (DRARD)
Gastroenterology and Renal Devices Branch (GRDB)
9200 Corporate Boulevard HFZ-470
Rockville, MD 20850
(240) 276-4151
jeffrey.cooper@fda.hhs.gov

Deficiencies:

(b)(4)



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

November 15, 2007

DERMAPORT, INC
C/O QUALITY & REGULATORY ASSOCIATES
800 LEVANGER LANE
STOUGHTON, WI 53589
ATTN: GARY SYRING

510(k) Number: K071202
Product: DERMAPORT PERCUTANEOUS VASCULAR ACCESS SYSTEM (PVAS)

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. Also, please note the new Blue Book Memorandum regarding Fax and E-mail Policy entitled, "Fax and E-Mail Communication with Industry about Premarket Files Under Review. Please refer to this guidance for information on current fax and e-mail practices at www.fda.gov/cdrh/ode/a02-01.html. On August 12, 2005 CDRH issued the Guidance for Industry and FDA Staff: Format for Traditional and Abbreviated 510(k)s. This guidance can be found at http://www.fda.gov/cdrh/ode/guidance/1567.html. Please refer to this guidance for assistance on how to format an original submission for a Traditional or Abbreviated 510(k).

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 in 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 questions, please contact the Division of Small Manufacturers International and Consumer Assistance (DSMICA) at (240)276-3150 or at their toll-free number (800) 638-2041, or contact the 510k staff at (240)276-4040.

Sincerely yours,

Marjorie Shulman
Supervisory Consumer Safety Officer
Premarket Notification Section
Office of Device Evaluation
Center for Devices and
Radiological Health

DermaPort

K071202/S1

November 14, 2007

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

Re: 510(k) K071202, DermaPort Percutaneous Vascular Access System (PVAS™),

We are writing in reply to the deficiency letter dated July 18th, 2007 requesting additional information pertaining to the *510(k) K071202, DermaPort Percutaneous Vascular Access System (PVAS™)*. Attached are two copies of our response to your requests, along with supporting data.

We believe the responses answer the questions asked and support a conclusion of substantial equivalence. Please contact me with any questions.

Regards,

Buzz Moran, President
DermaPort, Inc.
Phone: (661) 362-7901
Fax: (661) 362-7902
Email: bmoran@dermaport.com

K-13

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Attachment A

Research Report

(b) (4) [redacted]

Comparison of Tunnel Debris *in vitro:* PVAS versus Predicate Cuffed Catheter

(b) (4)

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Attachment B

DRAFT Instructions for Use

(b) (4)

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Attachment C

Biocompatibility Reports for Sheath

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Attachment E

Biocompatibility Reports (b)(4)

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Attachment F

PVAS Risk Analysis

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Attachment G

Literature Review References

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Restoration of Patency in Failing Tunneled Hemodialysis Catheters: A Comparison of Catheter Exchange, Exchange and Balloon Disruption of the Fibrin Sheath, and Femoral Stripping

Bertrand Janne d'Othée, MD, Jacques C. Tham, MD, and Robert G. Sheiman, MD

PURPOSE: To compare median patency times after treatment of malfunctioning tunneled hemodialysis catheters by one of three techniques: over-the-wire catheter exchange (CE), fibrin sheath stripping (FSS) from a femoral vein approach, and over-the-wire catheter removal with balloon dilation of fibrin sheath (DFS) followed by catheter replacement with use of the same tract.

MATERIALS AND METHODS: Retrospective study was conducted of 66 consecutive procedures performed over a period of 47 months for poor flow through tunneled hemodialysis catheters despite tissue plasminogen activator infusion trials (CE, $n = 33$; FSS, $n = 18$; DFS, $n = 15$). Baseline parameters (time since initial catheter placement, number of previous catheter interventions, catheter access site, and patient age and sex) were recorded to identify possible pretreatment differences among groups. Outcome comparison was based on duration of adequate catheter function on dialysis during follow-up.

RESULTS: No significant differences in baseline parameters were identified among the three groups ($P > .05$). Mean follow-up duration (67 ± 89 days; range, 0–398 d) was similar among the three groups. The immediate technical success rate was 100%, and there were no complications. Cumulative catheter patency rates were 73% (CE), 72% (FSS), and 65% (DFS) at 1 month; 43% (CE), 60% (FSS), and 39% (DFS) at 3 months; and 28% (CE), 45% (FSS), and 39% (DFS) at 6 months. Median duration of patency was similar among groups ($P = .60$).

CONCLUSIONS: All three therapies were equivalent in terms of immediate technical success, complication rates, and durability of catheter function during later follow-up. Hence, when one technique is chosen over another, factors other than the period of secondary patency should be considered, such as cost and patient and physician preference.

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Abbreviations: CE = catheter exchange, DFS = disruption/dilation of fibrin sheath (with catheter replacement), FSS = fibrin sheath stripping

THE use of tunneled central venous catheters remains a widely used solution to provide access for hemodialysis in the United States despite the emergence of guidelines warning against their use (1). These catheters have been associated with mean 1-year primary patency rates of 65%–75% (range, 3%–74%) (2) and mean durations of primary catheter function between 6 and 12 months (3). A common cause of catheter malfunction is obstruction by a fibrin sheath, for which two main endovascular therapies have been described after conservative thrombolysis has failed, namely (i) catheter exchange (CE) over a wire through the existing access site and (ii) fibrin sheath stripping (FSS) along the catheter with a snare introduced from another venous access. Few series have actually compared these two options, and controversy remains regarding their outcomes (3,4). In a randomized trial in 2000, Merport et al (3) showed much better patency rates with CE than with FSS. However, their 31% cumulative patency rate at 1 month after FSS was much lower than the outcomes of other published studies and was based on 15 procedures. Also, their 93% patency rate at 1 month after CE was higher than those usually reported. The same year, Gray

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Table 1
Patient Characteristics at Baseline

No. of Patients	CE (n = 33)	FSS (n = 18)	DFS (n = 15)
Male sex (%)	42	56	33
Mean age (y) ± SD (range)	66 ± 15 (22–86)	67 ± 14 (37–86)	60 ± 19 (25–85)
Mean time from initial catheter placement ± SD (d)	149 ± 158 (6–749)	142 ± 148 (10–562)	242 ± 334 (1–1,249)
Range of previous interventions on the catheter studied	0–4	0–3	0–3
0	14	9	7
1	5	4	6
2–4	10	3	2
Approach of catheter placement			
Right internal jugular vein	21 (64)	11 (61)	9 (60)
Left internal jugular vein	6 (18)	7 (39)	5 (33)
Right subclavian vein	4 (12)	0	1 (7)

Note.—There were no significant differences between treatment groups in any category. Values in parentheses are percentages.

et al (5) showed similar duration of catheter function after FSS or alteplase infusion through the catheter ports. In the present study, which was performed in a single population treated at a single institution, we propose to compare the secondary patency rates from these two techniques and an additional third technique, endovascular balloon disruption/dilation of the fibrin sheath (DFS) and catheter replacement, hereafter referred to as simply DFS.

MATERIALS AND METHODS

Study Design and Patient Selection

We retrospectively studied 66 consecutive interventions performed in 45 patients for malfunctioning tunneled hemodialysis catheters in our department between January 1, 2002, and December 1, 2005 (47 months). A waiver of informed consent was obtained from our institutional review board for the purpose of retrospective research investigation. Informed consent for all clinical procedures was obtained from patients according to standard of care. The patient inclusion process was started by reviewing all 768 interventions that were extracted from our interventional radiology case database with procedure codes for "tunneled catheter" (n = 716) or "catheter stripping" (n = 52) during the 47-month time period of interest. After reviewing the patients' history and images, we excluded 702 interventions (91%) that consisted of or included (i) de novo catheter placement, (ii) removal of an infected catheter, (iii) cases in which an evident cause of catheter malfunction other than a fibrin sheath was identified (eg, catheter kinking, malpositioning of catheter tip out of the right atrium, or leak at catheter hub), and (iv) manipulations limited to the internal lumens of the catheter (6). The remaining 66 interventions in 45 patients were subdivided into three groups according to the type of intervention to treat malfunction: (i) over-the-wire CE (n = 33 procedures), (ii) FSS from another venous access site (n = 18), and (iii) over-the-wire catheter removal with DFS followed by replacement with a new catheter through the same access (n = 15).

All patients were referred to our department only after the failure of trials to restore flow with tissue plasminogen activator infusion through the catheter lumens (1 mg per port for 30 minutes). Fibrin sheath–related malfunction was considered a diagnosis of exclusion after the aforementioned causes were not believed to be the cause of poor catheter flow. The assignment of fibrin sheath as a cause was made by any of four staff interventional radiologists with a minimum of 4 years of experience in the placement of tunneled dialysis catheters. Contrast angiography was routinely performed by successive injections through both ports in an attempt to detect the presence of fibrin sheath.

The choice of one therapeutic strategy over another was left to the attending radiologist performing the procedure and was therefore largely influenced by operator preference. The assignment of each operator to a given case was based on the timing and scheduled date of the procedure. No specific guideline was used to decide who would perform the procedure and what technique would be used by the operator. Overall, the type of procedure performed was randomized; no specific selection was used in choosing which procedure a specific individual would undergo.

Comparison of the three procedure types with respect to secondary patency can be performed if the study groups are similar at baseline with respect to (i) patient age, (ii) patient sex, (iii) time elapsed between initial placement of a tunneled catheter through that access site and the intervention of interest, (iv) number of earlier interventions performed on catheter(s) through that access site, (v) type of catheter placement (surgical vs interventional radiologic), and (vi) access site location of the catheter. Hence, these factors were assessed for each group and compared. None of the differences observed in any of these parameters was statistically significant among the three groups at baseline (**Table 1**). Among the 66 procedures included in this study, 45 (68%) were in patients who had not undergone any previous intervention for malfunction on their tunneled catheters before inclusion in this study. The remaining 21 interventions (32%) were in patients who had been included in the study once (14 procedures, 21%) or more times (seven procedures, 11%).

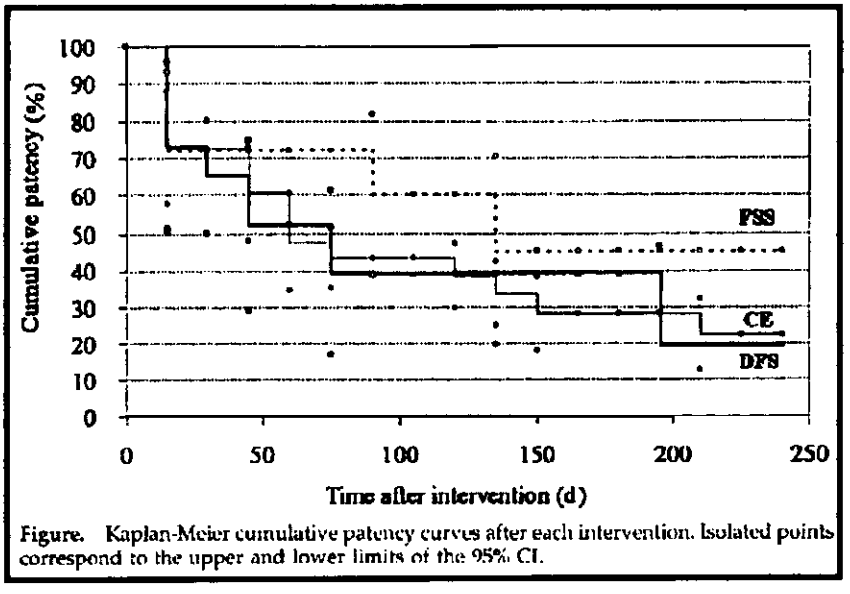

Figure. Kaplan-Meier cumulative patency curves after each intervention. Isolated points correspond to the upper and lower limits of the 95% CI.

Description of Procedures

Catheter stripping from a femoral approach (3,5–7) and CE (3,4,8,9) were performed according to well-described methods. Briefly, FSS was performed with use of a 15- to 20-mm nitinol snare from a right common femoral vein approach. CE was performed over one or two standard or Amplatz Super-Stiff wires (Boston Scientific, Natick, MA).

DFS was performed with the patient under local anesthesia and intravenous conscious sedation with fentanyl and midazolam. After removal of the existing tunneled catheter over two stiff Amplatz wires, a 23-cm-long 7-F Brite-Tip sheath (Cordis, Miami Lakes, FL) was advanced over one of the wires into the inferior vena cava. A balloon 8 to 12 mm in diameter was advanced through this vascular sheath, and dilation of the intravenous course of the previously placed catheter was performed. The balloon diameter was chosen to exceed the original dialysis catheter size but be small enough to avoid simultaneous dilatation of the vein wall itself. After complete dilation of the fibrin sheath, the inflated balloon was also advanced and withdrawn over the wire along the dilated course of the fibrin sheath to ensure its disruption. After removal of the balloon, pullback venography was performed through the 7-F sheath to confirm absence of fibrin sheath. The vascular sheath was then removed, and a new tunneled hemodialysis catheter was advanced over the two wires. Except for priming the catheter ports, no heparin was given systemically during any of the three types of procedures.

Outcome Assessment

Immediate technical success of the procedure was assessed by the presence of satisfactory flow rates observed during the next three hemodialysis sessions after the intervention. Thereafter, catheter patency was defined by uninterrupted satisfactory flow rates obtained during subsequent hemodialysis sessions. The adequacy of flow rates was determined individually by dialysis unit staff depending on patient needs (typically >250–300 mL/min when a non–high-flux system was used). The frequency of dialysis sessions varies among patients, but flow rate measurements were typically performed at least once per week as part of the routine dialysis procedure at our institution and related institutions.

Statistical Analysis

Outcome during the follow-up was assessed by the median survival time of catheter function in each group, comparison being made with the log-rank test. Because many of our patients had undergone multiple earlier interventions on their tunneled catheters before inclusion in this study, the basic unit for analysis was the intervention of interest (ie, CE, FSS, or DFS) and its corresponding subsequent follow-up period to the next additional procedure performed for catheter dysfunction (if any). Therefore, it was possible for a given patient to be included more than once in a given therapeutic group and/or in more than one group. Statistical analysis was performed with Stata 9.0 software (Stata, College Station, TX). A P value less than .05 was considered to indicate significance in two-tailed tests.

RESULTS

The immediate technical success rate for all three techniques was 100%. There were no early complications. Follow-up duration (mean, 67 ± 89 days [SD]; range, 0–398) was not statistically different among the three groups (50 days for DFS, 63 days for FSS, 78 days for CE; P = .15). During follow-up, the cumulative rates of persisting catheter function calculated by the Kaplan-Meier method (Figure) were 73% (CE), 72% (FSS), and 65% (DFS) at 1 month; 43% (CE), 60% (FSS), and 39% (DFS) at 3 months; and 28% (CE), 45% (FSS), and 39% (DFS) at 6 months. No group showed a significantly longer or shorter duration of patency compared with the other two groups (P = .60, log-rank test).

DISCUSSION

Our results for FSS and CE are in accordance with the findings of most series dealing with each technique individually or reports comparing CE and FSS (**Table 2**). Our cumulative patency rates at 1 and 3 months for these two techniques (65%–73% and 39%–60%, respectively) are in the range of those previously published (2–5,10) (31%–93% and 45%–56%, respectively). Six months after the procedure, our patency rates (28%–45%) are also similar to those reported (between 28% [11] and 46% [2]). Hence, we believe that the achievement of patency rates similar to those of other investigators for FSS and CE validates our results overall and allows the conclusion that minimally invasive restoration of function of a tunneled hemodialysis catheter obstructed by a fibrin

Table 2
Literature Review

Study	Sample Size	Technical Success (%)	Complications (%)	Cumulative Patency (%) 0.5	1	1.5	3	4	6	12 (months)	Median Duration of Function (d)
TPA infusion											
Gray et al, 2000	29	97		86	63	48					42
Stripping											
Crain et al, 1996	40	98					45		28		85
Haskal et al, 1996	24	92	4	8							
Brady et al, 1999	91	96	0				56		46		89
Gray et al, 2000	28	89		75	52	35					32
Merport et al, 2000	15	93	6		31			0			9
Current study	15	100	0		72		60		45		135
CE											
Duszak et al, 1998	42	93	15				51		37	30	85
Merport et al, 2000	22	100	0		93			23			40
Current Study	25	100	0		73		43		28		60
DFS											
Current Study	15	100	0		65		39		39		75

sheath can be equally achieved by all three methods we performed: CE, FSS, and DFS. All three techniques were equally successful in restoring immediate catheter function, none were associated with immediate complications, and all were associated with similar early outcomes and longer-term durability.

Brief summaries of DFS or mentions of a similar approach have been reported elsewhere (3,8,12) but have consisted of isolated reports without comparison versus other techniques in the same patient population. In the present report, removal and exchange of the dual-lumen catheter was combined with balloon angioplasty over the entire length of the fibrin sheath. The aim of DFS is to disrupt the existing sheath to fragment it or modify its geometry. An important technical aspect isolated to this procedure is potential dilation of the venipuncture site. This can be minimized by hand injection of contrast agent through the vascular sheath positioned in the central vein before balloon catheter insertion to allow for precise delineation of the vein contours (and, on occasion, confirmation of a fibrin sheath via a filling defect in the contrast agent column). Another potential disadvantage—but one that is not isolated to this technique—is fibrin sheath embolization to the lungs. This seems to be largely a theoretic complication because pulmonary embolism of fibrin sheath fragments has been very scarcely reported in the literature (13). Also of note, at our institution, the typical cost of the materials used was $542 for DFS, $342 for a typical CE, and $320 for uncomplicated FSS. Hence, because DFS shows no advantage compared with FSS and CE with respect to overall catheter patency, requires more costly equipment, and presents a potential unique disadvantage in the form of venipuncture site dilation, we no longer perform this procedure.

Obviously, the results of the present study must be understood in the context of its retrospective, nonrandomized design. The choice of one therapeutic strategy over another was left to the attending radiologist performing the procedure and was therefore largely influenced by operator preference. Even though 10 different interventional radiologists were involved in these procedures, each one preferred a given procedure: one operator performed 73% of the DFS interventions, another one performed 67% of the FSS procedures, and the eight others were involved in 88% of the CE procedures. Last, other parameters such as infection risk, patient preference, and procedure time (including radiation exposure) were not included in the present study. Although procedure times were not compared formally, in our experience, there is no dramatic difference among the three techniques. Further cost identification (14) and more cost-effectiveness analyses will be needed to put in perspective these cost values and integrate them with clinical and quality-of-life outcome parameters of such interventions (3,5,15–21).

The small sample size of our study may be interpreted as a study limitation. However, our cumulative survival curves (Figure) suggest that such a difference is unlikely, given the closeness between the lines for each of the three groups. In addition, the 95% CIs around our patency estimates are wide enough to overlap across the three groups. Therefore, unless there was a drastic change in the makeup of our study population in the future, our conclusions would likely not change. Another evident limitation of the present study relies on the presumptive nature of the diagnosis of fibrin sheath and of its role in flow reduction. Fibrin sheath formation remains a difficult diagnosis that is usually made after exclusion of other common causes of catheter malfunction such as catheter kinking, migration, or malposition. These causes are usually easily detected by fluoroscopy, and all patients with such findings were eliminated from our study. The exclusion of catheter obstruction by a thrombus around the catheter tip (another common cause of malfunction) can be made in 97% of cases (5) by successfully treating the clot by infusion of a

thrombolytic agent (eg, tissue plasminogen activator, urokinase) through the catheter ports (22) as a bolus (23,24) or in a prolonged infusion (5). Tissue plasminogen activator trials were undertaken and failed in all our patients before they were referred to the interventional radiology department. The suspicion of the presence of a fibrin sheath when flow rates are poor on catheter aspiration but better on flushing is clinically suggestive but inconstant. Contrast venography by injection through the catheter ports is also of limited value for the detection of fibrin sheath (2), with reported sensitivity rates of 50%; in addition, as a result of cost considerations, intravascular ultrasonography is not routinely performed for that indication. Therefore, we are confident that dysfunction resulted from the presence of fibrin sheath in our patient population by direct visualization or by default after exclusion of all other possibilities.

In conclusion, this retrospective comparison of three therapies for poor flow rates in tunneled hemodialysis catheters showed no clear benefit of one option over another in terms of immediate technical success or complications rates, or in terms of durability of catheter function later during follow-up. Hence, in the choice of one technique over another, consideration of factors other than the period of secondary patency should be considered.

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Replacement of Failing Tunneled Hemodialysis Catheters through Pre-existing Subcutaneous Tunnels: A Comparison of Catheter Function and Infection Rates for De Novo Placements and Over-the-Wire Exchanges[1]

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Index terms: Catheters and catheterization, complications • Dialysis

JVIR 1998; 9:321–327

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PURPOSE: Tunneled hemodialysis catheter dysfunction often occurs from fibrin sheath formation. As a way to preserve existing catheter venous access sites, the authors evaluated over-the-wire exchange of catheters through pre-existing subcutaneous tunnels as an alternative to catheter removal and de novo catheter replacement.

PATIENTS AND METHODS: One hundred nineteen catheters were placed in 68 patients. Seventy-seven catheters were placed de novo and 42 catheters were placed through the pre-existing subcutaneous tunnels of failing catheters. Technical success, short-term complications, infection rates, and functional catheter longevity were evaluated.

RESULTS: Technical success for catheter exchange was 93%. Infection rates were comparable to those of de novo catheter placement: 0.15 and 0.11 infections per 100 catheter days for de novo and exchanged catheters, respectively. Catheter duration of function was not significantly different for de novo versus exchanged catheters: 63% and 51% at 3 months, 51% and 37% at 6 months, and 35% and 30% at 12 months, respectively.

CONCLUSIONS: Over-the-wire exchange of tunneled hemodialysis catheters is safe and easily performed. It causes no increase in infectious complications and provides similar catheter longevity to de novo catheter placement. The procedure is an important option for prolonging tunneled hemodialysis catheter access sites.

TUNNELED catheters are widely used for hemodialysis access. They provide a bridge to maturation or revision of arteriovenous fistulas, prosthetic access grafts, or transplantation. In addition, they are used as a permanent access in patients who have no remaining access sites. Although these catheters can be rapidly placed and immediately used, they are prone to repeated failure because of infection or pericatheter fibrin sheaths or thrombus (1–6).

As with other implanted devices, infected catheters are typically removed and replaced at another site after an appropriate course of anti-

biotic therapy. Although some authors disagree, there is evidence that infection rates in tunneled catheters are lower than nontunneled catheters, presumably because of the protective barrier effect of the subcutaneous tract, which limits passage of pathogenic skin flora into the venous system (7).

Catheters that fail because of fibrin sheaths are treated with thrombolytic agents and, more recently, with transvenous fibrin sheath removal (8–12). When these methods fail to restore satisfactory catheter flow rates, catheters are traditionally removed and new catheters are placed at different venous entry sites.

Repeated placement of hemodialysis catheters at different sites carries several risks. These include all the risks of new catheter placement, and, if placed operatively, the risk of anesthesia. In addition, catheters can rapidly lead to venous stenoses or occlusions. In a study of 52 patients with temporary subclavian and internal jugular dialysis catheters, Cimochowski found that 50% of patients with subclavian catheters developed marked venous stenoses with a mean catheter dwell time of just 11.5 days (13). The development of a subclavian or brachiocephalic vein stenosis or occlusion imperils the outflow of an existing ipsilateral arteriovenous access graft or fistula, or entirely precludes its surgical placement. As the life expectancy of patients with chronic renal failure increases, preservation of existing central venous catheter sites becomes of paramount importance.

The guide wire exchange procedure is being rapidly disseminated among interventional radiologists to salvage failing, noninfected catheters and preserve venous access sites. Several authors have reported the use of pre-existing tunnels to salvage hemodialysis catheters. Egglin et al reported success in replacing tunneled catheters after accidental removal (14). Carlisle et al and Shaffer salvaged infected catheters by guide wire exchange and systemic antibiotic therapy (15,16). To the best of our knowledge, there are no published studies evaluating exchange as a routine method of salvaging noninfected failing tunneled catheters. We describe our results and compare our experience with exchanged catheters and de novo placement of tunneled hemodialysis catheters.

PATIENTS AND METHODS

From 1993 to 1995, 119 tunneled central venous hemodialysis catheters were placed in 68 patients with chronic renal failure. These patients were either awaiting maturation of surgically created arteriovenous fistulas or required permanent catheter dialysis because of repeatedly failed peripheral access grafts or fistulas. Seventy-seven catheters were placed de novo in 64 patients (that is, through fresh venous access sites and newly created tunnels). In 42 cases (29 patients), failing catheters were exchanged over guide wires through their existing subcutaneous tunnels. PermCaths (Quinton Instrument, Bothell, WA) were used in most cases. Single-barrel, multisidehole catheters, such as the Tesio (Medcomp, Harleysville, PA) or Duocath (Angiodynamics, Queensbury, NY) were not used in this study.

The patients consisted of 34 men and 34 women. The preferred primary site for catheter placement was the right internal jugular vein because of its straight line access into the right atrium. When this vein was occluded, stenotic, or when future ipsilateral arm graft surgeries were anticipated, the left internal jugular vein was used. When neither internal jugular vein was suitable, the subclavian, external jugular, and lastly, femoral veins were used. The leading tips of the thoracic catheters were placed within the lower superior vena cava or right atrium. The choice of either location was determined by the operator preference and several technical factors, including available catheter lengths.

Failing hemodialysis catheters were defined as devices that could not be infused or aspirated (either by the dialysis staff or interventional radiologists), or catheters that did not consistently sustain minimum acceptable hemodialysis flow rates (greater than 250 mL/min) throughout a dialysis treatment. As is the typical practice at our institution, the dialysis staff was allowed free and repeated use of low-dose transcatheter urokinase dwells (Abbokinase Open-Cath; Abbott Laboratories, North Chicago, IL), using 5,000 U per port (17). No catheter exchanges were performed in patients with catheters that were infected or presumed infected. In cases of bacteremia, or clinically evident or suspected site or tunnel infection, the catheters were completely removed. Temporary, nontunneled femoral, jugular, or subclavian catheters were used until blood cultures proved negative and antibiotic therapy was well established.

• Catheter Placement Techniques

All de novo catheter placements and exchanges were performed percutaneously under the sterile conditions of the interventional radiology suites. All operating physicians wore gloves, gowns, and masks. The skin and catheter entry sites were scrubbed with antiseptic soap and sterilely draped in the standard fashion that we use for all percutaneous procedures. Laminar flow operating room ventilation was not present. All patients received 1 g of cefazolin sodium intravenously as antibiotic prophylaxis. Patients with significant and relevant penicillin drug allergies received 1 g of vancomycin instead.

• De Novo Catheters

The procedures were performed under either local anesthesia alone or light intravenous conscious sedation with local anesthesia. Pulse oximetry, blood pressure, and electrocardiographic monitoring were used in each case. Anatomic landmarks or sonographic guidance was used to guide the venous puncture. A Rosen (Cook, Bloomington, IN) or

straight Newton LLT (Cook) wire was advanced into the right atrium or inferior vena cava under fluoroscopic guidance. The venotomy site was serially dilated to allow introduction of the peel-away introducer sheath that accompanied the specific catheter set. The length and position of the chest wall subcutaneous tunnel were chosen by taking into account the body habitus of the patient. In the case of jugular or subclavian access, catheters were tunneled laterally over the chest wall, exiting a short distance below the clavicle. In cases of femoral access, the catheters were tunneled laterally over the upper thigh away from the inguinal crease and skin pannus.

The tunnel path was infiltrated with lidocaine mixed with epinephrine. The tunnel was created with blunt dissection with use of a standard hemostat and blunt tunneling device included in the catheter kits. The catheter was attached to the trailing end of the tunneling device and drawn through the tunnel, exiting at the venotomy incision, adjacent to the peel-away sheath. The dilator was removed from within the peel-away sheath, and the catheter was looped back into it. The sheath was slowly split or cut back as the catheter was held in place, until it was removed in its entirety. The catheters were rotated under fluoroscopic guidance to ensure that their leading tips were satisfactorily positioned and oriented within the vessel lumen. The fabric fixation cuff was intentionally positioned only a few centimeters from the tunnel entry site (ie, within the reach of a hemostat). This allowed easy dissection of the fixation cuff from the site of tunnel exit at the time of catheter exchange, eliminating the need for incising the skin over the cuff. The venotomy sites were sutured closed with interrupted, nonresorbable or resorbable, subcuticular sutures and Steri-Strips (3M Medical Surgical Division, St. Paul, MN). The venotomy and catheter exit sites were dressed with sterile gauze and polyurethane (Tegaderm; 3M) or permeable adhesive dressings (Medipore; 2M). The catheters were flushed with the manufacturers' recommended volumes and concentrations of heparin. The patients were discharged after an appropriate period of observation, commensurate with the amount of sedation administered.

- **Exchange of Pre-existing Failing Catheters**

Patients referred for catheter exchange typically had functional evidence of fibrin sheath formation, manifest by the inability to infuse one or aspirate one or both ports at rest or during dialysis, or inability to maintain sufficient flow rates during dialysis treatments. All catheters were evaluated in the interventional suite prior to their exchange. The indwelling heparin within the catheter lumina was aspirated if possible. Digital subtraction contrast studies of each catheter lumen were performed to assess for pericatheter thrombus, fibrin sheaths, and vein stenoses.

After sterile skin preparation, the catheter entry site and subcutaneous catheter course were infiltrated with lidocaine. As our experience with catheter exchange increased, we switched to using lidocaine with epinephrine to minimize oozing at the tunnel entry site. A standard hemostat was used to free the incorporated fixation cuff of the catheter within the tunnel. In one case, a cutdown over the cuff was performed to allow it be dissected free of the surrounding tissue. Under fluoroscopic guidance, a 0.085-inch or 0.038-inch regular or stiff shaft hydrophilic guide wire (Terumo; Medi-tech/Boston Scientific, Watertown, MA) was inserted through a catheter lumen into the inferior vena cava. In some cases, a second such guide wire was placed through the other catheter lumen to further stabilize the subcutaneous tunnel and to ensure the ability to rethread the fresh catheter through the same tract. The old catheter was removed and simply exchanged for a new tunneled catheter, of similar or slightly longer length. An attempt was made to place the tip of the new catheter outside the culprit fibrin sheath. This was performed by either extending the new catheter central to the position of the old one or exiting the fibrin sheath proximally along its course with a guide wire before introducing the new catheter. This was done either by using a slightly longer catheter or by simply positioning the catheter deeper within the subcutaneous tunnel. The catheter was tested with rapid manual injection of saline and rapid aspiration. A radiograph was obtained to document catheter position, and the device was sutured to the skin at the tunnel exit site. The catheter was sterilely dressed and flushed with the indicated heparin dose. In many instances, the catheter exchange was performed without any intravenous sedation and patients were discharged shortly after the procedure.

- **Data Collection and Statistical Analyses**

All patients were followed up at our inpatient or outpatient hemodialysis centers. Catheter function was discussed during a weekly interdisciplinary interventional radiology, nephrology, and access surgery conference. Hospital charts and data regarding catheter function, flow rates, and clinical visits were reviewed. Catheters were followed until their removal, or until exit from follow-up. "Functional longevity" was defined as the period (in days) that the catheter provided adequate access for hemodialysis. Catheter longevity was evaluated with use of life-table analysis. Infection rates were calculated in the traditional fashion, with respect to both infections per catheter, as well as infections per 100 catheter days at risk. Infections within the first 30 days after catheter placements were specifically identified. χ^2 and Kaplan Meier analysis were used to determine statistical significance.

RESULTS

One hundred nineteen tunneled catheters were successfully placed

in 68 patients through a variety of access sites. Fifty-four catheters were placed through the right internal jugular vein (35 de novo and 19 exchanged), 27 left internal jugular (20 de novo and seven exchanged), 14 right subclavian (eight de novo and six exchanged), 13 left subclavian (five de novo and eight exchanged), six right common femoral (five de novo and one exchanged), two left common femoral (one de novo and one exchanged), and three right external jugular veins (three de novo).

Seventy-seven catheters were placed de novo in 64 patients. Forty-two exchanged catheters were placed in 29 patients. Of the exchanged catheters, 32 were initially placed by the interventional radiology service and 10 by the surgical service.

The leading tips of the catheters were positioned in the right atrium in 78 cases (47 de novo, 31 exchanged). In 41 cases, the tips lay within the vena cava—in the majority of cases within the distal superior vena cava at its junction with the right atrium. Femoral catheters were positioned so that their tips were within the infrarenal inferior vena cava.

The technical success for de novo catheter placement was 100%. There were three early failed attempts to exchange catheters through tracts due to tortuosity of the tracts, resulting in a technical success of 93%. All three of these patients had de novo catheters placed immediately thereafter (without leaving the interventional suite). In one case, an incision over the fixation cuff site was required to allow catheter removal. This catheter had been placed by a surgeon; its cuff lay deep within the subcutaneous tunnel beyond the reach of a standard hemostat.

The mean duration of catheter follow-up was 110 days (range, 1–501 days; SD, 105 days). De novo catheters were followed for 124 days (range, 3–501 days; SD, 110 days) and exchanged catheters for 85 days (range, 1–426 days; SD, 93 days).

Infection Data for All, De Novo, and Exchanged Hemodialysis Catheters

	All Catheters	De Novo	Exchanged
Catheters placed	119	77	42
Catheters infected	17	13	4
Episodes of infection	18	14	4
Line sepsis	13	12	1
Exit site infections	5	2	3
Percent total of catheters infected	14%	17%	10%
Infections requiring catheter removal (% of all catheters)	12 (10%)	10 (13%)	2 (5%)
Infections per 100 catheter days	0.14	0.15	0.11
Infections during first 30 days (% of all catheters)	7 (6%)	5 (7%)	2 (5%)

• Complications

Prolonged oozing from the tunnel was noted in two cases, one after de novo placement and one after wire exchange. Both resolved with prolonged manual compression and administration of desmopressin acetate, without the need for hospital admission.

One patient, with a history of intermittent tachyarrhythmias, developed supraventricular tachycardia during exchange of a catheter. This was controlled with intravenous verapamil. After medical clearance, the patient was sent home shortly after the procedure. Another patient with severe coronary artery disease and unstable angina developed transient hypotension during a catheter exchange. This was attributed to excessive sedation and resolved without further intervention or consequence.

There were no cases of pneumothorax or air embolism.

• Infection Rate

A total of 18 episodes of catheter-related infections were identified involving 17 catheters, providing an overall infection rate of 14% for all catheters. These occurred a mean of 96 days from catheter placement (range, 8–419 day; SD, 117). This corresponded to 0.14 infections per 100 catheter days. Thirteen infections were believed to be line-related bacteremia or sepsis, requiring the removal of 10 catheters. Five infections were identified as local exit site infections, requiring the removal of two catheters.

De novo catheters.—Fourteen infections were identified in 13 catheters, corresponding to infections in 17% of catheters, or 0.15 infections per 100 catheter days. These occurred a mean of 112 days from catheter placement (range, 8–419 days; SD, 135).

Exchanged catheters.—Four infections were identified in four catheters, corresponding to infections in 10% of catheters, or 0.11 infections per 100 catheter days at risk. These occurred a mean of 46 days after placement (8, 26, 33, and 116 days). In the patient presenting with sepsis at day 8, the catheter was suspected as the source, but catheter cultures yielded negative findings. Exit site infections occurred in the other three patients; two were treated successfully with antibiotics, without catheter removal. The infection data are presented in the Table.

There was no statistically significant difference between infection rates (either for percent catheters infected or infections per 100 days) for de novo and exchanged catheters ($P = .27$). Because early infections (ie, within 2–4 weeks of catheter placement) could be attributed to the insertion procedure, it is important to compare early infection rates. The incidence of infection during the first 30 days after new catheter placements or exchanges was not significantly different ($P = .70$).

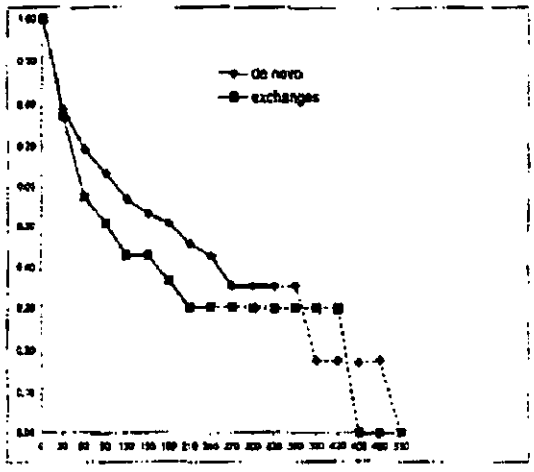

Figure. Functional life of de novo and exchanged catheters (dotted lines indicate where the standard error exceeds 10%). Time intervals on x axis are in days.

• Catheter Functional Longevity

Life table comparison of catheter longevity is illustrated in the Figure. The exchanged catheters tended to function for slightly shorter periods. Respective rates of acceptable function were 63% and 51% at 3 months, 51% and 37% at 6 months, and 35% and 30% at 12 months.

The authors observed that catheter tips directed medially (ie, away from the right lateral wall of the superior vena cava or right atrium) were less prone to catheter flow related problems, but the difficulty in confidently evaluating catheter tips retrospectively from final procedural spot films precluded quantitative evaluation.

DISCUSSION

Tunneled central venous catheters have been used for more than 2 decades to provide long-term or permanent central venous access (18,19). These catheters provide a low rate of infection compared with nontunneled catheters, partly because of the protective effect of the subcutaneous tunnel, and perhaps partly because of the barrier effect of the fabric cuffs that become fixed within the tracts by fibroblast ingrowth.

Historically, tunneled catheters have been placed by surgeons in operating rooms. Because of inherent similarities to other procedures they perform, interventional radiologists have been performing these procedures in interventional suites with increasing frequency during the last 5 years. The potential advantages and comparable success and complication rates have been well described for both low-flow (chemotherapy, parenteral nutrition) and high-flow (hemodialysis) catheters (1,6,20).

Many tunneled dialysis catheters fail because of either fibrin sheath formation or infection. As the prevalence of high-speed dialyzers grows, flow rates in excess of 400 mL/min become more routine. While fibrin sheaths contribute to dysfunction of many central venous catheters, the effect on such high-flow hemodialysis catheters may be more clinically apparent because of their high flow demands. Infections may be more frequent in dialysis catheters, as well, possibly because of their more frequent use and handling.

Fibrin sheath formation has long been recognized as a major cause of catheter dysfunction. This scabbard-like tissue spreads from sites of catheter and vein contact and intimal injury; it has been identified as early as 1 day after catheter placement (21). By enveloping the leading edge of the catheter, the fibrin sheath acts as a one-way valve. In non-high-flow catheters, such as those used for total parenteral nutrition or chemotherapy, this may prove inconvenient by preventing blood aspiration yet may still allow satisfactory fluid or medication infusions. In the case of hemodialysis or plasmapheresis catheters, however, fibrin sheaths can very quickly lead to complete loss of catheter function because of the inability to sustain the necessary high flow rates.

The first line in treating fibrin sheaths and pericatheter thrombus is instillation of relatively low-dose urokinase (eg, 5,000 U per lumen) into the catheters (16). Occasionally, more prolonged, 6-hour infusions can be used (22). In many cases, these will restore sufficient function to allow dialysis to continue. Traditionally, when these methods fail, the dysfunctional catheter is removed and a new catheter is inserted at a new access site.

Percutaneous fibrin sheath stripping was reported as a procedure to salvage tunneled and implanted central venous catheters by Crain and Mewissen in 1994 (23) and Knelson et al in 1995 (24). In a larger study, Crain reported prolongation of hemodialysis catheter

function in 24 patients, although 11 required multiple interventions (11). We evaluated this identical procedure and found that, although it was capable of immediately restoring satisfactory catheter function, this beneficial effect disappeared by the fifth subsequent dialysis session (12). Because of the femoral vein access required for this procedure, fibrin sheath stripping requires a period of several hours of bedrest and immobilization after the procedure. At our institution, the hospital costs alone for fibrin sheath stripping approaches $1,000.

These results led us to explore over-the-wire catheter exchange to restore catheter function while preserving the existing venous access site and tunnel. This technique raises three natural questions. First, can this procedure be performed with a sufficiently high degree of ease and technical success to make it a feasible treatment option? Second, does passing a new catheter through a sterilely prepared preexisting tunnel predispose the patient to higher infection rates? Third, what is the subsequent functional durability of the exchanged catheters compared with new catheters or failing catheters managed by other means (such as fibrin stripping)?

• Technical Issues

Our de novo catheter placements were designed to allow easy subsequent catheter removal or exchanges by keeping the subcutaneous tunnels relatively short (15 cm or less), and by positioning the fixation cuffs within several centimeters of the skin exit site. By passing a hemostat alongside the catheter at its exit site, the fixation cuff could be reached and bluntly dissected free. Once this glistening fibrous tissue was sharply detached from the cuff, the catheter became freely mobile. We found stiff, kink-resistant, hydrophilic nitinol guide wires to be much better suited to the exchange process than stiff Teflon-coated wires that tended to kink and bind within the silicone-type catheters. On occasion, when additional stiffness was necessary for exchange, two such wires were used, placing one in each catheter lumen.

One point worth emphasizing is the importance of aspirating the heparin solution from both ports. Typically, each lumen is filled with 5,000 U of heparin after hemodialysis. In cases when no blood was initially aspirable, contrast material injection to study the occluded lumen will deliver this large bolus of heparin to the patient. This unintended anticoagulation can lead to prolonged oozing after the catheter exchange. More preferable is freeing of the fixation cuff and slight withdrawal of the catheter; this often allows aspiration of the luminal heparin. After this step, the catheter study, guide wire introduction, and catheter exchange proceeds.

• Catheter Infection

When studying central venous catheters, two methods of reporting infections have typically been used: infections per catheter and infections per 100 catheter days at risk. We report both of these, in addition to infections developing within the first 30 days after catheter placement or exchange. We believe that infections occurring beyond 30 days, and perhaps even beyond 2 weeks, are unlikely to be related to the method of placement. Rather, these probably reflect the chronic, finite risk of infection carried by all patients with catheters that are accessed for prolonged periods several times a week. We found no difference in infections between de novo and exchanged catheters during this early window. Our infection rates of 14.3% of catheters and 0.14 per 100 catheter days compared favorably to those in other series. Lund et al reported infections in 14.4% of catheters and 0.20 per 100 catheter days (1). Identifying all possible infections (ie, not just those necessitating catheter removal), Trerotola et al report infection in 18.6% of catheters and 0.16 infections per 100 catheter days (6).

Our results suggest that exchanging hemodialysis catheters through pre-existing tunnels carries no increased risk of infection, if performed with the same sterile technique of the initial de novo catheter insertion. This seems to refute the conventional surgical wisdom that a fresh subcutaneous tunnel is an inviolable barrier to infection. In fact, infection rates overall were surprisingly lower with the exchanged catheters, although not significantly different.

• Functional Longevity

Function of the exchanged catheters was not significantly different than that of de novo catheters. The somewhat decreased longevity may be because the exchanged catheters inherit some of the problems that may have led to failure of the initial catheter, such as suboptimal tunnel or a venous stenosis. This is balanced against the relatively simple, rapid, outpatient nature of an over-the-wire catheter exchange. Although we attempted to exit beyond or through the fibrin sheath, we are aware of no data that the sheath will not continue to "grow" and cause failure of the new catheter. In any event, use of that specific venous access site is clearly preserved and extended with each newly exchanged catheter.

Fibrin sheath stripping has been reported as an effective percutaneous method of prolonging catheter function (11). In sharp contrast, we were unable to demonstrate a durable benefit from the same technique (12). On the other hand, functional catheter longevity of exchanged tunneled catheters compares favorably to Crain's report of stripping: 51% versus 45% at 3 months and 87% versus 28% at 6 months. Because femoral vein access is not necessary for exchanges, most patients were discharged immediately after the procedure, eliminating the need for several hours of bedrest and groin observation in the hospital ambulatory care facility.

Although more investigation is necessary to evaluate the optimal management of failing hemodialysis catheters and, in particular, the often culprit fibrin sheath, we have

shown percutaneous exchanges through the tunnel to be safe, offering comparable longevity to new catheters. As such, this technique adds another option to the management of these difficult access patients.

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Fibrin Sheath Stripping versus Catheter Exchange for the Treatment of Failed Tunneled Hemodialysis Catheters: Randomized Clinical Trial[1]

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Index terms: Catheters and catheterization, central venous access • Catheters and catheterization, complications • Dialysis, shunts

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Abbreviations: EX = over-the-wire catheter exchange, PFSS = percutaneous fibrin sheath stripping

PURPOSE: To compare the effectiveness of two treatments for tunneled hemodialysis catheter malfunction: percutaneous fibrin sheath stripping (PFSS) and over-the-wire catheter exchange (EX).

MATERIALS AND METHODS: Adult patients with poorly functioning tunneled hemodialysis catheters (flow rates < 200 mL/min) were randomly assigned to receive either PFSS or EX. Over the course of 20 months, 30 patients (37 encounters) referred to a single institution met the inclusion criteria and consented to participate. PFSS employed transcatheter snares via femoral vein puncture, whereas EX was performed over a guide wire with use of fluoroscopic guidance. Patients were followed up to determine the duration of continued adequate hemodialysis via manipulated catheters for up to 4 months (primary outcome measure).

RESULTS: Overall technical success rate was 97%. Mean catheter patency for the PFSS group was 24.5 ± 29.3 days, and 52.2 ± 43 days for the EX group ($P < .0001$). After EX, patency rates at 1, 2, 3, and 4 months were 71%, 33%, 27%, and 27%, compared to 31%, 16%, 7%, and 0% after PFSS ($P = .04$, logrank test). Exchanged catheters were significantly more likely to be patent for as long as 4 months (23% versus 0%; $P < .05$, χ^2 test).

CONCLUSIONS: Malfunctioning tunneled hemodialysis catheters treated by means of EX are significantly more likely to remain patent for up to 4 months than are those treated by means of PFSS. According to the results of this trial, PFSS should not be performed as a routine therapy for catheter malfunction.

ACCORDING to the United States Renal Data System 1999 annual data report, 79,102 new patients started treatment for end-stage renal disease in 1997 (1). Of those treated with use of hemodialysis, cuffed central venous catheters account for approximately 10%–15% of chronic temporary access (2). While hemodialysis access catheters offer the benefit of "painless" hemodialysis, this is offset by an increased incidence of infection compared with hemodialysis grafts or fistulas, and lower durability. Mean duration of catheter function has been reported to be between 6–12 months, with 1-year probability of patency ranging from 3% to 74% (2–4). Reasons for catheter malfunction include malposition, kinking, thrombosis, and fibrin sheath formation. Of these, malposition and kinking usually are recognized during the first hemodialysis session after placement. Fibrin sheath formation (**Fig 1**) occurs to some extent on all indwelling vascular

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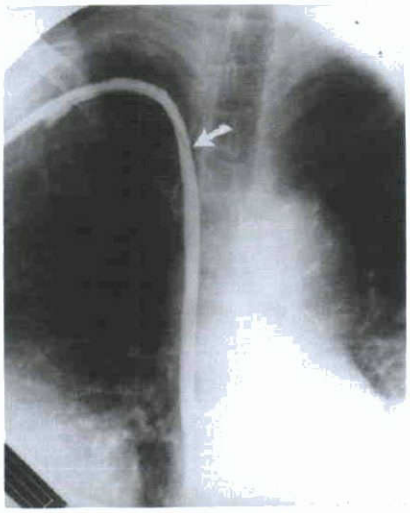

Figure 1. Fibrin sheath. The catheter was withdrawn almost to the venous entry (arrow). Contrast material was injected and outlined the fibrin sheath in the shape of the catheter.

access catheters. Flow limitation due to fibrin sheaths occurs later than malpositon or kinking, and probably accounts for most late failures of tunneled hemodialysis catheters due to decreased flow.

Increasing longevity of the hemodialysis patient requires preservation of vascular access sites. Mechanical means of correcting catheter malfunction, such as percutaneous fibrin sheath stripping (PFSS) (3–8) or over-the-wire catheter exchange (EX) (9,13), are routinely utilized to restore hemodialysis catheters. Because both PFSS (5) and catheter exchange (9) may be performed on a repeated basis, duration of catheter patency provided by each of these interventions is an important indicator of its clinical effectiveness. The reported patency rates after PFSS and EX vary widely. While a single PFSS procedure prolonged catheter life for more than 4 months in one report (7), another found that the catheter function returns to unacceptable level by the fifth hemodialysis treatment (6). However, comparison of the efficacy of EX with PFSS as a routine therapy for malfunctioning tunneled hemodialysis catheters has not been done. We designed a prospective randomized clinical trial to compare efficacy of these alternative treatments.

PATIENTS AND METHODS

• Study Design

The study was designed as a prospective randomized clinical trial to compare two interventional treatments for malfunctioning tunneled hemodialysis catheters. Patients were randomized by a custom computer program designed to maintain balance throughout patient accrual (permuted block design with eight-item blocks). For sample size calculations, we assumed that catheter exchange over a guide wire would result in continuing function for 3 months in 50% (9). To detect a difference in the probability of continuing function in the PFSS group of 30%, with a chance of type I error of 0.05 and 80% power, we would need a sample size of 37 encounters. Sample size estimates were done with a commercially available software program (nQuery; Statistical Solutions, Saugus, MA).

• Patients

Patients were recruited between October 1, 1997, and April 16, 1999. The study was performed at one institution, and approval of the institutional review board for human subjects was obtained. Patients were included in the study when they were referred to the vascular and interventional radiology service because of malfunction of their tunneled hemodialysis catheter (flow <200 mL/min), which had been known to function with acceptable flow rates during hemodialysis previously. Patients who had their catheter newly placed, replaced, or stripped within 72 hours prior to this visit were excluded. Patients were randomized based on the intention to treat malfunctioning catheters; randomization process occurred before the patient was examined by the physician, or underwent chest fluoroscopy.

Seventeen patient encounters randomized for PFSS, and 20 encounters for EX of the catheter. Two patients from the PFSS group subsequently had to have their catheters exchanged, one because the catheter did not extend into the superior vena cava and the second because the cuff was found to be external to the tunnel after randomization. These patients had procedural and follow-up data analyzed with the EX group.

There were 20 women and 10 men, ranging in age from 34 to 87 years (mean, 68.9 years). Four patients had multiple patient encounters included, but not on the same day. One patient was seen four times (two PFSS, two EX), one patient was seen three times (all EX), and two patients were seen twice (one underwent PFSS twice, one underwent EX twice). There were two patients who were randomized to PFSS but who could not be treated with PFSS alone and were crossed-over to EX. In one of these patients, the catheter cuff was noted to be external to the body after randomization, and one other patient had the catheter tip located in the brachiocephalic vein. There were more male patients in the PFSS group than in the EX group (seven of 15 encounters [47%] versus five of 22 encounters [23%]; $P = .15$). The ages of patients analyzed by encounter were also not significantly different (PFSS = 64.3y ± 17.2, EX = 70.8y ± 14.2; $P > .05$).

• Catheters

For 33 encounters, patients presented with 14-F Quinton oval catheters (Quinton Instrument, Seattle, WA); on four occasions, patients presented with Vascath (Vascath, Mississauga, ON, Canada) catheters. For 30 of 37 encounters (81%), the catheter was positioned via right internal jugular vein, four (11%) were in left internal jugular vein (two in each study group), two (5%) were in the right subclavian vein (both in the EX group), and

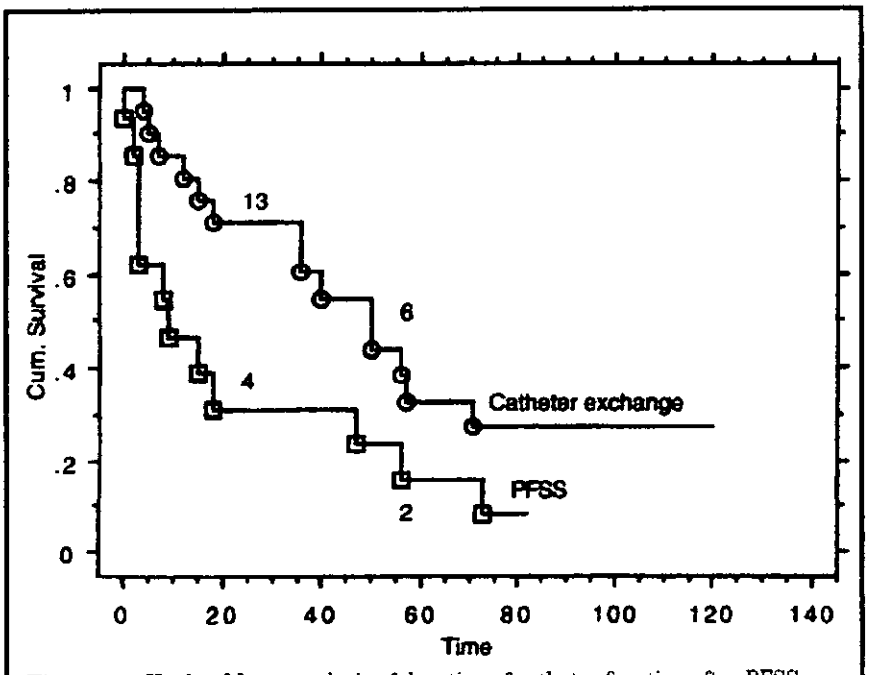

Figure 2. Kaplan-Meyer analysis of duration of catheter function after PFSS or EX. Event times expressed in days.

one (3%) was in the left subclavian vein (PFSS group).

• Description of Procedures

PFSS was performed by means of methods similar to those previously described (5–8). The right common femoral vein was accessed under local anesthesia, and 15- or 25-mm-diameter Amplatz Gooseneck snares (Amplatz; Microvena, White Bear Lake, MN) were used. Hemodialysis catheters were snared (sometimes with the assistance of the guide wire advanced through the venous port of the catheter into the inferior vena cava), and multiple passes were performed to strip the fibrin sheath off the catheter. The distal 10 cm of the catheters were stripped, ensuring that the proximal sidehole was included in the stripping procedure. The procedure was considered completed when adequate aspiration and forward flow through both ports was demonstrated. The snare and its catheter were then removed; hemostasis was achieved by manual compression. The catheter was flushed, filled with indwelling heparin, and dressed. The patient was monitored by the nurse of the radiology recovery unit and discharged after institutional discharge criteria were met.

If the patient was assigned to undergo replacement of the catheter, local anesthetic (lidocaine 2%) was infiltrated along the catheter tunnel. A hydrophilic guide wire (Boston Scientific/Medi-tech, Watertown, MA) was introduced through one of the catheter lumens to preserve access, and blunt dissection was performed to release the cuff. The catheter was removed. In five of 20 patients, a J-tipped guide wire (Cook, Bloomington, IN) (n = 1), a 7-F pig-tail catheter (Cook) (n = 2), or a balloon catheter (6-F Thru-Lumen Fogarty embolectomy catheter; Baxter, Irvine, CA) (n = 2) was used in attempts to disrupt the fibrin sheath. A new hemodialysis catheter of the same brand and size was then inserted over the guide wire and positioned appropriately. Adequate aspiration and forward flow was ensured. The catheter was secured to the skin with use of a nonabsorbable suture, dressed in the usual manner, and filled with indwelling heparin. The patient was monitored by the nurse of the radiology recovery unit and discharged after institutional discharge criteria were met.

• Follow-Up

Patients were followed-up until their catheters stop functioning again, or for 4 months, whichever came first. Follow-up data sheets were delivered to the hemodialysis units and were filled out by the hemodialysis unit nurse. The follow-up consisted of the assessment of the adequacy of hemodialysis treatment during the first treatment after the intervention, and then every month until the catheter ceased functioning, or 4 months passed. Two patients were lost to follow-up (one PFSS and one EX) and one (PFSS) had discrepancies between hospital records and hemodialysis records that could not be reconciled. Follow-up data from this last patient were discarded.

Uniform bills were obtained for each patient encounter when the procedure was performed on an outpatient basis (34 patients). Hospital charges were compared between the PFSS and EX groups.

• Outcome Criteria

Malfunction of the catheter was defined as inability to achieve flow rates of at least 200 mL/minute. When malfunction of the catheter occurred and the patient was referred for another intervention, the date of unsuccessful hemodialysis was noted. Patient follow-up information was confirmed by review of outpatient records, interventional radiology procedure reports, and the department's quality assurance information system (HI-IQ, Society of Cardiovascular and Interventional Radiology, Fairfax, VA).

• Definitions

We considered the procedure a success if at least one hemodialysis treatment could be performed after

the procedure with acceptable flow rates (≥200 mL/min). Complications were defined as adverse clinical events possibly related to the intervention or indwelling catheter that required additional treatment or hospital admission. The patency rate was defined as the duration of adequate catheter function in days.

- **Statistics**

Data were analyzed with use of a commercially available software package (StatView; SAS Institute, Cary, NC). Durability of interventions was plotted with use of Kaplan-Meier analysis; comparison of curves was done with the logrank test. Proportions of patients with continued catheter patency at various time intervals were compared with use of the χ^2 test. Mean catheter patency and mean patient age comparisons between treatment groups was done using Student *t* test. Differences were considered statistically significant at the $P \leq .05$ level.

Summary of Results of Comparison of PFSS and EX for Malfunctioning Dialysis Catheters

	PFSS	EX	*P* Value
Patient Encounters	15	22	NA
Technical Success	94%	100%	NS
Complication Rate	6%	15%	NS
Mean Catheter Life (d)	25	52	<.001
Median Catheter Life (d)	9	40	NA
1-month Patency	31%	93%	<.01
4-month Patency	0	23%	.05
Charge	$3,022	$2,584	<.01

Note.—NA = not applicable; NS = not significant.

RESULTS

Overall technical success rate of procedures for malfunctioning catheters was 97%. The only failure to restore the function of the catheter and provide at least one hemodialysis was in the stripping group (one patient). Mean catheter patency for the stripping group was 24.5 ± 29.3 days, and 52.2 ± 43.0 days for the EX group ($P < .0001$). After revision of a failing catheter, the median durability in the EX group was 40 days, and in the PFSS group median patency was only nine days. Thirteen patients in the PFSS group were followed-up for at least 1 month, nine of whom lost patency in that time. Fourteen patients in the EX group were followed-up for at least 1 month, but only one patient lost patency in that time ($P < .01$). For the EX group, five of 22 patients (23%) went the entire 4-month follow-up period with functioning catheters. In the PFSS group, no patient had a functioning catheter for 4 months ($P = .05$). The longest that a catheter functioned adequately after PFSS was 82 days. Patency rates with use of Kaplan-Meier analysis at 1, 2, 3, and 4 months for EX were 71%, 33%, 27%, and 27%, compared to 31%, 16%, 7%, and 0% after PFSS ($P = .04$, logrank test) (**Fig 2**). Although the number of patients followed-up for the entire 4-month follow-up interval was small, this was mostly due to catheter malfunction, which eliminated patients from their follow-up requirement. The standard error of the EX curve was 0.10 at 4 months, and it was 0.07 at 2 months for PFSS.

There was one complication within 30 days in the PFSS group (6%); a patient who developed groin hematoma and was admitted for observation. The patient, however, did not require further treatment. There were three patients in the EX group who developed complications within 30 days of their procedure (13.6%). The difference in the incidence of complications was not statistically different between treatment groups ($P > .10$). Two of the patients in the EX group developed periprocedural bleeding that required desmopressin acetate administration, one of these patients was admitted for observation, and one patient in the EX group developed a catheter infection that required catheter removal on day 12. A review of our hospital's uniform bills reveals charges for outpatient PFSS in this group of patients was $3,021.65 ± 695.78, and was $2,583.66 ± 798.66 for EX ($P < .01$). Results are summarized in the **Table**.

DISCUSSION

Fibrin sheaths are probably the most common reason for delayed failure of tunneled hemodialysis access catheters. The occurrence of this sheath was first described by Broviac et al in 1973 (10). According to the animal research studies, "fibrin sheath" formation starts at the venous entry site as early as 2–3 days after the catheter implantation, and matures over several weeks (11). Although occasional clinical reports demonstrated the presence of fibrin and platelets as the main components of the sheath in humans, an experimental animal study showed that the sheath starts as red thrombus containing fibrin, which progresses to become vascularized fibrous connective tissue (11).

In 1996, Crain et al (5) and Haskal et al (6) reported their experience with a mechanical method of salvaging the catheters—PFSS with use of a Gooseneck snare. The procedure has been shown to extend catheter life, however, long-term results were rather discouraging. Haskal et al noted that, on average,

after their fifth hemodialysis treatment, patients required another intervention. Crain et al reported that single PFSS has added, on average, 2.8 months to catheter life, with only 28% being patent at 6 months after the procedure. Repeated interventions, on the other hand, resulted in 72% patency at 6 months. More recently, Rockall et al (7) reported that PFSS prolonged catheter life for 4.25 months, however, the success rate of the procedure in that series was only 79%. Johnstone et al (8) claim 100% technical success, but only 75% of their patients were able to undergo at least one hemodialysis treatment after the intervention. The life of the catheter was extended, on average, for 126 days.

Duszak et al, in 1998 (9), reported their experience with replacing failing hemodialysis catheters through the existing tunnel over a guide wire. The authors found no significant difference in the catheter life between those catheters placed primarily compared with those placed through a preexisting tunnel. The patency rate of the replaced catheters was 37% after 6 months. The authors addressed the issue of the "fibrin sheath" by placing the new catheter deeper, or with use of a longer catheter than the one being replaced. The important finding of this study was the fact that there was no increased incidence of tunnel or catheter infection after replacement of the catheter over the wire. The safety of the replacement of the catheter through the preexisting tunnel was further demonstrated by Egglin et al (12) in their series of accidentally removed catheters. Garofalo et al recently reported 42% primary patency at 60 days and 16% at 120 days after replacement of the catheters over the wire (13).

We observed considerably lower patency for PFSS than described in previous reports (5,7,8), but our observations were fairly similar to those described by Haskal (6). The explanation for the variability in published and observed durability of PFSS is not obvious. Although one may consider that we did not perform PFSS properly, this is refuted by the fact that we used standard technique and had lower immediate failure rate; that is, we were able to restore adequate flow (≥200 mL/min) for at least one hemodialysis session in all patients except one.

Attempts to compare the two approaches used to revise malfunctioning hemodialysis catheters with use of existing literature was difficult, if not impossible. Differences in technique, catheter type, and reporting standards have led to great variability in reported results. Our study uses randomization to reduce patient selection bias. Although the number of patients in this series is small, we were able to demonstrate a large and statistically significant difference in durability of the interventional treatment alternatives favoring catheter exchange. Catheter exchange is also less expensive. A review of our hospital's uniform bills forms reveals charges for outpatient PFSS in this group of patients was \$3,021.65 ± 695.78, and \$2,583.66 ± 798.66 for EX ($P < .01$). The hospital charge may not be representative of the true cost of the procedure; however, within a single cost center of a single institution this comparison probably indicates real difference.

The ease of the hemodialysis catheter exchange over the wire may suggest that the procedure may be performed at the bedside in the hemodialysis center without the use of fluoroscopic guidance. This may eliminate the need to utilize costly interventional radiology facilities. Further investigation in this direction may prove beneficial.

The study has some limitations. We evaluated only primary catheter patency after the single intervention. It seems intuitive that the repeated interventions would accumulate the benefit of the EX versus PFSS. However, long-term outcome study may be necessary to confirm this assumption.

In summary, catheter exchange of malfunctioning tunneled hemodialysis catheters over a guide wire should be the standard interventional treatment for this condition. Based on the results of this study, routine performance of PFSS for failing tunneled hemodialysis catheters should not be done.

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Exchange of Poorly Functioning Tunneled Permanent Hemodialysis Catheters

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OBJECTIVE. The usefulness of exchanging poorly functioning tunneled permanent hemodialysis catheters in patients with end-stage renal disease was evaluated.

MATERIALS AND METHODS. We retrospectively reviewed case histories of 51 consecutive patients who underwent 88 catheter exchanges because of poor flow rates. All hemodialysis catheters were initially placed by the radiology service using image guidance. Catheter exchanges were performed through the existing subcutaneous tract over two stiff hydrophilic guidewires and without additional interventions such as fibrin sheath stripping or venoplasty. Life table analysis was performed to evaluate catheter patency rates after initial placement (primary patency) and after multiple exchanges (secondary patency).

RESULTS. The technical success rate for hemodialysis catheter exchange was 100%. Primary catheter patency was 42% at 60 days and 16% at 120 days. Secondary patency was 92% at 60 days and 82% at 120 days. The cumulative infection rate was 1.1 per 1000 catheter days. No complications from the procedure occurred.

CONCLUSION. Catheter exchange is an effective means of prolonging catheter patency in patients with end-stage renal disease and limited central venous access.

Maintaining uninterrupted vascular access for hemodialysis is of critical importance in the treatment of patients with end-stage renal disease. Although surgically placed Brescia-Cimino forearm fistulas and synthetic arteriovenous grafts are well-established routes for peripheral hemodialysis, they have a limited life expectancy. The mean patency of forearm fistulas is 34 months versus 20 months for arteriovenous grafts [1]. Once use of an arteriovenous graft or fistula is no longer possible, placement of central venous catheters for hemodialysis becomes a valuable option in maintaining vascular access for hemodialysis. Furthermore, central venous catheters may serve as a bridge to renal transplantation or creation and maturation of native fistulas and synthetic grafts.

The management of poorly functioning hemodialysis catheters is important. Complications resulting in catheter malfunction include fibrin sheath formation, catheter tip migration, catheter leak, constricting suture, and abutment of the catheter tip against the vein wall [2]. An alternative to de novo placement of tunneled catheters for malfunctioning hemodialysis catheters is attractive because future venous access sites are preserved and the potential complications associated with initial placement are avoided. A variety of techniques has been developed to address the problem of catheter malfunction, such as fibrin sleeve stripping [3], exchange over a guidewire [4, 5], and local or systemic lytic therapy [6]. We conducted a retrospective review to determine the usefulness of exchanging malfunctioning catheters through the same subcutaneous tract.

Materials and Methods

Patients with poorly functioning hemodialysis catheters were referred to the interventional radiology service. All catheters had been originally placed in the radiology department. Catheter malfunction was defined as inability to aspirate from each lumen or failure to maintain a minimum blood flow rate of 200 ml/min. Initial catheter evaluation was performed by a nephrology fellow in the dialysis unit. After eliminating obvious causes of catheter malfunction such as kinking or pinching, local fibrinolytic therapy was used with intracatheter urokinase (5000 IU/ml) (Abbokinase Open Cath; Abbott Laboratories, North Chicago, IL). This method is typically 80–90% successful at restoring flow in occluded catheters [7]. When these methods failed, the patient was referred to the interventional radiology service for catheter exchange.

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Patients and Catheters

From November 1995 to February 1997, 51 consecutive patients (32 women and 19 men; age range, 19–89 years old; mean age, 48 years) underwent 88 catheter exchanges for catheter malfunction. The permanent tunneled central venous catheters used at our institution include the Hickman hemodi: .ysis catheter (Bard Access Systems, Salt Lake City, UT) and the Permcath (Quinton Instruments, Bothell, WA). The preferred initial site for catheter placement was the right internal jugular vein. If thrombosis or stenosis occurred or if a right upper extremity graft was planned, the left internal jugular vein was used.

Technique

Initial placement of tunneled hemodialysis catheters was performed by the radiology service as described by Trerotola et al. [8]. Patients presenting for catheter exchange were monitored with pulse oximetry, blood pressure cuffs, and electrocardiographic recordings. The catheter entry site, ipsilateral chest, and neck were scrubbed with antiseptic soap and draped. The skin surrounding the proximal portion of the subcutaneous tunnel was anesthetized with 1% lidocaine. One gram of ceftizoxime sodium (Cefizox; Fujisawa Pharmaceutical, Deerfield, IL) was routinely administered IV to all patients 1 hr before the procedure unless the patient was already receiving antibiotic therapy or had a documented allergy to this antibiotic. In cases of allergy, vancomycin (Lederle Laboratories, Wayne, NJ) was used. Conscious sedation, when deemed necessary, was achieved with fentanyl citrate (Sublimaze; Abbott Laboratories) and midazolam hydrochloride (Versed; Hoffmann-La Roche, Nutley, NJ). The retention suture was removed and the indwelling heparin was aspirated from each lumen if possible.

Catheter exchange was performed according to a previously described method [5]. Briefly, one or two stiff hydrophilically coated angled-tip 0.035-inch guidewires (Glidewire; Medi-tech, Watertown, MA) were advanced through each port and then into the inferior vena cava. Two guidewires provided slightly better intravascular purchase. The catheter was withdrawn over the guidewires with moderate initial resistance that was attributed to the retention cuff. If the cuff was well incorporated into the subcutaneous tissue, the cuff was carefully dissected and cut away from the fibrous tissue and then carefully removed along with the catheter. A separate cutdown procedure was not needed in any of our procedures because all cuffs were placed approximately 2 cm from the incision site by the radiology service. The catheter was removed. Back tension on the guidewires was provided as a new catheter was advanced over the guidewires through the subcutaneous tract into the central venous system. The hemodialysis catheter was advanced under fluoroscopic guidance to ensure appropriate final positioning in either the distal superior vena cava or the proximal right atrium. The catheter was secured to the skin at the entrance site with 0 Ethibond (Ethicon, Somerville, NJ).

Catheter function was confirmed by rapid blood return from each lumen with aspiration using a 10-ml syringe. If brisk blood return was not achieved, catheter position was altered by either advancing or withdrawing the catheter slightly over the two hydrophilically coated guidewires. After confirming catheter function, 1.5 ml of heparin (1000 U/ml) was instilled into each port. The routine dose of 1.5 ml of heparin (5000 U/ml) was not used because intermixing with blood prolongs bleeding from the catheter entry site. In addition, many of these patients went directly to dialysis and received standard heparin after their hemodialysis treatment. IV contrast material was not uniformly used because detection of an incidental thrombus or a fibrin sheath would not have altered our protocol.

Fibrin sheath stripping of the catheter tip or venoplasty was not used during the period of this study.

Statistical Analysis

Kaplan-Meier life table analysis was performed to determine primary and secondary catheter patency rates. Catheter primary patency was defined as the time from initial placement to failure to achieve adequate blood flow rates for hemodialysis. The primary patency after a single catheter exchange procedure was defined as the patency of the catheter after a single catheter exchange procedure. Catheter secondary patency was defined as duration of function irrespective of the number of catheter exchanges. The end point for catheter secondary patency was catheter removal because of low blood flow rates or infection. Infection was defined as fever and positive findings on blood culture. Technical success was achieved if catheter exchange was accomplished and adequate blood flow rates were present at the first hemodialysis session.

Follow-up was available using nephrology and radiology medical records in 50 of 51 patients. Total follow-up was 9632 catheter days.

Results

Fifty-one patients underwent permanent tunneled hemodialysis catheter exchange through the same subcutaneous tract. Thirty-one patients had one exchange, 11 patients had two exchanges, four had three exchanges, three had four exchanges, one had five exchanges, and one had six exchanges. One patient was lost to follow-up. Three patients had left internal jugular catheters, and the remainder had right internal jugular catheters. All catheter exchanges were technically successful (Fig. 1). The pri-

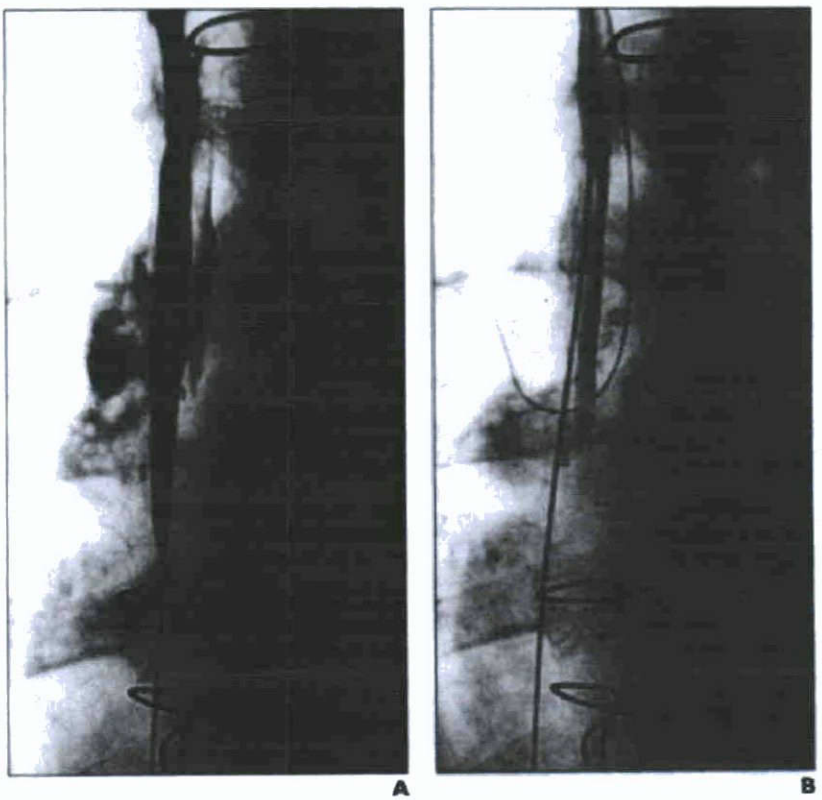

Fig. 1.—73-year-old man requiring catheter exchange because of poor catheter flow.
A, Digital radiograph shows contrast tracking around catheter after infusion of contrast material, which indicates presence of large fibrin sheath.
B, Digital radiograph shows guidewires that have been advanced through hemodialysis catheter and exiting from sides of fibrin sheath.

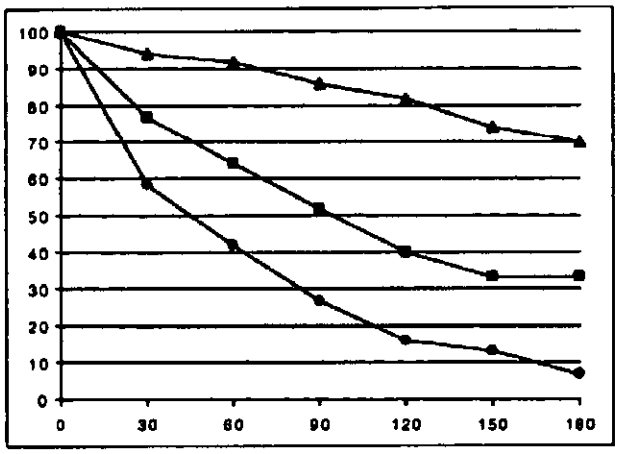

Fig. 2.—Graph of life table analysis. Primary patency (●) was defined as time from initial placement to failure to achieve adequate blood flow rates for hemodialysis. Patency after single catheter exchange (■) procedure was defined as duration of catheter function after single catheter exchange procedure. Secondary patency (▲) was defined as duration of function irrespective of number of catheter exchanges.

mary catheter patency was 42% at 60 days and 16% at 120 days (Fig. 2). The primary patency after a single catheter exchange procedure was 64% at 60 days and 40% at 120 days. The secondary catheter patency was 92% at 60 days and 82% at 120 days.

Five catheters were removed because of infection, with an infection rate requiring catheter removal of 0.52 per 1000 catheter days. In each of these cases, the catheter was removed because the patients' bacteremia did not resolve with antibiotics. All cases of bacteremia were caused by *Staphylococcus aureus*. Six additional patients had episodes of bacteremia that responded to antibiotics and the catheters were not removed. The cumulative infection rate was 1.1 per 1000 catheter days.

Five patient deaths were attributed to stroke, pneumonia, pulmonary edema, emphysematous cholecystitis, and septic shock. The death resulting from septic shock was likely related to long-standing central venous catheterization, and initial signs of infection were evident 27 days after catheter exchange. No episodes of symptomatic upper extremity venous thrombosis or of superior vena cava occlusion occurred during our study.

Four patients had catheters placed in the left internal jugular vein after repeated episodes of malfunction of the right internal jugular vein catheter. This placement was done at the request of the clinical service when each subsequent catheter exchange provided progressively shorter periods of catheter function.

Discussion

Preservation of long-term central venous access sites is of vital importance in the patient population dependent on life-long hemodialysis. Our initial choice for tunneled hemodialysis catheter placement is the right internal jugular vein [9] because it has been well documented that subclavian vein access results in a higher incidence of stenosis [10] and thrombosis. In patients with catheter malfunction who are unresponsive to local fibrinolytic therapy, we prefer to exchange the tunneled catheters through the same tract—a practice that preserves each site for as long as possible before using other locations such as the left internal jugular vein, subclavian veins, or femoral veins or resorting to other techniques such as recanalization of occluded veins [11]. Exchanging tunneled subclavian catheters by making an infraclavicular incision to localize the catheter and changing the catheter through the incision over a guidewire have been described [4, 12–14]. The technique we use does not require an incision [5].

Tunneled hemodialysis catheter exchange through the same subcutaneous tract is a safe and effective method of managing catheter malfunction. Inherent mechanical problems such as catheter leak or constricting suture are solved by catheter replacement. Catheter exchange is performed under fluoroscopic guidance to ensure proper tip position. We believe that fibrin sheath formation around the catheter is also addressed with this technique. Fibrin sheath formation has been shown to occur within 24 hr of catheter placement and is thought to be a consequence of intimal injury. The injury takes place where the catheter enters the vessel wall and where the tip of the catheter is in contact with the vessel wall. Consequently, during fibrin sheath formation there is both antegrade and retrograde propagation around the catheter [15], which is a significant cause of catheter malfunction and accounted for 57% of cases of catheter malfunction as described by Cassidy et al. [2].

It is our hypothesis that during catheter exchange, the guidewires pass outside of the fibrin sheath and that during catheter replacement, the fibrin sheath is at least partially disrupted as the catheter tracks along the guidewires. Venography before catheter removal showing a fibrin sheath and venography after catheter exchange often showing minimal residual fibrin sheath support this presumption. Percutaneous fibrin sheath stripping with a snare from a femoral venous approach has been described by Knelson et al. [16] and by Crain et al [3]. This technique requires an additional percutaneous venous puncture, and Haskal et al. [17] found that this technique provides no durable benefit in improving function of failing hemodialysis catheters. Embolization of fibrin sleeve fragments has been reported [15] and undoubtedly occurs in catheter exchange and in percutaneous fibrin sleeve stripping. Currently, in patients who have undergone multiple catheter exchanges, we do use venography and venoplasty with angioplasty and occlusion balloons. However, these patients are still in the minority of our patients undergoing catheter exchange.

We routinely used antibiotics for all procedures on dialysis patients at the request of the nephrology service. Antibiotics are used prophylactically for catheter exchanges and for the initial catheter placement. Antibiotic prophylaxis has been shown to be beneficial in peritoneal dialysis catheter placement and in catheter placement of pediatric central venous catheters [18, 19]. We believe that antibiotic use for catheter exchanges is beneficial because catheter exchange is, theoretically at least, a less sterile procedure.

We did not perform catheter exchange in patients with signs or symptoms of infection. Patients who developed infections necessitating catheter removal after initial catheter placement, but before a catheter exchange procedure had been performed, were eliminated from the study. Our cumulative infection rate is identical to the infection rate of 1.1 infections per 1000 catheter days reported by Duszak et al. [5] for patients who underwent catheter exchange. This infection rate compares favorably with that described by Trerotola et al. [8] of 2.2 per 1000 catheter days in patients who had de novo placement of an internal jugular vein tunneled hemodialysis catheter. Our infection rate for de

novo catheter placement during the study period was 1.2 infections per 1000 catheter days, which is nearly identical to our infection rate for catheter exchanges. De novo catheter placement, presumably in a sterile field, requires two incisions, each site potentially allowing entry of bacteria. Catheter exchange does not create any new incisions, although the original entry site is likely not sterile, despite cleansing with povidone-iodine (Betadine; Purdue Frederick, Norwalk, CT). Regardless of the mechanism, we hope that our study, together with the study by Duszak et al., will help alleviate the unfounded fears of increased infection expressed in the literature for catheter exchange [20].

Duszak et al. [5] found that percutaneous exchanges through the subcutaneous tunnel offered comparable longevity to new percutaneously introduced catheters. Our assisted primary patency of 52% at 90 days and 33% at 180 days is similar to their rates of 51% at 3 months and 37% at 6 months. However, our primary patency rate for de novo placement of 42% at 3 months and 16% at 6 months is lower than their rate of 63% at 3 months and 51% at 6 months. Our primary patency rate is low because we intentionally excluded all patients with tunneled catheters that had not yet malfunctioned. It is interesting to note that patients who had catheter malfunction after de novo placement actually had a longer duration of catheter function after exchange when compared with initial placement. Our secondary patency rates were 92% at 60 days and 82% at 120 days, indicating that the duration of catheter-mediated hemodialysis at the same venous access site can be prolonged considerably by catheter exchange without increasing the risk of infection compared with de novo placement.

We preferred to perform catheter exchange of the right internal jugular vein rather than switch to the left side even if the most recent catheter exchange did not give a good long-term patency. Each catheter exchange allows placement of the catheter tip in a slightly different location, which may give good long-term function even if the preceding catheter exchange did not. Alternatively, a different catheter, Hickman hemodialysis catheter versus Permcath, for each subsequent procedure was also used. In general, we preferred to exhaust all possibilities before changing locations, even if it meant several repeated procedures within 1 week. A specific clinical end point was not established. However, in four patients, the clinical service requested that the site be changed to the left internal jugular vein because each exchange procedure was giving progressively shorter patencies.

Exchange of malfunctioning tunneled permanent hemodialysis catheters through the same subcutaneous tract is a technically uncomplicated procedure that is well tolerated, has a low infection rate, and in our series of patients was without complications. It is an effective alternative to other methods of catheter salvage that have been described and is a valuable technique in the preservation of vascular access.

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Outcome of Tunneled Hemodialysis Catheters Placed via the Right Internal Jugular Vein by Interventional Radiologists[1]

PURPOSE: To assess the outcome of interventional radiologic placement of tunneled hemodialysis catheters via the right internal jugular vein.

MATERIALS AND METHODS: In 194 patients, the catheter was placed via the right internal jugular vein unless thrombosis was present. Real-time ultrasound-guided puncture and fluoroscopic guidance were used. Patients were followed up until catheter removal or death. Outcomes evaluated included infection, thrombosis, and catheter malfunction.

RESULTS: In 175 patients, 250 consecutive catheters were placed via the right internal jugular vein with 100% success. All catheters functioned immediately after placement. Procedural complications were limited to clinically unimportant air embolus ($n = 2$). No instances of pneumothorax, hemothorax, or substantial bleeding complications occurred. Follow-up was available in 173 (99%) patients. Mean and median "catheter duration" were 87 and 56 days, respectively. Catheter-related symptomatic venous thrombosis or stenosis was not observed. The rate of infection was 0.08 per 100 catheter days, and the rate of malfunction that necessitated removal was 0.22 per 100 catheter days. Definite or possible catheter thrombosis that necessitated removal occurred at a rate of 0.16 per 100 catheter days.

CONCLUSION: Interventional radiologic placement of tunneled hemodialysis catheters via the right internal jugular vein showed equal or better long-term results than those reported for surgical placement. Interventional radiologic placement should be the method of choice.

PLACEMENT of tunneled hemodialysis catheters, whether as temporary or permanent access, is frequently necessary in patients undergoing hemodialysis. Traditionally, tunneled catheters were placed in the operating room by surgeons, but interventional radiologists have recently challenged this traditional approach with excellent results (1,2). The largest series to date in which placement of hemodialysis catheters by radiologists was assessed involved almost exclusively subclavian vein catheterization (1). However, there has been a growing trend toward primary use of the right internal jugular vein for catheter access for hemodialysis due to the recognition that access via the subclavian route may result in central venous stenosis in this patient population (3–7).

The purpose of our study was to determine the outcome of placement of tunneled hemodialysis catheters via the right internal jugular vein by interventional radiologists.

MATERIALS AND METHODS

From September 1993 to May 1996, 194 patients (124 men, 70 women) were referred to the Department of Interventional Radiology for placement of 299 tunneled hemodialysis catheters. According to our policy, the right internal jugular vein was the access of choice if it was patent at ultrasound (US) performed in the interventional radiology suite. If the vein was not patent, another site was chosen on the basis of a number of factors including previous permanent access (graft, fistula), existing or planned permanent access, and available vessels. In those patients in whom the right internal jugular vein was not patent, eight catheters were placed via the left internal jugular vein, 12 via the left subclavian vein, six via the right subclavian vein, five via the right external jugular vein, one via the supraclavicular right subclavian route, and 17 via the translumbar inferior vena cava.

One hundred seventy-five patients met the criterion of having a patent right internal jugular vein; 250 catheters were placed via the right internal jugular vein in these patients. During the study period, 126 patients received one catheter, 33 patients received two catheters, 12 patients received three catheters, two patients received four catheters, one patient received six catheters, and one patient received eight catheters.

Data regarding the catheters were collected prospectively as part of our section's quality assurance program. These data included catheter type, localization method, initial complications, late complications, length of time the catheter was in place, and reason for catheter removal. Follow-up was performed through August 1996.

The primary catheter used in the study was the 13.5-F silicone dual lumen (Davol; Bard Access, Salt Lake City, Utah). A total of 165 catheters of this type were placed: 96 catheters measured 36 cm (19 cm tip to cuff), and 69 catheters measured 40 cm (23 cm tip to cuff). In addition to this type of catheter, 81 12.5-F silicone dual-lumen catheters (Medcomp, Harleysville, Pa; 22 cm tip to cuff), one dual 10-F silicone catheter set (Tesio; Medcomp), and three 11.5-F polyurethane dual-lumen catheters (Vas-

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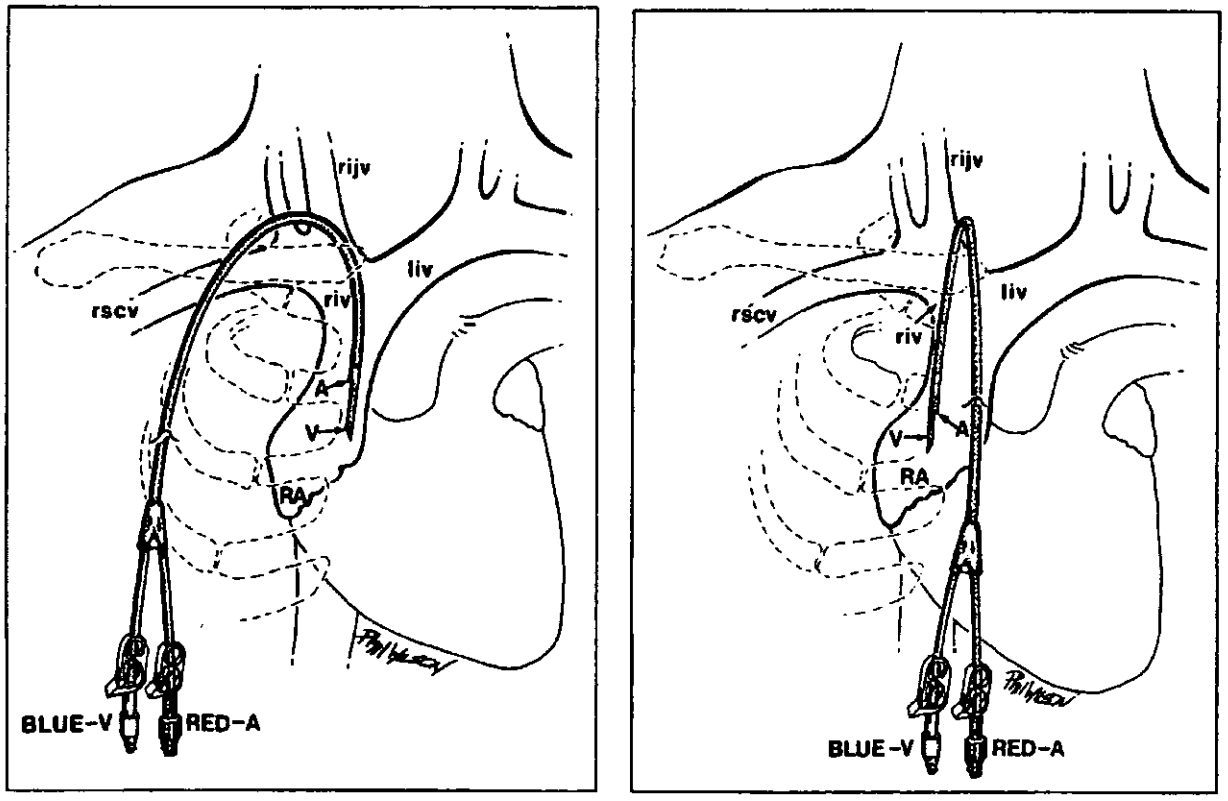


1. 2.

Figures 1, 2. *liv* = left innominate vein, *RA* = right atrium, *rijv* = right internal jugular vein, *riv* = right innominate vein, *rscv* = right subclavian vein. Diagrams show optimal tip orientation for catheters with (1) laterally oriented and (2) parasternal tunnels. (1) The catheter curve directs the tip against the medial wall of the junction between the superior vena cava and the right atrium. By orienting the venous (*BLUE-V, V*) lumen medially (ie, along the cephalic aspect of the curve), flow is optimized by allowing the arterial (*RED-A, A*) lumen to aspirate freely. (2) The catheter tends to lie against the lateral wall of the superior vena caval–right atrial junction. To allow the arterial (*RED-A, A*) lumen to aspirate freely, the venous (*BLUE-V, V*) lumen should be oriented laterally with this type of tunnel.

Cath, Bard Access; 19 cm tip to cuff) were placed.

Patient preparation consisted of correction of the platelet count to 50,000/mm³ or greater and the prothrombin time international normalization ratio to 1.3 or less when necessary. Prophylactic antibiotics were not administered. Conscious sedation was achieved with midazolam hydrochloride (Versed; Hoffmann-LaRoche, Nutley, NJ) and fentanyl citrate (Abbott Laboratories, North Chicago, Ill) as needed.

Catheter placement was similar to that described previously (1,2) for a right internal jugular vein approach. All personnel in the room, as well as the patient, wore a cap and mask. The operating interventional radiologists performed a complete surgical scrub before they donned surgical gowns and gloves. The right side of the neck and upper chest of the patient was cleansed with a chlorhexidine gluconate solution (Hibiclens; Zeneca Pharmaceuticals, Wilmington, Del) followed by povidone-iodine (Betadine; Purdue Frederick, Norwalk, Conn). A 7.5-MHz US transducer (128; Acuson, Mountain View, Calif) was covered with a sterile drape (Surgi; Civco, Kalona, Iowa) and used to localize the right internal jugular vein. After administration of a local anesthetic, real-time US-guided puncture of the right internal jugular vein was performed just cephalad to the clavicle with a 21-gauge needle (Micropuncture; Cook, Bloomington, Ind). After successful puncture, the 0.018-inch wire from the Micropuncture set was introduced and the dilator set passed over it. The wire was then used to mark the caval-atrial junction during full inspiration, bent at the hub, and set aside. The inner dilator was removed and a 0.035-inch wire placed into the superior vena cava. A flow switch (Medi-tech/Boston Scientific, Natick, Mass) was used to lock the wire to the dilator. Then, depending on the body habitus, a catheter of appropriate length was chosen.

By using the bent 0.018-inch wire as a guide, the desired length of subcutaneous tunnel could be determined by holding the wire against the catheter. The tunnel was created in a right parasternal or right upper chest location, depending on patient body habitus (parasternal tunnels for obese and large-breasted individuals), as well as operator preference. After the catheter was tunneled, the venotomy was sequentially dilated and the appropriate peel-away sheath (usually from the catheter kit) was placed into the superior vena cava. The catheter was passed through the peel-away sheath as quickly as possible to avoid air emboli. The Trendelenburg position was not used, as our angiographic tables cannot be placed in this position. Air emboli were minimized by pinching the peel-away sheath and/or instructing the patient to hum to increase intrathoracic pressure. The catheter tip was positioned spanning the caval-atrial junction during deep inspiration. The lumina were oriented differently depending on the position of the tunnel. For tunnels angled across the right upper chest, it was preferable to orient the venous lumen medially (Fig 1). For right parasternal tunnels, we found optimal flows were achieved with the arterial lumen oriented medially (Fig 2). Tip position was adjusted in individual patients to allow the best flow possible.

After the procedure, tip position was checked with an erect anteroposterior chest radiograph. The patient usually underwent hemodialysis immediately after the procedure. Catheter placement was performed as an outpatient procedure unless the patient was already hospitalized for another reason.

Catheter exchange was performed by means of a small incision made near the venous entry site of the catheter, dissecting the catheter free and transecting it to

Status of Catheters and Complications at Follow-up

Status and Complications	No. of Catheters
Functioning catheter	14
Functioning catheter at death	24
Lost to follow-up	3
Electively removed (n = 145)	
Mature permanent access	85
Converted to continuous ambulatory peritoneal hemodialysis	37
Patient recovered	9
Fever, culture negative	8
Patient refused hemodialysis	3
Allergy to catheter	1
Transplantation	1
Planned ipsilateral access	1
Removed for malfunction (n = 47)	
Low flow	23
Refractory clot or sheath	11
Dislodged	5
Too far in	2
Broken catheter	3
Kink	3
Removed for infection (n = 17)	
Bacteremia	9
Exit site	7
Tunnel	1
Total	250

allow passage of a guide wire into the superior vena cava. The catheter was removed and replaced with a hemostatic sheath through which venography was performed. Any remaining fibrin sheath was disrupted mechanically with an angled catheter and/or guide wire; this procedure was uniformly effective. The hemostatic sheath was then replaced with the peel-away sheath from the catheter set, and a new catheter was placed with creation of a new tunnel.

Definitions

Technical success was defined as establishment of access via the chosen vein (right internal jugular vein) satisfactory for hemodialysis. Initial catheter failure was defined as the inability to perform hemodialysis adequately despite successful catheter placement. Late failure was defined as the inability to achieve satisfactory flow rates for hemodialysis after the initial session regardless of the reason (thrombosis, mechanical problem, catheter dislodged) and resultant catheter removal. Primary catheter function (patency) ended when any intervention was performed to alleviate malfunction (eg, repositioning) or, if no such intervention was performed, when the catheter was removed. Secondary catheter function (patency) ended when the catheter was removed. Infection of the exit site was defined as a localized infection within 2 cm of the exit site. Tunnel infection was defined as localized infection more than 2 cm from the exit site. Catheter-related bacteremia was defined as positive blood cultures, even if catheter-tip cultures were subsequently negative. If catheters were removed for fever only but the catheter-tip culture was negative, this was not considered an infection.

Catheter Management

Catheter care was performed by nurses in the hemodialysis unit, with dressing changes at each hemodialysis session. Catheters were dressed with a nonocclusive dressing and povidone-iodine ointment. Exit-site and tunnel infections were cultured and treated with intravenous administration of 1.0–1.5 g vancomycin hydrochloride (Eli Lilly, Indianapolis, Ind); if the infection failed to improve after 48 hours, the catheter was removed. Persistent bacteremia was treated by means of catheter removal. Catheter malfunction was treated initially with low-dose urokinase (Open-Cath; Abbott Laboratories), 5,000 U per lumen with a 30-minute dwell. If this treatment was unsuccessful, a chest radiograph was obtained to ensure the catheter was well positioned. If the catheter was found to be positioned correctly, a contrast material–enhanced study was performed in the interventional radiology department. If a fibrin sheath was documented, urokinase infusion was performed in the hemodialysis unit, with 20,000 U/h through each lumen for a 6-hour infusion (total dose, 240,000 U). If treatment was successful, no further study or intervention was performed. If treatment was unsuccessful, the catheter was exchanged for a new catheter, and a new tunnel was created. Creation of a new tunnel rather than over-the-wire exchange is based on our belief that the existing tunnel may be colonized with bacteria, thus potentially increasing the risk of infection. Fibrin sheath stripping was not performed.

Statistical Analysis

All survival curves were estimated with the Kaplan-Meier method (8). Survival curves were generated for overall catheter "survival," infection, and malfunction. Since some episodes of catheter malfunction were corrected by means of repositioning the catheter or thrombolysis without catheter removal, primary and secondary survival curves were generated for malfunction and overall survival. Differences were considered statistically significant if the P value was less than .05.

RESULTS

Catheter placement was successful in all patients. One patient (who was combative) interrupted the procedure; placement was repeated the next day without incident. Thus, the technical success rate was 99.6% for the first attempt. Furthermore, of the 299 catheters requested during the study period, satisfactory catheter access for hemodialysis was achieved in 100%. All catheters functioned adequately immediately after placement (0% initial failure rate).

Immediate complications of catheter placement were limited to two clinically silent air emboli. These emboli were recognized at fluoroscopy but necessitated no treatment. Local bleeding at the exit site that responded to compression and did not necessitate further therapy was not considered a complication; this type of mild oozing of blood is relatively common in these patients because of poor platelet function. No instances of pneumothorax, hemothorax, hemomediastinum, or vascular perforation occurred.

In our study population, there were 21,572 catheter days, with catheters in place for a mean of 87 days (range, 2–643 days; median, 56 days). At final follow-up, 14 catheters were still in place, and 24 patients had died with functional catheters. Reasons for catheter removal are listed in the Table. Follow-up was achieved in 173 (99%) patients. Catheter survival curves are shown in Figures 3–7. Probability of catheter survival (secondary) was 85% at 30 days, 64% at 180 days, and 50% at 1 year. Primary catheter survival differed little: 81% at 30 days, 62% at 180 days, and 48% at 1 year. Probability of freedom from infection was 95% at 30 days, 92% at 180 days, and 74% at 1 year.

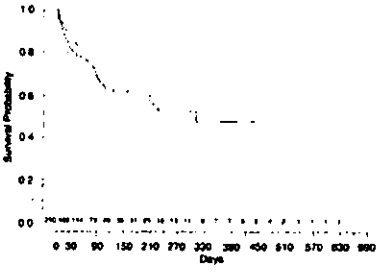
Late complications included 17 (6.8%) infections that necessitated catheter removal, or 0.08 per 100 catheter days, and 17 infections that did not necessitate removal. Many of the latter cases were not clearly documented as catheter infections; the patients may have had other potential sources of infection but were treated empirically as having catheter infections. Five of these cases were well-documented exit-site infections treated successfully with antibiotics. In the remaining 12 patients, single positive cultures from blood samples obtained through the catheter prompted antibiotic treatment, but cultures from repeat tests were sterile. Whether these episodes were truly catheter-related bacteremia is unclear, as they generally resolved completely with a single dose of antibiotics. Mean time to development of infection was 67 days (range, 4–310 days). Four infections developed within the 1st week.

There were 47 (18.8%) episodes of catheter malfunction that necessitated removal, or 0.22 per 100 catheter days. Catheter malfunctions that necessitated removal included poor flow with-

out obvious cause (n = 23), fibrin sheaths refractory to thrombolysis (n = 11), dislodged catheter (n = 5), catheter too far in (after the patient lost fluid weight while receiving hemodialysis [n = 2]), catheter breakage (n = 3), and kinks in the catheter (n = 3). Thus, of the catheter failures, 34 were definitely or possibly related to thrombosis (0.16 per 100 catheter days). Symptomatic central venous stenosis or thrombosis was not observed in any patients during the study period.

Sixteen episodes of catheter malfunction occurred in which removal was not necessary. These included two kinks and six episodes of poor flow relieved by means of catheter repositioning, two catheter breakages repaired with the manufacturer's repair kit (Bard), and six fibrin sheaths successfully treated with urokinase infusion.

Urokinase infusion as described previously for thrombosis refractory to low-dose urokinase was attempted in 11 catheters, with restoration of catheter function in six catheters (55% success rate). No complications occurred related to the infusion. Duration of patency after successful infusion was 8–70 days (mean, 31 days ± 22).



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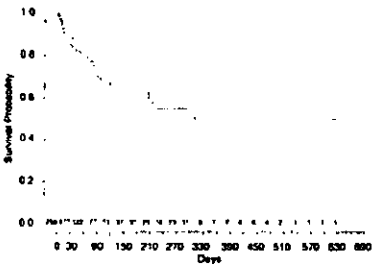

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Figures 3, 4. Survival curves show probability of overall (3) primary and (4) secondary catheter function. Numbers of catheters at risk are shown above the x axis. Dotted lines show the 95% confidence interval.

DISCUSSION

Percutaneous placement of tunneled hemodialysis catheters is an integral part of care of the patient undergoing hemodialysis. Whether as temporary access during maturation of more permanent access such as a native fistula or graft, as a bridge to transplantation or continuous ambulatory peritoneal hemodialysis, or as permanent access, these catheters are an invaluable adjunct to the practicing nephrologist. There has been a growing trend toward nonsurgical placement of such catheters at the bedside (9) or in the interventional radiology suite (1,2).

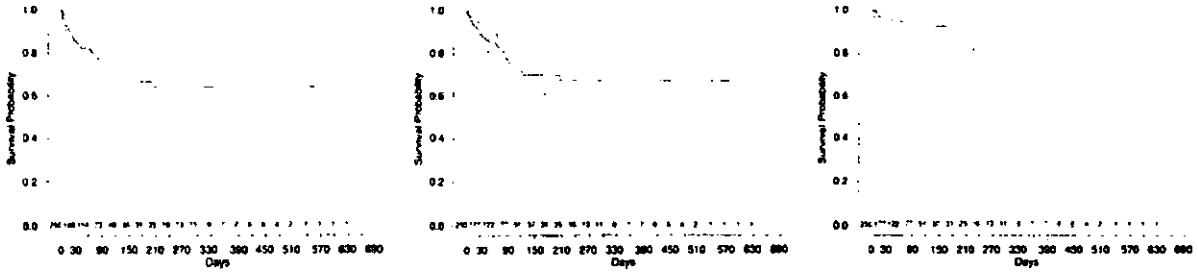
Concerns that such approaches might yield an increase in complication rates, particularly infection rates, have proved unfounded. Lund et al (1), in a large series of patients, showed that excellent outcomes could be achieved with interventional radiologic placement of tunneled subclavian hemodialysis catheters. In that study of 236 catheters in 190 patients, the investigators reported an infection rate of 0.20 episodes per 100 catheter days; the rate of infection that necessitated removal was 0.15 per 100 catheter days. The overall catheter failure rate was 0.81 per 100 catheter days, with 28% of catheters removed because of failure. The technical complication rate was extremely low, limited primarily to pneumothorax (2.5%). Other investigators who assessed percutaneous catheter placement outside the operating room have achieved similar results (9).

However, there is a growing recognition that the subclavian approach for hemodialysis catheter placement should be avoided due to the risk of central venous stenosis. In studies of nontunneled catheters, rates of 42%–50% for central venous stenosis and/or thrombosis have been reported for subclavian catheters compared with 0%–10% for those placed via the right internal jugular vein (3,4). These studies have led to a widespread change in practice resulting in the right internal jugular vein as the access of choice for tunneled hemodialysis catheters. Lund et al (1) acknowledged this change in practice; they used the subclavian vein because their study dated from 1991 to 1992. Consequently, only 3% of the catheters in that series were placed via the right internal jugular vein. Given the growing recognition that the right internal jugular vein is the access of choice for tunneled hemodialysis catheters, our policy since 1993 has been to use the right internal jugular vein for access if patent.

We have shown that by using the right internal jugular vein for catheter placement, procedure-related complications can be reduced further compared with those associated with the subclavian approach. Specifically, we had no instances of pneumothorax, hemothorax, hemomediastinum, catheter malposition, vascular perforation, or substantial bleeding complication. Our complications were limited to two clinically silent air emboli, which, had we not been using fluoroscopic guidance, would certainly not have been recognized. The lack of puncture-related complications underscores the importance of real-time US-guided access to the right internal jugular vein. Our complication rate compares favorably with those of published surgical reports in which overall procedural complication rates are as high as 5.9% (10,11). Specifically, these include pneumothorax (0%–1.8%), hemothorax (0%–0.6%), hemomediastinum (0%–1.2%), recurrent laryngeal nerve palsy (0%–1.6%), and bleeding that necessitates reexploration and/or transfusion (0%–4.7%) (10–20).

The other theoretic advantage of access via the right internal jugular vein is a reduction or elimination of central venous stenosis, which is an important cause of morbidity in this patient population. However, in the series of Lund et al (1), the occurrence of symptomatic central venous thrombosis and/or stenosis was less than 1% (compared with 15.9% in one surgical series [19]), indicating that, even with subclavian access, interventional radiologic catheter placement may decrease the complication rate substantially compared with non–imaging-guided methods (1). We believe that with a combination of access via the right internal jugular vein and interventional radiologic placement, the rate of central venous thrombosis and stenosis may approach zero, as suggested by the absence of symptomatic central venous thrombosis or stenosis in our series.

Previous series in which surgical and percutaneous approaches were assessed have generally not indicated the technical success of the procedure (11–14,16–20). Uldall et al (15) noted that in 6% of bedside catheter insertions, transportation of the patient to the radiology department was necessary to complete the procedure. McDowell et al (10), who assessed percutaneous placement in the operating room, reported a 1.7% failure rate of the percutaneous approach and a



Figures 5–7. Survival curves show probability of freedom from (5, 6) catheter malfunction and (7) infection. Dotted lines show the 95% confidence interval. Numbers of catheters at risk are shown above the x axis. (5) Curve indicates primary survival. (6) Curve indicates secondary survival, thus including those catheters in which malfunctions were remedied without catheter removal.

0.6% failure rate overall (the remaining procedures in which percutaneous access was unsuccessful were completed successfully with a cutdown procedure). In most surgical series, a mixture of cutdown and percutaneous insertion is performed, with cutdown insertion reserved as a backup when percutaneous insertion fails. Cutdown insertion may result in loss of the vein for future access, whereas the percutaneous approach nearly always preserves patency of the jugular vein, as shown by Agraharkar et al (21), who found a 33% thrombosis rate in right internal jugular veins cannulated surgically (by means of cutdown insertion) versus only 2% with percutaneous insertion.

Not only did we have nearly 100% technical success in percutaneous catheter placement, but such success was achieved in placement of the catheter via the desired vein (ie, the right internal jugular vein) when it was patent at US. In fact, our single initial placement failure was due to a combative patient who refused to allow catheter placement halfway through the procedure. The catheter was placed without incident the next day when the patient was less combative. This degree of technical success can probably be achieved only by means of combined US and fluoroscopic guidance available in the interventional radiology suite. Perhaps even more important than technical success, however, is our 0% rate of initial catheter malfunction. Previous surgical series have reported a variable rate of initial catheter malfunction of 9.0%–14.5% (12,16,17).

The disparity in initial function rates between surgically placed and radiologically placed catheters was one of the most important factors in the conversion from surgical to radiologic placement of hemodialysis catheters at our institution. This success can be attributed to careful positioning of the catheter tip at the caval-atrial junction, as well as fluoroscopic confirmation that there are no kinks throughout the course of the catheter. Both of these technical facets of the procedure deserve further discussion.

Catheter-tip placement is of critical importance not only in prevention of late complications such as thrombosis but in achievement of adequate flow rates. According to the tunneling technique used (Figs 1, 2), the catheter tip may lie along the medial or lateral wall of the superior vena cava. The arterial (red) lumen should be oriented so that it does not abut the wall, as this will result in poor flow. Tunneling the catheter laterally can result in substantial catheter excursions between the supine and upright positions, especially in obese and large-breasted individuals. This observation was also made by Lund et al (1). To prevent such excursion, we have increasingly used the more medial, parasternal location for the tunnel, especially in such individuals (Fig 2).

Parasternal tunneling can render the apex of the curve of the internal jugular vein catheter more prone to kinking. Because of the high flow rates needed for hemodialysis, even subtle kinks can be extremely detrimental to successful hemodialysis. In an effort to eliminate kinks, some manufacturers have produced precurved catheters. We do not use the precurved catheters; such catheters do not allow us to achieve optimal tip positioning because the catheter curve dictates where the tip will be located in the patient. As can be seen from our results with use of nonprecurved catheters, excellent results can be achieved by using fluoroscopic guidance. We had three catheters that needed to be replaced due to kinks (at 2, 35, and 43 days, respectively), as well as two other catheters that needed slight manipulation (catheter repositioning under fluoroscopic guidance) to remove kinks (at 5 days each). None of these kinks were present at initial placement, even in retrospect. Two of the three catheters removed and one of the catheters repositioned for kinks were the thinner-walled 12.5-F catheters, which we found to be much less resistant to kinks than the 13.5-F Bard silicone catheter. Late-developing catheter kinks and malpositions may result from loss of fluid weight during initial hemodialysis; such weight loss may be substantial even in the first few days. Since this weight loss shortens the distance between the skin and the catheter-tip location, it can result in kinking and/or inward migration of the catheter tip, which ultimately necessitates correction. Such inward migration was seen in three patients in our series.

Catheter infection and failure due to thrombosis remain the most important drawbacks to catheter hemodialysis. Lund et al (1) summarized the existing data with regard to catheter infection and malfunction rates, as well as the problems in comparison of various series. As recommended by Lund et al, we reported our infection and failure rates as the number of episodes per 100 catheter days and used Kaplan-Meier survival analysis; these reporting methods take into account the duration of catheterization. With use of events per 100 catheter days, the published infection rates were 0.2–0.8 per 100 catheter days. Thus, our infection rate of 0.08 per 100 catheter days compares favorably. We reported infection that necessitated removal, which does not take into account the successfully treated infections, and we did not consider fever alone with negative catheter-tip cultures an infection, since fever with tunneled catheters has been shown not to be predictive of catheter infection (22). Even if we included treated infections

(the majority of which were not clearly documented infections), the infection rate in our series would have been 0.16 per 100 catheter days, still below the rate reported in surgical series. Lund et al (1) did not address isolated fever. We disagree with Lund et al that it is misleading to report infection that necessitates removal. Liberal antibiotic use in our hemodialysis unit results in treatment of many episodes that almost certainly are not catheter-related infection (low-grade fever, minimal nonpurulent exit-site discharge, minimal tunnel tenderness without erythema). Not surprisingly, the vast majority of these episodes resolve with a single antibiotic dose, yet it would be misleading to label them all as infectious episodes that were successfully treated. The only clinically meaningful infectious episodes are those that result in catheter loss, bacteremia or sepsis, or hospitalization, and these are all accounted for with our reporting method. Further, we can use persistent bacteremia, for which catheter removal is the rule at our institution, to compare our results with those of other series without the question of treated infections coming into play.

Our bacteremia rate of 0.04 per 100 catheter days compares favorably with that of 0.14 reported by Lund et al (1), 0.34 reported by Mosquera et al (16), 0.08 reported by McDowell et al (10), and 0.27 reported by Swartz et al (9). Catheter infection nonetheless remains an important cause of catheter failure. Although some investigators reported that bacteremia can be eradicated with a combination of intravenous antibiotics and catheter exchange (23,24), in our patient population this has not been our experience, with bacteremia always resulting in catheter removal. The exception is the 12 episodes in which a single culture obtained from the catheter was positive and a repeat culture after a single dose of antibiotics was negative. It is doubtful that this finding constitutes successful treatment of bacteremia; it is more likely that the initial cultures were contaminated. New measures aimed at reduction of catheter infection, such as catheter bonding with antibiotics or other antibacterial agents, will remain the subject of further study.

Our results reemphasize, however, that despite the fact that interventional radiology suites are used for various procedures, both "clean" and "dirty", as well as the fact that no special air handling is used in these suites, our occurrence of infection is comparable with that in the operating room. We believe, like others, that such results are due to careful attention to patient and operator preparation and sterile technique in the interventional radiology suite (1).

Unlike Lund et al (1), we did not use preprocedure antibiotics. Lund et al used 1 g of cefoxitin before the procedure because that was the surgical practice at their institution. The surgical practice at our institution was to not use preprocedure antibiotics; therefore, we did not. The fact that we found a lower rate of infection than Lund et al suggests that use of such antibiotics is unnecessary; this idea has also been suggested for other tunneled catheter placements (22,25, 26). Elimination of preprocedure antibiotics further decreases the cost of the procedure, as well as the risk of an allergic reaction.

Catheter failure due to malfunction also remains a vexing problem with tunneled hemodialysis catheters. Our overall catheter survival (62% 6-month and 48% 1-year primary survival) compares well with those in recent reports: Swartz et al (9) reported 60% 6-month and 30% 1-year survival, and Lund et al (1) reported 44% 6-month and 25% 1-year survival. Other investigators have reported longer survival: McDowell et al (10) reported 57% 1-year survival, and Gibson and Mosquera (13) reported 74% 1-year survival; however, these older reports do not reflect the higher flow requirements of current hemodialysis technique.

As can be seen from the Table, a variety of causes of catheter failure may be encountered; however, the majority are related to thrombosis. Even in cases where no clear-cut catheter-tip thrombosis is identified, when those catheters are removed and replaced with an identical catheter in an identical position they nearly always function well, indicating that there was probably a fibrin sheath on the catheter that was below the limits of resolution of a contrast material–enhanced study. Thus, we have a liberal policy of catheter exchange when catheter malfunction is experienced in the absence of an obvious fibrin sheath.

The management of fibrin sheaths continues to be a matter of personal preference. We have preferred to use urokinase infusion as our initial measure when low-dose urokinase has failed. Lund et al (1) reported a 79% success rate with this approach; our results were slightly less than this. Other investigators have reported successful use of fibrin sheath stripping rather than urokinase infusion. Crain et al (27) reported a series of 40 procedures in 23 patients in which percutaneous fibrin sheath stripping was used in hemodialysis catheters with 98% success. However, this concept has recently been challenged by Haskal et al (28), who reported poor results with fibrin sheath stripping in a series of 24 procedures in 20 patients. Although initial technical success was high, by the fifth subsequent hemodialysis session, poor flow rates had returned in nearly all catheters, seriously calling into question the durability of the stripping procedure.

We believe initial urokinase infusion is the most cost-effective way of restoring catheter function, since it can be performed as an outpatient procedure in the hemodialysis unit and the cost is only that of the vial of urokinase ($330). In contrast, fibrin sheath stripping was reported by Crain et al (29) to average $1,840 per procedure. Catheter exchange is considerably less expensive, averaging $1,300 at our institution. In addition, catheter exchange is not associated with the risks and inconveniences of transfemoral catheterization, namely, deep venous thrombosis (2.5% in the series of Crain et al [27]) and the necessary postprocedure observation in the interventional radiology recovery area. However, randomized cost analysis studies in which fibrin sheath stripping, urokinase infusion, and catheter exchange are compared are clearly needed to help determine what is the most cost-effective means of restoring flow in cases of this complication.

In conclusion, percutaneous placement of tunneled hemodialysis catheters via the right internal jugular vein can be performed by interventional radiologists with excellent technical success rates and long-term outcomes. Placement of these catheters in the interventional radiology suite should be the procedure of choice. ■

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A Reconstituted In Vitro Clot Model for Evaluating Laser Thrombolysis

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Abstract. Background/Objective: **Laser thrombolysis is the selective removal of thrombus from occluded blood vessels using laser energy. A reconstituted clot model with reproducible optical absorption properties was developed to evaluate the effect of various laser parameters on thrombus removal rate.**

Study Design/Materials and Methods: **Reconstituted clots were made with known fibrinogen concentrations and hematocrits. *Ex vivo* clots were collected from ten swine. Four red gelatin phantoms were prepared. Mass removal rates and ablation efficiencies were determined using a 577 nm, 1 μsec pulsed dye laser. The ablation efficiencies of the three clot models were compared at an energy of 25 mJ and a repetition rate of 4 Hz. In addition, the reconstituted clot model was ablated as pulse energy and repetition rate were varied with average power held constant at 100 mW.**

Results: **The mean ablation efficiency for *ex vivo* clots ranged from 0.4 ± 0.1 to 3.4 ± 0.7 μg/mJ/pulse, with significant differences between groups (ANOVA $p < 0.05$). Reconstituted clots of varied fibrinogen content had ablation efficiencies of 1.5 ± 0.2 to 1.6 ± 0.3 μg/mJ/pulse at this energy and repetition rate. Gelatin ablation efficiency was inversely proportional to protein content and ranged from 0.5 ± 0.3 to 2.0 ± 0.7 μg/mJ/pulse. Reconstituted clot mass removal rates (in μg/s) were clinically similar for settings ranging from 13 mJ at 8 Hz to 33 mJ at 3 Hz.**

Conclusions: **The reconstituted model clot is a reproducible and biologically relevant thrombolysis target. *Ex vivo* clot lacks reproducibility between individuals and gelatin phantoms lack clinical relevance. At a constant average power, varying laser parameters did not affect mass removal rates to a clinically significant degree.**

Key Words. **ablation, mass removal rate, stroke**

Introduction

Laser thrombolysis is the photomechanical removal of thrombus. Pulsed laser energy is absorbed by the hemoglobin pigment in the clot, causing the formation of a cavitation bubble. The collapse of this bubble mechanically disrupts and eventually removes the clot [1,2]. Earlier work utilizing laser thrombolysis for the treatment of acute myocardial infarction [3–5] and pre-clinical studies in a swine cerebral thromboemboli model [6] indicate that this therapy is a viable, selective, and safe method for the recanalization of occluded cerebral arteries. This study develops and validates a new reconstituted clot model that is more physiologically relevant than previous gelatin clot models used in laser ablation studies [7]. This clot model was used to test five sets of laser parameters, having equal average power.

Laser thrombolysis for acute stroke therapy is currently being tested in a clinical trial [8]. The laser thrombolysis system delivers laser energy to the clot through a flexible fluid core catheter [9]. The laser is coupled into a fused silica fiber, which carries the laser energy to nearly the end of the catheter. Radiopaque contrast solution is continuously injected through the catheter. After the laser light exits the fiber it is transmitted through the optically clear contrast solution to the occluding thrombus with a spot size of approximately 0.8 mm^2 [10]. The contrast solution is atraumatic, angiographically visible, removes ablated thrombus particles, and convectively cools the area. Because the fiber terminates before the end of the catheter, potentially dangerous contact with arterial tissue is prevented.

Hemoglobin is the primary absorbing chromophore in thrombus at wavelengths ranging from 400–590 nm. Within this spectrum, light selectively ablates thrombus and not vascular tissue [11]. The catheter system tested uses a 1-μsec pulsed dye laser emitting at 577 nm (Palomar 3010, Beverly MA). This pulse duration is much less than the time required for thermal confinement [11]. At 577 nm, thrombus has a much lower ablation threshold (0.02–0.03 J/mm^2) than the damage threshold for vessel tissue (1.1 J/mm^2 in saline, 0.16 J/mm^2 in blood) [11]. The ablative event is due to the formation and rapid collapse of a cavitation bubble, the force of which increases with energy [1]. In the confined space of a cerebral artery, the force of this bubble collapse becomes a potential safety concern. It may be possible to increase the safety margin of this therapy without compromising efficiency of clot removal by lowering

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the energy level and proportionally increasing the repetition rate [12].

For this study, a new *in vitro* model clot was developed to test the effects of varying pulse energy and repetition rate on the ablation of thrombus. Previous investigations have successfully measured the effects of altering laser parameters on red-dye gelatin phantoms [1,7], but the clinical relevance of a non-biological clot target is questionable. *Ex vivo* thrombus (static clot), formed by allowing whole blood to clot in tubing, has been used for thrombolysis [2,7,13–18]. This model clot lacks reproducibility, due to variations between donor individuals in hemoglobin concentration (hematocrit) and fibrinogen concentration.

The reconstituted clot model was developed to provide a simple, reproducible yet clinically relevant clot target in which the hemoglobin and fibrinogen concentrations were controlled. The fibrinogen concentration has previously been demonstrated to be directly proportional to the mechanical strength of the clot [19]. The mechanical properties of the model clots are the result of enzymatic reactions that mimic those found in the final common pathway of the clotting cascade *in vivo*. In short, fibrinogen is added to whole blood, then converted to fibrin by thrombin. It is important to note that this model does not take into account additional biochemical events that occur during clotting *in vivo*. These include fibrin-fibrin crosslinking by fibrin stabilizing factor (Factor XIII) [20] and the clot contraction through the action of platelets. Extensive remodeling of the thrombus also occurs intravascularly over time through the action of plasmin. Characterization and optimization of these phenomena were outside the scope of this study.

The effects of alterations in laser energy and repetition rate on ablation rate ($\mu g/s$) were assessed using fibrinogen concentrations of 300 mg/dL. The normal range of fibrinogen in swine is 100–500 mg/dL [21], and 200–400 mg/dL in human plasma. Therefore, the 300 mg/dL reconstituted model clot represents a median concentration for both human and swine thrombus. The majority of thrombotic emboli in ischemic stroke are caused by atrial fibrillation [22]. Freshly formed, this clot typically has approximately the same amount of hemoglobin containing erythrocytes as found in whole blood [23]. The reconstituted clot model most closely models thrombus of this type.

The goals of this study were to (1) develop a reproducible clot model using native blood components and to (2) compare the reproducibility of this reconstituted clot to that of static and gelatin clot models, (3) use scanning electron microscopy (SEM) to investigate the structural differences between the static and reconstituted model clots, and (4) test the effects of various laser parameters on ablation rates of a reconstituted model clot at an average power of approximately 100 mW as pulse energy was decreased and repetition rate was proportionally increased.

Materials and Methods

Thrombus models

Static clot

Whole blood was drawn from domestic swine into a 25–35 cc syringe with an 18G needle and immediately injected into (2.5 mm ID) IV tubing (Baxter Healthcare Corp., Deerfield IL). The tubing was folded in half and suspended for 12–24 hours at room temperature. Hematocrit was measured for each animal, and ranged from 25.3–33.8%. Six preparations were ablated within 24 hrs of collection and 4 were ablated at 96 hrs. The 96 hr. blood samples were analyzed for fibrinogen concentration (Beckman Electra 1600C Coagulation Analyzer). This procedure is adapted from the method for forming static clots previously reported by other investigators [2,7,13–18].

Reconstituted clot A

Whole blood from domestic swine was collected in citrated blood donor bags (CPDA1, Baxter Healthcare Corp.) and centrifuged at 2280 × g for 20 min. at 4°C. The plasma supernatant was frozen at −70°C for at least 24 hr and slowly thawed at 4°C. The cryoprecipitate, which contains most of the fibrinogen [24] was removed. Porcine fibrinogen (Fraction I, Sigma, St. Louis MO) was added to a concentration of 300 mg/dL plasma. The erythrocytes were mixed with Adsol preservative (Baxter Healthcare Corp.) and stored up to 30 days. Prior to recombination, this red blood cell preservative was removed by centrifuging at 1000 × g for 5 min. at 4°C. The separated erythrocytes and plasma were then recombined to a hematocrit of 40–45%, the normal human range. To form the reconstituted clot, 250 US units of bovine thrombin (Jones Pharma, Middleton WI) in 1 mL Tris buffered saline (TBS) with 5 mM $CaCl_2$ was drawn into a 35 mL syringe followed by 34 mL of whole blood. This mixture was immediately injected into 2.5 mm inner diameter IV drip tubing (Baxter) and then incubated in a 37°C water bath for 1 hour.

Reconstituted clot B

Whole blood from swine was collected in CPDA1 donor bags (Baxter) and centrifuged at a relative centrifugal force of 2100 × g for 30 min. at 4°C. The plasma supernatant was heated to 53–56°C for 3 min., causing the fibrinogen to precipitate from solution [14]. Plasma fibrinogen was measured and determined to be <60 mg/dL (Electra 1600C Coagulation Analyzer, Beckman). Porcine fibrinogen (Sigma, Fraction I) was added to a concentration of 300, 600 or 1,200 mg/dL. The separated erythrocytes and plasma were then recombined to a hematocrit of 28%. To form the reconstituted clot, 1,000 US units of

thrombin (bovine, Jones Pharma) (in 1 mL TBS with 40 mM $CaCl_2$) was drawn into a 35 mL syringe followed by 34 mL of whole blood. This mixture was immediately injected into IV drip tubing and then incubated in a 37°C water bath for 1 hour.

All procedures used in this study were conducted in accordance with institutional guidelines at Oregon Health and Science University concerning the care and use of experimental animals.

Gelatin phantom

300 Bloom Gelatin (Sigma) was mixed with a 0.18% aqueous solution of Direct Red 81 dye (Sigma) in proportions of 5, 10, 15, and 20% gelatin (wt/wt). The mixtures were allowed to soak for 4 hr, then heated to 65°C for 25 min. The solutions were injected into IV tubing (Baxter, 2.5 mm ID). The samples were allowed to cure in a 10°C water bath for 18 hr. prior to testing. These methods were adapted from gelatin bloom strength measurement standards [25].

Scanning electron microscopy

Samples of the static and reconstituted model A clots were fixed in 4% glutaraldehyde $\geq$12 hr, then rinsed with phosphate buffered saline (PBS). The samples were serially dehydrated with increasing concentrations of ethanol, then exchanged into increasing concentrations of Amyl acetate (Sigma). The Amyl acetate was removed with liquid CO_2 in a critical point dryer (CPD2, Pelco International, Redding CA). Samples were anchored to aluminum posts using colloidal silver paint (Ted Pella Inc., Redding CA) and sputter coated in a Hummer IV Sputtering System (Technics Corp., Alexandria, VA). Scanning electron microscopy was performed in an Amray 1810 SEM.

Laser ablation

The laser thrombolysis (ablation) experiments were performed with a Palomar 3010 pulsed dye laser emitting a 1-μsec pulse at 577 nm. Energy was measured before and after each experimental set (EM400, Molectron, Portland OR). The average value of these two measurements was used as the effective laser pulse energy. For all the ablation experiments, the average power was approximately 100 mW for 30 seconds. These parameters mimic those in the current clinical trial. To determine the effects of decreasing pulse energy while proportionally increasing repetition rate, the effective energy was 12.6, 14.7, 20, 24, and 32.8 mJ with corresponding repetition rates of 8, 7, 5, 4, and 3 Hz, respectively.

A fluid core catheter (approximately 1.0 mm ID) and a 200 μm fused silica fiber (SpecTran, Avon CT) were used in this study. The fluid core catheter acts as a conduit for the radiopaque contrast dye (Hypaque 60, Nycomed, Atlanta GA) and the fiber. The contrast dye was injected at a rate of 4.2 mL/min. Laser energy is transmitted through this fluid to the occluding clot. The catheter was positioned within 1–3 mm of the model clot. This distance from the proximal surface was maintained as the target was ablated.

A 3 cm section of tubing was cut and the model clot was released into phosphate buffered saline (PBS). The clot was drawn into a 6.5 cm long section of Silastic silicone tubing (Dow Corning, Midland MI) with a 3.4 mm inner diameter and a 4.7 mm outer diameter. This inner diameter corresponds to that of vessels encountered in the cerebral circulation targeted for clinical application. The Silastic tubing with model clot was fixed in an ablation holder which had a diverting piece of tubing that allows flow of contrast solution and ablated particles from the lumen of the tubing (see Fig. 1). The fluid core catheter was advanced into the tubing containing the model clot until the catheter tip was 1–2 mm from the proximal face of the target. During ablation, the catheter was manually kept within 3 mm of the model clot. Contrast solution at 37°C was injected for 30 s to build

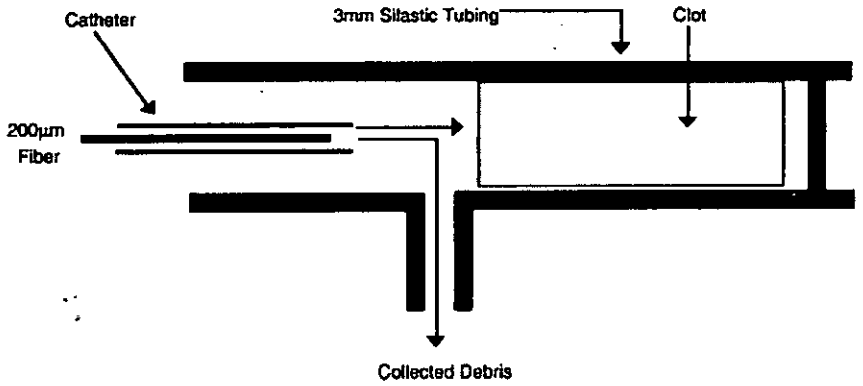

Fig. 1. The in vitro laser thrombolysis experimental set up. Laser energy is delivered through the fluid core catheter to the clot in the ablation chamber. The ablation chamber contains a 3 mm inner diameter section of tubing which holds the clot and has a bypass for the collection of effluent.

up to a 4.2 mL/min flow rate. Laser firing was performed for 30 s with simultaneous contrast injection. Following ablation, the proximal tubing was flushed with deionized water to collect all ablated fragments. Effluent was collected during the entire experiment and flushing. Deionized water was added to each effluent sample to bring the total volume to 10 mL. The effluent for both static and reconstituted clot ablations contained small fragments that were mechanically crushed. Intact erythrocytes were osmotically lysed in the hypotonic solution. Effluent samples from the gelatin ablations were slightly heated to liberate the dye. Control experiments with contrast flow but no energy were performed at the end of each experiment ($N = 3$) to account for mass removal due to non-ablative mechanical forces and fluid flow from the laser thrombolysis catheter system.

The absorbance of a solution at a given wavelength is directly proportional to its hemoglobin concentration. When the total volume is known, the mass of absorber is readily obtained from the concentration. The relationship is summarized in the following equation:

$$\text{Mass ablated } (g) = \frac{\text{Absorbance (410 nm)} - \text{Absorbance (800 nm)}}{k}$$

where the constant k is experimentally determined and is equal to the slope of the graph of absorbance difference versus mass. The hemoglobin in the reconstituted thrombus absorbs strongly at 410 nm; this wavelength provides the necessary sensitivity at the low concentrations of dissolved hemoglobin found in ablated samples. Direct Red dye from the gelatin samples absorbs strongly at 510 nm. There is minimal absorbance by hemoglobin and Direct Red at 800 nm, therefore this wavelength was used to correct for variation in the plastic cuvettes used in the experiments. This method was adapted from the method of Sathyam et al. (1996). To generate a calibration curve, a range of clot or gelatin fragments similar in mass to those that would be produced in the experiment were blotted for 10 sec on filter paper (Qualitative P8, Fisher Scientific, Pittsburg PA) and weighed to the nearest 0.1 mg in 50 mL beakers. 10 mL of deionized water was added to each sample and the clot was manually crushed and osmotically lysed. A 3 mL aliquot from each sample was measured using a spectrophotometer (HP 8425 Diode Array). Absorbance was measured at 410 nm and 800 nm for clot and 510 nm and 800 nm for gelatin, and the difference was plotted against mass (For an example, see Fig. 2). The slope of a linear curve fit is the calibration constant k (in g^{-1}). A new calibration curve was generated for every static and reconstituted model clot preparation. A single calibration curve was generated for the four gelatin phantoms which all contained the same dye concentration. The

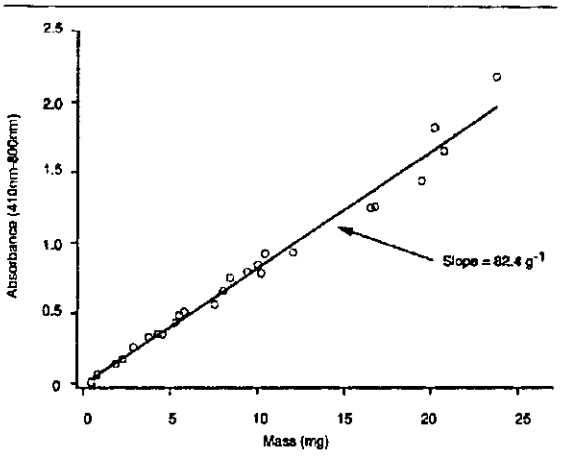

Fig. 2. Calibration curve. Absorbance difference between 410 nm and 800 nm vs., mass (g), slope (k) = 82.4 g^{-1}. Each clot model formulation had its own calibration curve value. Absorbance values were measured at 510 nm and 800 nm for gelatin phantoms. The r^2 value for all linear regressions was ≥0.90.

absorbance values were divided by the constant (k) to determine the total mass ablated during each 30 sec experiment. This calculation gives the mass removal rate in μg/sec. The ablation efficiency (μg/mJ/pulse) is calculated by dividing this value by the laser pulse energy (in mJ) and repetition rate (in Hz).

Mass removal rates at ~100 mW

Table 1 summarizes the experimental models utilized in each experiment. Static clot was collected from 10 domestic swine for the purpose of comparing the reproducibility of this model to the newly developed reconstituted clot model. Six of the static clot samples were ablated within 24 hrs. of collection and 4 more static clot samples were ablated 96 hrs. after collection. To measure the mass removal due to mechanical disruption by the fluid flow of the catheter system, 3 control (flow only) samples were tested from each clot. For the 24 hr. old clots, 6 samples were ablated from each, while 10 samples were ablated from each of the 96 hr old static clots.

Reconstitituted clot B was made from the recombination of plasma and cells from 4 animals. Fibrinogen concentrations were 300, 600, and 1,200 mg/dL Hematocrit was 28% for all three clots. Gelatin samples (5, 10, 15, and 20%) with Direct Red dye were also made. Ten samples of each of the reconstituted clot and gelatin phantoms were ablated, with 3 contrast flow-only controls. The model clots were ablated at an energy of approximately 25 mJ and a repetition rate of 4 Hz as described above.

The 300 mg/dL reconstituted clot A model was used in the increased energy (12.6, 14.7, 20, 24, and 32.8 mJ) and decreased repetition rate (8, 7, 5, 4, and 3 Hz) experiments. Average power was

Table 1. Experimental Thrombus Models. Fibrinogen Concentration is Expressed in mg/dL Plasma

Model	Age	N	Fibrinogen	Hct (%)	Clots/sample	Controls	Experiment
Static	24 h	36		25–34	6	3	Mass removal
Static	96 h	40	200–309	25–34	10	3	Mass removal
Reconst A	24 h	100	300	43	20	3	Energy/Rep rate
Reconst B	24 h	30	300–1,200	28	10	20	Mass removal
Gelatin	24 h	40			10	3	Mass removal

approximately constant (100 mW). Twenty experiments were performed at each setting and twenty contrast flow-only controls were performed. The reconstituted clot samples in this set of experiments all came from the same preparation. Hematocrit was 43%.

Statistical Analysis

Reported ablation rates and ablation efficiencies values are means ±1 standard deviation. Significance of difference was determined by one-way analysis of variance (ANOVA) and t-tests using SPSS (Version 10.0, Chicago IL). Significance was defined as $p < 0.05$.

Results

Scanning electron microscopy

The ultrastructure of the static clot appeared to be more complex and the clot matrix to be more heterogeneous in size than in the reconstituted 300 mg/dL model clot (Fig. 3). The reconstituted clots exhibited fibrin fibers of uniform diameter (approximately 300 nm). Spheroid morphology (rather than the physiological biconcave shape) of erythrocytes was observed in all SEM prepared samples, due to the glutaraldehyde fixation and/or dehydration.

Mass removal rates at ~100 mW

The results of the ablation experiments are summarized in Figures 4–6. The mass removal rate (μg/mJ/pulse) experiments comparing the static, reconstituted, and gelatin clot models are summarized in Figures 4 and 5. For clarity, the ablated samples in Figures 4 and 5 have the model-appropriate control values (contrast flow only) rate subtracted. The mean control mass removal rates ranged from 4–65%, 2–23%, 4–9%, and 30–57% of the mean ablated mass for the 24 h static clots (1–6), 96 h static clots (A–D), reconstituted clots, and gelatin models, respectively. The 24 h static clots varied significantly (ANOVA, $F = 6.327$, $p < 0.001$) in ablation efficiency, as did the 96 h static clots (ANOVA, $F = 66.782$, $p < 0.001$). The age of the static clot (24 versus 96 h) significantly affected ablation efficiency (2 tailed t-test, $p < 0.001$). The blood donors utilized for static clots ablated at 96 hrs (Samples A–D, Fig. 4) were tested for fibrinogen concentration. The concentrations were 200, 216, 264, and 309 mg/dL for samples A, B, C, & D, respectively. There was no significant difference in ablation efficiency between the reconstituted clots of varying fibrinogen concentration (ANOVA, $F = 0.701$, $p = 0.505$). The gelatin models (Fig. 5) varied significantly (ANOVA, $F = 21.261$, $p < 0.001$) in ablation efficiency, with significant differences between 5–10% and 15–20% protein concentrations (Tamhane's T2, $p < 0.05$).

Figure 6 shows the results from the decreased energy, increased repetition rate experiments. The control value is contrast flow only. There were significant differences in the mass removal rate (μg/s) among the groups (ANOVA, $F = 17.472$, $p < 0.001$). The level of difference detectable at this experimental power is considered in detail in the discussion. The highest mass removal rate (400 ± 50 μg/s) was achieved at 20 mJ, 5 Hz and the lowest rate (270 ± 60 μg/s) was seen both at 14.7 mJ, 7 Hz and 24 mJ, 4 Hz. The largest difference in mean mass rate was 130 μg/s, between 20 mJ, 5 Hz and 24 mJ, 4 Hz.

Discussion

The overall goal of this study was to develop and characterize a reproducible reconstituted clot model using native blood components, and to compare this new model clot to the more widely used static clot and gelatin phantoms. Another objective was to measure the effects of varying laser parameters on the mass removal rate (μg/sec) and ablation efficiency (μg/mJ/pulse) of laser thrombolysis at 577 nm.

The lack of reproducibility in the strength of static model clots as well as variance in the hematocrits between individuals motivated the development of the reconstituted clot model. The mass removal rate of the static model clots varied significantly among the clots from the six swine. The static clot model is variable and unpredictable, both in fibrinogen and hemoglobin concentration (hematocrit ranging from 25–34%), for accurate *in vitro* testing of laser thrombolysis parameters. Since the age of thrombus *in vivo* correlates with its optical properties [26] and mechanical properties [20], these results suggest that stroke clots of varying ages may be removed clinically with the laser parameters previously discussed, although older clots will be removed significantly more slowly.

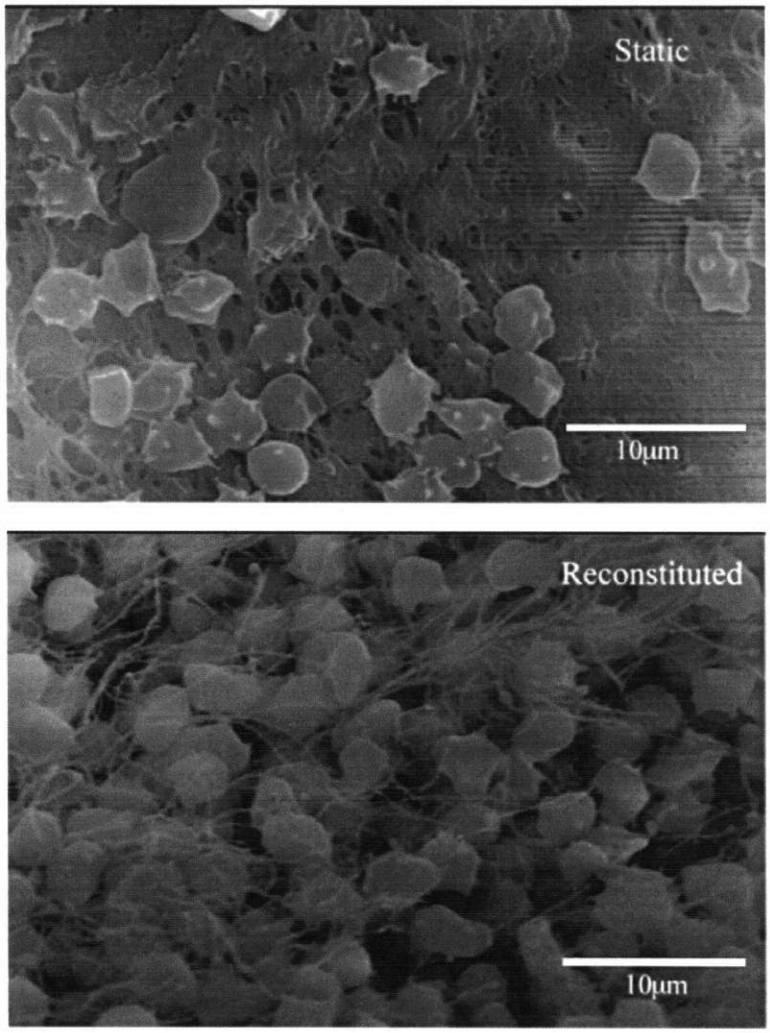

Fig. 3. *Scanning electron microscopy (SEM) of static and 300 mg/dL fibrinogen reconstituted model clots. The static clot was more heterogeneous than the reconstituted clot.*

Earlier gelatin phantom studies are consistent with our results, due to the homogeneity in strength and absorption coefficients between samples [7,13]. Detwiler (1991) used a similar gelatin phantom to measure the effect of unconfined compression modulus on ultrasonic thrombolysis. They concluded that ultrasonic ablation decreased with increasing protein content of their gelatin target [27]. These conclusions are supported by the current study of laser thrombolysis ablation of gelatin phantoms (see Fig. 5). Both ultrasonic angioplasty and the laser thrombolysis system under study remove target material through the formation and collapse of cavitation bubbles. The collapsing bubble generates a shock wave that is transmitted through the material, breaking it into smaller pieces. The differences demonstrated in the ablation of gelatin phantoms of varied protein content diminishes the value of gelatin as a thrombus phantom. Gelatin is a suspension of partially denatured collagen molecules, while clot is held together by a meshwork of fibrin. These structural differences appear to have an effect on the ablation of the models.

The ablation efficiency (μg/mJ/pulse) has previously been demonstrated to be independent of radiant exposure above threshold [1,2,7,11]. Previous experiments [12] with this reconstituted clot model and *in vitro* setup demonstrated no difference in ablation efficiency as the parameters of energy and repetition rate were varied with average power held constant at approximately 100 mW. The number of trials in this earlier study was chosen to be $N = 10$.

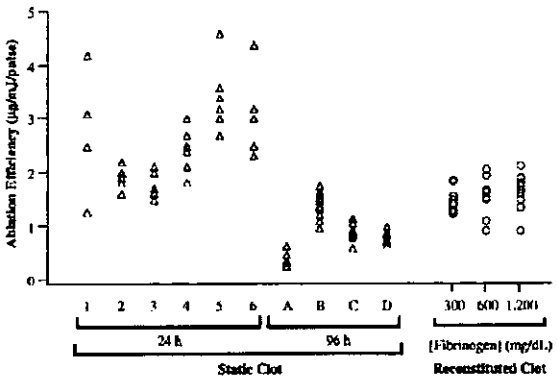

Fig. 4. Ablation efficiency of the static and reconstituted clot models. Static clots are represented by open triangles, and each static clot category (1–6, A–D) represents clot from a different individual. Reconstituted clot is represented by open circles, and is reconstituted model B. There are significant differences among the static clot samples of each age group and between age groups (separate ANOVAs, $p < 0.001$). The reconstituted clot samples at 300, 600 and 1,200 mg/dL fibrinogen did not have statistically different ablation efficiencies.

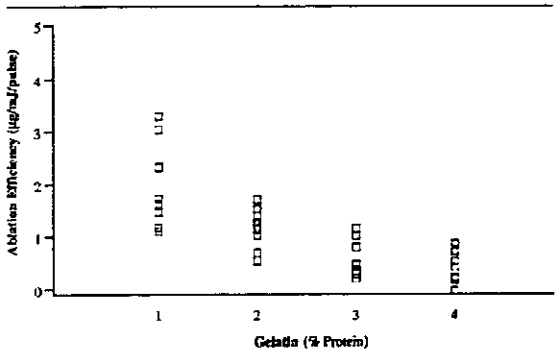

Fig. 5. Mean ablation efficiency of the gelatin clot models. The gelatin models varied significantly (ANOVA, $p < 0.001$) in ablation efficiency, with significant differences between 5–10% and 15–20% protein concentrations.

For the present experiments, a power calculation was performed using the previous investigation [12] as preliminary data. With $N = 20$, this study had 85% power to detect differences of at least standard deviations between groups. At this extremely high level of sensitivity, significant differences were demonstrated between most groups. The largest difference in mean mass removal was only 130 μg/s. The highest mean mass removal rate observed (at 20 mJ, 5 Hz) was 400 ± 50 μg/sec, while the lowest (at 24 mJ, 4 Hz) was 270 ± 60 μg/sec. With the sample size used in these experiments, the detectable difference (less than 0.2 standard deviation) in clot removal rates would translate to less than 2 μg/sec, which is too small to be clinically significant. These results

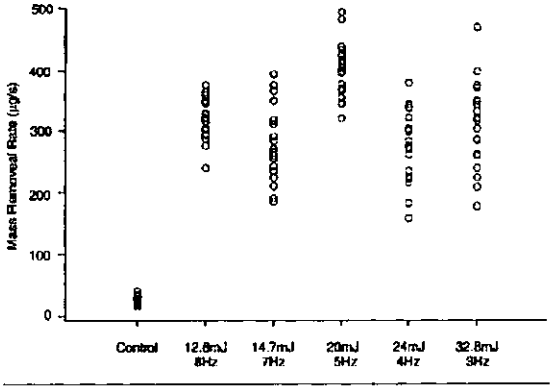

Fig. 6. Mass removal rate of reconstituted model A clot at varying laser pulse energy (mJ) and repetition rates (Hz). Average power was approximately 100 mW. There were statistically, but not clinically significant differences among the groups.

demonstrate that the clot mass removal rate can be maintained as pulse energy is decreased, as long as average power is approximately constant at 100 mW. This would reduce the force generated by the collapse of the cavitation bubble, which in the confined space of a cerebral artery, may be a potential safety concern.

The differences in ablation efficiency between the 24 hr and 96 hr static clots may have been due to crosslinking by Factor XIII over the additional time. The reconstituted clot models A and B also demonstrated significantly different mean ablation rates ($p < 0.05$), with the model A reconstituted clot ablating at approximately twice the rate as that of model B. The fibrinogen concentration was equal for the 300 mg/dL clots, therefore the differences in ablation rate appear to be due to differences in thrombin or calcium concentration, both of which have been previously shown to affect clotting [28,29]. The reconstituted model B clots had similar ablation efficiencies across a range of fibrinogen concentrations. These results agree with previous studies that demonstrate equivalent clot removal for similar model clots tested for tensile strength [30] and resistance to compression [10].

In this study as well as earlier ablation studies of thrombus, the static model clot was variable [1,2,7]. Gelatin phantom studies were shown to be more consistent due to the homogeneity in strengths and absorption coefficients between samples [7]. The reconstituted clot model is a reproducible and more biologically relevant *in vitro* target for bench top studies of laser thrombolysis parameters. The mass removed during control (contrast flow only) experiments on the reconstituted clots resulted in the lowest variation among the models. This decreased the error in the measurement of ablated mass due to laser energy, and further supports the usefulness of this

model over the others. The reconstituted clot model has some differences from static clot formed *ex vivo*. This is to be expected from a simplified clot phantom that lacks platelets and the complexity of the full hemostatic complement of the coagulation cascade. The static clot is limited to the endogenous concentration of thrombin generated by the *in vivo* clotting cascade, while the reconstituted model clot polymerizes much more quickly, with an excess of thrombin.

Future optimization studies of laser thrombolysis are now possible using this clot model. The reconstituted clot model has predictable optical properties and is a more biologically representative thrombus phantom than red gelatin because it consists of blood components, making it an ideal clot target for *in vitro* and even *in vivo* studies of laser thrombolysis as well as other mechanical thrombolysis therapies.

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Treatment of infected tunneled venous access hemodialysis catheters with guidewire exchange

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Treatment of infected tunneled venous access hemodialysis catheters with guidewire exchange. Cuffed venous access catheters have become commonplace for hemodialysis access. The major complications of these catheters are catheter thrombosis, catheter fibrin sheathing and infection. When catheter associated bacteremia occurs treatment with antimicrobial therapy alone has been unsuccessful in providing acceptable cure rates. Failed antimicrobial therapy exposes the patient to the risks of prolonged bacteremia, while the alternative, catheter replacement at a new site can lead to central venous stenosis and compromise future long-term upper extremity access. Catheter guidewire exchange when the tunnel tract is clinically not infected theoretically allows the preservation of future access sites and yields a higher treatment success rate while avoiding temporary non-cuffed access placement. We report a series of 23 cases of hemodialysis patients with tunneled cuffed catheters and bacteremia related to the catheter who were treated with the exchange of a new catheter over a guidewire combined with three weeks of systemic antibiotics. Patients eligible for the study required no evidence of tunnel tract infection and defervescence within 48 hours of antimicrobial therapy. Technique failure was defined as repeat infection from any organism within 90 days of catheter exchange. Four patients (18%) redeveloped bacteremia within 90 days of the exchange. The bacteremias developed at 4, 19, 63 and at 74 days days after the exchange. Guidewire exchange in combination with intravenous antibiotics in cases of catheter related bacteremia has an acceptable rate of treatment success and is a viable treatment option in a carefully selected patient population.

Cuffed tunneled venous access catheters are commonly used for temporary and permanent access for hemodialysis patients [1–4]. These catheters serve an essential role providing hemodialysis access to patients awaiting the maturation or placement of permanent arteriovenous (AV) access and providing permanent access in patients in whom all other access options have been exhausted. The predominant complications with the use of these tunneled catheters are catheter thrombosis, catheter fibrin sheathing and infection [1–6].

Catheter dysfunction caused by thrombosis has been shown to respond to a series of therapeutic techniques [5, 7], and in our experience thrombotic episodes, although frequent, are treatable. Catheter mediated bacteremia and catheter tunnel infection, however, are currently the primary reasons for catheter access failure [5, 6]. In a study from our institution, the mean catheter life in catheters intended for permanent use was 12.7 months with almost all catheters lost due to infection [5].

In a prospective study by Marr and colleagues at Duke University, we demonstrated an infection rate of 3.9 infections per 1000 catheter days of use [6], which was consistent with the cuffed hemodialysis catheter infection rates at other centers [8]. Complication from these infections ranged from minimal systemic signs to endocarditis, septic arthritis, and epidural abscess. In the study by Marr and colleagues using the same patient base as the current study, there were no differences in systemic complications between those patients in whom catheter salvage was attempted and in those it whom it was not [6]. However, Kovalik and colleagues noted an increased frequency of epidural abscesses and bacterial endocarditis when these catheters were used chronically when compared to AV access [9]. Thus, infectious complications have emerged as the dominant problem with long-term chronic cuffed catheter use.

Cuffed catheter related bacteremia has been treated by attempted salvage with intravenous antibiotics or removal of the catheter. As reported by Marr et al, the successful rate of salvage with antimicrobial therapy alone was only 32% [6]. The alternate clinical approach to attempted catheter salvage has been catheter removal, with use of temporary access for a period of time followed by catheter replacement at a new site. With repeated new sites of access there is an increased risk for the development of central venous stenosis compromising the longevity of upper extremity AV access.

Several studies have shown that in the intensive care unit (ICU) setting, guidewire exchange of non-cuffed catheters may be successfully performed without any increased risk of infection compared to placement of a new catheter at a new site [12–17]. This approach, however, has not been universally recommended [15].

Carlisle et al reported a series of patients with hemodialysis catheter related sepsis who underwent catheter exchange over a guidewire who had treatment failures only in the presences of purulence at the exit site [16]. Shaffer reported a series of thirteen patients with cuffed tunneled catheter related sepsis who were treated with antimicrobial therapy and guidewire exchange [17]. We report here a cohort of patients with systemic infections associated with cuffed tunneled catheters who were treated with guidewire exchange in addition to intravenous antibiotic therapy.

Key words: hemodialysis, bacteremia, catheters-indwelling, infection in access site, thrombosis, defervescence, antibiotics.

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Table 1. Catheter infection outcomes

Catheter bacteremia episodes	40	100%
Immediate catheter removal	17/40	42%
Catheter exchanges	23/40	58%
Exchange technique success (infection free > 90 days)	19/23	83%
Exchange technique failure [recurrent infection (any organism) < 90 days]	4/23	17%

Table 2. Causes of bacteremia

Organism	Number of cases
Staphylococcus aureus	8
Enterococcus sp.	3
Staphylococcus Coag neg	5[a]
Diptheroids sp.	1
Serratia marcescans	1
Escherichia coli	1
Hemophilus Parainfluenza	1
Streptococcus viridans	1
Xanthomonas Maltophilia	1
Polymicrobial	1

[a] 2 cultures, catheter tip only

METHODS

Patients seen at Duke University Medical Center (DUMC) with clinically suspected catheter related sepsis were evaluated for potential guidewire exchange. These patients were seen over the period of July 1, 1996 though September 30, 1997. Requirement for consideration for guidwire exchange were: (*1*) end-stage renal disease (ESRD), (*2*) bacteremia without an identifiable source except the catheter, (*3*) defervescence with intravenous antibiotics within forty-eight hours, and (*4*) no sign of catheter tunnel tract infection. Patients with purulence at the exit site were ineligible for guidewire exchange. Patients who underwent guidewire exchange were continued on antibiotic therapy for three to four weeks at the discretion of the clinician.

Patients who presented with fever and leukocytosis without an identifiable infection source except the catheter underwent blood cultures and received an initial empiric antibiotic therapy of vancomycin and gentamicin. Patients with positive cultures were then entered into the study. After culture results, antibiotic therapy was based on susceptibilities. A treatment failure was considered any bacteremia within 90 days after exchange.

Patients who met eligibility criteria were taken to the interventional radiology suite for the catheter exchange. The catheters used in this study were of a single type (Perm Cath™; Quinton Instrument Co., Seattle, WA, USA). The catheter and skin site were prepped with a betadyne scrub (×3) and the betadyne was allowed to dry and draped in sterile fashion. Fentanyl and Versed were administered intravenously for conscious sedation; 10 cc was aspirated from each catheter port and discarded. Each port was flushed with 10 cc of heparinized saline (1,500 Units of heparin in 500 cc normal saline). Using fluoroscopic guidance, a stiff shaft hydrophilic guidewire (Glidewire SS, Medi-tech; Boston Scientific Corporation, Watertown, MA, USA) 0.035 inches in diameter, 150 cm in length, was passed through each of the two catheter lumens to the level of the right atrium. The Dacron cuff was bluntly dissected from the subcutaneous tissue via the tunnel. Catheters were placed in such a manner that the cuff could be reached with forceps inserted via the tunnel. The catheter was exchanged for a new catheter over the guidewires into the same tunnel. The guidewires were removed and 5 cc were aspirated from each lumen. Five thousand units of heparin were injected into each lumen and caps placed on the ports; 2-0 silk was used to anchor the catheter to the skin for 10 days.

RESULTS

During the study 40 catheter-related infection episodes (fever, chills, leukocytosis without an identifiable infection source except the catheter) were evaluated for possible guidewire exchange. Patients not entered into the study had their catheter removed either because they were judged clinically unstable (hypotension), had a possible infected catheter tunnel tract, or failed to become afebrile within 48 hours of initiation of antibiotic therapy (Table 1).

There were 23 catheter exchanges in 21 patients. The patient population included 10 men and 11 women with a mean age of 59 years. Seventeen of the catheters were right internal jugular insertion and 6 were left internal jugular. Catheters had been in place for a range of one month to 1.6 years. Organisms isolated from blood cultures were *staphylococcus aureus* (8 cases), *enterococcus sp.* (3 cases), *staphylococcus Coagulase negative* (3 cases), and one case each of *diptheroids, serratia marcescans, streptococcus viridans, E. coli*, and *hemophilus parainfluenzae*, respectively. One patient had a polymicrobial infection with four organisms. Two patients had positive catheter tip cultures but negative blood cultures (both *staphylococcus Coagulase negative*). One patient who was initially culture negative later redeveloped fever and grew *Xanthomonas maltophia*, which resulted in catheter removal and treatment failure (Table 2).

There were four treatment failures, defined as bacteremia from any organism within 90 days of catheter exchange. These failures occurred at 4, 19, 63, and 78 days post-catheter exchange. The treatment failure at four days was associated with recurrent fever and *staphylococcus aureus* bacteremia. The technique failure at 19 days was with *xanthomonas maltophilia* in a patient who was initially blood culture negative. The treatment failure at 63 days occurred in a patient who initially grew *enterococcus* but developed *staphylococcus aureus* bacteremia at 63 days. The treatment failure at 78 days was a recurrence of *Coagulase negative staphylococcus*.

In addition, the patient with a polymicrobial infection with *E. coli, streptococcus viridans, staphylococcus coagulase negative*, and *enterococcus sp.* bacteremia, developed *staphylococcus Coagulase negative* bacteremia and L4-L5 discitis 144 days after the catheter exchange. It is our belief that this infection represents new and not recurrent infection, as this patient had developed sacral decubiti prior to the event. There were no discernable correlations between organism and treatment failure.

DISCUSSION

This prospective observational series supports the finding by Shaffer that guidewire exchange of cuffed venous hemodialysis catheters is a reasonable approach to catheter related bacteremia in the clinical setting of defervescence within 48 hours after the administration of intravenous antibiotics in the absence of exit site infection [9]. Data reported by Marr et al from our institution in

the study that preceded our study documented a very low (32%) rate of successful catheter salvage with intravenous antibiotics alone [6]. Although patient selection is different in these studies, (no exclusion of tunnel tract infections in the study by Marr et al), the results of our study and the study by Shaffer support the finding that in the correct clinical setting guidewire exchange can be done safely.

Due to the high incidence of bacteremia associated with cuffed venous access catheters, it is unreasonable to expect that there will be no repeat infections at follow-up. The infection rate 90 days after exchange in this series is comparable to the rate in *de novo* catheter use. Only four of the 23 cases (17%) had a repeat infection 90 days post-exchange. The series of patients reported by Shaffer had 3 of 13 cases with repeat bacteremia ranging from 2.5 months to 13 months, with two of three recurrences being with the originally cultured organism. In our study only one of the four bacteremias was with the original cultured organism, while one original culture failed to grow an organism. It is possible that our treatment failures may represent either a new infection or an infection introduced at the time of catheter exchange rather than failure to eradicate the original infection. Regardless of the cause, all represent a catheter exchange technique failure and are reported in this manner. This study is also in agreement with the observations of Beathard (personal communication) that in the correct setting that catheters can be successfully salvaged by the use of guidewire exchange.

In conclusion, preservation of access sites is in the best long-term interest of the dialysis patient. When used in the proper clinical situation, guidewire catheter exchange can be performed with a low likelihood of treatment failure. Successful guidewire exchange can preserve sites of access while allowing the patient to avoid temporary non-cuffed hemodialysis access placement. We believe when the conditions of clinical improvement after 48 hours of intravenous antibiotics and absence of tunnel tract infection are met, then guidewire exchange is a viable treatment option.

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Bacteremia associated with tunneled dialysis catheters: Comparison of two treatment strategies

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Bacteremia associated with tunneled dialysis catheters: Comparison of two treatment strategies.

Background. Tunneled dialysis catheters are often used for temporary vascular access in hemodialysis patients, but are complicated by frequent systemic infections. The treatment of bacteremia associated with infected tunneled catheters requires both antibiotic therapy and catheter replacement. We compared the outcomes of two treatment strategies for catheter-associated bacteremia: exchange of the existing catheter with a new one over a guidewire versus catheter removal with delayed replacement.

Methods. We retrospectively analyzed the outcomes of all cases of tunneled dialysis catheter-associated bacteremia during a two-year period. The infection-free survival time of the subsequent catheter was evaluated in two groups of patients: group A (31 catheters), exchange of the existing infected catheter with a new catheter over a guidewire, and group B (38 catheters), removal of the infected catheter followed by delayed catheter replacement 3 to 10 days later. Patients in both groups received three weeks of systemic antibiotic therapy. Cox proportional hazard models were used to evaluate the factors predictive of infection-free survival time of the replacement catheter.

Results. On univariate proportional hazard regression analysis, the infection-free survival time of the replacement catheter was similar for groups A and B ($P = 0.72$), whereas the hazard of infection was significantly greater for patients with hypoalbuminemia (serum albumin < 3.5 g/dL), as compared with patients with a normal serum albumin (hazard ratio 2.81, 95% CI, 1.21, 6.53, $P = 0.016$). The infection-free survival time was not affected by patient age, sex, diabetic status, or type of organism (gram-positive coccus vs. gram-negative rod).

Conclusions. The infection-free survival time associated with the subsequent catheter is similar for the two treatment strategies. However, exchanging the catheter for a new one over a guidewire minimizes the number of separate procedures required by the patient. Hypoalbuminemia is the major risk factor for recurrent bacteremia in the replacement catheter.

Key words: hemodialysis, dialysis catheter, infection, hypoalbuminemia, vascular access.

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Tunneled dialysis catheters placed in a central vein are used frequently in hemodialysis patients as a temporary vascular access until an arteriovenous (AV) fistula or a polyfluoroethylene (PTFE) graft is ready to use [1]. In addition, dialysis catheters are used as a permanent vascular access in some patients who have exhausted all options for placement of a fistula or graft. A large proportion of hemodialysis patients in the United States dialyze through a catheter at any time. In a recent survey, nearly 20% of the prevalent patients required a dialysis catheter for vascular access [2]. As compared with fistulas and grafts, tunneled dialysis catheters offer the advantage of ease of placement and the ability to be used immediately for dialysis. However, they suffer from several disadvantages, including poor blood flow [3], frequent thrombosis and infection [3–5], risk of central vein stenosis [6–8], and limited longevity [5, 9].

Infections are the most serious complication of tunneled dialysis catheters. The frequency of catheter-associated bacteremia has been about two to four per 1000 patient-days in a number of studies, equivalent to 0.7 to 1.5 per catheter year [5, 10–12]. In contrast, the frequency of infections is approximately 0.2 per patient-year for AV grafts and 0.05 per patient-year for AV fistulas [13]. Moreover, catheter-associated bacteremia often results in serious systemic infections, including endocarditis, osteomyelitis, epidural abscess, septic arthritis, and even death [11]. Treatment of catheter-associated bacteremia with systemic antibiotics without catheter removal is not usually effective. Only 22 to 32% of tunneled catheters can be salvaged without catheter removal [5, 10, 11, 14]. Moreover, attempting to salvage the infected catheter with antibiotics alone incurs the risk of serious systemic complications, including endocarditis and epidural abscess [15]. On the other hand, the removal of the dialysis catheter creates a short-term vascular access hardship until a new catheter can be placed, frequently necessitating the insertion of one or more femoral dialysis catheters and requiring utilization of an inpatient dialysis unit.

Several recent observational studies have reported that exchanging infected dialysis catheters over a guidewire, in combination with systemic antibiotics, results in successful resolution of the infection [12, 16, 17]. Unfortunately, none of these studies reported a concurrent control group for comparison of the outcomes.

The present study retrospectively analyzed the outcomes of the replacement catheters following all episodes of dialysis catheter-associated bacteremia during a two-year period. We compared two treatment strategies at our institution: exchange of the infected catheter with a new one over a guidewire versus removal of the infected catheter followed by delayed placement of a new catheter 3 to 10 days later. Both patient groups received systemic antibiotics for three weeks. We used prospective, computerized records [18] to track the catheter events.

METHODS

Patient population

The University of Alabama at Birmingham (UAB) provides chronic dialysis to approximately 350 in-center hemodialysis patients. About 15% of the prevalent patients dialyze with tunneled dialysis catheters. The demographics of the patients dialyzing with catheters are as follows: 26% of the patients are age 65 or older; 51% of the patients are female; 84% of the patients are black, and 16% are white; 41% of the patients have diabetes. All patient hospitalizations, surgical procedures, and radiologic procedures are done at UAB Hospital. The vast majority of dialysis catheter procedures are performed by interventional radiology.

Dialysis catheter placement and management

Double-lumen cuffed dialysis catheters were placed by one of four experienced interventional radiologists. All catheters were placed through the internal jugular vein using ultrasound guidance. The tip of the catheter was positioned in the right atrium using fluoroscopy, with the distal end tunneled through the subcutaneous tissue in the anterior chest wall and the Dacron cuff positioned within the tunnel. Aseptic techniques were used by the dialysis nurses to access the catheters for hemodialysis. Catheter thrombosis was treated by instilling 5000 units of urokinase into each lumen [4]. When this maneuver failed to re-establish patency, the catheter was replaced over a guidewire with a new dialysis catheter, utilizing the same subcutaneous tunnel.

Management of dialysis catheter-associated bacteremia

Infection was suspected whenever patients with a dialysis catheter developed fevers or chills, in the absence of an alternative source of infection. Treatment with empiric broad spectrum antibiotics (vancomycin and gentamicin) was initiated immediately after obtaining blood cultures from a peripheral vein. Patients with clinical sepsis (some combination of high fever, persistent shaking chills, or hypotension) were hospitalized for further management, whereas those with milder symptoms (low grade fever and stable blood pressure) were managed as outpatients. The dialysis catheter was removed promptly (within 24 to 48 h) if there was an exit site infection, severe sepsis (persistent shaking chills or hypotension) in spite of antibiotics, or persistent fever 48 hours after the initiation of antibiotic therapy. In the remaining cases of catheter-associated bacteremia, one of two treatment strategies was followed, at the discretion of the nephrologist. The first strategy (group A) consisted of replacing the infected dialysis catheter with a new one over a guidewire within a few days once the bacteremia was clinically resolved (absence of fever or chills). Documentation of negative blood cultures following antibiotic administration was not required prior to catheter replacement. The second strategy (group B) consisted of removal of the dialysis catheter within 1 to 2 days of the onset of clinical symptoms and placement of a new tunneled dialysis catheter 3 to 10 days later. In the interim, these patients were dialyzed with a femoral dialysis catheter. Patients in both groups A and B received three weeks of systemic antibiotic therapy, which was tailored to the culture and sensitivities reported. The differences in the strategies selected by the individual nephrologists were largely due to their subjective impressions regarding the severity of clinical sepsis.

Data collection

A full-time dialysis access coordinator scheduled all of the dialysis access procedures and maintained a computerized record of all procedures performed [18]. Consent for review of the patients' medical records for research purposes was obtained from the UAB Institutional Review Board. Removal of infected dialysis catheters was performed by either interventional radiology or access surgery, whereas exchange of infected catheters or placement of new catheters was performed by one of four experienced interventional radiologists. We identified all cases of dialysis catheter-associated bacteremia occurring during the two-year period between January 1, 1997, and December 31, 1998. If a patient had more than one episode of catheter-associated bacteremia during the study period, only the first infection was included in the analysis. We excluded cases in which a replacement catheter was not inserted within 10 days of removal of the infected catheter. (In most instances, this was due to having a permanent access ready to use, persistent fever after catheter removal, or patient death.) The following demographic and clinical information was collected for each patient: age, sex, race, diabetic status, serum albumin, and the organism grown from the blood

Table 1. Baseline clinical features of patients with catheter-associated bacteremia

	Group A	Group B	*P* value	All catheters
Number of catheters	31	38		69
Age (mean ± SD)	52 ± 16	52 ± 16		52 ± 16
Age >65 years	8 (26%)	10 (26%)	0.96	18 (26%)
Age <65 years	23 (74%)	28 (74%)		51 (74%)
Sex				
Male	13 (42%)	21 (55%)	0.27	34 (49%)
Female	18 (58%)	17 (45%)		35 (51%)
Race				
Black	26 (84%)	32 (84%)	0.97	58 (84%)
White	5 (16%)	6 (16%)		11 (16%)
Diabetes				
Yes	11 (35%)	17 (45%)	0.44	28 (41%)
No	20 (65%)	21 (55%)		41 (59%)
Type of organism				
Gram-positive coccus	22 (71%)	22 (58%)	0.26	44 (64%)
Gram-negative rod	9 (29%)	16 (42%)		25 (36%)
Serum albumin*				
<3.0 m/dL	11 (38%)	9 (25%)	0.48	20 (31%)
3.0–3.9 m/dL	15 (52%)	21 (58%)		36 (55%)
>4.0 m/dL	3 (10%)	6 (17%)		9 (14%)
Serious complications				
Yes	7 (23%)	6 (16%)	0.47	13 (19%)
No	24 (77%)	32 (84%)		56 (81%)
Outcome of the replacement catheter				
Infection	16 (52%)	16 (42%)	0.86	32 (46%)
Elective removal	5 (16%)	7 (18%)		12 (17%)
Malfunction	8 (26%)	11 (29%)		19 (28%)
Death	2 (6%)	4 (10%)		6 (9%)

Groups are defined as: Group A, exchange of catheter over guidewire; Group B, removal of catheter with delayed placement of new catheter.
*Values missing in four cases

cultures. Finally, each patient's medical records was reviewed to evaluate for serious complications associated with catheter-associated bacteremia.

We then evaluated the infection-free survival time of the replacement catheter. The longevity of each replacement catheter (groups A and B) was calculated as the number of days from catheter placement (or exchange) and catheter removal. The indication for catheter removal was categorized as infection, malfunction (thrombosis or poor flow), or elective (permanent vascular access ready to use). When urokinase was unsuccessful in restoring blood flow, the patient was referred to interventional radiology for an elective exchange. We also determined the organism responsible for the infections in the replacement catheters.

Statistical analysis

Descriptive statistics were used to summarize the sample data. The time from catheter replacement (exchange or delayed replacement) until recurrent infection was calculated. Survival analysis techniques were used to model infection-free survival time. Patients whose catheter malfunctioned was electively removed (permanent vascular access ready to use) or who died with a functioning catheter were considered censored. Univariate Cox proportional hazard models were fit. Multivariable Cox proportional hazard models allowed for the evaluation of the significance of several independent variables in the presence of each other. Hazard ratios and the associated 95% confidence intervals were computed. Survival distributions were plotted using the Kaplan–Meier method.

RESULTS

We analyzed the outcomes of all cases of dialysis catheter-associated bacteremia during the two-year period from January 1, 1997, to December 31, 1998. After excluding patients who did not receive a replacement catheter within 10 days of catheter removal, we were left with 69 cases of documented catheter-associated bacteremia. The age, sex, racial distribution, and frequency of diabetes among this group of patients (Table 1) were similar to that in the prevalent dialysis population at UAB. Approximately two thirds of the patients were infected with a gram-positive organism (mostly *Staph aureus* or *Staph epi*), and the remainder had gram-negative infections. Serious complications occurred in 19% of all episodes of catheter-associated bacteremia. These included endocarditis (2 patients), septic arthritis (3), septic emboli to the brain (1), and severe sepsis requiring hospitalization in the intensive care unit (7).

The patients were classified retrospectively into two groups according to the clinical management of the catheter. Group A patients had the infected catheter replaced

Table 2. Univariate proportional hazard regression analysis of clinical factors as predictors of infection-free catheter survival

Variable	Hazard ratio	95% C.I.	*P* value
Treatment group	0.88	(0.43, 1.79)	0.72
Serum albumin (<3.5 vs. ≥3.5 g/dL)	2.81	(1.21, 6.53)	0.016
Age	1.00	(0.98, 1.02)	0.74
Sex	1.49	(0.73, 3.05)	0.27
Race	0.64	(0.22, 1.84)	0.41
Diabetic status	1.72	(0.83, 3.58)	0.15
Type of organism	1.60	(0.69, 3.73)	0.28

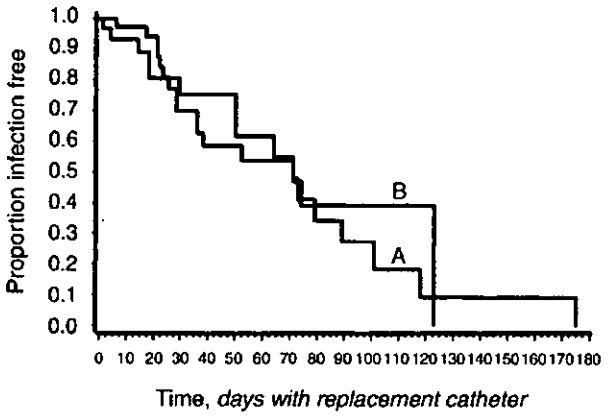

Fig. 1. Life-table analysis (Kaplan–Meier survival curves) for infection-free survival of the replacement catheter in patients whose dialysis catheter was replaced with one of two strategies (group A, replacement over a guidewire; group B, removal of the catheter with delayed replacement 3 to 10 days later, $P = 0.72$).

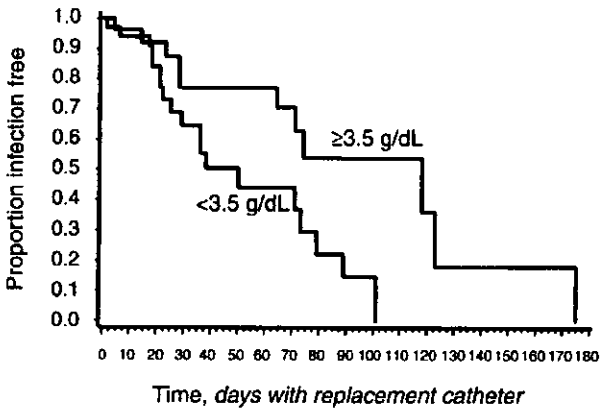

Fig. 2. Life-table analysis (Kaplan–Meier survival curves) for infection-free survival of the replacement catheter in patients with hypoalbuminemia (serum albumin < 3.5 g/dL) versus patients with a normal serum albumin, $P = 0.016$).

with a new one over a guidewire. Group B patients had their infected dialysis catheter removed, with delayed placement of a new catheter 3 to 10 days later. Patients in both treatment groups were treated with three weeks of systemic antibiotics. The patients in both groups were similar to each other in terms of age, sex and race distribution, frequency of diabetes, type of infective organism, and severity of infection, as inferred from the frequency of serious complications (Table 1).

Of the 69 replacement dialysis catheters, 32 had to be removed because of a second infection (Table 1). In addition, 19 catheters were replaced because of malfunction (thrombosis or poor flow). Twelve were removed electively because the patient had a fistula or graft that was ready to use, and six were patent and uninfected at the time of patient death or date of study analysis. On univariate proportional hazard regression analysis of infection-free catheter survival time, there was no significant difference between patients in groups A and B (Table 2 and Fig. 1). Patients with hypoalbuminemia (serum albumin < 3.5 g/dL) had a higher hazard of a second episode of catheter-associated bacteremia than patients with a normal serum albumin (Table 2 and Fig. 2). The infection-free survival time was not significantly affected by patient age, sex, race, diabetic status, or type of infective organism (Table 2). Finally, using multivariable stepwise proportional hazard regression analysis, only low serum albumin and male sex had increased hazard of catheter infection (this was true whether serum albumin was treated as a categorical or continuous variable).

Among patients whose initial infection was with a gram-positive organism, the second infection was with another gram-positive organism in 88% of the cases. In contrast, following a gram-negative, catheter-associated bacteremia, the next infection was equally likely to be with a gram-positive or gram-negative organism.

DISCUSSION

We observed a high frequency of infections of the replacement dialysis catheter following an initial episode of catheter-associated bacteremia. Although this was not a randomized study, the patients in groups A and B were closely matched in terms of their clinical characteristics (Table 1). The infection-free survival time was similar whether the initial dialysis catheter was exchanged with a new one over a guidewire (group A) or whether it was removed with delayed placement of a new catheter 3 to 10 days later (group B). The former strategy requires a single, relatively brief procedure by interventional radiology, without an interruption of the outpatient hemodialysis schedule. In contrast, the second strategy involves two separate radiologic procedures, at least one femoral dialysis catheter placement, and at least one dialysis session in the inpatient dialysis unit. Moreover, the removal of an infected catheter carries the risk of losing a potential vascular access site as a result of occlusion of a central vein. Thus, from the perspective of cost-benefit analysis,

as well as patient convenience, the strategy of catheter exchange is clearly preferable in those patients who qualify.

The inverse relationship between the risk of recurrent infection in the replacement catheter and serum albumin was striking. Previous studies have found an association of hypoalbuminemia with systemic infection in hemodialysis patients [13]. The mechanism by which hypoalbuminemia predisposes to recurrent infection remains to be elucidated.

The frequency of serious complications following catheter-associated bacteremia was remarkably high, but consistent with a previous report [11]. At our institution, 14% of the prevalent hemodialysis population were using a tunneled dialysis catheter for vascular access. A recent survey by the Centers for Disease Control reported that 17.5% of patients in the United States were dialyzing with a dialysis catheter [2]. The ongoing Dialysis Outcomes and Practice Patterns Study (DOPPS) found that 62% of new U.S. hemodialysis patients and 31% of prevalent patients were using a dialysis catheter, rates that are substantially higher than those observed in European hemodialysis patients (personal communication from David Goodkin, M.D., Amgen Corporation, Thousand Oaks, CA, USA). Extrapolating our experience to the U.S. dialysis population suggests the occurrence of a very large number of catheter-associated infections in the United States, resulting in serious morbidity in many of these patients. The current study suggests that a strategy of elective catheter exchange in patients with catheter-associated bacteremia is an acceptable alternative to catheter removal with delayed placement of a new catheter. Moreover, the catheter exchange strategy should reduce the number of procedures, decrease the cost, and minimize the disruption of the outpatient hemodialysis schedule.

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Catheter-Related Sepsis Complicating Long-Term, Tunnelled Central Venous Dialysis Catheters: Management by Guidewire Exchange

David Shaffer, MD

● Standard therapy of catheter-related sepsis of long-term, tunnelled, silicone dialysis catheters is catheter removal, parenteral antibiotics, and catheter replacement in a new venous site after documented clearing of bacteremia. This leads to loss of future venous access sites. Thirteen consecutive cases of dialysis catheter-related sepsis in 10 patients successfully managed by guidewire exchange with preservation of the same central venous access site are reported. Although the most common cause of catheter sepsis in this series was coagulase-negative staphylococcus, guidewire exchange also was successful in cases due to gram-negative rods and yeast. To preserve future venous access sites in the chronic hemodialysis population, long-term, tunnelled dialysis catheter-related sepsis should be managed by a short course of parenteral antibiotics and by changing the catheter over a guidewire using the same venous insertion site.

INDEX WORDS: Vascular access catheter; hemodialysis; infection.

PROVIDING long-term vascular access for chronic hemodialysis remains an ongoing challenge for surgeons and nephrologists. In an increasing number of patients, an autogenous vein or synthetic graft arteriovenous fistula cannot be created or maintained due to age, cardiac or peripheral vascular disease, or multiple previous failed accesses. In these patients, tunnelled, dual-lumen, silicone central venous dialysis catheters have provided an alternative method of long-term hemodialysis access.[1-4]

While providing satisfactory vascular access in these high-risk patients, infection and thrombosis remain the major factors limiting their long-term use. In a previous study, we reported a 6-month actuarial catheter patency rate of 53%, with sepsis accounting for almost half the cases of catheter failure.[1] Standard therapy of catheter-related sepsis involving tunnelled, long-term silicone catheters is catheter removal and systemic antibiotics followed by a new catheter at a new venous site after eradication of the bacteremia.[5] In the chronic dialysis population, this has the disadvantage of loss of a venous access site in a group with limited vascular access and in whom maintenance of indefinite vascular access is critical. It also leads to prolonged hospitalization, multiple procedures, and increased costs. In an effort to preserve central venous access sites and limit hospitalization, the author began to manage catheter-related sepsis in long-term, tunnelled central venous dialysis catheters by changing the catheter over a guidewire under antibiotic coverage using the same venous site, similar to the management of suspected catheter sepsis from short-term, nontunnelled central venous catheters used for hyperalimentation, chemotherapy, or hemodynamic monitoring.[5-7] The following is a report of the author's initial experience with 13 consecutive episodes of tunnelled, hemodialysis catheter-related sepsis in 10 patients managed by guidewire exchange.

MATERIALS AND METHODS

Between October 1992 and April 1994, 98 tunnelled, dual-lumen, silicone central venous dialysis catheters (Quinton PermCath; Quinton, Seattle, WA) were inserted. The majority were inserted for prolonged temporary vascular access until an autogenous vein or synthetic graft arteriovenous fistula was available. Due to the risk of subclavian vein stenosis or thrombosis, the preferred insertion site was the internal jugular vein. Seventy-seven catheters were inserted into the right internal jugular vein, 15 into the left internal jugular vein, two into the right external jugular vein, and four into the femoral vein. Sixty-eight catheters were inserted percutaneously using a Seldinger technique and pull apart introducer (Quinton), and the remainder (predominantly left-sided) were inserted by surgical cutdown as previously described.[1] All catheters were inserted in the operating room under local anesthesia with intravenous sedation. Fluoroscopy was not used, but correct catheter tip placement was confirmed by chest x-ray films in all cases prior to leaving the operating room.

One gram of cefazolin intravenously was given preoperatively at the time of initial catheter insertion as antimicrobial prophylaxis. One gram of vancomycin was given in patients

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Table 1. Management of Catheter-Related Sepsis by Guidewire Exchange

Patient No.	Onset of Catheter Sepsis (Months Postinsertion)	Blood Catheter	Blood (Venipuncture)	Catheter Tip	Follow-Up
1	3	SCN	SCN	Negative	SCN *Xanthomonas maltophilia* infection at 2.5 mo; guidewire exchange
2	2.5	SCN, *X maltophilia*	Negative	Negative	Clotted at 1 mo, culture-negative; guidewire exchange; functioning at 4 mo; kidney transplant
3	2.5	ND	*Staphylococcus aureus*	Negative	Functioning at 4 mo
4	40	*Serratia marcescens*	*S marcescens*	Negative	SCN infection at 3 mo; guidewire exchange
5	3	SCN	SCN	Negative	Clotted at 4 mo, culture-negative; re-sited
6	7.5	Enterococcus	Enterococcus	Positive	Functioning at 1 wk; died of myocardial infarction
7	14	*Bacillus* sp	Negative	Negative	Functioning at 6 mo
8	3	SCN	Negative	Positive	Functioning at 1 mo; changed to peritoneal dialysis
9	17	SCN	SCN	Negative	SCN infection at 13 mo; guidewire exchange
10	18	SCN, *Candida* sp	ND	Positive, Candida	Functioning at 3 mo; died of myocardial infarction
11	4.5	SCN	SCN	Negative	Functioning at 5 mo
12	0.5	SCN	ND	Negative	Functioning at 5 mo
13	13	SCN	SCN	ND	Functioning at 6 mo

Abbreviations: ND, not done; SCN, coagulase-negative staphylococcus.

allergic to penicillin. A total of 5,000 U of heparin was instilled in each catheter port immediately after insertion and after each subsequent hemodialysis treatment. Catheters were handled aseptically by the dialysis nursing staff; the exit site was swabbed with povidone-iodine solution and covered with gauze and a clear plastic occlusive dressing (Tegaderm; 3M, St Paul, MN) after each treatment. Patients were asked to keep the exit site dry at all times.

In cases of frank tunnel infection, catheters were removed and re-sited under systemic antibiotic coverage. In cases of persistent bacteremia despite systemic antibiotics without frank tunnel infection, catheters were changed over a guidewire via a 1-cm cervical incision using the same central venous insertion site but with creation of a new tunnel and exit site. The catheter tip was sent for routine bacteriologic cultures and repeat blood cultures were obtained via the catheter at the next hemodialysis treatment. Systemic antibiotics were continued 1 to 2 weeks following guidewire exchange. Blood cultures were repeated via the catheter at least 1 week after completion of the course of antibiotics.

RESULTS

Over the 18-month study period, 17 episodes of catheter-related sepsis in 14 patients were documented. Four patients had frank tunnel infections with a tender, erythematous subcutaneous tunnel and grossly purulent exit site drainage. In these cases the catheter was removed under systemic antibiotic coverage, a temporary catheter was placed in the femoral vein, and a new tunnelled catheter was inserted in a new central venous site several days later following clearing of the bacteremia.

Ten patients developed 13 episodes of catheter-related sepsis associated with long-term tunnelled central venous dialysis catheters; these were treated by guidewire exchange (Table 1). All patients were symptomatic at the time blood cultures were obtained; surveillance cultures were not routinely obtained. Catheters had been in place a mean of 10.3 months (range, 2 weeks to 40 months) prior to the onset of sepsis. Patients received a variable course of preoperative antibiotic therapy (range, 1 day to 6 weeks) depending on symptoms and culture results in an attempt to eradicate the infection with the catheter in place prior to surgical referral and guidewire exchange. All patients, however, continued to have positive blood cultures (either via the catheter, venipunc-

ture, or both) on antibiotic therapy at the time of guidewire exchange.

Three patients were treated a second time by guidewire exchange for recurrent catheter-related sepsis 2.5, 3, and 13 months after the initial episode (Table 1; patients no. 1, 4, and 9). Each appeared to be a de novo infection since each patient had negative interval blood cultures. In addition, the bacteriology in two of the three recurrent infections was different than the initial episode, making it likely that there was a second infection rather than failure to eradicate the initial infection by guidewire exchange. In the third patient, although the isolated organism was coagulase-negative staphylococcus (SCN) in both episodes, the two episodes occurred 13 months apart, again suggesting a second, de novo infection.

The bacteriology of catheter-related sepsis in this series is also summarized in Table 1. Coagulase-negative staphylococcus was the predominant organism (nine cases). In one patient the catheter became secondarily infected with *Serratia marcescens* 1 week following removal of an infected hip prosthesis; persistent bacteremia despite parenteral antibiotics cleared following guidewire exchange. Two patients had a second organism isolated in addition to SCN. In the first patient, both blood drawn via the catheter and the catheter tip at the time of guidewire exchange grew *Candida albicans*. This patient received a 10-day course of oral fluconazole following guidewire exchange with clearing of both organisms. It is noteworthy that this patient had received 8 weeks of intravenous vancomycin in an attempt to eradicate persistent SCN bacteremia prior to surgical referral. In addition to SCN, a culture of *Xanthomonas maltophilia* was grown from the second patient, who received 1 week of intravenous ceftazidime following guidewire exchange; clearing of both organisms also occurred in this patient.

Catheter tip cultures were positive in three patients at the time of guidewire exchange and were negative in the remaining cases. Clearing of catheter-related sepsis was documented in two of the three cases with positive catheter tip cultures, with both catheters functioning without evidence of infection at 1 and 3 months postoperatively. In the third patient with a positive catheter tip, blood cultures immediately following guidewire exchange were negative, but the patient died of an acute myocardial infarction 1 week later.

DISCUSSION

While the use of dual-lumen, tunnelled, silicone central venous catheters has become commonplace for prolonged temporary hemodialysis access, catheter-related sepsis remains a major problem limiting their long-term or permanent use.[1-3] This is due in part because conventional therapy of tunnelled catheter-related sepsis has been catheter removal with parenteral antibiotics and subsequent catheter reinsertion in a new venous site after documented clearing of the bacteremia. In the hemodialysis population, this leads to loss of critical central venous access sites. Catheter exchange over a guidewire has been advocated by some[5-7] but not others[8,9] for sepsis complicating short-term, nontunnelled central venous catheters. Similarly, the management of sepsis complicating long-term, tunnelled catheters remains controversial. While some investigators recommend intravenous antibiotics initially for treatment only of SCN infections complicating long-term silicone catheters, with catheter removal and replacement in a new site in all cases of polymicrobial, gram-negative, or fungal infections and in those cases of SCN infections that do not respond to a short course of parenteral antibiotics,[5,10] other investigators have successfully managed catheter-related sepsis with intravenous antibiotics and guidewire exchange alone.[4] In addition, most previous reports of the use of intravenous antibiotics or guidewire exchange for the treatment of catheter-related sepsis have included only catheters used for hyperalimentation, chemotherapy, or hemodynamic monitoring,[5-10] with less data on the management of sepsis specifically complicating long-term hemodialysis catheters.[4]

This report of 13 consecutive infections in long-term, tunnelled hemodialysis catheters demonstrates that in the absence of a frank subcutaneous tunnel infection, catheter-related sepsis can be successfully managed by guidewire exchange under a short course of antibiotic coverage with preservation of the same central venous insertion site. Guidewire exchange appeared to be adequate therapy for catheter-related sepsis due to SCN that failed to respond to a prolonged course of parenteral antibiotics alone, given in one case for as long as 2 months. The absence of reinfection due to intraoperative contamination may be due to the fact that although the same central

venous insertion site was used, a new subcutaneous tunnel was created in all cases. Although the experience was limited to five cases, guidewire exchange also appeared to be adequate therapy for catheter-related sepsis due to more virulent organisms, such as gram-negative rods and yeast. Finally, guidewire exchange in the three cases with a positive catheter tip culture also successfully cleared the catheter infection.

These data support those reported in an earlier study by Carlisle et al in which 17 of 21 episodes of catheter-related sepsis complicating tunnelled, silicone dialysis catheters were eradicated by guidewire exchange and antibiotics.[4] The four cases requiring complete removal and re-siting of the catheter all had frank exit site or tunnel infection.

In conclusion, guidewire exchange with a short perioperative course of antibiotics is adequate to treat most cases of catheter-related sepsis complicating long-term, tunnelled hemodialysis catheters. This allows preservation of central venous access sites and makes dual-lumen, tunnelled catheters a viable long-term option for chronic hemodialysis in patients with limited vascular access.

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This guidance was written prior to the February 27, 1997 implementation of FDA's Good Guidance Practices, GGP's. It does not create or confer rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both. This guidance will be updated in the next revision to include the standard elements of GGP's.

Center for Devices and Radiological Health

Office of Device Evaluation

Division of Gastroenterology/Urology and

General Use Devices

Guidance on 510(k) Submissions for Implanted Infusion Ports

October 1990

General Submission Requirements

A person proposing to begin the introduction of a new implanted drug infusion/blood sampling port into interstate commerce must submit a premarket notification (510[k]) submission to FDA at least 90 days prior to its introduction.

The general requirements for 510(k) submissions are provided under 21 CFR 807, Subpart E. The 510(k) submissions for implanted ports are evaluated by the General Hospital and Personal Use Devices Branch, Division of Gastroenterology/Urology and General Use Devices.

Overview

A score of implanted ports have been found substantially equivalent through the 510(k) process. The great majority of these ports have been indicated for intravascular (intravenous and intraarterial) use. These substantially equivalent determinations have been based upon comparisons of design specifications with other marketed ports and analysis of performance data derived from in vitro and in vivo testing.

Tens of thousands of ports are now implanted yearly. The design features and clinical experience with ports have matured to a point where FDA believes that the clinical performance of a new intravascular port is predictable provided it has the same intended use and technological characteristics as other marketed ports, satisfactory in vitro testing, and adequate instructions for use.

Thus, in general, in vivo (animal or clinical) data are unnecessary to evaluate equivalence in a 510(k) application of a port for intravascular use that meets the above criteria. However, as detailed below, in certain instances FDA may request in vivo data to establish equivalency.

Total adherence to the specifics of this guidance is not mandatory. It does, however, present important elements to address in a 510(k) submission. Alternatives or modifications to any portion of the guidance may be submitted but should be justified.

Specific Data Requirements for Implanted Ports for Intravascular Use

1. Description of Device

   a. Specifications of port and catheter (specifications must also include catheter physical tests, e.g., tensile, burst)

   b. Engineering drawings (or equivalent)

c. Exact identification of materials, not simply 'stainless steel'

2. Labelling/Instructions for Use

a. Description and specifications of the port components

b. Indications/route of administration, e.g., IV, IA, blood sampling, drug administration, bolus, continuous administration, etc.

Note: If any specific drugs are indicated in the labelling for infusion by the port, the drugs must be approved for the indicated route of administration.

c. Contraindications for those with known or suspected infections, allergies, intolerance to implants, etc.

d. Complications

e. Warnings and Precautions

f. Site selection

g. Implantation

Preparation of the patient
Preparation of the port
Implant procedure
Post-operative care

h. Use of the port for bolus infusion (and continuous, if indicated), or blood sampling, noting needle type and size used, use of heparin, and clearing blockages

3 Table of Comparisons

a. Similar Ports vs. Specifications Grid

Provide a grid comparing the subject device to other ports with comparable characteristics for which equivalence is claimed.

Specifications include dimensions, reservoir volume, catheter ID/OD, materials, septum size, catheter, and catheter lock system.

b. Provide a detailed analysis of comparability based upon the grid.

4. Provide a sample, if possible.

5. In Vitro Test Data

NOTE: All in vitro evaluations should consist of replicate tests and a complete statistical analysis of each segment of testing. Pass/fail criteria must be stated for each test and justified in terms of actual use conditions. The manufacturer must submit the protocol for each test, results and data analysis, explanation for any failures, and conclusions. FDA will provide quantitative information on pass/fail criteria in the next major revision of this guidance (late 1991) based upon the literature and comparative data in 510(k)s. In the interim only qualitative criteria are described.

a. Catheter To Port Connection Tests

Purpose: To test the strength of the catheter to port connection.

Pass: Strength of connection meets specifications based upon worst case in vivo conditions.

Test the catheter to port connection under dry and wet conditions. The wet condition simulates both the external and internal fluid environment to which the catheter to port connection will be exposed, e.g., interstitial fluid, blood, drugs, or flushing solutions. A series of external wet conditions may be tested first followed by exposure of the port to catheter connection to a series of combined external and internal wet conditions. Internal simulation media should include saline, water, dextrose, a heparin-lock, heparinized blood and/or a fluid that approximates the viscosity of blood (see example below of a blood simulation fluid). The external media may include those noted above but must include at least the ~~actual~~ or ~~simulated~~ blood media.

Ports and catheters that are not preattached by the manufacturer must be connected in the wet medium unless labelling indicates connection prior to implantation.

Load conditions vary under actual use. To simulate the variables encountered several types of replicated simulations should be considered. These include:

(1.) axial and lateral loads for each test

(2.) a test where a load equal to the specification is applied for 5-10 seconds

(3.) a test where a load equal to the specification is applied after the connection is exposed for 72 hours to

the wet medium

(4.) an increasing load to failure test

(5.) a test with a minimal load applied for 1-2 weeks with the port in the wet medium to evaluate any creep

(6.) a test with a cyclic load of 1-2 weeks duration

The tests should demonstrate that the catheter meets the specifications or pass/failure criteria for the connection and does not exhibit leaks to air under pressure after loading.

The catheter/port may be removed from the wet medium for connection strength determinations, if necessary, but the connection must remain wet.

Preparation of saline/glycerine solution: distilled, deionized water mixed with 45% glycerine by weight. Titrate with NaCl (2.9 gm/l) for a resistance of approximately 150 ohms at 37°C.

b. Septum Puncture

Purpose: To test the durability of the septum.

Pass: Septum withstands maximum possible punctures (punctures/day x days) plus a safety factor.

Use only the needles listed in labelling on series of ports. Typically, noncoring needles are used. The number of punctures that must be sustained depends upon the life of the port, anticipated punctures per day, plus a safety factor of 1/3. Conduct air leak test after punctures with applied internal pressure equivalent to that encountered in vivo, in a 37°C water bath checking for bubbles. Increase pressure and report the pressure at which the septum exhibits air leaks. Justify the puncture specification based on the data.

c. Port Leak Testing

Purpose: To test the integrity of the whole port.

Pass: Port does not leak under extremes of expected in vivo conditions.

The test regimen should consist of both intermittent and continuous applied pressure to a series of ports to simulate bolus injection and continuous fluid administration by pump. The pressures applied must be

justified in view of those encountered with syringe or pump use and backpressure conditions. Test in 37° C water bath. Check for port seam and septum leaks.

Increase pressure to failure point of port and report maximum pressure attained.

d. Fluid Dynamics Tests

(1.) Clearance Test (see attached)

Purpose: To test clearance kinetics of the port and catheter, and flushing volume requirements of the port and catheter.

Pass: Port clears with reasonable amount of flushing volume and applied syringe pressure.

Attach the catheter to the port, if it is a two piece port. Fill the port with 150 ohm glycerine/saline solution noted above. Put impedance transducer on catheter. Insert non-coring needle in septum. Attach a specified syringe, e.g, 10 ml, with specific volume of flushing solution that has an impedance less than the glycerine/saline solution (e.g. 0.9% NaCl/distilled water giving 50 ohms at 37°C). Submerge the port in a 37°C bath and let the system equilibrate. Instill flushing solution at a specific rate. Record impedance change over time.

The data should be used to gauge the clearance capabilities of the port and adequacy of labelling directions pertaining to flushing.

Results from alternative test methods that address clearance kinetics and flushing requirements may be submitted along with the test protocol.

(2.) Blood Flow Dynamics

Blood is a unique liquid which exhibits flow characteristics and other properties that cannot be fully duplicated by substitute liquids more amenable to laboratory procedures. While the clearance test [5.d.(1.) above] approximates the clearance of a liquid with the viscosity of blood, the test is not an ideal substitute for evaluating actual blood sampling and flushing. FDA encourages manufacturers to develop <u>in vitro</u> methodology to simulate flow patency under repeated blood sampling/flushing and other forward injection/aspiration procedures.

Situations Which Require Additional Data

1. New designs

   Port designs which are not similar to those currently on the market may require additional in vitro and in vivo data. The requirement for additional data will be made on a case by case basis. Such design characteristics could include, for example, a new profile or angle of septum access, a unique catheter lock, or a new type of catheter.

2. New material

   There are several commonly used materials for port construction. A material not previously used for implantable ports will require more extensive biocompatibility, material specifications, and drug interaction data.

3. New route of administration

   a. Until there is further experience with intraperitoneal (IP) use, an IP indication must be supported by clinical data.

   b. Intraspinal administration (epidural or intrathecal catheter implantation) is Class III and requires premarket approval through a PMA application.

4. Comparative or expanded labelling claims, e.g., reduction of infection or occlusion, may require supportive clinical or other data.

5. Indications for pediatric use must be accompanied by a risk analysis for this population and may require supporting data.

ANY COMMENTS ON THIS GUIDANCE DOCUMENT SHOULD BE DIRECTED TO:

Chief, General Hospital
and Personal Use Devices Branch
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EVALUATION OF CLEARANCE KINETICS OF A PORTAL VASCULAR ACCESS SYSTEM

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ABSTRACT

A portal vascular access system is a totally implantable system comprised of a fluid reservoir with an attached catheter. The system provides easy access for patients requiring a continuous supply of medication or repeated blood sampling. To ensure no obstruction of flow, the system must be flushed to clear the port and catheter, making it important to establish the clearance parameters. This paper describes a method to obtain these parameters using a tetrapolar impedance cell to monitor the relative impedance change using two solutions of different resistivities to fill and flush the system. The resulting impedance dilution curve allows calculation of time delay, dilution time, clearance time and clearance volume. This method and resulting data may be used to characterize a portal vascular access system and provide a basis for comparative analysis of newly introduced systems.

INDEX WORDS: portal vascular access system, clearance volume, impedance dilution curve, clearance parameters

For the patient requiring repeated injections, continuous infusion of drugs or fluids, or repeated blood samples, the portal vascular access system simplifies blood access. The system includes a fluid reservoir commonly called a "port" and a catheter extending from the reservoir (see Figure 1). For venous access, catheters most commonly extend to the superior vena cava through the subclavian vein for venous access. Ports are also used for infusion into the arterial blood vessels, the peritoneum and the central nervous system. Thousands of portal access systems are implanted yearly and the number is increasing. (Figure 1)

Once implanted, a port is accessed by insertion of a needle through the skin into the rubber septum covering the port. Drugs or fluid can be injected or blood can be sampled through the needle. After access is accomplished, but before removing the needle, sterile flushing solution must be injected to clear the port and catheter of drugs or blood. Insufficient flushing may result in clogging or clotting of the catheter and patency will be lost. The volume and flow rate of fluid required for adequate flushing (clearance) depend upon the fluid dynamics of the particular system. The clearance volume is different for different flow rates.

To determine the clearance volume, impedance dilution with two sample solutions of different impedances (one for filling and one for flushing) may be used. After filling the portal access system with the filling solution, injection of a flushing solution of different impedance will produce a record of impedance dilution. Measuring the elapsed time required for a maximum impedance change (reaching

the impedance of the flushing solution) allows calculation of the clearance volume for a given flow rate. This report describes an approach for the measurement of clearance volume of the port reservoir and attached catheter.

METHODS

To detect relative impedance change and thereby calculate the clearance volume of the portal access system, two solutions of different resistivities were prepared: one for filling the system and another for flushing the system. The filling solution chosen was a saline/glycerine mixture, approximating the viscosity of blood, comprised of distilled water mixed with 45% glycerine by weight with added NaCl (2.9 gm/l). The flushing solution chosen was a 0.9% saline mixture. To maintain temperature equilibrium, one beaker containing 0.9% saline and one beaker containing the glycerine/saline solution were placed in a 37°C bath of distilled water.

In order to detect the relative change in impedance which occurs as the flushing solution replaces the filling solution, a tetrapolar impedance cell was implemented at the end of the catheter (see Figure 2). The impedance cell employed four electrodes; current was supplied between the outer two electrodes while the inner two electrodes measured the voltage produced by the current passing through the solution; impedance is the implied voltage divided by the applied current according to Ohm's law. (Figure 2)

The measured resistance, R, is equal to the resistivity of the solution, ρ, multiplied by the cell constant, k. Resistivity of a saline solution can be related to concentration by the equation

$$\rho = 379.1 / C^{0.9149},$$

where C is the concentration of saline at 37°C, and therefore the measured resistance is related to concentration by

$$R = 379.1\ k / C^{0.9149}$$

(Geddes and Baker, 1989). For application in this study, the precise values of ρ and R are not needed since clearance parameters may be obtained from relative impedance change.

A slit of approximately 3 mm in length was cut in the catheter wall near the distal end of each of the two sizes of catheters (1.0 and 1.5 mm ID) which were supplied with the vascular access system studied (VITAL-PORT™ Vascular Access System, Cook Pacemaker Corporation, Leechburg, PA). A tetrapolar impedance cell was affixed in the slit without impeding flow using Locktite 406 (Loctite Corp., Newington, CT) with the electrodes perpendicular to the direction of flow through the catheter. The electrodes were located 63.9 and 67.5 cm distal to the port for the 1.0 and 1.5 mm ID catheters, respectively. The output of the impedance cell was plotted on a strip chart recorder.

Using a resistivity bridge, the measured resistance of the glycerine/saline solution was 160 ohms and the measured resistance of the 0.9% saline solution was 52 ohms. The entire system, including the catheter, was submerged in a 37°C bath. The portal access system was filled with the glycerine/saline solution and allowed to thermally equilibrate. With the chart recorder activated at a paper speed of 25 cm/min and a stable voltage signal from the impedance cell reflecting the impedance of the system filled with the glycerine/saline solution, a constant flow rate (5, 25 or

50 ml/min) of flushing solution (0.9% saline) was delivered by an automatic pump with a 20 cc syringe attached to a 22 gauge 1.5 inch Huber non-coring needle. Measurements were made with the needle placed in various locations in the septum as well as facing various angles with respect to the port outlet tube (needle orientation at 0, 90 and 180 degrees). System filling and flushing were repeated three times for each flow rate (5, 25 and 50 ml/min) for each needle orientation to obtain an average delay time, dilution time, clearance time and clearance volume.

Upon injection of the flushing solution, the relative impedance change between the filling solution and the flushing solution was evident on the strip chart recorder (see Figure 3). Knowing the flow rate of the flushing solution and the paper (Figure 3) speed of the strip chart recorder, measurements were made of the delay time, dilution time, total clearance time and total clearance volume. The time delay was measured between the onset of injection of the flushing solution and the onset of an impedance change. This delay is related to the static volume within the reservoir and catheter. Dilution time was measured between the beginning and ending of the impedance change. Total clearance time was measured between the onset of injection and the end of the impedance change. Clearance volume was obtained as the product of flow rate and clearance time, and can be cross checked with the actual injected volume.

The above procedure was repeated with a 1.5 mm ID catheter attached to the portal access system. Filling and flushing solutions prepared for the 1.5 mm ID catheter had measured resistances of 155 ohms and 52 ohms, respectively. Again, system filling and flushing were repeated three times for each flow rate and needle

orientation to obtain an average delay time, dilution time, clearance time and clearance volume with respect to each flow rate.

In order to relate flow rates (ml/min) to infusion pressure (PSI) in the portal vascular access system, a stainless steel diaphragm pressure transducer (Foxboro/ICT model 1221-08G-K5L) was used to obtain pressures at the needle hub.

RESULTS

For the VITAL-PORT™ Vascular Access System, there were no significant differences in the clearance volume data related to the orientation (angle of the needle with respect to the port outlet tube) using either the attached 1.0 mm or 1.5 mm ID catheters. Although data recorded with respect to the location of the needle in the septum (proximal edge, middle or distal edge) were not exhaustive, no significant differences were noted. Data for each flow rate, independent of needle position, were therefore averaged for each catheter size.

The delay times, dilution times, total clearance times and clearance volumes are tabled for the 1.0 mm ID (see Table I) and the 1.5 mm ID (see Table II) catheters. (Table I) (Table II)
In general, higher flow rates require higher clearance volumes, but shorter clearance times and delay times between initial injection and onset of dilution. The 1.5 mm ID catheter requires more clearance volume and clearance time than the 1.0 mm ID catheter.

Infusion pressures for the 1.0 and 1.5 mm ID catheters resulting from flow rates of 50, 25, and 5 ml/min are tabled for the filling (see Table III) and flushing (see Table IV) solutions. As expected, higher flow rates yield higher pressures. The difference in pressures between solutions demonstrates the effect of different viscosities of the filling and flushing solutions. (Table III) (Table IV)

DISCUSSION

Data from this study may be used to determine clearance volumes for the Vital-Port™ Vascular Access System. The procedure, however, may be applicable for any portal vascular access system.

In assessing the data from this study for constant flow rates of 5, 25 and 50 ml/min, it should be noted that a flow rate of 5 ml/min corresponds to a very slow hand-delivered injection rate. A flow rate of 50 ml/min more closely approximates probable hand-delivered flow rates through the system.

While this technique yields the clearance volume of a population sample of systems, the recommended clearance volume should be at least 30% higher than the measured clearance volume obtained in the study, allowing for a safety factor to assure adequate clearance of the system in clinical practice. Assuming the rate of injection by hand approximates 50 ml/min, at least 5.2 ml should be injected to assure clearance (30% increase over the mean value, 3.99 ml found in Table I) for the VITAL-PORT™ Vascular Access System using the 1.0 mm ID (64.0 cm long) catheter. For complete clearance through this same portal system using the 1.5 mm

ID (67.5 cm long) catheter, at least 7.5 ml of solution should be injected (30% increase over the mean value, 5.79 ml at a flow rate of 50 ml/min found in Table II).

The measured and suggested clearance volumes are based on the maximum length catheter. In clinical application, the site for the portal access system is selected and the catheter is cut to the appropriate length, usually 30 cm or less. This results in a reduction in the volume capacity of the system of approximately 0.7 ml using the 1.5 mm ID catheter and 0.3 ml using the 1.0 mm ID catheter. For most situations, to ensure clearance using this portal access system, it would therefore be adequate to inject 4.9 ml (5.2 ml - 0.3 ml) through the portal system using the 1.0 mm ID catheter and 6.8 ml (7.5 ml - 0.7 ml) using the 1.5 mm ID catheter. However, for the sake of simplicity and safety, the maximum clearance volumes may be the recommendation of choice.

Results of this study describe the clearance characteristics for the VITAL-PORT™ Vascular Access System using maximum length pre-attached catheters for injecting solutions with the viscosity of 0.9% saline. For applications using different catheters of varying lengths and/or alternate solutions, flow characteristics and other properties of the solution as well as of the catheter must be kept in mind in determining flow rates, pressures and clearance volumes. Although this study showed no effect of needle orientation for this system, it would be inappropriate to conclude needle orientation is unimportant in other systems. The effect of needle orientation should be considered in each new design. Given all the assumptions are understood and considered, this procedure appears to offer a simple technique for comparative analysis of vascular access systems.

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Table I.

CLEARANCE PARAMETERS FOR THE 1.0mm ID CATHETER

FLOW RATE (ml/min)	AVG. DELAY TIME(sec)	AVG. DILUTION TIME(sec)	AVG. CLEARANCE TIME(sec)	AVG. CLEARANCE VOLUME(ml)
5	6.2±0.7	17.6±1.9	23.9±1.8	1.99±0.15
25	1.6±0.2	6.0±0.6	7.5±0.6	3.14±0.23
50	1.1±0.1	3.7±0.5	4.8±0.5	3.99±0.41

Table II.

CLEARANCE PARAMETERS FOR THE 1.5mm ID CATHETER

FLOW RATE (ml/min)	AVG. DELAY TIME(sec)	AVG. DILUTION TIME(sec)	AVG. CLEARANCE TIME(sec)	AVG. CLEARANCE VOLUME(ml)
5	11.6±1.3	29.1±5.5	40.7±6.0	3.39±0.50
25	2.7±0.1	10.0±1.1	12.8±1.0	5.31±0.43
50	1.7±0.2	5.3±0.2	6.9±0.3	5.79±0.24

Table III.

NEEDLE HUB PRESSURE (PSI) FOR
FILLING SOLUTION (45% GLYCERIN IN SALINE)

FLOW RATE (ml/min)	Catheter Size 1.0mm ID	1.5mm ID
5	3.1	2.1
25	17.0	12.2
50	36.0	33.9

Table IV.

NEEDLE HUB PRESSURE (PSI) FOR
FLUSHING SOLUTION (0.9% SALINE)

FLOW RATE (ml/min)	Catheter Size 1.0mm ID	1.5mm ID
5	1.0	0.6
25	6.3	5.0
50	18.8	16.9

FIGURE LEGENDS

Figure 1. Photograph of the VITAL-PORT™ Vascular Access System. A rubber septum covers the port or fluid reservoir to which a supplied catheter is pre-attached through a port outlet tube. The oblong holes in the wall of the port provide suture sites.

Figure 2. Diagram showing set-up for obtaining impedance dilution curves to obtain clearance parameters for the VITAL-PORT™ Vascular Access System.

Figure 3. Impedance dilution curve obtained from a strip chart recorder. The impedance of the filling solution is indicated by Z_1. As the flushing solution is injected, there is a time delay (t) before the change in impedance (ΔZ) occurs. As flushing continues, an impedance dilution curve results over a period of time (T_D). When the port and catheter have been completely flushed or cleared, the impedance of the flushing solution (Z_2) is evident. The clearance time (T) is the period between injection of flushing solution and end of impedance change.

Figure 1.

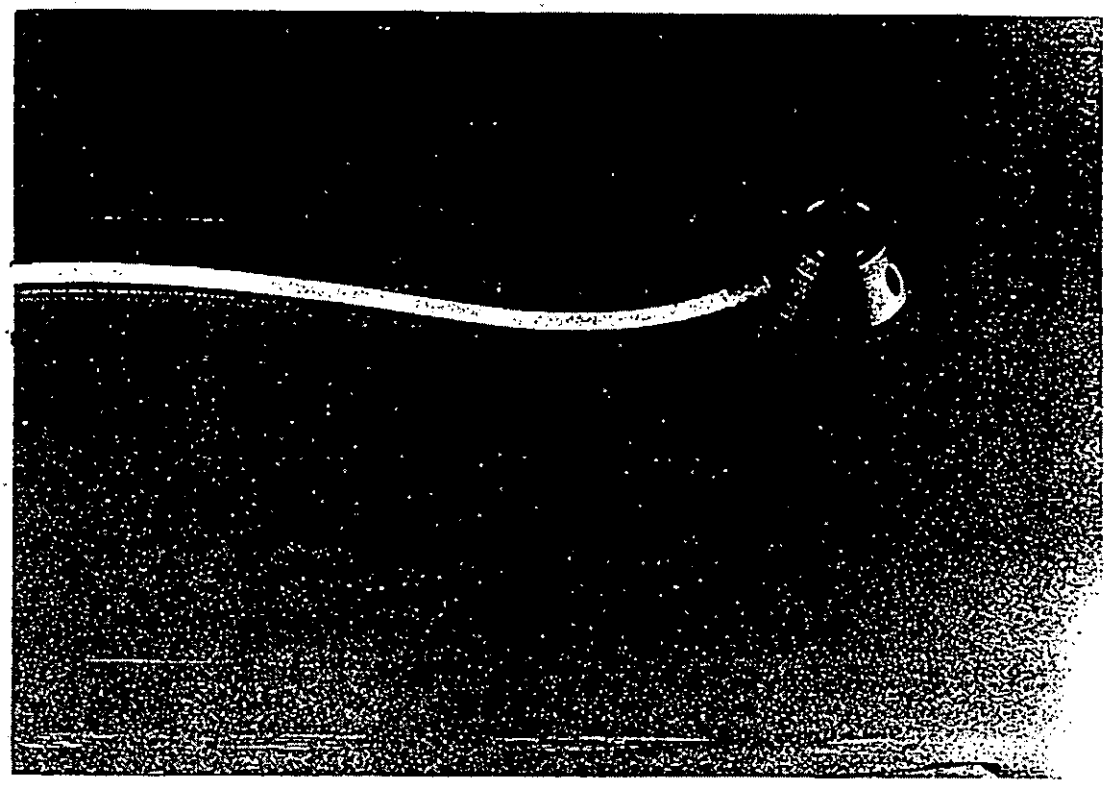


Figure 2.

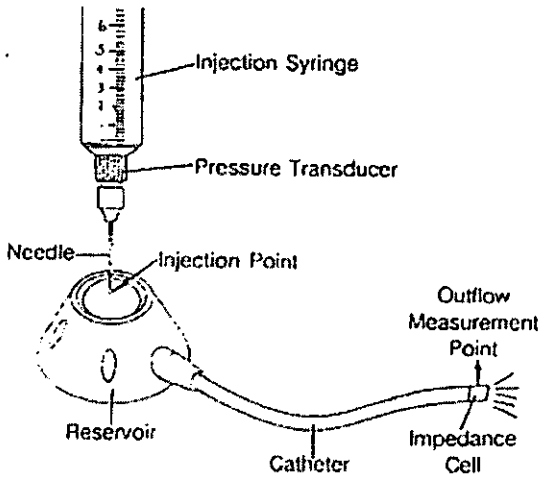
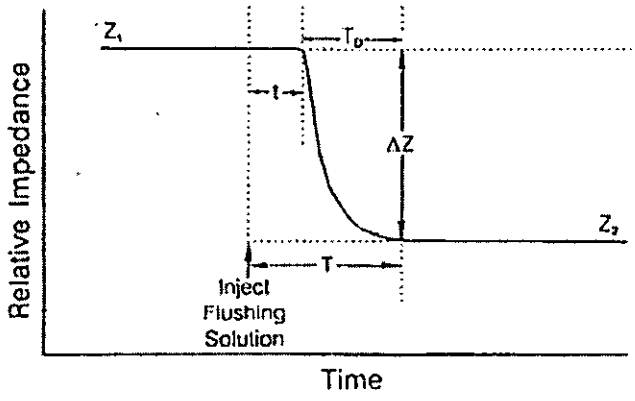

Injection Syringe
Pressure Transducer
Needle
Injection Point
Outflow
Measurement
Point
Reservoir
Catheter
Impedance
Cell

Figure 3.



Where: Z_1 = Impedance of Filling Solution
Z_2 = Impedance of Flushing Solution
t = Time Delay (sec.)
T = Time Required for Clearance (sec.)
T_0 = Dilution Time

THE EFFECTS OF PROLONGED ETHANOL EXPOSURE ON THE MECHANICAL PROPERTIES OF POLYURETHANE AND SILICONE CATHETERS USED FOR INTRAVASCULAR ACCESS

Christopher J. Crnich, MD, MS; Jeremy A. Halfmann, BS; Wendy C. Crone, PhD; Dennis G. Maki, MD

ABSTRACT

BACKGROUND: Products containing alcohol are commonly used with intravascular devices at insertion, to remove lipids from occluded intravascular devices used during parenteral nutrition, and increasingly for the prevention and treatment of intravascular device–related bloodstream infection. The effects of alcohol on the integrity of intravascular devices remain unknown.

METHODS: Two types of widely used commercial peripherally inserted central catheters, one made of polyetherurethane and one made of silicone, were exposed to a 70% ethanol lock solution for up to 10 weeks. Mechanical testing was performed to identify force-at-break, stress, strain, modulus of elasticity, modulus of toughness, and wall area of ethanol-exposed and control catheters.

RESULTS: No significant differences between exposed and unexposed catheters were identified for any of the mechanical parameters tested except for a marginal reduction in the modulus of elasticity for both polyetherurethane and silicone catheters and minor increases in the wall area of polyetherurethane catheters.

CONCLUSIONS: These data indicate that exposure to a 70% ethanol lock solution does not appreciably alter the integrity of selected commercial polyetherurethane and silicone catheters. Given the greatly expanded use of alcoholic solutions with intravascular devices of all types, we believe that manufacturers would be well advised to subject their catheters and other intravascular devices to formal testing of the type employed in this study (*Infect Control Hosp Epidemiol* 2005;26:708-714).

The use of intravascular devices in clinical practice has greatly expanded during the past two decades; more than 200 million intravascular devices are now used in hospitals, clinics, and the outpatient setting each year.[1] The wide array of available intravascular devices has enhanced our capacity to administer a large number of parenteral medications and total parenteral nutrition as well as intravenous fluids and blood products.

Unfortunately, every intravascular device, no matter the type, carries some risk of associated bloodstream infection (BSI).[2] As a result, the Healthcare Infection Control Practices Advisory Committee of the Centers for Disease Control and Prevention has periodically published evidence-based guidelines for the prevention of intravascular device–related BSI. The 2002 guidelines[3] now recommend, for the first time, use of a 2% solution of chlorhexidine for cutaneous antisepsis at the time of intravascular device insertion. Currently, the only chlorhexidine-based antiseptic commercially available for use with intravascular devices approved by the Food and Drug Administration contains 2% chlorhexidine gluconate in 70% isopropyl alcohol (Chloraprep, Medi-Flex, Leawood, KS). Many hospitals across the United States have adopted this product for vascular access. Medical-grade ethanol has also been used for many years for the removal of insipissated lipids from occluded intravascular devices used for parenteral nutrition.[4,5] Moreover, recent reports suggest that 25% to 70% ethanol used as a lock solution may be of value both as an adjunct to the treatment of intravascular device–related BSI[7] and for the prevention of infection with the use of long-term intravascular devices.[8]

The increasing use of alcohols for vascular access raises questions about their effects on the mechanical integrity of catheters. However, the studies addressing this important issue have been limited. McHugh et al. reported that luminal surfaces and wall thickness of polyurethane catheters exposed to ethanol for as long as 19 days were not significantly different from those of control

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catheters exposed to normal saline when examined by scanning electron microscopy; however, qualitative softening was observed for catheters exposed to ethanol." The authors did not undertake formal mechanical testing of the catheter materials evaluated. Studies performed in Japan found that the constant infusion of etoposide, which incorporates ethanol into its vehicle, was associated with microcracking of polyurethane catheters[10]; similar degradation was not seen for catheters made of polyvinyl chloride or silicone.

Given the rapidly growing exposure of all types of intravascular devices to alcohols, we studied the effects of prolonged exposure to 70% ethanol on the mechanical integrity of polyetherurethane and silicone intravascular catheters commonly used for long-term vascular access.

METHODS

Experimental Procedure

Standard tensile tests were conducted to evaluate the effects of prolonged exposure to ethanol on the mechanical integrity of two types of widely used peripherally inserted central catheters (PICCs): a 4 French single-lumen catheter (Arrow International Inc., Reading, PA) made of an aromatic thermoplastic polyetherurethane containing 20% barium sulfate for radiopacity and a 5 French single-lumen catheter (Cook Critical Care, Bloomington, IN) made of silicone. The inner and outer diameters of both types of catheter were determined after cross-sectioning by optical measurement using a Nikon Eclipse Optical Microscope (Nikon USA, Melville, NY) and Metamorph imaging software (version 5.02; Universal Imaging Corp., Downington, PA); the average cross-sectional area was 0.85 mm^2 for the polyetherurethane catheter and 1.75 mm^2 for the silicone catheter.

One set of catheters (15 polyetherurethane and 16 silicone catheters) was locked with 70% ethanol, whereas control catheters (17 polyetherurethane and 17 silicone catheters) were left empty (ie, were not locked with any solution). Study catheters in both groups were then immersed in prepared Hank's balanced salt solution held at 37°C, to simulate the effect of the human bloodstream, for 1 to 10 weeks. Mechanical testing was performed on ethanol-exposed and control catheters after 1, 2, 3, 5, 6, and 9 weeks for polyetherurethane catheters and after 1, 2, 3, 4, 7, 9, and 10 weeks for silicone catheters.

Preparation of Catheter Segments

At the time of mechanical testing, two or three test catheters from each treatment arm were removed from the Hank's balanced salt solution. The ethanol was drained from the treated catheters, and the catheters were allowed to air dry at room temperature. A minimum of three but as many as nine 25-mm segments were prepared from the tubular portion distal to the hub of each catheter, excluding the tip (Table). A solid steel core was introduced into each of the gripped ends to minimize the stress concentration effects and reduce the risk of failure due to pinching of the ends of the segment (Fig. 1). If such a failure occurred, the data were discarded and an additional specimen from the same catheter was tested. Mechanical testing of catheter segments was conducted on an Instron 5566 Universal Testing Machine (DatapointLabs, Ithaca, NY).

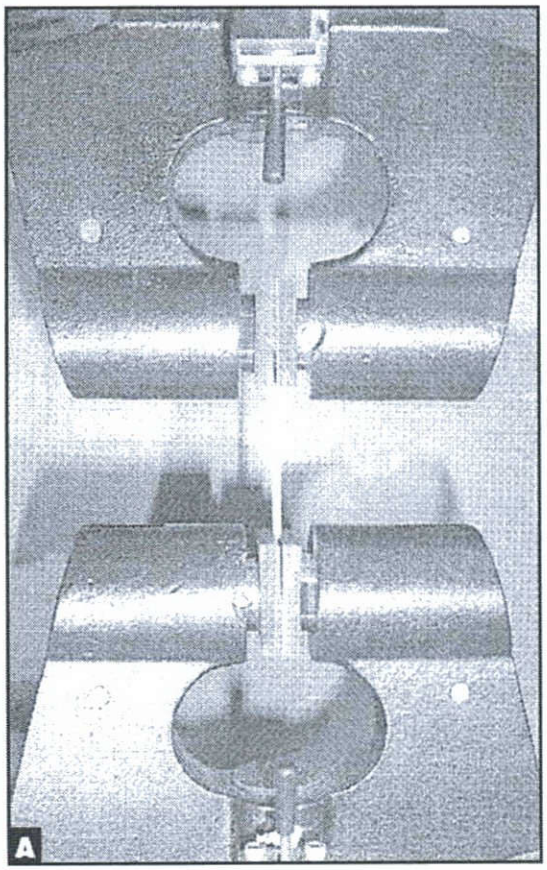
TABLE
NUMBER OF CATHETER SEGMENTS USED AT EACH EXPOSURE INTERVAL FOR POLYETHERURETHANE AND SILICONE CATHETERS

Catheter Material	Test Day	Ethanol	Control
Polyurethane	0	7	5
	14	9	7
	21	5	7
	36	7	6
	47	8	6
	67	5	3
Silicone	7	6	5
	15	6	6
	21	8	3
	29	5	5
	50	4	9
	67	3	4
	72	6	6

Tensile Testing

Tensile strength testing to determine force-at-break was conducted as delineated in standard 10555-1 of the International Organization for Standardization.[11] The conditioning procedure described in the standard was replaced by the experimental immersion procedure described above. Catheter junctions and hubs were not subjected to testing. All testing was conducted at room temperature. Force was measured in newtons (N), stress—the force per unit area—was recorded in megapascals (MPa), and strain—a dimensionless property characterizing stretch—was measured as the ratio of the change in length of the catheter segment to the original length of the catheter segment. Catheter segments were loaded while force and strain data were continuously recorded at 0.5-second intervals. A strain rate of 500 mm/min was employed to satisfy the 20 mm/min/mm strain rate recommended by the International Organization for Standardization standard.[11]

The mechanical properties of segments, including force-at-break (N), failure stress (MPa), elongation at failure (mm), maximum strain (change in length [mm]/original length [mm]), modulus of elasticity (MPa), modulus of toughness (MPa), and wall thickness, were measured for each of the study catheters. The elongation of catheter segments at failure (mm) was measured as the displacement of the grips at the time of breakage; direct placement of an extensometer on segments was not possible because they were too soft. Standard stress–strain curves were created from data generated during displacement-controlled loading of the catheter



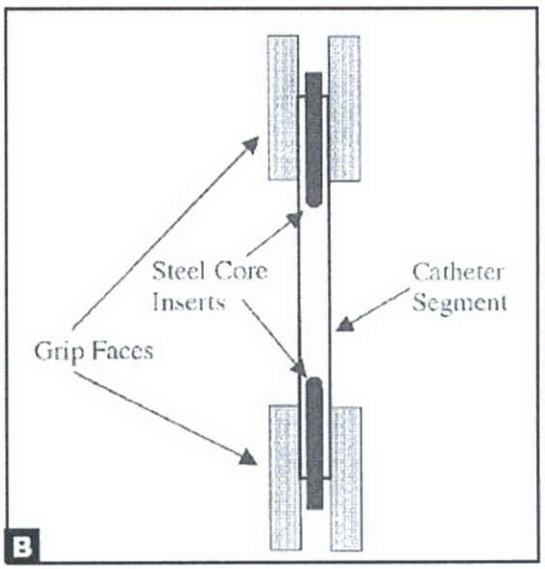


FIGURE 1. (A) A catheter segment loaded into an Instron 5566 Universal Testing Machine (DatapointLabs, Ithaca, NY) and (B) the location of the steel core inserts within the catheter segment to facilitate gripping within the testing apparatus.

segments. These curves were then used to calculate the modulus of elasticity (Young's modulus) and modulus of toughness.

Figure 2 shows a typical stress–strain curve for a silicone catheter segment. The initial slope of the curve is taken to be the elastic modulus, beyond which the specimen undergoes plastic deformation. Typically, after significant strain, the slope of the curve changes again. Rubbery polymers, such as polyurethanes and silicones, may exhibit an increase in stress prior to breakage as a result of strain-induced crystallization caused by molecular orientation in the direction of applied stress.[12] The modulus of elasticity was calculated from the slope of the linear region of the curve below 0.25 strain for silicone catheters and below 0.10 strain for polyurethane catheters. The modulus of toughness of a material represents the total amount of work the specimen is able to withstand before it fails and is proportional to the area under the entire stress–strain curve.

Wall Area

Wall area in square nanometers (nm^2) was determined by subtracting the inner wall area from the outer wall area, as determined by the optical measurement methods described above. The initial intent was to obtain multiple measurements from a single catheter segment and take the average of these measurements. However, within the first week of testing of silicone catheters, it became apparent that the wall area was not uniform throughout the length of the catheter lumen. Based on this knowledge, measurements were obtained from several different catheter segments along the length of the catheter lumen and the average of these measurements was recorded as the wall area for each exposure interval. As a result, the wall areas for silicone catheters at day 7 of exposure were not included in the final analysis. This modified method of assessing wall area was used at all exposure intervals for tested polyetherurethane catheters. Mislabeling of polyetherurethane catheter segments selected for wall area determination on day 36 of exposure did not allow for accurate identification of exposed and control catheters, and wall area measurements of polyetherurethane catheters on day 36 of exposure were not included in the final analysis.

Statistical Analysis

The measurements obtained at each exposure interval from each treatment group were averaged for polyetherurethane and for silicone catheters. Unpaired Student's *t* tests with Welch correction were used to compare mean values for each mechanical property measured.

RESULTS

The mechanical properties of polyetherurethane catheters exposed to a 70% ethanol lock solution for as long

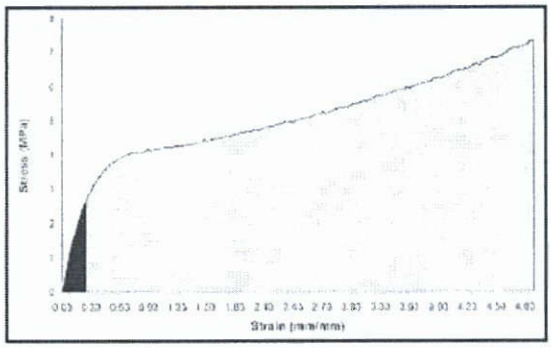


FIGURE 2. Typical stress–strain curve for a silicone catheter segment. The area under the entire curve represents the modulus of toughness, whereas the slope of the portion of the curve highlighted in black represents the modulus of elasticity (Young's modulus). MPa = megapascals.

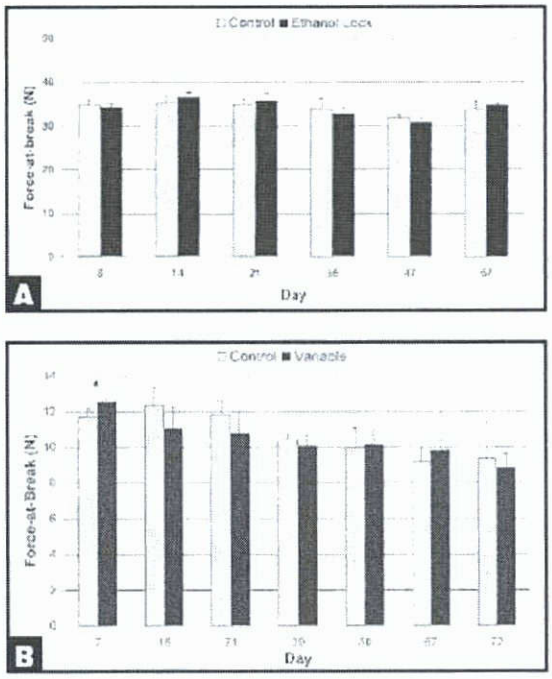


FIGURE 3. Force-at-break (in newtons [N]) at various exposure intervals for (A) polyetherurethane and (B) silicone catheters. Data are the mean force-at-break (N) of catheter segments tested (the table contains the number of segments tested at each exposure interval). Vertical bars represent standard error. *$P < .05$.

as 67 days and of silicone catheters exposed to a 70% ethanol lock solution for as long as 72 days are depicted in Figures 3 through 5.

The force-at-break or stress-at-break was consistently higher in the polyetherurethane catheters compared with the silicone catheters, and the force or stress required to break the silicone catheters tended to decrease the longer they remained in the Hank's solution (Figs. 3 and 4). No significant difference in the force required to break segments was found between the catheters exposed to ethanol and the unexposed, control catheters within each group, regardless of the exposure time (Fig. 3). The maximum stress-at-break was found to be reduced at a single exposure interval in both types of catheter (day 47 of exposure for the polyetherurethane catheters and day 7 of exposure for the silicone catheters), but no significant differences between exposed and control catheters were found at any of the other exposure intervals (Fig. 4).

The maximum segment elongation and strain immediately prior to breakage tended to be greater for the silicone catheters than for the polyetherurethane catheters, although this difference diminished the longer the catheters were immersed in Hank's solution. No differences in elongation and strain were seen between the catheters exposed and those unexposed to a 70% ethanol lock solution, for either the polyetherurethane or the silicone catheters, regardless of the exposure time.

As expected, the modulus of elasticity (Fig. 5) and the modulus of toughness were higher for the polyetherurethane than for the silicone catheters. The modulus of toughness of the polyetherurethane catheters exposed to ethanol was not significantly different from that of the unexposed, control catheters. Although the modulus of toughness of the silicone catheters exposed to ethanol was found to be reduced at a single exposure interval (day 21), no differences were seen between the catheters exposed to ethanol and the unexposed, control catheters at any of the other testing intervals. In contrast, the modulus of elasticity of both the polyetherurethane and the silicone catheters exposed to 70% ethanol was found to be slightly but significantly lower at several of the exposure intervals (Fig. 5).

Wall areas of segments of the control polyetherurethane and silicone catheters did not change appreciably over time during prolonged immersion in Hank's solution at 37°C. On comparison of the ethanol-exposed catheters with the unexposed, control catheters, the wall area of the silicone catheter segments was not consistently altered by exposure to 70% ethanol. In contrast, the polyetherurethane catheters exposed to 70% ethanol showed a consistent trend toward increasing wall thickness with prolonged exposure times, although statistical significance was reached at only one of the testing intervals (day 47 of exposure).

DISCUSSION

Ethanol and other alcohol-containing solutions are commonly used with intravascular devices as topical antiseptics during insertion or at the time of dressing changes[13,14] and as flush solutions to remove insipissated lipids from occluded catheters.[4–6] Moreover, there is growing interest in the use of ethanol as a novel intraluminal disinfectant for the treatment[7] and prevention[8] of intravascular device–related BSI.

Previous studies have raised questions about the effects of ethanol exposure on the mechanical integrity of polyurethane catheters,[9,10] although, to our knowledge, no studies have examined the effect of ethanol on silicone

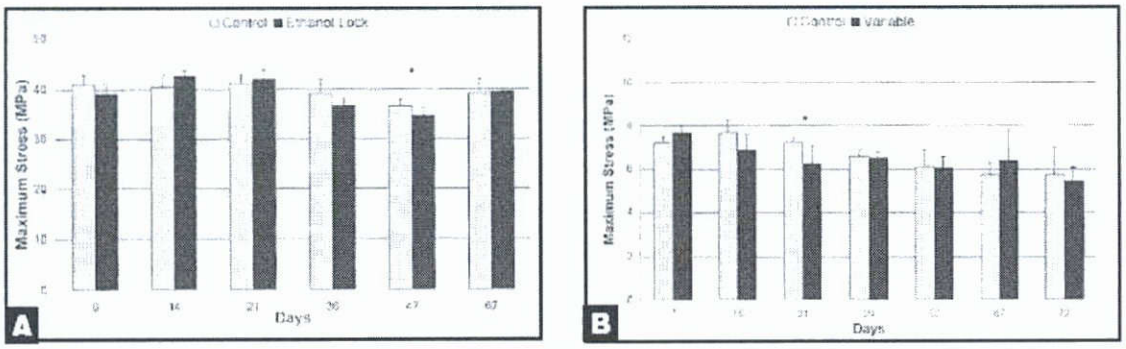


FIGURE 4. Maximum stress (in megapascals [MPa]) at break at various testing intervals for (A) polyetherurethane and (B) silicone catheters. Data are the mean stress (MPa) of catheter segments tested (the table contains the number of segments tested at each exposure interval). Vertical bars represent standard error. *$P < .05$.

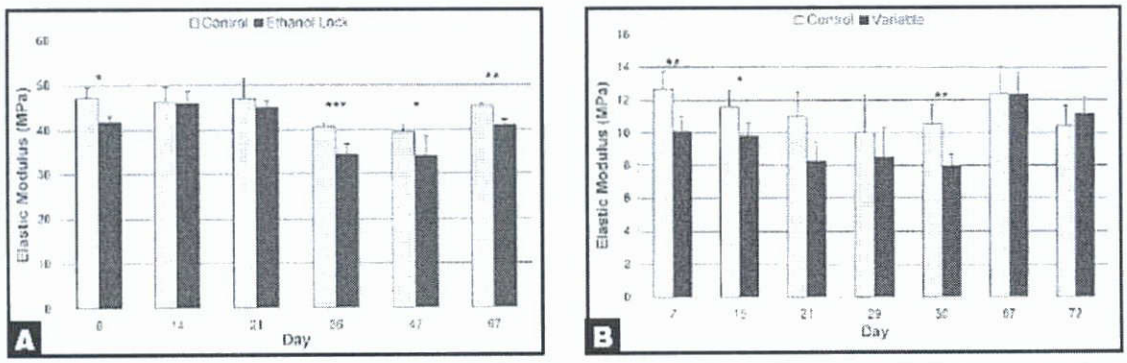


FIGURE 5. Modulus of elasticity (in megapascals [MPa]) of catheter segments at various exposure intervals for (A) polyetherurethane and (B) silicone catheters. Data are the mean modulus of elasticity (MPa) of catheter segments tested (the table contains the number of segments tested at each exposure interval). Vertical bars represent standard error. *$P < .05$; **$P < .01$; and ***$P < .001$.

catheters. Our study went beyond the qualitative assessments made in these earlier studies by rigorously assessing the effects of prolonged ethanol exposure on the mechanical integrity of widely used polyetherurethane and silicone catheters, employing industry standards wherever possible.[11] Although it has been reported that polyurethanes may dissolve in polar organic solvents,[12] our study failed to show any consistent reductions in the mechanical integrity of polyetherurethane or silicone catheters exposed to a 70% ethanol lock solution for as long as 10 weeks.

Our study was designed to provide a worse-possible-case challenge to the mechanical integrity of the catheters tested: the durations of continuous exposure to 70% ethanol were hundreds of times greater than an intravascular device material is likely to experience in clinical practice. We did find minimal differences in the modulus of elasticity between the ethanol-exposed and the control polyetherurethane catheter segments at several of the exposure intervals (Fig. 5). However, no consistent trend toward a sustained reduction in the modulus of elasticity was found for the silicone catheters (Fig. 5). Prolonged ethanol exposure appeared to produce slight swelling of the walls of the polyetherurethane catheters, but no consistent effect was seen for the silicone catheters tested. These findings may represent a type I error or may be the result of measurement error. However, the latter seems unlikely given that the exposed and unexposed catheters were measured in a similar fashion.

Even if the modest differences seen in the modulus of elasticity and wall thickness are real, their effect on the clinical performance of these catheters in practice is likely to be negligible because the force required to break a catheter segment (Fig. 3), the stress at break (Fig. 4), the maximum elongation before breakage, the maximum strain before breakage, and the modulus of toughness were unaffected by prolonged exposure to 70% ethanol. We believe these properties are more reliable predictors of the integrity of intravascular devices during clinical use. In fact, the sole mechanical property of catheter lumens recommended for testing in the International Organization for Standardization standard is the force-at-break.[11] As such, we interpret our findings as strong evidence supporting the safety of using ethanol and alcohol-containing solutions with selected polyetherurethane and silicone catheters in clinical practice.

Our study has limitations. First, we assessed only the mechanical integrity of the tubular portion of the polyetherurethane and silicone catheters. As a result, the impact of prolonged ethanol exposure on the integrity of the catheter hub and junction (at the interface of the hub and the tubular portion of the catheter) remains unknown. However, 70% alcohols have long been used to clean catheter hubs prior to blood draws or connections to administration sets, and we have been unable to find any published reports of cracking or fracturing of catheter hubs linked causally to repeated exposure to alcohol. Moreover, a review of the Food and Drug Administration's Manufacturer and User Facility Device Experience Database (MAUDE),[15] which includes data on complications with devices in use from 1992 to 2004, failed to identify any reports of mechanical failure of catheter hubs linked to alcohol exposure. However, if such effects did occur, a damaged hub could be easily repaired without replacing the entire catheter.

The other limitation of our study was our testing of only one manufacturer's polyurethane catheter. Many intravascular device manufacturers have advised against exposure of their polyurethane catheters to alcohol and acetone because of concerns about accelerated environmental stress cracking.[16] We have been unable to identify any published studies that corroborate these concerns. However, MAUDE contains 195 reports, all except one submitted by three companies (Bard Access Systems, Salt Lake City, UT; Boston Scientific Corp., Salt Lake City, UT; and Medcomp Medical Components, Harleysville, PA), describing environmental stress cracking of central venous catheters, usually at the junction of the catheter hub and lumen, which was ascribed to exposure of the devices to alcohol-containing antiseptics or acetone. Because environmental stress cracking of vascular catheters may occur in clinical practice without any clear inciting cause, the causal relationship of exposure to alcohol in each of these reports is unclear.

Of the 195 reports in MAUDE, 154 involved a cuffed hemodialysis catheter (Ash Split 1 Hemodialysis Catheter, Medcomp Medical Components) manufactured from an aliphatic polyetherurethane called Tecoflex (Thermedics, Wilmington, MA), a compound that reportedly swells more than 25% in the presence of ethanol or isopropyl alcohol[17] and is known to develop microcracks after prolonged implantation times.[18] The manufacturer has since introduced a next-generation hemodialysis catheter (Ash Split Hemodialysis Catheter II) made of Carbothane (Carboline, St. Louis, MO), an aliphatic polycarbonate–based polyurethane that has been shown to be compatible with several cutaneous antiseptics, including chlorhexidine and isopropyl alcohol.[19] Fourteen reports pertained to a polyurethane PICC (Vaxcel PICC, Boston Scientific Corp.), although we have been unable to obtain information on the exact polyurethane formulation used in its manufacture; however, information in MAUDE indicates that the manufacturer recently modified the production procedure to make the catheter material more resistant to the effects of isopropyl alcohol.[20] Of the remaining 27 reports, 26 were from a manufacturer (Bard Access Systems) that apparently has not modified the material used in the manufacture of its catheter (Polyurethane Per-Q-Cath PICC) and, as a result, continues to recommend against the use of alcohol or alcohol-containing solutions with its catheter.

The type of polyurethane catheter evaluated in this study is manufactured from an aromatic thermoplastic polyetherurethane that is similar, but may not be identical, to polyurethanes used in the manufacture of intravascular devices produced by other companies. Aromatic polyurethanes may be more resistant to the effects of organic solvents than aliphatic polyurethanes,[12] but the effects of ethanol exposure on the integrity of other types of aromatic polyurethanes used in the manufacture of intravascular devices are unknown. Our findings combined with the reports submitted to MAUDE highlight the heterogeneity among polyurethanes and suggest potential differences in the effects of alcohols and other organic solvents on the integrity of these devices. They also point out that manufacturers must understand that alcohols will be used increasingly with their devices, regardless of labeling instructions, and the importance of using materials in the manufacture of intravascular devices that are resistant to the degrading effects of these agents. Given the greatly expanded use of alcoholic solutions with intravascular devices of all types, we believe that manufacturers would be well advised to subject their catheters and other intravascular devices to formal testing of the type employed in this study.

This was the first study to systematically evaluate the effect of ethanol on the integrity of two types of vascular catheters commonly used in clinical practice. The findings suggest that a 70% ethanol lock solution has a negligible impact on the mechanical properties of polyetherurethane and silicone catheters, despite continuous exposure times as long as 10 weeks. These findings should allay fears about the use of alcohol-containing antiseptic solutions with vascular catheters made of silicone and aromatic polyetherurethanes and should prompt further study of ethanol as an anti-infective lock solution for the prevention[6] and treatment[7] of intravascular device–related BSI in clinical practice.

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