



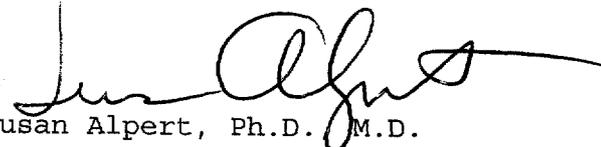
Memorandum

Date MAR 10 1997
From Director, Office of Device Evaluation (HFZ-400)
Center for Devices and Radiological Health (CDRH)
Subject Premarket Approval of ELA Medical, Inc.
Chorus RM Model 7034 DDR Pacemaker System and Opus RM Model 4534
SSIR Pacemaker System - ACTION
To The Director, CDRH
ORA _____

ISSUE. Publication of a notice announcing approval of the subject PMA.

FACTS. Tab A contains a FEDERAL REGISTER notice announcing:
(1) a premarket approval order for the above referenced medical device (Tab B); and
(2) the availability of a summary of safety and effectiveness data for the device (Tab C).

RECOMMENDATION. I recommend that the notice be signed and published.


Susan Alpert, Ph.D. M.D.

Attachments
Tab A - Notice
Tab B - Order
Tab C - S & E Summary

DECISION

Approved _____ Disapproved _____ Date _____

Prepared by Marian Kroen, CDRH, HFZ-450, January 7, 1997, 443-8517
Jan Donelson, CDRH, HFZ-450, January 7, 1997, 443-8320
Lynne Reamer, CDRH, HFZ-450, January 7, 1997, 443-8320

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION

[DOCKET NO. _____]

ELA Medical, Inc.; PREMARKET APPROVAL OF Chorus RM Model
7034 DDDR Pacemaker System and Opus RM Model 4534 SSIR
Pacemaker System

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is
announcing its approval of the application submitted by ELA
Medical, Inc., Plymouth, MN, for premarket approval, under
the Federal Food, Drug, and Cosmetic Act (the act), of
Chorus RM Model 7034 DDDR Pacemaker System and Opus RM Model
4534 SSIR Pacemaker System. FDA's Center for Devices and
Radiological Health (CDRH) notified the applicant, by letter
of March 10, 1997, of the approval of the application.

DATES: Petitions for administrative review by (insert date
30 days after date of publication in the FEDERAL REGISTER).

ADDRESSES: Written requests for copies of the summary of
safety and effectiveness data and petitions for
administrative review, to the Dockets Management Branch
(HFA-305), Food and Drug Administration, 12420 Parklawn Dr.,
rm. 1-23, Rockville, MD 20857.

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FOR FURTHER INFORMATION CONTACT:

Marian Kroen,
Center for Devices and Radiological Health (HFZ-450),
Food and Drug Administration,
9200 Corporate Blvd.,
Rockville, MD 20850,
301-443-8517.

SUPPLEMENTARY INFORMATION: On January 18, 1996, ELA Medical, Inc., Plymouth, MN 55441, submitted to CDRH an application for premarket approval of Chorus RM Model 7034 DDDR Pacemaker System and Opus RM Model 4534 SSIR Pacemaker System which includes an IBM compatible microcomputer which has been configured and furnished by ELA Medical, Inc. with CSO 2.46 programming software and is connected to a CPR1 programming lead. These devices are implantable cardiac pacemakers and are indicated for:

Rate adaptive pacing in patients who may benefit from increased pacing rates concurrent with increases in minute ventilation; and

The generally accepted patient conditions warranting chronic cardiac pacing which include:

- Symptomatic paroxysmal or permanent second or third-degree AV block;
- Symptomatic bilateral bundle branch block;
- Symptomatic paroxysmal or transient sinus

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node dysfunctions with or without associated AV conduction disorders;

- Bradycardia-tachycardia syndrome to prevent symptomatic bradycardia or some forms of symptomatic tachyarrhythmias; and
- Vaso-vagal syndromes or hypersensitive carotid sinus syndromes.

The Chorus RM is also indicated for dual-chamber and atrial tracking modes in patients who may benefit from maintenance of AV synchrony. Dual-chamber modes are specifically indicated for treatment of conduction disorders that require restoration of both rate and AV synchrony which include:

- Various degrees of AV block to maintain the atrial contribution to cardiac output; and
- VVI intolerance (e.g., pacemaker syndrome) in the presence of persistent sinus rhythm.

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory System Devices Panel of the Medical Devices Advisory Committee, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.



On March 10, 1997, CDRH approved the application by a letter to the applicant from the Director of the Office of Device Evaluation, CDRH.

A summary of the safety and effectiveness data on which CDRH based its approval is on file in the Dockets Management Branch (address above) and is available from that office upon written request. Requests should be identified with the name of the device and the docket number found in brackets in the heading of this document.

Opportunity For Administrative Review

Section 515(d)(3) of the act, (21 U.S.C. 360e(d)(3)) authorizes any interested person to petition, under section 515(g) of the act, for administrative review of CDRH's decision to approve this application. A petitioner may request either a formal hearing under part 12 (21 CFR part 12) of FDA's administrative practices and procedures regulations or a review of the application and CDRH's action by an independent advisory committee of experts. A petition is to be in the form of a petition for reconsideration under §10.33(b) (21 CFR 10.33(b)). A petitioner shall identify the form of review requested (hearing or independent advisory committee) and shall submit with the petition supporting data and information showing that there is a genuine and substantial issue of material fact for resolution through administrative review. After reviewing

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the petition, FDA will decide whether to grant or deny the petition and will publish a notice of its decision in the FEDERAL REGISTER. If FDA grants the petition, the notice will state the issue to be reviewed, the form of the review to be used, the persons who may participate in the review, the time and place where the review will occur, and other details.

Petitioners may, at any time on or before (insert date 30 days after date of publication in the FEDERAL REGISTER), file with the Dockets Management Branch (address above) two copies of each petition and supporting data and information, identified with the name of the device and the docket number found in brackets in the heading of this document. Received petitions may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.



This notice is issued under the Federal Food, Drug, and Cosmetic Act (secs. 515(d), 520(h) (21 U.S.C. 360e(d), 360j(h))) and under authority delegated to the Commissioner of Food and Drugs (21 CFR 5.10) and redelegated to the Director, Center for Devices and Radiological Health (21 CFR 5.53).

Dated: _____.

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Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

Ms. Catherine Goble
Regulatory Affairs Manager
ELA Medical, Incorporated
2950 Xenium Lane North
Plymouth, Minnesota 55441

MAR 10 1997

Re: P950029
Chorus RM Model 7034 DDDR Pacemaker System and
Opus RM Model 4534 SSIR Pacemaker System
Filed: January 18, 1996
Amended: February 15, March 8, June 14, July 16 and 19,
August 19, October 15 and 22, November 1 and 21,
December 24 and 31, 1996; and January 2, 1997

Dear Ms. Goble:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) for the Chorus RM Model 7034 DDDR Pacemaker System and Opus RM Model 4534 SSIR Pacemaker System which includes an IBM compatible microcomputer which has been configured and furnished by ELA Medical, Incorporated with CSO 2.46 programming software and is connected to a CPR1 programming head. These devices are indicated for:

Rate adaptive pacing in patients who may benefit from increased pacing rates concurrent with increases in minute ventilation; and

The generally accepted patient conditions warranting chronic cardiac pacing which include:

- Symptomatic paroxysmal or permanent second or third-degree AV block;
- Symptomatic bilateral bundle branch block;
- Symptomatic paroxysmal or transient sinus node dysfunctions with or without associated AV conduction disorders;
- Bradycardia-tachycardia syndrome to prevent symptomatic bradycardia or some forms of symptomatic tachyarrhythmias; and
- Vaso-vagal syndromes or hypersensitive carotid sinus syndromes.

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The Chorus RM is also indicated for dual-chamber and atrial tracking modes in patients who may benefit from maintenance of AV synchrony. Dual-chamber modes are specifically indicated for treatment of conduction disorders that require restoration of both rate and AV synchrony which include:

- Various degrees of AV block to maintain the atrial contribution to cardiac output; and
- VVI intolerance (e.g., pacemaker syndrome) in the presence of persistent sinus rhythm.

We are pleased to inform you that the PMA is approved subject to the conditions described below and in the "Conditions of Approval For Cardiac Pacemakers and Programmers" (enclosed). You may begin commercial distribution of the device upon receipt of this letter.

The sale, distribution, and use of these devices are restricted to prescription use in accordance with 21 CFR 801.109 within the meaning of section 520(e) of the Federal Food, Drug, and Cosmetic Act (the act) under the authority of section 515(d)(1)(B)(ii) of the act. FDA has also determined that to ensure the safe and effective use of the devices that the devices are further restricted within the meaning of section 520(e) under the authority of section 515(d)(1)(B)(ii) insofar as the sale, distribution, and use must not violate sections 502(q) and (r) of the act.

Expiration dating for these devices has been established and approved at one year. This is to advise you that the protocol you used to establish this expiration dating is considered an approved protocol for the purpose of extending the expiration dating as provided by 21 CFR 814.39(a)(8).

CDRH will publish a notice of its decision to approve your PMA in the FEDERAL REGISTER. The notice will state that a summary of the safety and effectiveness data upon which the approval is based is available to the public upon request. Within 30 days of publication of the notice of approval in the FEDERAL REGISTER, any interested person may seek review of this decision by requesting an opportunity for administrative review, either through a hearing or review by an independent advisory committee, under section 515(g) of the act.

Failure to comply with the conditions of approval invalidates this approval order. Commercial distribution of a device that is not in compliance with these conditions is a violation of the act.

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You are reminded that, as soon as possible and before commercial distribution of your devices, you must submit an amendment to this PMA submission with copies of all approved labeling in final printed form.

All required documents should be submitted in triplicate, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing.

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

In addition under section 522(a) of the act manufacturers of certain types of devices identified by the act or designated by FDA are required to conduct postmarket surveillance studies. FDA has identified under section 522(a)(1)(A) the above noted devices as requiring postmarket surveillance.

Upon approval and within thirty (30) days of first introduction or delivery for introduction of these devices into interstate commerce you will be required to submit to FDA certification of the date of introduction into interstate commerce, a detailed protocol which describes the postmarket surveillance study, and a detailed profile of the study's principal investigator that clearly establishes the qualifications and experience of the individual to conduct the proposed study. For your information, general guidance on preparing a protocol for a postmarket surveillance study is enclosed.

At that time you should submit five (5) copies to:

Postmarket Studies Document Center
1350 Piccard Drive (HFZ-544)
Rockville, Maryland 20850

Within sixty (60) days of receipt of your protocol, FDA will either approve or disapprove it and notify you of the Agency's action in writing. Do not undertake a postmarket surveillance study without an FDA approved protocol.



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Failure to certify accurately the date of initial introduction of your devices into interstate commerce, to submit timely an acceptable protocol, or to undertake and complete an FDA approved postmarket surveillance study consistent with the protocol, will be considered violations of section 522.

In accordance with the Medical Device Amendments of 1992, failure of a manufacturer to meet its obligations under section 522 is a prohibited act under section 301(q)(1)(C) of the act (21 U.S.C. 331(q)(1)(C)). Further, under section 502(t)(3) of the act (21 U.S.C. 352(t)(3)), a device is misbranded if there is a failure or refusal to comply with any requirement under section 522 of the act. Violations of sections 301 or 502 may lead to regulatory actions including seizure of your product, injunction, prosecution, or civil money penalties or other FDA enforcement actions including (but not limited to) withdrawal of your PMA.

If you have questions concerning postmarket surveillance study requirements, contact the Postmarket Surveillance Studies Branch, at (301) 594-0639.

Under section 519(e) of the act (as amended by the Safe Medical Devices Act in 1990), manufacturers of certain devices must track their products to the final user or patient so that devices can be located quickly if serious problems are occurring with the products. The tracking requirements apply to (1) permanent implants the failure of which would be reasonably likely to have serious adverse health consequences; (2) life sustaining or life supporting devices that are used outside of device user facilities the failure of which would be reasonably likely to have serious adverse health consequences; and (3) other devices that FDA has designated as requiring tracking. Under section 519(e), FDA believes that your devices are devices that are subject to tracking because they are permanent implants whose failure would be reasonably likely to have serious adverse consequences.

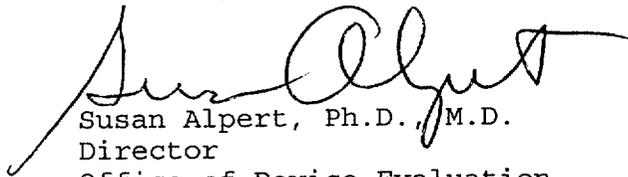
FDA's tracking regulations, published in the FEDERAL REGISTER on August 16, 1993, appear at 21 CFR Part 821. These regulations set out what you must do to track a device. In addition, the regulations list example permanent implant and life sustaining or life supporting devices that FDA believes must be tracked at 21 CFR § 821.20(b) and the devices that FDA has designated for tracking at 21 CFR § 821.20(c). FDA's rationale for identifying these devices is set out in the FEDERAL REGISTER (57 FR 10705-10709 (March 27, 1991), 57 FR 22973-22975 (May 29, 1992), and 58 FR 43451-43455 (August 16, 1993)).

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If you have questions concerning this approval order, please contact
Marian Kroen at (301) 443-8517.

Sincerely yours,

A handwritten signature in cursive script, appearing to read "Susan Alpert". The signature is written in black ink and is positioned above the typed name and title.

Susan Alpert, Ph.D., M.D.
Director

Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosures

A small, handwritten mark or signature in the bottom right corner of the page, consisting of a few loops and a vertical stroke.

CONDITIONS OF APPROVAL

APPROVED LABELING. As soon as possible, and before commercial distribution of your device, submit three copies of an amendment to this PMA submission with copies of all approved labeling in final printed form to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration (FDA), 9200 Corporate Blvd., Rockville, Maryland 20850.

ADVERTISEMENT. No advertisement or other descriptive printed material issued by the applicant or private label distributor with respect to this device shall recommend or imply that the device may be used for any use that is not included in the FDA approved labeling for the device. If the FDA approval order has restricted the sale, distribution and use of the device to prescription use in accordance with 21 CFR 801.109 and specified that this restriction is being imposed in accordance with the provisions of section 520(e) of the act under the authority of section 515(d)(1)(B)(ii) of the act, all advertisements and other descriptive printed material issued by the applicant or distributor with respect to the device shall include a brief statement of the intended uses of the device and relevant warnings, precautions, side effects and contraindications.

PREMARKET APPROVAL APPLICATION (PMA) SUPPLEMENT. Before making any change affecting the safety or effectiveness of the device, submit a PMA supplement for review and approval by FDA unless the change is of a type for which a "Special PMA Supplement-Changes Being Effected" is permitted under 21 CFR 814.39(d) or an alternate submission is permitted in accordance with 21 CFR 814.39(e). A PMA supplement or alternate submission shall comply with applicable requirements under 21 CFR 814.39 of the final rule for Premarket Approval of Medical Devices.

All situations which require a PMA supplement cannot be briefly summarized, please consult the PMA regulation for further guidance. The guidance provided below is only for several key instances.

A PMA supplement must be submitted when unanticipated adverse effects, increases in the incidence of anticipated adverse effects, or device failures necessitate a labeling, manufacturing, or device modification.

A PMA supplement must be submitted if the device is to be modified and the modified device should be subjected to animal or laboratory or clinical testing designed to determine if the modified device remains safe and effective.

A "Special PMA Supplement - Changes Being Effected" is limited to the labeling, quality control and manufacturing process changes specified under 21 CFR 814.39(d)(2). It allows for the **addition** of, but **not the replacement** of previously approved, quality control specifications and test methods. These changes may be implemented before FDA approval upon acknowledgment by FDA that the submission is being processed as a "Special PMA Supplement - Changes Being Effected." This acknowledgment is in addition to that issued by the PMA Document Mail Center for all PMA supplements submitted. **This procedure is not applicable to changes in device design, composition, specifications, circuitry, software or energy source.**

Alternate submissions permitted under 21 CFR 814.39(e) apply to changes that otherwise require approval of a PMA supplement before implementation of the change and include the use of a 30-day PMA supplement or annual postapproval report. FDA must have previously indicated in an advisory opinion to the affected industry or in correspondence with the applicant that the alternate submission is permitted for the change. Before such can occur, FDA and the PMA applicant(s) involved must agree upon any needed testing protocol, test results, reporting format, information to be reported, and the alternate submission to be used.

POSTAPPROVAL REPORTS. Continued approval of this PMA is contingent upon the submission of postapproval reports required under 21 CFR 814.84 at intervals of 1 year from the date of approval of the original PMA. Postapproval reports for supplements approved under the original PMA, if applicable, are to be included in the next and subsequent annual reports for the original PMA unless specified otherwise in the approval order for the PMA supplement. Two copies identified as "Annual Report" and bearing the applicable PMA reference number are to be submitted to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Blvd., Rockville, Maryland 20850. The postapproval report shall indicate the beginning and ending date of the period covered by the report and shall include the following information required by 21 CFR 814.84:

- (1) Identification of changes described in 21 CFR 814.39(a) and changes required to be reported to FDA under 21 CFR 814.39(b).
- (2) Bibliography and summary of the following information not previously submitted as part of the PMA and that is known to or reasonably should be known to the applicant:
 - (a) unpublished reports of data from any clinical investigations or nonclinical laboratory studies involving the device or related devices ("related" devices include devices which are the same or substantially similar to the applicant's device); and

- (b) reports in the scientific literature concerning the device.

If, after reviewing the bibliography and summary, FDA concludes that agency review of one or more of the above reports is required, the applicant shall submit two copies of each identified report when so notified by FDA.

ADVERSE REACTION AND DEVICE DEFECT REPORTING. As provided by 21 CFR 814.82(a)(9), FDA has determined that in order to provide continued reasonable assurance of the safety and effectiveness of the device, the applicant shall submit 3 copies of a written report identified, as applicable, as an "Adverse Reaction Report" or "Device Defect Report" to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Blvd., Rockville, Maryland 20850 within 10 days after the applicant receives or has knowledge of information concerning:

- (1) A mixup of the device or its labeling with another article.
- (2) Any adverse reaction, side effect, injury, toxicity, or sensitivity reaction that is attributable to the device and
 - (a) has not been addressed by the device's labeling or
 - (b) has been addressed by the device's labeling, but is occurring with unexpected severity or frequency.
- (3) Any significant chemical, physical or other change or deterioration in the device or any failure of the device to meet the specifications established in the approved PMA that could not cause or contribute to death or serious injury but are not correctable by adjustments or other maintenance procedures described in the approved labeling. The report shall include a discussion of the applicant's assessment of the change, deterioration or failure and any proposed or implemented corrective action by the applicant. When such events are correctable by adjustments or other maintenance procedures described in the approved labeling, all such events known to the applicant shall be included in the Annual Report described under "Postapproval Reports" above unless specified otherwise in the conditions of approval to this PMA. This postapproval report shall appropriately categorize these events and include the number of reported and otherwise known instances of each category during the reporting period. Additional information regarding the events discussed above shall be submitted by the applicant when determined by FDA to be necessary to provide continued reasonable assurance of the safety and effectiveness of the device for its intended use.

REPORTING UNDER THE MEDICAL DEVICE REPORTING (MDR) REGULATION. The Medical Device Reporting (MDR) Regulation became effective on December 13, 1984, and requires that all manufacturers and importers of medical devices, including in vitro diagnostic devices, report to FDA whenever they receive or otherwise became aware of information that reasonably suggests that one of its marketed devices

- (1) may have caused or contributed to a death or serious injury or
- (2) has malfunctioned and that the device or any other device marketed by the manufacturer or importer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

The same events subject to reporting under the MDR Regulation may also be subject to the above "Adverse Reaction and Device Defect Reporting" requirements in the "Conditions of Approval" for this PMA. FDA has determined that such duplicative reporting is unnecessary. Whenever an event involving a device is subject to reporting under both the MDR Regulation and the "Conditions of Approval" for this PMA, you shall submit the appropriate reports required by the MDR Regulation and identified with the PMA reference number to the following office:

Division of Surveillance Systems (HFZ-531)
Center for Devices and Radiological Health
Food and Drug Administration
1350 Piccard Drive, 340
Rockville, Maryland 20850
Telephone (301) 594-2735

Events included in periodic reports to the PMA that have also been reported under the MDR Regulation must be so identified in the periodic report to the PMA to prevent duplicative entry into FDA information systems.

Copies of the MDR Regulation and an FDA publication entitled, "An Overview of the Medical Device Reporting Regulation," are available by written request to the address below or by telephoning 1-800-638-2041.

Division of Small Manufacturers Assistance (HFZ-220)
Center for Devices and Radiological Health
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

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Summary of Safety and Effectiveness Data

I. GENERAL INFORMATION

Device Generic Name: Implantable Pacemaker Pulse Generator

Device Trade Name: Chorus RM Model 7034 DDDR Pacemaker System
Opus RM Model 4534 SSIR Pacemaker System

Applicant's Name and Address: ELA Medical, Inc.
2950 Xenium Lane North, Suite 120
Plymouth, MN 55441

Pre-Market Approval (PMA)
Application Number: P950029

Date of Notice of Approval
to the Applicant: MAR 10 1997

II. INDICATIONS FOR USE

The Chorus RM and Opus RM pacemaker systems are indicated for:

Rate adaptive pacing in patients who may benefit from increased pacing rates concurrent with increases in minute ventilation; and

The generally accepted patient conditions warranting chronic cardiac pacing which include:

- Symptomatic paroxysmal or permanent second or third-degree AV block;
- Symptomatic bilateral bundle branch block;
- Symptomatic paroxysmal or transient sinus node dysfunctions with or without associated AV conduction disorders;
- Bradycardia-tachycardia syndrome to prevent symptomatic bradycardia or some forms of symptomatic tachyarrhythmias; and

- Vaso-vagal syndromes or hypersensitive carotid sinus syndromes.

The Chorus RM is also indicated for **dual-chamber and atrial tracking modes** in patients who may benefit with maintenance of AV synchrony. Dual-chamber modes are specifically indicated for treatment of conduction disorders that require restoration of both rate and AV synchrony which include:

- Various degrees of AV block to maintain the atrial contribution to cardiac output; and
- VVI intolerance (e.g., pacemaker syndrome) in the presence of persistent sinus rhythm.

III. DEVICE DESCRIPTION

Chorus RM

The Chorus RM Model 7034 DDDR Pacemaker is a multiprogrammable DDDR (dual chamber, rate adaptive) implantable pacemaker pulse generator powered by a lithium iodine cell. It is encapsulated in a hermetically sealed titanium case. It can be externally programmed and interrogated via bi-directional telemetry using an IBM compatible microcomputer which has been configured and furnished by ELA Medical Inc. with CSO version 2.46 programming software and is connected to a CPR1 programming head. A complete description of the Chorus RM Model 7034 appears in the Physician's Manual.

This programmable polarity device has two bipolar 3.2mm connectors compatible with the IS-1 standard (ISO/DP 58413) It incorporates the same features as the PMA-approved Chorus 6034 pulse generators including algorithms designed to help in cases of endless loop tachycardia (Retro P algorithm), bradycardia (Rate Smoothing), and atrial tachycardia (Fallback), while adding minute ventilation as the indicator for rate adaptive pacing. (Minute ventilation is a second order indicator of metabolic demand during exercise.)

The purpose of rate response is to adjust the pacing rate to the patient's activity level. When programmed to a rate-responsive mode, the Chorus RM and Opus RM pacemakers will vary the pacing rate in response to the patient's respiratory activity.

Minute Ventilation as the Indicator

Minute ventilation is the product of respiratory rate and tidal volume. This physiological indicator

closely reflects the metabolic demand during exercise. Minute ventilation is a 2nd order indicator [1]. Resting minute ventilation is approximately 6 l/min and can rise up to 60 l/min during severe exercise. It can even increase to 150 l/min in well-trained athletes during strenuous exercise. Minute ventilation correlates to oxygen consumption and heart rate [2]. Minute ventilation also rapidly increases at the onset of exercise [3].

[1] Rate responsive pacing : biosensor reliability and physiological sensitivity, P. Rossi, PACE, vol 10, 1987.

[2] Normal and abnormal heart rate response to exercise, H.K. Hammond and V.F Froehlicher, Progress in Cardiovascular diseases, Vol 27, No 4, 1985 : 271.

[3] Relationship between heart rate and minute ventilation, tidal volume and respiratory rate during brief and low level exercise, F. Vai, JL. Bonnet, P. Ritter, G. Pioger, PACE, Vol 11, 1988 : 1860

Minute Ventilation Sensor

Minute ventilation is determined by the measurement of transthoracic impedance. A linear relationship exists between the measured impedance and tidal volume. A bipolar electrode is necessary for measuring minute ventilation. Low amplitude (400 μ amps) and short duration (15 μ seconds) output pulses are delivered at a 8 Hz frequency to the distal electrode. Impedance is measured between the proximal electrode of the lead and the pacemaker case.

Impedance increases with inspiration and decreases with expiration. The signal measured is filtered to allow the detection of respiratory rates between 6 and 45 cycles per minute. The respiration period and amplitude are derived from the detected rates. Ventilation is calculated every respiratory cycle as a function of the Amplitude/Period ratio.

The sensor circuitry has a 3rd order low pass filter with a cut-off frequency of 45 min^{-1} . If the rate of the signal is higher, the signal will be attenuated by the filter.

The effect of this attenuation is to lower the effective respiration used by the pacemaker. Thus, above a respiration of 45 per minute, the pacemaker will use a lower effective respiration rate to calculate a minute ventilation value. This lower minute ventilation value will result in a lower rate responsive rate. The higher the respiration rate, the more attenuated the signal. The more attenuated the signal, the lower the effective respiration value used to calculate minute ventilation. Thus, depending upon other factors including tidal volume, at some high respiration rate above 45 per minute, the rate responsive rate can equal the basic rate.

The behavior for rate response for high respiration rates is subject to the same constraints as for respiration rates below 45 per minute. The response will be smoothed since minute ventilation is averaged over four respiratory cycles and the change in rate responsive rate cannot be faster than the programmed acceleration and recovery values allow.

Rate Response: Calculation of the Pacing Rate

Rate response is based on the linear relationship between minute ventilation and heart rate. Minute ventilation is calculated every respiratory cycle and an average is computed over four respiratory cycles. The sensor-driven rate is calculated every fourth, eighth or twelfth cycle from this average. This frequent calculation allows the pacemaker to respond rapidly to changes in the patient's activity.

Different parameters allow the appropriate adjustment of the pacemaker response according to the patient need. Rate responsive operation is available in two modes: fixed calibration and auto calibration. In the fixed mode, a single slope is selected from one to fifteen in increments of one. The slope stays fixed at the starting slope unless programmed to another fixed slope. In the autocalibration mode, the slope starts at a value of 11, however the slope is continually adjusting from a possible range of 1 to 15 in increments of 0.1.

Additional Device Features

The Chorus RM has the ability to switch to rate adaptive function (VVIR) when fallback occurs, providing the patient with the ability to adjust the pacing rate when needed, based on minute ventilation, even in the presence of atrial tachycardia. Both the Chorus RM and Opus RM devices include diagnostic features such as the Holter functions, which can be used to collect patient heart activity data passively.

Several additional tools are available to adjust or assess the performance of the rate adaption. Simulation allows the physician to collect approximately 20 minutes of minute ventilation and cardiac data. The data are stored in the pulse generator's random access memory (RAM) and may then be downloaded to the programmer for simulation of the rate response at various programmed settings, to adjust the response for the patient's needs.

When the pulse generator is programmed to automatic calibration mode, curves of the calibration parameters are also available. Three curves are recorded, showing the resting ventilation, the exercise ventilation, and the rate response slope number. The physician can use this feature to review the activity level of the patient over the last thirty days, and to monitor the behavior of the automatic adjustment of the rate adaptive slope in response to the activity.

Histograms of the sensor driven rate are also available. Chorus RM records the value of the sensor driven rate in three individual 24-hour histograms, each with eight channels (automatically set between the basic rate and the sensor driven maximum rate). These histograms provide information for the physician in the analysis of the pacemaker rate as determined by the minute ventilation sensor. Statistics indicate the number of paced beats that were due to the rate response calculation for comparison to the number of beats due to sinus node activity or lower rate pacing.

Opus RM

The device description for the Opus RM Model 4534 Pacemaker is identical to that given for the Chorus RM Model 7034 Pacemaker, except:

- Opus RM is an SSIR (single-chamber, rate adaptive) rather than DDDR (dual-chamber, rate adaptive) pacemaker
- Opus RM has one bipolar 3.2 mm connector rather than the two bipolar 3.2 mm connectors used by the Chorus RM
- Opus RM does not have those parameters that are applicable only to dual chamber devices:
 - Basic AV Delay
 - Minimum AV Delay
 - Maximum AV Delay
 - AV Delay Hysteresis
 - Atrial Absolute Refractory Period
 - PVARP
 - Blanking Period
 - ELT Protection (Retro P)
 - AV Modulation
 - Maximum VP Variation
 - Fallback

IV. CONTRAINDICATIONS

- This device is contraindicated in patients with an implanted cardioverter-defibrillator (ICD) because the pulses used in the measurement of minute ventilation may cause unwanted delivery of ICD therapy.
- Single-chamber atrial pacing is contraindicated in patients with impaired AV nodal conduction.
- Dual-chamber and single-chamber atrial pacing are contraindicated in patients with chronic refractory atrial tachyarrhythmias.

V. WARNINGS

- **Rate adaptive pacing** should be used with care in patients unable to tolerate increased pacing rates.

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- **Minute ventilation rate response pacing** may be inappropriate for patients who can achieve respiratory cycles shorter than 1.33 seconds (greater than 45 breaths per minute). Higher respiratory rates attenuate the impedance signal which diminishes the MV rate response, i.e., the pacing rate will drop toward the programmed basic rate.
- **Asynchronous pacing (DOO/VOO/AOO)** may be proarrhythmic in the presence (or likelihood) of competition between paced and intrinsic rhythms.
- **Single chamber ventricular pacing** should be used with care in patients who may develop pacemaker syndrome or who may have a need for maximum atrial contribution.
- **Crosstalk** results in atrioventricular (AV) pacing with a 94 ms AV delay. This may be avoided by appropriate choice of blanking periods and sensitivities.
- **Slow retrograde conduction**, especially with conduction time >450 ms, may induce pacemaker-mediated tachycardia.
- **Magnetic resonance imaging** of pacemaker patients has resulted in significant adverse effects (see PRECAUTIONS).
- **Therapeutic diathermy** can induce current in the pacing leads and may cause fibrillation, burning of the myocardium, and irreversible damage to the pulse generator.

VI. PRECAUTIONS

Programming

- **Rate response or autocalibration** should not be enabled before implantation, because the sensor will be incorrectly initialized, resulting in inappropriate rates.
- During **automated threshold testing**, the programming head must be removed when capture ceases to restore preprogrammed pulse amplitude, otherwise the pacemaker will continue the threshold test for the 20 cycles of the test without pacing the patient (i.e., without capture of the heart).

Storage and sterilization

- Store the device between 5° C and 50° C, because temperatures outside this range can damage components.
- A device should not be implanted if sterility is not assured:
 - ⇒ If its sterility indicator within the inner package is not green, it might not have been sterilized;
 - ⇒ If its storage package has been pierced or altered, this could have rendered it non-sterile.
- Do not implant a device when:
 - ⇒ It has been dropped after it has been removed from its sterile packaging;
 - ⇒ Its "use before" date has expired, because this can adversely affect pulse generator longevity.
- Do not resterilize devices. Return unimplanted devices in their storage packages to ELA Medical for resterilization.

Lead Evaluation and Lead Connection

- For Chorus RM, do not use a unipolar atrial lead if rate response is required, because the device's rate response function will only operate with a bipolar lead.
- For Opus RM, do not use a unipolar lead if rate response is required.
- Do not use any lead with this pulse generator without first verifying IS-1 compatibility, because use with other leads can damage the connector or result in a leaking or intermittent connection.
- Do not use as-shipped pulse generator values for pacing amplitude and sensitivity without verifying that they are appropriate for the patient, because this may result in shortened battery longevity or improper sensing.
- Consider lead maturation in choice of pacing amplitude and sensitivity, because:
 - ⇒ acute pacing thresholds > 1 V or 2 mA or chronic pacing thresholds > 3 V or 6 mA can result in loss of capture because thresholds increase after implantation.
 - ⇒ R wave amplitude < 5 mV or P wave amplitude < 2 mV can result in undersensing because sensed amplitude decreases after implantation.
- Exercise extreme caution if testing leads using line-powered equipment, because leakage current exceeding 10 microA can induce ventricular fibrillation.

- Do not insert a lead in the pacemaker connector without first visually verifying that the setscrews are sufficiently retracted to allow insertion.
- Do not insert a lead or setscrew wrench in the pacemaker connector without first lubricating the lead connector body or the wrench tip with silicone lubricant, because failure to do so can damage the connector.
- Do not tighten the setscrews without a lead connector inserted. This can damage the connector block.

Environmental and Medical Therapy Hazards

Patients should exercise reasonable caution in avoidance of devices which generate a strong electric or magnetic field. If a pulse generator should inhibit or revert to asynchronous operation at the programmed pacing rate or at the magnet rate while in the presence of EMI, moving away from the source or turning it off will allow the pulse generator to return to its normal mode of operation.

Hospital and Medical Environments

- **Mechanical ventilators** may cause pacing rate changes. Program the pacemaker to a non-rate responsive mode during ventilation.
- **Electrosurgical cautery** could induce ventricular arrhythmias and/or fibrillation, or may cause asynchronous or inhibited pulse generator operation or operation in standby mode. If use of electrocautery is necessary, the current path and ground plate should be kept as far away from the pulse generator and leads as possible.
- **Magnetic Resonance Imaging (MRI)** among pacemaker patients has been contraindicated by MRI manufacturers. Clinicians should carefully weigh the decision to use MRI with pacemaker patients.
 - ⇒ Magnetic and radio-frequency (RF) fields produced by MRI may: increase ventricular pacing beyond the rate limit, result in total inhibition of pacing output, result in pacing at random rates, or result in synchronous pacing.
 - ⇒ Magnetic fields may activate magnet mode operation and cause asynchronous pacing.
 - ⇒ Pacemaker patients treated with MRI should be closely monitored and programmed parameters should be verified upon cessation of MRI.
- **Lithotripsy** may damage the pulse generator. If lithotripsy must be used, do not focus the beam near the pulse generator.
- **External defibrillation** may damage the pulse generator. Attempt to minimize current flowing through the pulse generator and lead system by following these precautions

- ⇒ Position defibrillation paddles as far from the pulse generator as possible. Attempt to minimize current flowing through the pulse generator and leads by positioning the defibrillation paddles perpendicular to the implanted pulse generator/lead system.
- ⇒ Use the lowest clinically appropriate energy output (watt seconds).
- ⇒ Confirm pacemaker function following any internal or external defibrillation.
- **Transcutaneous electrical nerve stimulation (TENS)** may interfere with pacemaker function. If necessary, the following measures may reduce interference:
 - ⇒ Place the TENS electrodes as close to each other as possible.
 - ⇒ Place the TENS electrodes as far from the pulse generator/lead system as possible.
 - ⇒ Monitor cardiac activity during TENS use.
- **High radiation sources** such as cobalt 60 or gamma radiation should not be directed at the pulse generator. If a patient requires radiation therapy in the vicinity of the pulse generator, place lead shielding over the device to prevent radiation damage.

Home and Occupational Environments

- **High voltage power transmission lines** may generate enough EMI to interfere with pulse generator operation if approached too closely.
- **Communication equipment** such as microwave transmitters, linear power amplifiers, or high-power amateur transmitters may generate enough EMI to interfere with pulse generator operation if approached too closely.
- **Commercial electrical equipment** such as arc welders, induction furnaces, or resistance welders may generate enough EMI to interfere with pulse generator operation if approached too closely.
- **Home appliances** which are in good working order and properly grounded do not usually produce enough EMI to interfere with pulse generator operation. There are reports of pacemaker disturbances caused by electric hand-tools or electric razors used directly over the skin over the pulse generator

Cellular Phones

Recent studies have indicated there may be a potential interaction between cellular phones and pacemaker operation. Potential effects may be due to either the radio frequency signal or the magnet within the phone and could include inhibition or asynchronous pacing.

Based on testing to date, effects resulting from an interaction between cellular phones and the



implanted pacemakers have been temporary. Simply moving the phone away from the implanted device will return it to its previous state of operation. Because of the great variety of cellular phones and the wide variance in patient physiology, an absolute recommendation to cover all patients cannot be made.

Patients having an implanted pacemaker who operate a cellular phone should:

- Maintain a minimum separation of 6 inches (15 centimeters) between a hand-held personal cellular phone and the implanted device. Portable and mobile cellular phones generally transmit at higher power levels compared to hand held models. For phones transmitting above 3 watts, maintain a minimum separation of 12 inches (30 centimeters) between the antenna and the implanted device.
- Patients should hold the phone to the ear opposite the side of the implanted device. Patients should not carry the phone in a breast pocket or on a belt within 6 inches (15 centimeters) of the implanted device as some phones emit signals when they are turned ON but not in use (i.e., in the listen or standby mode). Storing the phone in a location opposite the side of implant is recommended.

Pulse Generator Disposal

- Do not incinerate pacemakers, because they can explode if subjected to incineration or cremation temperatures.
- Return all explanted pacemakers to ELA Medical for analysis and safe disposal.
- Do not implant an explanted pacemaker in another patient as sterility, functionality, and reliability cannot be assured.



VII. ADVERSE EVENTS

The Chorus RM was evaluated in a clinical study involving 350 devices implanted in 346 patients. As of June 17, 1996, total device exposure was 3622 device months, and individual patient exposure averaged 10 months (ranging from 0.3 to 32 months). A total of 27 patients died during the study. None of these deaths were judged related to the device. Seven devices were explanted from six patients. None of the explants were judged to be due to device malfunction. Four device explants were secondary to late postoperative infection, and three were explanted prophylactically.

The Opus RM was evaluated in a clinical study involving 74 devices implanted in 74 patients. As of June 17, 1996, total device exposure was 513 device months, and individual patient exposure averaged 7 months (ranging from 0.1 to 18.2 months). A total of 8 patients died during the study. None of these deaths were judged related to the device.

Observed Adverse Events

Table 1 reports the adverse events on a per patient and a per patient-month basis in descending order of frequency by category, for Chorus RM.

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Table 1. Adverse Events Reported in > 1 Study Patient
(n=350 devices in 346 patients, 3622 device months)

Adverse Event	# of Patients	% of Patients	# of Events	Events per device-year
Complications¹				
<i>Atrial lead revision/replacement</i>	20	5.7%	20	6.6%
<i>Setscrew problem</i>	4	1.2%	4	1.3%
<i>Infection and sequelae</i>	4	1.2%	4	1.3%
<i>Ventricular lead revision/replacement</i>	3	0.9%	3	0.99%
<i>Diaphragmatic/Phrenic nerve stimulation</i>	3	0.9%	3	0.99%
Observations²				
<i>Diaphragmatic/Phrenic nerve stimulation</i>	19	5.5%	25	8.3%
<i>Tachycardia, endless-loop</i>	17	4.9%	20	6.6%
<i>Atrial tachyarrhythmias</i>	16	4.6%	16	5.3%
<i>Sensor over/under-response to effort</i>	13	3.8%	13	4.3%
<i>Atrial loss of capture</i>	10	2.9%	10	3.3%
<i>Atrial loss of sensing</i>	6	1.7%	7	2.3%
<i>Atrial loss of capture and sensing</i>	6	1.7%	6	2.0%
<i>Muscle stimulation</i>	4	1.2%	4	1.3%
<i>Ventricular loss of capture</i>	4	1.2%	4	1.3%
<i>Programmer/memory error</i>	3	0.9%	3	0.99%
<i>Sensor over/under-response at rest</i>	3	0.9%	3	0.99%
<i>Standby mode operation</i>	3	0.9%	3	0.99%
<i>Ventricular loss of sensing</i>	3	0.9%	3	0.99%
<i>Atrial sensing of skeletal muscle artifact</i>	2	0.6%	2	0.66%
<i>Ventricular sensing of skeletal muscle artifact</i>	2	0.6%	2	0.66%
<i>Crosstalk</i>	2	0.6%	2	0.66%

¹Complications are adverse events requiring invasive measures to correct, e.g., surgical intervention.

²Observations are adverse events which are correctable by noninvasive measures, e.g., reprogramming.

Table 2 reports the adverse events on a per patient and a per patient-month basis in descending order of frequency by category, for Opus RM.

Table 2. Adverse Events Reported in > 1 Study Patient

(n=74 patients, 513 device months)

	# of Patients	% of Patients	# of Patients	Events per device year
<i>Observations¹</i>				
Ventricular loss of sensing	3	4.1%	3	0.6%

Potential Adverse Events

Adverse events (including those reported in Tables 1 and 2) associated with pacing systems based on historical implant experience include:

- Cardiac perforation
- Cardiac tamponade
- Transvenous lead-related thrombosis
- Elevated thresholds
- Erosion through the skin
- Pulse generator migration
- Body rejection phenomena
- Hematoma/seroma
- Nerve and muscle stimulation
- Myopotential sensing
- Local tissue reaction
- Fibrotic tissue formation

¹Observations are adverse events which are correctable by noninvasive measures, e.g., reprogramming.

VIII. ALTERNATIVE PRACTICES AND PROCEDURES

Electrical pacing of the heart with a cardiac pulse generator is the standard and accepted treatment modality for the indications described above in Section II. Other available dual chamber or single chamber rate responsive pacing systems may meet the needs of the patient with the indications described above in Section II.

IX. MARKETING HISTORY

The Chorus RM and Opus RM are currently distributed commercially outside the United States. The first worldwide implant of the Chorus RM occurred in August, 1992 and the Opus RM in May, 1993. As of October 10, 1995, over 6,000 Chorus RM and 2,400 Opus RM devices have been sold and/or implanted outside the United States. This device has not been withdrawn from the market in any country for any reason related to the safety and effectiveness of the device and is currently marketed in the following countries: France, Germany, Belgium, Great Britain, Italy, Spain, Japan, Austria, Switzerland, Greece, Turkey, Sweden, Republic of Czechlovakia, and Bulgaria.

X. SUMMARY OF STUDIES

A. Nonclinical Laboratory Studies

Nonclinical testing of the Chorus RM and Opus RM was conducted to ensure that the components and the finished device perform in accordance with their design specifications. Additionally, testing has previously been submitted in support of the safety and effectiveness evaluation of the Chorus Model 6034 and Opus 4034 which differ only in software and components related to rate adaptation in the Chorus RM and Opus RM, respectively. Such changes in software and electronics have no effect on the microbiological, toxicological, immunological, biocompatibility, stress, and wear characteristics of the device. (See attached Summary of Safety and Effectiveness Data for the Chorus Model 6034, which was approved under PMA Number P900022. The Opus 4034 is a subset of the Chorus 6034 hardware, and is approved for market under K894267).

These nonclinical tests show that the Chorus RM and Opus RM passed all validation tests, function within specification under normal operating conditions, and function appropriately when subjected to severe mechanical and electrical conditions.

1. Hazard analysis

The manufacturer performed a risk analysis to identify potential hazards in the pacemaker's electronic components and subassemblies. The device incorporates risk management measures identified in this analysis. The company performed in-vitro testing of components, the hybrid

subassembly, the electronic subassembly, and finished devices, to verify the effectiveness of these measures.

The manufacturer also performed a pacemaker software hazard analysis to identify potential hazards associated with pacemaker software and a programmer software hazard analysis to identify other potential hazards associated with the programming system. Both pacemaker and programmer include features designed to reduce risk due to these potential hazards. The company performed testing of pacemaker and programmer software to exercise these safety features.

2. *Electronic component tests*

The manufacturer tested all components that changed with respect to the commercially available products, Opus Model 4034 and Chorus Model 6034.

Capacitor, tantalum

Electrical characteristics were measured on 100 samples. These samples were separated into two groups of 50 each. The first group was subjected to voltage aging and thermal shock. The second group was first subjected to visual inspection, then ten were subjected to dimensional checking and terminal strength tests, and 40 were subjected to life test, 1000 hours at 85 °C. All 100 samples passed.

Capacitors, ceramic

Life test was performed on 100 samples for 1000 hours at 125 °C. All samples met all specifications for capacitance change, dissipation factor, and insulation resistance.

Diodes, small signal and Zener

Visual and electrical inspection was performed on 128 samples. All samples met all specifications.

Integrated circuits

The pacemaker uses four integrated circuits: a pacing circuit, a sensor circuit, a microprocessor, and a random-access memory. In addition to 1000 hour life test at 125 °C performed on these circuits after mounting on a hybrid subsystem, the manufacturer characterized critical analog and digital parameters on one sample of the pacing circuit and sensor circuit, on ten microprocessor samples, and on four memory samples. Current drain of the device was characterized using five samples of the pacing integrated circuit. Current drain as established by the above testing was deemed appropriate.

Resistor, discrete

Visual inspection and verification of resistance value were performed on 98 samples. All samples

passed.

Resistor, network

Thermal shock, visual inspection, and electrical inspection was performed on each of 34 resistors on four samples. All resistors on all samples passed.

3. *Hybrid subassembly tests*

This assembly consists of four integrated circuits and associated discrete components, mounted on a cofired ceramic substrate. The manufacturer measured critical analog parameters and temperature drift on five samples. They measured the effect of supply voltage on these parameters in one sample. All tested samples passed these parametric tests.

The manufacturer also performed physical characteristic testing on electronic subassemblies. This included the following tests:

Destructive bond pull and die shear strength tests were performed on ten samples before cover seal. Mechanical shock, temperature cycling, and vibration were applied to ten samples after cover seal. These ten samples then passed visual inspection, particle impact noise detection, and fine leak tests, after application of these stresses. All samples passed these tests.

Life tests were performed on 22 completed electronic subassemblies, for 1000 hours at 125 °C. Electrical parameters were measured before and after this life test, and parameter changes were evaluated between 0 and 1000 hours. All samples gave results within specified tolerances.

4. *Electronic subassembly tests*

This consists of a hybrid subassembly as described above, together with a flexible circuit and associated discrete components including a battery.

One sample electronic subassembly was subjected to simulated electrosurgery, in a saline solution, at 250 watts for the coagulation mode and 400 watts for the cutting mode. The subassembly reverted to its standby mode of operation or continued to operate as programmed.

5. *Finished device tests*

Five samples of finished devices, without packaging, were subjected to six mechanical shocks at 500 g and random vibration at frequencies from 5 to 510 Hz. All samples functioned correctly after these stresses.

Five packaged samples were subjected to drops of one to five meters to concrete. These devices operated correctly after the drop tests.

One sample was subjected to simulated defibrillator shocks at 0.2 and 0.5 amps peak. The device

continued to operate correctly after this test.

One sample was subjected to signals designed to simulate electromagnetic interference at 10 Hz to 20 MHz. The device met test criteria above 0.5 KHz at any programmed sensitivity setting, and below 0.5 KHz at programmed sensitivity above 2.0 mV. This device was also tested for spurious injected current from 20 Hz to 5 MHz and met requirements over that range. Finally, a 1 V peak to peak signal was applied to the device over the range from 20 Hz to 0.5 MHz, and the device operated correctly thereafter.

One sample in a saline solution torso model was tested with an analog cellular telephone, and a digital cellular telephone using formats TDMA-11 and TDMA-50.. No effect was noted with the telephone and antenna located at least 3 cm from the pacemaker case.

The company did not perform additional testing of pacemaker connector assemblies, because these did not change from the commercially available devices, Opus Model 4024 and Chorus Model 6034.

6. Pacemaker software tests

Testing began with design review, which established a one-to-one correspondence between a pseudocode Software Design Document and a natural-language Software Requirements Specification. Testing then included code inspection for one-to-one correspondence with the pseudocode. Functional testing evaluated respiration impedance measurement, respiration signal processing, rate response, basic pacemaker functions, Holter, initialization, and timing performance. Functional testing was performed on a single prototype device. Software corrections were implemented where necessary, and all tests were passed.

7. Programmer software tests

Functional testing was performed on a single finished programmer and pacemaker. Testing was performed on the following safety-related functions: Implant interrogation, programming to nominal mode, programming basic or pacing parameters, management of conflict between parameters, battery curve and magnet rate display, threshold and lead tests, software integrity verification with cyclic redundancy control, and version control. Software corrections were implemented where necessary, and all tests were passed.

8. *Biocompatibility*

The company did not conduct additional biocompatibility testing because these devices use identical materials and surface finishes used on the commercially available products, Opus Model 4034 and Chorus Model 6034.

9. *Conclusion concerning non-clinical tests*

The manufacturer conducted risk analyses and identified risk control measures for hardware, pacemaker software, and programmer software, and then conducted testing to evaluate these and other device features. All electronic components that changed from approved predecessor devices were tested. The hybrid subassembly, electronic subassembly, and finished device were subjected to stresses designed to simulate or exceed device use. Pacemaker and programmer software were tested functionally. The device passed all these tests.

B. *Clinical Studies*

Chorus RM

The clinical data provided in support of this PMA were accrued under a common investigational plan for the Chorus RM device, approved under G920150. The study began on October 12, 1993. As of June 17, 1996, 350 devices were implanted in 346 patients at 48 investigational sites. The average implant duration was 10.35 months, with a maximum implant duration of 32.0 months. The mean age of patients implanted with this device was 71.3 years old, with a standard deviation of 11.8 years.

Objectives: Evaluate oxygen consumption rate, peak heart rate, proportionality of rate increase, correlation with a literature standard³, and correlation with intrinsic rates.

Methods: Oxygen consumption and peak heart rate were obtained in a single-blind, randomized crossover design using paired exercise testing, comparing Chorus RM in DDDR mode to DDD mode. Proportionality and correlation were evaluated from the device's sensor-determined rate, patient intrinsic rate, and elapsed time during exercise. These effectiveness data were obtained at approximately one month post-implant.

All study subjects were selected from each investigator's general patient population with the overall requirement that each subject was a candidate for dual chamber pacing. In addition, early candidates for the study were examined for demonstration of chronotropic incompetence (CI) and were to be able to perform treadmill exercise tests. (CI was defined as the inability to achieve heart rates greater than 75% of the maximum predicted heart rate (MPHR = 220 - age).) Seven of the 63 tested patients exhibited chronotropic incompetence.

Exclusion criteria included the presence of any life-threatening diseases (including patients who had received an organ transplant), the presence of any serious disease which could necessitate noncompliance with the protocol, geographic instability, the presence of chronic supraventricular

tachycardia, and the inability to tolerate increases in pacing rate due to conditions such as severe coronary artery disease or severe aortic stenosis.

For inclusion in the randomized crossover study, patients were also required to demonstrate CI in a confirmation by laboratory testing.

Data concerning safety were gathered at: pre-implant, implant, pre-discharge, and at scheduled follow-up visits (1, 3, 6, 12, 18, 24, and 30 months post-implant). Safety data consisted of information concerning all device failures and replacements, patient deaths, observations and patient complaints, complications and patient discontinuations. They also consisted of data showing that the study adequately exercised all new device parameters, to expose any potential safety issues.

Results of the Study

Three hundred and forty-six patients were enrolled by 45 investigators at 48 sites. Mean age was 71.3 ± 11.8 (SD) years. Average implant duration was 10.35 ± 9.02 (SD) months, with a maximum of 32.0 months. Although diagnosis of chronotropic incompetence was a requirement for inclusion in Phase 1, only 7 of the 63 tested Phase 1 patients exhibited chronotropic incompetence in confirming laboratory testing, in which chronotropic incompetence was defined as inability to achieve 75% of their maximum predicted heart rate (220-age) in symptom-limited exercise testing.

Data concerning the effectiveness hypotheses of oxygen consumption and peak heart rate were gathered at paired exercise testing at approximately one month post-implant. This was symptom-limited treadmill testing according to the chronotropic assessment exercise protocol (CAEP). This was a single-blind, randomized crossover study where each patient served as their own control, comparing DDDR and DDD modes for both oxygen consumption and peak heart rate. Linearity or rate response and comparability with a literature standard³ were also measured at approximately one month post-implant using the CAEP protocol. The quantitative variables observed were: intrinsic heart rate, sensor-indicated rate and elapsed time.

Gender Bias Analysis

Of all patients enrolled, 67 (39%) were females. Inclusion and exclusion criteria were chosen to avoid gender bias. The preponderance of male patients reflected both the gender referral pattern for cardiac disease and the severity of the disease in the centers involved. In addition, the comparability of the gender distribution is supported by U.S. epidemiological data obtained nationwide in a 1988 survey of 122,310 individuals where the age-adjusted pacemaker prevalence in males was 1.5 times that in females (60% male: 40% female).

Safety and effectiveness data were analyzed by gender and no statistically significant differences were noted.

Four patients were unable to achieve rates higher than the Activities of Daily Living rate when performing treadmill testing. Investigation revealed that these patients' rate-response parameters were improperly initialized. Labeling has been provided to address this problem. Detailed instructions have been provided for obtaining a proper initialization, as well as a method to verify proper initialization immediately afterwards rather than waiting for a treadmill test. ELA suggests that the physician verify proper initialization by looking at the simulation data. Criteria for what constitutes both proper and improper initialization by looking at the simulation data has been provided in the Physician's manual.

Data not directly addressing effectiveness hypotheses were gathered through Chorus RM internal histograms of sensor-determined rate, external Holter monitoring, and testing of rate-response in activities of daily living.

Analyses of the 52 twenty-four hour Holter recordings taken at the one-month follow-up revealed some pacing and sensing abnormalities which were all resolved by reprogramming.

Results: Tables 3 and 4 summarize the results of exercise testing. The devices demonstrated a linear increase in sensor rates with exercise level, an appropriate response for a rate responsive pacemaker. The slope of increase was comparable to a literature standard² and to intrinsic rates. The slope of the regression of sensor-indicated rates versus a literature standard was 1.023 ± 0.067 which was not significantly different statistically from 1.0 ($p=0.735$). A slope of 1.0 would indicate identical performance to predicted values.

Table 3. Oxygen Consumption and Peak Heart Rate during Exercise Testing

(n=37 patients including 7 patients exhibiting chronotropic incompetence)

Parameter	# of Patients	DDDR mean \pm SD	DDD mean \pm SD	Difference (DDDR-DDD) [95% Conf. Interval]
Oxygen consumption rate (L/min)				
CI patients	6	0.70 \pm 0.35	0.71 \pm 0.38	0.011 [-.037, 0.059]
Peak heart rate (beats/minute)				
CI patients	7	122 \pm 6.2	92 \pm 15	30.3* [12.9, 47.7]
Non-CI patients	30	127 \pm 15	119 \pm 19	7.2* [1.5, 13]
All patients	37	126 \pm 14	114 \pm 21	11.6* [5.5, 17.6]

* Difference statistically significant ($p < 0.05$) by t-test

² Kay GN: Quantitation of chronotropic response: Comparison of methods for rate-modulating permanent pacemakers. J Am Coll Cardiol 20:1533, 1992

Table 4. Rate Sensor Proportionality during Exercise Testing
(n=38 patients including 7 patients exhibiting chronotropic incompetence)

Parameter	# of Patients	Correlation Coefficient [95% confidence interval]
Sensor indicated rate vs. exercise time	38	0.96 [0.89, 0.99]
Sensor indicated rate vs. method of Kay (slope = 1.023 ± 0.067)	38	0.99 [0.91, 0.99]
Sensor indicated rate vs. intrinsic rate	38	0.94 [0.89, 0.98]

Opus RM

The Opus RM was evaluated in a multi-center prospective study of the rate response in calibrated symptom-limited treadmill testing. Seventy-four patients were enrolled by 19 investigators at 21 sites. Mean age was 75.3 ± 10.9 (SD) years. Average implant duration was 6.92 ± 4.92 (SD) months, with a maximum of 18.2 months.

Objectives: Evaluate oxygen consumption rate, peak heart rate, proportionality of rate increase, correlation with a literature standard³, and correlation with intrinsic rates.

Methods: Oxygen consumption and peak heart rate were obtained in a single-blind, randomized crossover design using paired exercise testing, comparing Opus RM in VVIR mode to VVI mode. Proportionality and correlation were evaluated from the device's sensor-determined rate, patient intrinsic rate, and elapsed time during exercise. These effectiveness data were obtained at approximately one month post-implant.

Study subjects were selected from candidates for dual chamber pacing, able to perform treadmill exercise tests, in each investigator's general patient population. They were further required to have been diagnosed with chronotropic incompetence (CI), defined as the inability to achieve heart rates greater than 75% of the maximum predicted heart rate ($MPHR = 220 - \text{age}$). Although this diagnosis was a requirement for participation in paired exercise testing, only eight of the eleven tested patients in fact exhibited chronotropic incompetence.

All study subjects were selected from each investigator's general patient population with the overall requirement that each subject was a candidate for single chamber pacing. In addition, candidates for the early part of the study (effectiveness endpoints) were examined for

demonstration of chronotropic incompetence (CI) and were to be able to perform treadmill exercise tests. (CI was defined as the inability to achieve heart rates greater than 75% of the maximum predicted heart rate (MPHR = $220 - \text{age}$.)

Exclusion criteria included the presence of any life-threatening diseases (including patients who had received an organ transplant), the presence of any serious disease which could necessitate noncompliance with the protocol, geographic instability, the presence of chronic supraventricular tachycardia, and the inability to tolerate increases in pacing rate due to conditions such as severe coronary artery disease or severe aortic stenosis.

Data concerning safety were gathered at: pre-implant, implant, pre-discharge, and at scheduled follow-up visits (1, 3, 6, and 12 months post-implant). Safety data consisted of information concerning all device failures and replacements, patient deaths, observations and patient complaints, complications and patient discontinuations. They also consisted of data showing that the study adequately exercised all new device parameters, to expose any potential safety issues.

Data concerning effectiveness hypotheses were gathered at exercise testing at approximately one month post-implant. This was symptom-limited treadmill testing according to the chronotropic assessment exercise protocol (CAEP). Four quantitative variables were observed: intrinsic heart rate, oxygen consumption, sensor-indicated rate, and elapsed time.

Data not directly addressing effectiveness hypotheses were gathered through Opus RM internal histograms of sensor-determined rate and external Holter monitoring of twenty-nine patients.

Results: Table 5 summarizes the results of exercise testing. The devices demonstrated a linear increase in sensor rates with exercise level, an appropriate response for a rate responsive pacemaker. The slope of increase (3.79 ± 0.14) beats per minute per minute of exercise was comparable to a literature standard³ (3.48 ± 0.46). The slope of the regression of sensor-indicated rates versus a literature standard was 0.96 which was not significantly different statistically from 1.0. A slope of 1.0 would indicate identical performance to predicted values.

Table 5. Rate sensor proportionality during exercise testing

(n= 8 patients exhibiting chronotropic incompetence)

Parameter	# of Patients	Correlation Coefficient [95% confidence interval]
Sensor indicated rates vs. exercise time	8	0.99 [.973, .999]
Sensor indicated rate vs. method of Kay	8	0.93 [.708, .986]

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XI. CONCLUSIONS DRAWN FROM THE STUDIES

Chorus RM

- Both the bench testing and clinical testing demonstrate a reasonable assurance that the Chorus RM is safe and effective when used in accordance with its labeling.
- There were a total of 27 deaths and seven explanted devices. None of the deaths or explants were deemed due to device malfunction. Four device explants were secondary to late postoperative infection, and three were explanted prophylactically.
- All patients who completed the six-week follow-up exercise testing showed appropriate rate increase during the initial stages of exercise and an appropriate rate decrease following the cessation of exercise in the DDDR pacing mode.
- Analyses of the twenty-four hour Holter recordings from fifty-two patients taken at the one-month follow-up revealed some pacing and sensing abnormalities (2%). All pacing and sensing abnormalities were resolved by re-programming.
- There were no device malfunctions. All adverse events were either clinically insignificant or were resolved through reprogramming, programming correction, drug therapy or other medical interventions.
- Interaction of the programming system and associated software with the Chorus RM including interrogation, programming, and the use of other features was reliable.
- There have been no reports of clinical issues related to the chronic use of the device.

The effectiveness objectives and conclusions which were evaluated during exercise testing are presented below.

- Sensor rates in the Chorus RM increased proportionally (i.e., linearly) with exercise. The observed correlation coefficient (0.96) was significantly higher than the target value of 0.90.
- The observed rate of increase of 3.10 beats per minute, per minute of exercise, was not significantly different from that estimated using the method of Kay³.

- Sensor rates in Chorus RM were correlated with rates predicted by the method of Kay (observed correlation equalled 0.97). The observed slope (1.02) was not significantly different from the ideal value of 1.0.

Opus RM

- Both the bench testing and clinical testing demonstrate a reasonable assurance that the Opus RM is safe and effective when used in accordance with its labeling.
- All patients who completed the one-month follow-up exercise testing showed appropriate rate increase during the initial stages of exercise and an appropriate rate decrease following the cessation of exercise in the SSIR pacing mode.
- Analysis of the twenty-four hour Holter recordings from twenty-nine patients taken at the one-month follow-up demonstrated normal pacing and sensing behavior in 97% of the patients. One patient (3%) showed rare ventricular undersensing which was resolved by reprogramming.
- There were no device malfunctions.
- Interaction of the programming system and associated software with the Opus RM including interrogation, programming and the use of other features was reliable.
- There have been no reports of issues related to the chronic use of the device. The eight patient deaths in the study were not device related. There have been no explants.

The effectiveness objective exercise testing results are provided below.

- Sensor rates in the Opus RM increased proportionally (i.e., linearly) with exercise. The observed correlation coefficient was 0.99.
- The observed rate of increase of 3.79 beats per minute, per minute of exercise, was not significantly different from that estimated using the method of Kay, 3.48.
- Sensor rates in Opus RM were correlated with rates predicted by the method of Kay (observed correlation = 0.93). The observed slope (0.96) was not significantly different from the ideal value of 1.0

XII. PANEL RECOMMENDATION

Pursuant to section 515(f) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory System Devices Panel, an FDA advisory panel for review and recommendation because the information in the PMA substantially duplicated information previously reviewed by this panel.

XIII. CDRH DECISION

FDA issued an approval order on MAR 10 1997. The applicant's manufacturing facility was inspected on December 9-12, 1996 and was found to be in compliance with the device Good Manufacturing Practice regulations (21 CFR Part 820).

XIV. APPROVAL SPECIFICATIONS

Directions for use: See the labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions and Adverse Events in the Labeling.

Post-approval Requirements and Restrictions: See approval order.

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Summary of Safety and Effectiveness Data
for the ELA Medical, Inc. Chorus DDD Pacemaker Models 6001, 6003 and
6033, CPR1 Microcomputer Programmer and P2A Handheld Programmer

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SUMMARY OF SAFETY AND EFFECTIVENESS DATA

I. GENERAL INFORMATION

Device Generic Name: Implantable Pacemaker Pulse
Generator and Pacemaker Programmer

Device Trade Name: Chorus DDD Pacemaker Models 6001,
6003 and 6033, CPR1 Microcomputer
Programmer and P2A Handheld
Programmer

Applicant's Name and Address: ELA Medical, Inc.
15245 Minnetonka Boulevard
Minnetonka, Minnesota 55345

Pre-market Approval (PMA)
Application Number: P900022

Date of Notice of Approval
to the applicant: SEP - 6 1991

II. INDICATIONS AND CONTRAINDICATIONS FOR USE

Indications

Generally accepted indications for long-term cardiac pacing include, but are not limited to: sick-sinus syndrome; chronic symptomatic drug-resistant sinus arrhythmias, such as sinus bradycardia, sinus arrest, sinoatrial (SA) block as seen in sick-sinus syndrome; chronic, symptomatic second-degree or third-degree AV block; recurrent Adams-Stockes syndrome; symptomatic bilateral bundle branch block; and hypersensitive carotid sinus syndrome (carotid sinus syncope). Also symptomatic drug-resistant bradyarrhythmias that impair cardiac output are considered indications for pacing in patients with acute myocardial infarction. Dual chamber pacing is specifically indicated in patients requiring permanent pacemakers where restoration of atrioventricular synchrony and/or sinus modulated rate variability is indicated: to improve cardiac output or congestive heart failure related to bradycardia or VVI pacing intolerance (pacemaker syndrome); to protect against certain tachyarrhythmias by suppressing ectopic foci in both the atrium and the ventricle; to treat varying degrees of AV block with normal sinus activity; to treat patients with sick-sinus syndrome (conditions such as intermittent sinus bradycardia, sinus arrest, SA block, and bradytachy syndrome); and to use against certain drug-resistant and reentrant tachycardias by varying AV delay settings.

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Contraindications

There are no known contraindications to the use of ventricular demand pacemakers as a medical method for control of heart rate. However, a patient's physical and medical condition or age may dictate the particular pacemaker, lead, and surgical procedure used by the physician.

Application of this pacemaker to pace the atrium (i.e., in AOO, AAI, AAT modes) is contraindicated when atrioventricular conduction disturbances are present. Also synchronous pacing is contraindicated when there is competition between a patient's intrinsic rhythm and the pacemaker.

Contraindications for pacing in the DDD mode include patients exhibiting atrial fibrillation or atrial flutter, or patients exhibiting slow retrograde (VA) conduction greater than 450 ms which could give rise to pacemaker-mediated-tachycardias.

III. DEVICE DESCRIPTION

The Chorus DDD pacemakers are dual chamber, multiprogrammable pulse generators. The pacing system consists of the Model 6001, 6003 and 6033 pulse generators with commercially available pacing leads, the CPR1 Microcomputer and P2A Handheld Programmer. The Model 6001 is a unipolar device with two 5 mm connector ports which are compatible with the 6 mm standard ports. The only difference between the Model 6001 and the other Chorus pacemakers is the connector size. The Model 6003 is a unipolar device with two 3.2 mm IS-1 connectors. The Model 6033 is identical to the Model 6003 with the addition of Holter functions. The Model 6033 is available in the event that the physician desires to monitor the patient's cardiac activity. The Holter functions measure, record and display events selected by the physician. Event selections include atrial intervals, atrial pauses, ventricular intervals, ventricular pauses, AV intervals and nonsynchronous ventricular intervals. The Holter display of the collected statistical data consists of consecutive histograms which last the programmed period and are defined by the type of event and the boundaries which separate the histogram channels. A curve of battery status can also be displayed.

The CPR1 Microcomputer Programmer and P2A Handheld Programmer are intended to be used to noninvasively interrogate and program the three Chorus DDD pacemaker models. The Chorus pacemakers can be interrogated and programmed via bidirectional radio frequency telemetry using either the P2A Handheld programmer or the Model CPR1 Programmer head which is used with a microcomputer. The P2A Programmer has a built-in printer. The CPR1 microcomputer programmer system can be connected to a printer via a parallel printer port.

Pacing modes available include: DDD, DDI, DOO, VVI, VVT, VOO, AAI, AAT and AOO. Other programmable parameters are rate atrial and ventricular settings (amplitude, pulse width and sensitivity), hysteresis, AV delay, absolute refractory period, post ventricular atrial refractory period

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(PVARP), blanking and committed period and test rate and atrial threshold during threshold testing. The programmable pacing algorithms include: rate responsive AV delay; Pacemaker Mediated Tachycardia (PMT) protection; fallback; and rate smoothing. Telemetered measurements include: lead impedance (current and voltage); atrial and ventricular electrograms; markers; and serial number and model. Statistics include: atrial and ventricular sensed beats; atrial and ventricular paced beats; paced ventricular beat at the end of committed period; premature ventricular contractions; PMT reduction; fallback and programming. The Chorus pacemakers have runaway protection designed to prevent pacing rates in excess of 185 ppm.

The Chorus pacemakers are powered by a lithium iodine cell with a 1.6 Ampere-hour useable capacity. Calculated life time is 66 months based on 100 percent pacing in the DOO mode, 70 bpm, 5V, 0.49 msec and a 500 ohm load. The electric replacement indicator (ERI) is signalled by a magnet rate of 80 pulses per minute (ppm). At beginning of life (BOL) the magnet rate is 96 ppm, and decreases in steps to ERI. When ERI has been reached, a minimum of 3 months of battery life remains prior to the pacemaker end of life (EOL) which occurs at a magnet rate of 69.8 ppm.

IV. ALTERNATIVE PRACTICES AND PROCEDURES

Cardiac pacing is the accepted treatment for the indications described in Section II above. Other PMA approved systems, single or dual chamber, may meet the needs of the patients with the symptoms described in Section II above.

V. MARKETING HISTORY

The Chorus pacemakers were released for general marketing in France in June, 1988. Presently, the devices are being distributed in 12 countries. Approximately 5491 units have been distributed. There have been no adverse effects or complications reported about these devices.

VI. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Potential adverse effects associated with all pacemaker systems include: loss of normal pacemaker function due to battery failure or other component failure; inability to reprogram a pacemaker pulse generator because of programmer failure; infection; erosion; undesired muscle or nerve stimulation; and inadequate sensing or pacing. Any demand pulse generator can be affected by magnetic, electrical, and electromagnetic signals of sufficient strength or with characteristics which mimic cardiac function. Possible effects of electrical interference on pulse generator operation include reversion to synchronous pacing, inhibition of output pulses and rapid synchronous pacing. Certain environmental sources can couple sufficient energy into a cardiac pacing system to damage the pulse generator or cardiac tissue adjacent to the electrodes.

Potential adverse effects associated with dual-chamber pulse generators include crosstalk and PMT. The pulse generator may be reprogrammed to

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minimize or prevent the effects of these phenomena.

Failure of the pulse generator system to function properly may result in the patient experiencing the symptoms for which the pulse generator was originally indicated.

VII. SUMMARY OF STUDIES

A. Component Tests

Electrical and mechanical components were design verified in accordance with the applicant's specifications. Sixteen hybrid electronic modules underwent 1,000 hours of accelerated life testing at 125 degrees Centigrade. A series of tests were performed on the hybrids in accordance with the applicable sections of the appropriate military testing standard (MIL-STD-883). All hybrid electronic modules passed the tests. Tests on the device feedthroughs consisted of thermal cycling, electrical tests, and hermeticity. No failures were reported. The battery was subjected to a series of tests (vibration, mechanical shock, hermeticity after burn-in). No failures were observed. The test results demonstrated performance consistent with high reliability pacemaker requirements. The battery model is routinely used in marketed pacemakers.

B. Device Tests

Environmental testing on the finished devices consisted of: thermal cycling (0 degrees Centigrade (C) for 24 hours, 50 degrees C for 6 hours and 37 degrees C for 24 hours); vibration tests with the pacemaker in transport packaging (3 orthogonal axes, 4 cycles, 1 hour, 3 to 8 Hz vibration, 7.5 mm amplitude, then 8 to 0.3 Hz, with constant 2 g (gravity) peak acceleration); vibration tests on the device without packaging (3 orthogonal axes, with one cycle sweep for 30 minutes at 10 to 50 Hz with 4 mm amplitude, then 50 to 0.5 Hz at a constant 20 g peak acceleration, then 0.5 to 50 Hz return); mechanical shock (3 orthogonal axes both directions, 3 shocks each direction, 1/2 sinusoid, 30 g peak acceleration, 18 ms duration, then 2 shocks along 3 axes, 1/2 sinusoid, 0.5kg, 1 ms duration); magnetic field application (10 Hz to 10 kHz, 20 V/m equivalent electric field strength, repeated 2 kHz to 2.5 GHz); defibrillation (capacitor discharge 0.4 kJ at 0.4 kV through 10 k ohm resistor, 3 shocks); and hermeticity (maximum standard leak rate 0.31×10^{-9} atm/cc/sec air equivalent). Drop tests on the units with and without packaging, electromagnetic interference tests (10 Hz to 1 MHz), electrosurgery and high strength magnetic field effects on telemetry (at BOL and EOL) were also performed. All of the devices remained within the applicant's labeled specifications.

Electrical characterization tests were performed on three Model 6003 pacemakers to verify the performance to design specifications

over a range of battery conditions, load conditions and programmed settings. In all cases, the devices performed in accordance to the applicant's tolerances and specifications. The testing of the Model 6003, as described above, is sufficient for the Models 6001 and 6033 due to the identical basic electronic circuitry which is shared by the Chorus pacemakers.

The results of bench tests that support the accuracy of the pacemaker statistics and Holter functions employed by the Model 6033 were submitted. A heart simulator with a known number of types of events recorded in statistics was used in evaluating the pacemaker statistics function. The tests verified proper performance in storing and identifying atrial sensing and pacing events, ventricular detection and stimulation statistics, ventricular asynchronous beats and programmings. It was also verified that the statistics reset function operated as intended. In evaluating the Holter functions a series of tests were performed. Tests were done to verify the accuracy of the battery cell status recording. A resistance was connected in series with the cell voltage to simulate the cell resistance. The resistance values were set between 0 and 10 k ohms. A written record of the decade resistance setting and the time at which the setting was changed was maintained. The resistance was changed randomly up and down. It was verified that in all cases the data stored were correct. In evaluating the Model 6003 Holter functions, the device was set in the DDD mode to record atrial and ventricular intervals. The limits were set to 453, 500, 504, 703, 707, 906 and 1000 ms. The pacemaker was connected to a heart simulator that repeated a sequence of atrial and ventricular events with periods varying within the above limits. The average heartbeat interval in the sequence should be 805 ms which means that approximately 2235 events should be recorded per histogram or 248 events per channel (except in the channel for intervals longer than 1000 ms where 497 events should be found). The results demonstrated that the performance of the device conformed to specifications.

Biocompatibility

The biocompatibility of the tissue contact material used in the Chorus pacemakers has been well established. These materials include titanium and silicone rubber, and are being used in other ELA approved pacemakers.

C. Programmer Testing

A series of environmental, functional and software tests were performed to check the programming effectiveness. Test results indicated that the programmer performed according to the applicant's specifications which are consistent with the labeling.

D. Animal Studies

In lieu of the animal trials, data from European clinical trials were provided. The results of the studies demonstrated performance of the Chorus pacemakers to specifications.

E. Clinical Studies

The objectives of the clinical study of the Chorus pacemakers were to confirm the proper operation, safety and effectiveness of the Models 6001, 6003 and 6033 in providing dual-chamber pacing. Since there are no significant electronic differences between the Chorus pacemakers, the clinical data obtained are applicable to all three models.

The clinical study began in the United States on January 11, 1989. As of October 31, 1990, data had been collected at implant and post-implant on 239 patients (124 males and 115 females) by 37 investigators. The device models included one Model 6001, 213 Model 6003 and 25 Model 6033 pacemakers. The mean age for males was 71.7 years and for females was 73.3 years with a range from 30 - 96 years. The average implant time was over 252 days and the longest implant time was 658 days. Accumulated device months was approximately 2010 months. Since the only difference between the Model 6001 and the Model 6003 is that the Model 6001 has 5mm connector ports, the study of one unit was sufficient. The reliability of this connector port change was established through bench testing.

The indications for use of the Chorus pacemaker models included sick sinus syndrome (27 percent); various degrees of heart block (24 percent); complete heart block (18 percent) sinus bradycardia (18 percent); brady-tachy syndrome (3 percent); hypersensitive carotid (2 percent); battery replacement and unknown (8 percent).

Of the 239 patients implanted with the Chorus pacemakers, 145 patients had follow-up reports greater than 30 days, 116 patients were followed for more than 90 days and 83 patients had reports of 6 months or greater.

The study was divided into three phases. The follow-up schedule for phase I and phase II was at predischarge and at 1, 2 and 6 months thereafter. Data were collected during phase III at implant and at 6 months. In phase I, 30 patients were closely followed with either 24 hour Holter monitoring or bedside monitoring. Eight patients were Holter monitored for 24 hours and the remaining patients were monitored at the bedside. Occasional undersensing of P waves was noted which resulted in programming the atrial sensitivity to 0.8 mV from the nominal setting of 1 mV. One patient required adjustment of the blanking period from 24 ms to 31 ms. In order to assess effectiveness, exercise testing was performed on 16 of 30 phase I patients after 1 month. Sensing of

myopotentials by the atrial sense amplifier was noted in two patients, with crosstalk noted in one patient. The atrial sensitivity was changed from 0.6 mV to 1 mV. All of the device algorithms were represented in those patients who had exercise tests. Certain patients were programmed with more than one algorithm. Four patients were programmed with the rate smoothing algorithm ON; the PMT algorithm was programmed ON in nine patients; the automatic AV delay in six patients, and fallback in nine patients. One patient was exercised using automatic AV delay and fixed AV delay. Appropriate behavior was adequately documented.

Phase II involved the study of a total of 100 patients including the 30 patients followed according to the phase I protocol. During phase II, 30 U.S. patients were studied to evaluate the susceptibility of the Chorus pacemakers to crosstalk (sensing by the ventricular sense amplifier of the atrial pacing pulse) and the marker channel capability. The crosstalk study involved maintaining typical parameter settings and increasing the atrial pacing energy in increments until crosstalk was encountered. The energy factor for the atrial pulse was incremented while holding the ventricular sensitivity and blanking period constant until crosstalk was encountered. Also, crosstalk was assessed at different ventricular sensitivity levels and blanking periods. The study results demonstrated the following: (1) the majority of the patients were not susceptible to crosstalk until the atrial pulse width reached 0.173 ms when the blanking period was set at 31 ms (nominal); (2) crosstalk was never encountered when blanking was set at 47 ms (maximum setting); (3) it was demonstrated that crosstalk was directly related to atrial pulse width settings (wider pulse width). Several patients exhibited crosstalk at 0.98 ms pulse width at 5 volts and 7.5 volts atrial pulse amplitude, but crosstalk disappeared at both voltage settings when pulse width was reduced to less than 0.73 ms; and (4) crosstalk was revealed at the 24 ms blanking period. As a result of the studies, the preprogrammed blanking period was changed from 24 ms to 31 ms. Marker channel evaluations were done on 31 patients, proper functioning was observed.

During phase III, data was generated from studies involving the total patient population of 239 patients. The studies included verification of proper operation of the algorithms with an electrocardiograph (ECG) machine and/or by interrogating the three Chorus pacemakers for the statistics information. Algorithm activation increased slightly with each follow-up period. The automatic AV Delay was used on 128 patients, and the PMT algorithm was used on 117 patients. One hundred patients had the algorithm programmed ON during the last follow-up. Studies by several authors confirmed successful termination of PMT in several cases. The fallback algorithm was used on 41 patients and was programmed ON in 28 patients at the last follow-up. Appropriate behavior was demonstrated. The results of published studies (1, 2) also



provided support for the proper functioning of the algorithm. The rate smoothing algorithm was used on 21 patients and was programmed ON in 12 patients at the last follow-up. Proper operation of the algorithm was confirmed with a standard ECG and during exercise tests. The rate limit off feature was successfully used on five patients to pace at a rate higher than the pacemaker rate limit of 185 ppm during electrophysiological studies. The devices operated to specifications.

Proper functioning of all pacing modes was demonstrated. At the 180 day period, it was reported that 92.6 percent of the patient population was programmed in the DDD mode. The predominately used programmed settings were as follows: basic rate was 76 pulses per minute (ppm); the maximum rate was 120 ppm; PVARP was 297 ms; the most frequently used blanking period was 31 ms; atrial pulse amplitude was 2.5 volts; ventricular pulse amplitude at 25 volts; ventricular pulse width at 5 volts; and ventricular sensitivity at 2.2 mV.

The following tests were also performed in evaluating the performance of the Chorus pacemakers. Lead impedance measurements were done on 112 of 239 patients to assess the integrity of the atrial leads; and on 118 patients for the assessment of the ventricular leads. Intracardiac electrocardiograms were recorded on at least 20 percent of the patient population. The recordings demonstrated good pacemaker capture. The automatic threshold feature was used to estimate atrial thresholds in 51 patients and ventricular thresholds in 108 patients. Proper functioning was documented. The pacemaker statistics (number of paced and sensed atrial and ventricular beats, non synchronous and committed ventricular beats, PMT termination attempts and fallback starts and programming) were interrogated and documented at least once on 108 patients. Other patients were interrogated, however, without documentation. It was demonstrated that the statistics feature functioned as intended.

Clinical tests were done on 20 patients in France to assess the performance of PMT algorithm and the response to electromagnetic interference (EMI). Patients were programmed to conditions to promote induction of PMTs (long AV delays and short PVARPs). Twenty-four hour Holter recordings were made and pacemaker statistics were analyzed and compared to the Holter recordings. The data compared favorably. Full success of the algorithm was noted in all cases. Studies to assess cross sensing and cross stimulation and the response to electromagnetic interference algorithm were also performed. No ventricular sensing of the atrial pacing pulse, except during extreme circumstances, was noted. The device also performed to specifications during the electromagnetic interference (EMI) tests.

Complications included three acute lead repositionings, one open heart surgery to repair an atrial lead perforation, and cross-

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talk associated with an unstable lead which required repositioning. One patient required an increase in atrial sensitivity from 1 mV to 0.8 mV. Two problems were experienced with the printer used with the CPR1 programmer (clogging of inkjet cartridge and a blown fuse). Three units were explanted. In one case the investigator elected to explant the device after perforation of the ventricle by the ventricular lead. The decision was to remove the entire dual chamber system and replace it with a VVI unit. A second device was explanted when the connectors became damaged after a lead displacement. The results of analysis on the unit supported proper functioning of the device. The third unit was replaced when the investigator was unable to reinitialize the Chorus model operating in the standby mode (VVI) pacing after it was subjected to repeated defibrillation shocks. The device labeling warns against placing the defibrillation electrodes directly over the pulse generator. There have been ten deaths, all unrelated to the Chorus pacemakers. The results of analyses of the pacemakers confirmed proper operation.

VIII. CONCLUSIONS DRAWN FROM STUDIES

The in vitro test results and data from the clinical study provide reasonable assurance that the Chorus DDD Pacemaker Models 6001, 6003 and 6033, CPR1 Micro Computer Programmer and P2A Handheld Programmer perform as designed and are safe and effective when used as indicated in the labeling.

IX. RECOMMENDATIONS

The information in the application for the Chorus pacemakers and programming system which would be reviewed by the Circulatory System Devices Panel substantially duplicates information which has previously been reviewed by the Panel. Therefore, based on the review of the PMA application for the Chorus pacemakers and similar DDD pacemakers, and in accordance with Sec. 515(c)(2) of the Federal Food, Drug, and Cosmetic Act as amended by the Safe Medical Devices Act of 1990, CDRH determined that panel review was not indicated for the Chorus pacemakers.

X. FDA INSPECTION

On June 20, 1990, FDA completed an inspection of ELA Medical, Inc.'s manufacturing facilities and determined that the manufacturer was in compliance with the device Good Manufacturing Practices Regulation.

XI. APPROVAL SPECIFICATIONS

Directions for use: See attached labeling.

Conditions of approval: CDRH approval of this PMA is subject to

full compliance with the conditions described in the approval order.

XII. REFERENCES

1. M. Limousin, J.L. Bonnet and the Investigators of the Multicenter Study. "A New Algorithm to Solve Endless Loop Tachycardia in DDD Pacing: A Multicenter Study of 91 Patients," Pace, July, 1990. XIII:867-874.
2. Sylvie Girodo Marcel Limousin, Philippe Ritter, et al. "New Algorithm for Prevention and Termination of Pacemaker Endless-Loop Tachycardia," New Perspectives in Cardiac Pacing, Futura Publishing Company, 1988.

LABELING

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Chorus RM 7034

Dual Chamber Rate Responsive Pacemaker System

Caution: *Federal Law restricts this device to sale by or on the order of a physician (or properly licensed practitioner).*

1. DEVICE DESCRIPTION

Chorus RM (Model 7034) is a dual-chamber, bipolar, rate responsive, implantable pulse generator which uses a minute ventilation sensor. It is powered by a lithium-iodine cell and encapsulated in a hermetically sealed titanium case. Chorus RM can be programmed and interrogated via bi-directional telemetry using an IBM PC compatible microcomputer (programming software CSO 2.46 or higher and operating system configured and furnished by ELA Medical with that software) connected to a CPR1 programming head. Model 7034 is fitted with two IS-1 standard 3.2 mm connectors (ISO/DP 5841-3).

2. INDICATIONS

The Chorus RM pacemaker system is indicated for:

Rate adaptive pacing in patients who may benefit from increased pacing rates concurrent with increases in minute ventilation;

The accepted patient conditions warranting chronic cardiac pacing which include:

- Symptomatic paroxysmal or permanent second or third-degree AV block;
- Symptomatic bilateral bundle branch block;
- Symptomatic paroxysmal or transient sinus node dysfunctions with or without associated AV conduction disorders;
- Bradycardia-tachycardia syndrome to prevent symptomatic bradycardia or some forms of symptomatic tachyarrhythmias; and
- Vaso-vagal syndromes or hypersensitive carotid sinus syndromes.

The Chorus RM is also indicated for **dual-chamber and atrial tracking modes** in patients who may benefit from maintenance of AV synchrony. Dual-chamber modes are specifically indicated for treatment of conduction disorders that require restoration of both rate and AV synchrony which include:

- Various degrees of AV block to maintain the atrial contribution to cardiac output; and
- VVI intolerance (e.g., pacemaker syndrome) in the presence of persistent sinus rhythm.

3. CONTRAINDICATIONS

- This device is contraindicated in patients with an implanted cardioverter-defibrillator (ICD) because the pulses used in the measurement of minute ventilation may cause unwanted delivery of ICD therapy.
- Single-chamber atrial pacing is contraindicated in patients with impaired AV nodal conduction.
- Dual-chamber and single-chamber atrial pacing are contraindicated in patients with chronic refractory atrial tachyarrhythmias.

4. WARNINGS

- **Rate adaptive pacing** should be used with care in patients unable to tolerate increased pacing rates.
- **Minute ventilation rate response pacing** may be inappropriate for patients who can achieve respiratory cycles shorter than 1.33 seconds (greater than 45 breaths per minute). Higher respiratory rates attenuate the impedance signal which diminishes the MV rate response, i.e., the pacing rate will drop toward the programmed basic rate.
- **Asynchronous pacing (DOO/VOO/AOO)** may be proarrhythmic in the presence (or likelihood) of competition between paced and intrinsic rhythms.
- **Single chamber ventricular pacing** should be used with care in patients who may develop pacemaker syndrome or who may have a need for maximum atrial contribution.
- **Crosstalk** results in atrioventricular (AV) pacing with a 94 ms AV delay (see section 11). This may be avoided by appropriate choice of blanking periods and sensitivities.
- **Slow retrograde conduction**, especially with conduction time >450 ms, may induce pacemaker-mediated tachycardia.
- **Magnetic resonance imaging** of pacemaker patients has resulted in significant adverse effects (see PRECAUTIONS, section 5.4.1)
- **Therapeutic diathermy** can cause fibrillation, burning of the myocardium, and irreversible damage to the pulse generator, due to induced currents.

5. PRECAUTIONS

5.1 Programming

- **Rate response or autocalibration** should not be enabled before implantation because the sensor will be incorrectly initialized resulting in inappropriate rates.
- During **automated threshold testing**, the programming head must be removed when capture ceases, to restore preprogrammed pulse amplitude, otherwise the pacemaker will

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continue the threshold test for the 20 cycles of the test without pacing the patient (i.e., without capture of the heart).

5.2 Storage and sterilization

- Store the device between 5 °C and 50 °C because temperatures outside this range can damage components.
- A device should not be implanted if sterility is not assured:
 - ⇒ If its sterility indicator within the inner package is not green, it might not have been sterilized;
 - ⇒ If its storage package has been pierced or altered, this could have rendered it non-sterile.
- Do not implant a device when:
 - ⇒ It has been dropped after it has been removed from its sterile packaging;
 - ⇒ Its “use before” date has expired, because this can adversely affect pulse generator longevity.
- Do not resterilize devices. Return unimplanted devices in their storage packages to ELA Medical for resterilization.

5.3 Lead Evaluation and Lead Connection

- Do not use a unipolar atrial lead if rate response is required, because the device’s rate response function will only operate with a bipolar atrial lead.
- Do not use any lead with this pulse generator without first verifying IS-1 compatibility, because use with other leads can damage the connector or result in a leaking or intermittent connection.
- Do not use as-shipped pulse generator values for pacing amplitude and sensitivity without verifying that they are appropriate for the patient, because this may result in shortened battery longevity or improper sensing.
- Consider lead maturation in choice of pacing amplitude and sensitivity, because:
 - ⇒ acute pacing thresholds > 1 V or 2 mA or chronic pacing thresholds > 3 V or 6 mA can result in loss of capture because thresholds increase after implantation.
 - ⇒ R wave amplitude < 5 mV or P wave amplitude < 2 mV can result in undersensing because sensed amplitude decreases after implantation.
- Exercise extreme caution if testing leads using line-powered equipment, because leakage current exceeding 10 microA can induce ventricular fibrillation.
- Do not insert a lead in the pacemaker connector without first visually verifying that the setscrews are sufficiently retracted to allow insertion.
- Do not insert a lead or setscrew wrench in the pacemaker connector without first

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lubricating the lead connector body or the wrench tip with silicone lubricant, because failure to do so can damage the connector.

- Do not tighten the setscrews with no lead connector inserted. This can damage the connector block.

5.4 Environmental and Medical Therapy Hazards

Patients should exercise reasonable caution in avoidance of devices which generate a strong electric or magnetic field. If a pulse generator should inhibit or revert to asynchronous operation at the programmed pacing rate or at the magnet rate while in the presence of EMI, moving away from the source or turning it off will allow the pulse generator to return to its normal mode of operation.

5.4.1 Hospital and Medical Environments

- **Mechanical ventilators** may cause pacing rate changes. Program the pacemaker to a non-rate responsive mode during ventilation.
- **Electrosurgical cautery** could induce ventricular arrhythmias and/or fibrillation, or may cause asynchronous or inhibited pulse generator operation or operation in standby mode. If use of electrocautery is necessary, the current path and ground plate should be kept as far away from the pulse generator and leads as possible. (see Section 12)
- **Magnetic Resonance Imaging (MRI)** among pacemaker patients has been contraindicated by MRI manufacturers. Clinicians should carefully weigh the decision to use MRI with pacemaker patients.
 - ⇒ Magnetic and radio-frequency (RF) fields produced by MRI may: increase ventricular pacing beyond the rate limit, result in total inhibition of pacing output, result in pacing at random rates, or result in synchronous pacing.
 - ⇒ Magnetic fields may activate magnet mode operation and cause asynchronous pacing.¹
 - ⇒ Pacemaker patients treated with MRI should be closely monitored and programmed parameters should be verified upon cessation of MRI.
- **Lithotripsy** may damage the pulse generator. If lithotripsy must be used, do not focus the beam near the pulse generator. (see Section 12)
- **External defibrillation** may damage the pulse generator. Attempt to minimize current flowing through the pulse generator and lead system by following these precautions (see Section 12)
 - ⇒ Position defibrillation paddles as far from the pulse generator as possible. Attempt to minimize current flowing through the pulse generator and leads by positioning the defibrillation paddles perpendicular to the implanted pulse generator/lead system.
 - ⇒ Use the lowest clinically appropriate energy output (watt seconds).
 - ⇒ Confirm pacemaker function following any internal or external defibrillation.
- **Transcutaneous electrical nerve stimulation (TENS)** may interfere with pacemaker

¹ Holmes, Hayes, Gray, et al. The effects of magnetic resonance imaging on implantable pulse generators. PACE 1986; 9 (3): 360-70.

function. If necessary, the following measures may reduce interference:

- ⇒ Place the TENS electrodes as close to each other as possible.
- ⇒ Place the TENS electrodes as far from the pulse generator/lead system as possible.
- ⇒ Monitor cardiac activity during TENS use.

- **High radiation sources** such as cobalt 60 or gamma radiation should not be directed at the pulse generator. If a patient requires radiation therapy in the vicinity of the pulse generator, place lead shielding over the device to prevent radiation damage. (see Section 12).

5.4.2 Home and Occupational Environments

- **High voltage power transmission lines** may generate enough EMI to interfere with pulse generator operation if approached too closely. (see Section 12)
- **Communication equipment** such as microwave transmitters, linear power amplifiers, or high-power amateur transmitters may generate enough EMI to interfere with pulse generator operation if approached too closely. (see Section 12)
- **Commercial electrical equipment** such as arc welders, induction furnaces, or resistance welders may generate enough EMI to interfere with pulse generator operation if approached too closely. (see Section 12)
- **Home appliances** which are in good working order and properly grounded do not usually produce enough EMI to interfere with pulse generator operation. There are reports of pacemaker disturbances caused by electric hand-tools or electric razors used directly over the skin over the pulse generator (see Section 12)

5.4.3 Cellular Phones

Recent studies have indicated there may be a potential interaction between cellular phones and pacemaker operation. Potential effects may be due to either the radio frequency signal or the magnet within the phone and could include inhibition or asynchronous pacing.

Based on testing to date, effects resulting from an interaction between cellular phones and the implanted pacemakers have been temporary. Simply moving the phone away from the implanted device will return it to its previous state of operation. Because of the great variety of cellular phones and the wide variance in patient physiology, an absolute recommendation to cover all patients cannot be made.

Patients having an implanted pacemaker who operate a cellular phone should:

- Maintain a minimum separation of 6 inches (15 centimeters) between a hand-held personal cellular phone and the implanted device. Portable and mobile cellular phones generally transmit at higher power levels compared to hand held models. For phones transmitting above 3 watts, maintain a minimum separation of 12 inches (30 centimeters) between the antenna and the implanted device.
- Patients should hold the phone to the ear opposite the side of the implanted device. Patients should not carry the phone in a breast pocket or on a belt within 6 inches (15 centimeters) of the implanted device as some phones emit signals when they are turned ON but not in use (i.e., in the listen or standby mode). Storing the phone in a location opposite the side of implant is recommended.

5.5 Pulse Generator Disposal

- Do not incinerate pacemakers, because they can explode if subjected to incineration or cremation temperatures.
- Return all explanted pacemakers to ELA Medical for analysis and safe disposal.
- Do not implant an explanted pacemaker in another patient as sterility, functionality, and reliability cannot be assured.

6. ADVERSE EVENTS

The Chorus RM was evaluated in a clinical study involving 350 devices implanted in 346 patients. As of June 17, 1996, total device exposure was 3622 device months, and individual patient exposure averaged 10 months (ranging from 0.3 to 32 months). A total of 27 patients died during the study. None of these deaths were judged related to the device. Seven devices were explanted from six patients. None of the explants were judged to be due to device malfunction. Four device explants were secondary to late postoperative infection, and three were explanted prophylactically.

6.1 Observed Adverse Events

Table 1 reports the adverse events on a per patient and a per patient-month basis in descending order of frequency by category.

Table 1. Adverse Events Reported in > 1 Study Patient
(n=350 devices in 346 patients, 3622 device months)

Adverse Event	# of Patient	% of Patients	# of Events	Events per device- year
Complications¹				
Atrial lead revision/replacement	20	5.7%	20	6.6%
Setscrew problem	4	1.2%	4	1.3%
Infection and sequelae	4	1.2%	4	1.3%
Ventricular lead revision/replacement	3	0.9%	3	0.99%
Diaphragmatic/Phrenic nerve stimulation	3	0.9%	3	0.99%
Observations²				
Diaphragmatic/Phrenic nerve stimulation	19	5.5%	25	8.3%
Tachycardia, endless-loop	17	4.9%	20	6.6%
Atrial tachyarrhythmias	16	4.6%	16	5.3%
Sensor over/under-response to effort	13	3.8%	13	4.3%
Atrial loss of capture	10	2.9%	10	3.3%
Atrial loss of sensing	6	1.7%	7	2.3%
Atrial loss of capture and sensing	6	1.7%	6	2.0%
Muscle stimulation	4	1.2%	4	1.3%
Ventricular loss of capture	4	1.2%	4	1.3%
Programmer/memory error	3	0.9%	3	0.99%
Sensor over/under-response at rest	3	0.9%	3	0.99%
Standby mode operation	3	0.9%	3	0.99%
Ventricular loss of sensing	3	0.9%	3	0.99%
Atrial sensing of skeletal muscle artifact	2	0.6%	2	0.66%
Ventricular sensing of skeletal muscle	2	0.6%	2	0.66%
Crosstalk	2	0.6%	2	0.66%

¹ Complications are adverse events requiring invasive measures to correct, e.g., surgical intervention.

² Observations are adverse events which are correctable by noninvasive measures, e.g., reprogramming..

6.2 Potential Adverse Events

Adverse events (including those reported in Table 1) associated with pacing systems based on historical implant experience include:

- Cardiac perforation
- Cardiac tamponade
- Transvenous lead-related thrombosis
- Elevated thresholds
- Erosion through the skin
- Pulse generator migration
- Body rejection phenomena
- Hematoma/seroma
- Nerve and muscle stimulation
- Myopotential sensing
- Local tissue reaction
- Fibrotic tissue formation

7. CLINICAL STUDIES

The Chorus RM was evaluated in a multi-center prospective study of the rate response in calibrated symptom-limited treadmill testing.

Objectives: Evaluate oxygen consumption rate, peak heart rate, proportionality of rate increase, correlation with a literature standard², and correlation with intrinsic rates.

Methods: Oxygen consumption and peak heart rate were obtained in a single-blind, randomized crossover design using paired exercise testing, comparing Chorus RM in DDDR mode to DDD mode. Proportionality and correlation were evaluated from the device's sensor-determined rate, patient intrinsic rate, and elapsed time during exercise. These effectiveness data were obtained at approximately one month post-implant.

Study subjects were selected from candidates for dual chamber pacing, able to perform treadmill exercise tests. Chronotropic incompetence (CI) was defined as the inability to achieve heart rates greater than 75% of the maximum predicted heart rate (220 - age). Seven of the 63 tested patients exhibited chronotropic incompetence.

Results: Tables 2 and 3 summarize the results of exercise testing. The devices demonstrated a linear increase in sensor rates with exercise level, an appropriate response for a rate responsive pacemaker. The slope of increase was comparable to a literature standard² and to intrinsic rates. The slope of the regression of sensor-indicated rates versus a literature standard was 1.023 ± 0.067 which was not significantly different statistically from 1.0 ($p=0.735$). A slope of 1.0 would indicate identical performance to predicted values.

² Kay GN. Quantitation of chronotropic response: comparison of methods for rate-modulated pacemakers. J Am Coll Cardiol 1992; 20: 1533.

Table 2. Oxygen Consumption and Peak Heart Rate during Exercise Testing
(n=37 patients including 7 patients exhibiting chronotropic incompetence)

Parameter	# of Patients	DDDR mean \pm SD	DDD mean \pm SD	Difference (DDDR-DDD) [95% Conf. Interval]
Oxygen consumption rate (L/min)				
CI patients	6	0.70 \pm 0.35	0.71 \pm 0.38	0.011 [-.037, 0.059]
Peak heart rate (beats/minute)				
CI patients	7	122 \pm 6.2	92 \pm 15	30.3* [12.9, 47.7]
Non-CI patients	30	127 \pm 15	119 \pm 19	7.2* [1.5, 13]
All patients	37	126 \pm 14	114 \pm 21	11.6* [5.5, 17.6]

* Difference statistically significant ($p < 0.05$) by t-test

Table 3. Rate sensor proportionality during Exercise Testing
(n=38 patients including 7 patients exhibiting chronotropic incompetence)

Parameter	# of Patients	Correlation Coefficient [95% confidence interval]
Sensor indicated rate vs. exercise time	38	0.96 [0.89, 0.99]
Sensor indicated rate vs. method of Kay (slope = 1.023 \pm 0.067)	38	0.99 [0.91, 0.99]
Sensor indicated rate vs. intrinsic rate	38	0.94 [0.89, 0.98]

8. STORAGE AND STERILIZATION

Chorus RM and its accessories are sterilized with ethylene oxide gas and are hermetically sealed in a dual plastic package in accordance with international standard. Sterility is ensured if:

- the sterility indicator within the inner container is green, and
- the external packaging is neither pierced nor altered

8.1 Shelf Life

The "use before" date on the storage package is calculated twelve months from the time of manufacture. Pacemakers not implanted before the "use before" date should be returned to Ela Medical.

8.2 Resterilization

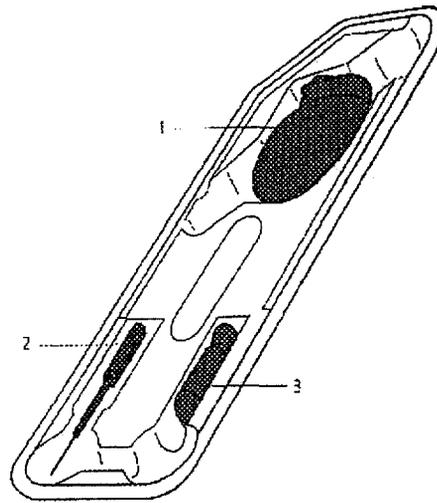
If the pulse generator needs to be resterilized, return it in its storage package to ELA Medical.

9. IMPLANT INFORMATION

9.1 Sterile Package Description and Handling

The sterile inner package contains the following items :

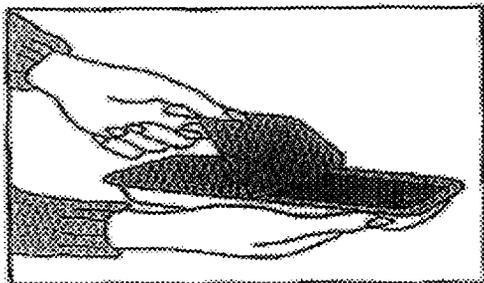
1. Chorus RM pulse generator
2. Hexagonal screwdriver
3. Bottle of silicone lubricant



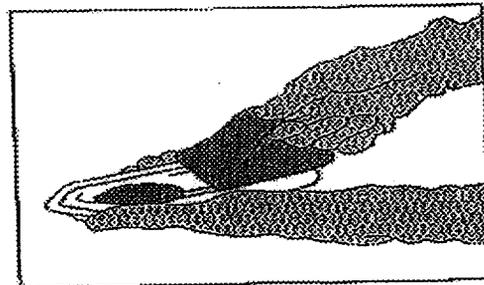
The non-sterile cardboard package also contains the following items :

1. Physician's manual
2. Patient ID card
3. Individual technical data sheet
4. Warranty form

Before opening the package, examine the label to verify that the package contains the desired pacemaker. Inspect the package to make sure that (1) the "use before" date has not been exceeded and (2) the sterile trays are still intact and have not been opened, pierced or broken.



Open the first plastic package and present it to the sterile field.



The physician takes the internal package and opens it as shown above.

Handwritten signature

9.2 Threshold Tests at Implant

9.2.1 External pulse generator

Pacing thresholds as well as the amplitude of P and R waves should be measured at implant. A battery-powered external pulse generator or a pacing system analyzer should be used for this purpose. Slew rates can also be measured using the external system.

9.2.2 Measuring pacing thresholds

- Set the rate of the external pulse generator higher than the patient's spontaneous rate
- Program the external pacer's pulse width to the value desired for the pulse generator to be implanted
- Program the external pacer's output to 7.5 V and/or 15 mA
- Connect the implanted leads to the external pulse generator following the manufacturer's instructions.
- Gradually decrease the external pulse generator amplitude while observing the ECG for loss of capture. The lowest amplitude at which capture is reacquired after it has been lost is the pacing threshold. Acute thresholds should be less than 1 V or 2 mA. Chronic thresholds should be less than 3 V or 6 mA.

9.2.3 Measuring sensing thresholds

Follow the external generator manufacturer's instructions to measure the recorded amplitude of R and P waves. The minimum amplitude of R waves and P waves that can be sensed by Chorus RM depends on the slew rate and the lead impedance.

The slew rate usually lies between 0.5 and 1.5 V/s in the atrium and 1.6 and 2.2 V/s in the ventricle. In most cases, an R wave greater than 5 mV during acute threshold measurement will be adequate with Chorus RM programmed to a ventricular sensitivity of 2.2 or 2.5 mV. In most cases, a P wave with an amplitude greater than 2 mV during acute measurement will be adequate with Chorus RM programmed to an atrial sensitivity of 1.0 mV. The programming of either 0.4 or 0.6 mV sensitivity should be used only for lower amplitude P waves because such settings enhance the pacemaker's sensitivity to interference.

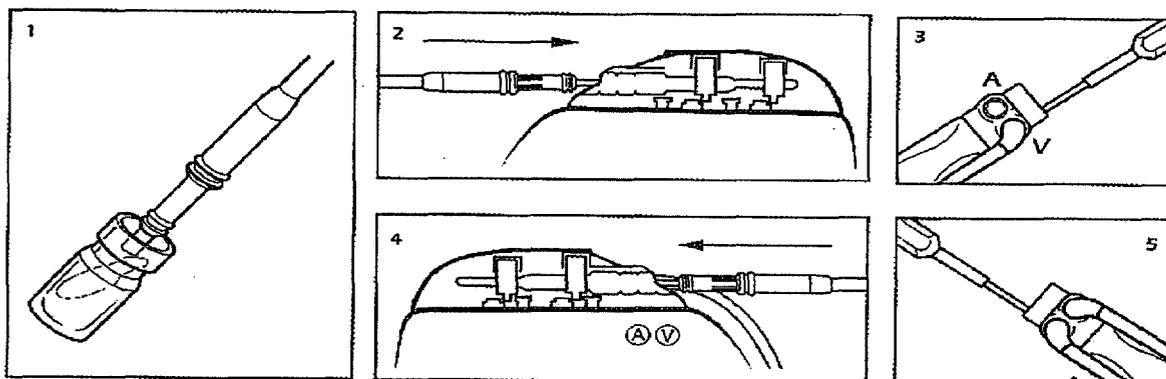
9.3 LEAD CONNECTION

It is imperative that each lead be properly connected to the corresponding pacemaker connector. Ensure that the pre-inserted setscrews are sufficiently retracted to allow insertion of the lead connector into the pacemaker connector.

1. Apply a small amount of silicone lubricant to the silicone rubber body of the connector.
2. Insert the ventricular lead connector into the right port. The lead pin must be visible through the opposite end of the connector block.
3. Lubricate the tip of the hexagonal wrench and pass it through the ventricular lead terminal seal. Tighten the pre-inserted setscrews.
4. After lubricating the atrial lead connector, insert it into the left port. The lead pin must be visible through the opposite end of the connector block.

5. Lubricate the tip of the hexagonal wrench and pass it through the ventricular terminal seal. Tighten the pre-inserted setscrews.

Lead pin should be visible here



10. PACEMAKER INTERROGATION

Chorus RM can be interrogated and programmed via telemetry using a CPR1 programming head connected to a microcomputer. Refer to the computer software (CSO) manual supplied with the programmer for details concerning its use.

11. PACEMAKER PROGRAMMING

11.1 BASIC PARAMETERS

11.1.1 Mode and Pacing Mode Selection

NOTE: *Contraindications, Warnings and Precautions in Sections 3, 4 and 5 above should be considered before selection of a pacing mode.*

Ten programmable modes are available on Chorus RM. Six of them can be associated with rate responsive pacing :

- AOO mode : asynchronous atrial pacing

Atrial pacing is provided at the programmed rate regardless of the patient's intrinsic rhythm.

Use for: Diagnostic evaluation

Avoid use in: AV block, conduction system disease, atrial flutter, atrial fibrillation, supraventricular tachyarrhythmia

no

- AAI(R) mode : inhibited atrial pacing

Atrial pacing is provided at the programmed rate (AAI) or at the sensor-driven rate (AAIR) in the absence of intrinsic atrial activity. A sensed P wave inhibits pacing.

Use for: Sick sinus syndrome with symptoms

Avoid use in: AV block, conduction system disease, supraventricular tachyarrhythmia, atrial flutter, atrial fibrillation

- AAT(R) mode : atrial triggered pacing

Atrial pacing is provided at the programmed rate (AAT) or at the sensor-driven rate (AATR) in the absence of intrinsic atrial activity. A sensed P wave triggers pacing.

Use for: Diagnostic evaluation³

Avoid use in: AV block, conduction system disease, atrial flutter, atrial fibrillation, supraventricular tachyarrhythmia

- VOO mode : asynchronous ventricular pacing

Ventricular pacing is provided at the programmed rate regardless of the patient's intrinsic rhythm.

Use for: Diagnostic evaluation

Avoid use in: Competitive intrinsic rhythm, pacemaker syndrome

- VVI(R) mode : inhibited ventricular pacing

Ventricular pacing is provided at the programmed rate (VVI) or at the sensor-driven rate (VVIR) in the absence of intrinsic rhythm. A sensed R wave inhibits pacing.

Use for: Bradycardia with chronic atrial fibrillation

Avoid use in: Pacemaker syndrome, need for maximum atrial contribution

- VVT(R) mode : triggered ventricular pacing

Ventricular pacing is provided at the programmed rate (VVT) or at the sensor-driven rate (VVTR) in the absence of ventricular intrinsic activity. A sensed R wave triggers pacing.

Use for: Diagnostic evaluation³

Avoid use in: Pacemaker syndrome

- DOO mode : asynchronous AV pacing

Both chambers are paced at the programmed rate regardless of the patient's intrinsic rhythm.

Use for: Diagnostic evaluation³

Avoid use in: Competitive intrinsic rhythm

³Allows diagnostic evaluation without having to reinitialize the device to rate response.

- DVI (noncommitted) mode : AV sequential ventricular inhibited pacing

Both chambers are sequentially paced at the programmed rate in the absence of ventricular activity regardless of the atrial intrinsic activity. A sensed R wave inhibits ventricular pacing if it occurs during the AV delay after the blanking and committed periods. It inhibits atrial and ventricular pacing if it occurs outside the AV delay.

Use for: AV block with sick sinus syndrome, intolerance to fast pacing rates or rate fluctuations because of severe coronary artery disease or rate dependent ventricular arrhythmias

Avoid use in: Persistent supraventricular tachyarrhythmias

- DDI(R) mode : dual-chamber non tracking mode

Both chambers are sequentially paced at the programmed rate (DDI) or at the sensor-driven rate (DDIR). A sensed P wave inhibits atrial pacing for the cycle in progress but does not initiate an AV delay. A sensed R wave inhibits ventricular pacing if it occurs after atrial pacing and inhibits atrial and ventricular pacing if it occurs outside the AV delay.

Use for: AV block with sick sinus syndrome or supraventricular tachyarrhythmias, intolerance to fast pacing rates or rate fluctuations because of severe coronary artery disease or rate dependent ventricular arrhythmias, paroxysmal AV block

Avoid use in: Permanent complete heart block

- DDD(R) mode : Dual-chamber tracking mode

Both chambers are paced at the programmed rate (DDD) or at the sensor-driven rate (DDDR) in the absence of intrinsic activity. In both chambers, pacing may be inhibited by sensed activity. A sensed P wave inhibits atrial pacing and triggers ventricular pacing after the programmed AV delay. A sensed R wave inhibits ventricular pacing if it occurs during the AV delay and inhibits atrial and ventricular pacing if it occurs outside the AV delay.

Use for: Atrial bradyarrhythmias with or without AV block, normal sinus activity with AV block, required AV synchrony

Avoid use in: Supraventricular tachyarrhythmias, inadequate atrial sensing, angina pectoris with symptoms at fast pacing rates

11.1.2 Basic rate

The programmed basic rate is the programmable lower limit for the pacing rate in the absence of sensed events. The programmed basic rate minus the programmed hysteresis is the intrinsic lower limit. If the patient's intrinsic rate falls below this limit, the pacemaker starts pacing.

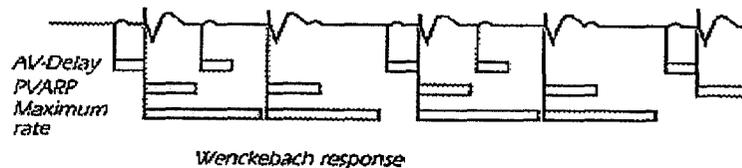
Notes :

- 1. In special modes, such as during the magnet or threshold tests, the pacing rate is independent of the programmed basic rate.*
- 2. If rate smoothing or the rate responsive function is ON, the escape rate can be higher than the programmed basic rate.*
- 3. If rate responsive pacing is ON, the lower limit of the programmable pacing rate is 55 bpm.*

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11.1.3 Maximum tracking rate

The maximum tracking rate is the highest rate in DDD mode at which the pacemaker can synchronize ventricular pacing to each sensed atrial beat. If the atrial rate is higher than the programmed maximum tracking rate, the PV interval between atrial sensing and ventricular pacing will be progressively lengthened until a P wave falls into the PVARP (Wenckebach response). If the atrial rate is even higher, only every second P wave will be sensed and trigger ventricular pacing (2:1, or at still higher rates, higher degree blocks such as 3:1 can occur).



Notes :

1. The upper tracking response is limited by the Total Atrial Refractory Period (TARP). The programmer displays a message if the programmed TARP limits pacing to a rate lower than the programmed maximum tracking rate.
2. The maximum tracking rate is also the maximum AV pacing rate allowed for rate smoothing.
3. The maximum tracking rate is the highest programmable value for the sensor-driven rate.

11.1.4 Pulse amplitude

The programmed pulse amplitude determines the voltage applied to the heart while pacing. Use the "as shipped" pulse amplitude immediately after implant to avoid loss of capture due to the early rise in threshold. This acute threshold level can be up to five times the implant threshold level. After threshold stabilization, a setting which provides a suitable safety margin (twice the chronic threshold) and saves pacemaker battery can be found. Pulse amplitude is programmed independently for atrial pacing and for ventricular pacing.

11.1.5 Pulse width

The pulse width is the duration the programmed pulse amplitude is applied to the heart during pacing. Pulse width can be used to adjust pacemaker output. Pulse width is programmed independently for atrial pacing and for ventricular pacing.

11.1.6 Sensitivity

The pacemaker sensing circuit is designed to sense P waves and R waves. If the pacemaker does not correctly sense the intrinsic signal, a higher sensitivity (lower value) may be programmed. However, extracardiac signals should not be sensed. If the pacemaker senses signals other than intrinsic cardiac signals, a lower sensitivity (higher value) can be programmed as long as a sufficient safety margin of two to four times the amplitude of the recorded signal is maintained.

MB

11.1.7 Polarity

Although mechanically configured like a bipolar pulse generator, Chorus RM may be programmed either to unipolar or bipolar configuration. Pacing and sensing polarity configuration can be programmed independently for the atrial and ventricular channels. The pacemaker is shipped with unipolar sensing and pacing configuration programmed for each channel. To avoid programming the pacemaker to bipolar configuration when connected to a unipolar lead, the lead impedance is measured during programming to bipolar configuration.

Notes:

- 1. Due to this protection, the pacemaker cannot be programmed to a bipolar configuration while it is still in the storage package. It must be connected to a bipolar lead with an appropriate impedance.*
- 2. Although measuring transthoracic impedance requires a bipolar atrial lead, sensing and pacing in the atrium can be programmed either to unipolar or bipolar mode.*

Pacing polarity

In unipolar pacing configuration, the anode (positive pole) is the pacemaker's titanium case and the distal electrode is the cathode (negative pole). In bipolar pacing configuration, the proximal electrode is the anode (positive pole) and the distal electrode is the cathode (negative pole). One of the advantages of bipolar pacing is to avoid nerve and muscle stimulation. One of the advantages of unipolar pacing is a larger pacing pulse, which can be more visible on a surface ECG.

Sensing polarity

In unipolar sensing configuration, the potential difference is measured between the pacemaker titanium case and the distal tip of the lead. In bipolar sensing configuration, the potential difference is measured between the proximal ring and the distal tip of the lead. One advantage of bipolar sensing is a lower susceptibility to detection of myopotentials and electromagnetic interference. In unipolar sensing configuration, the measured signal is wider than that obtained in bipolar configuration.

11.1.8 Refractory periods

Refractory periods prevent the pacemaker from sensing extracardiac signals. There are two types of refractory periods :

- Absolute refractory periods during which there is no sensing.
- Relative refractory periods during which signals can be sensed, but sensing does not recycle the pacemaker.

The following is a description of all refractory periods available on Chorus RM.

Absolute atrial refractory period

- In DDI or DDD mode, an absolute atrial refractory period starts with atrial pacing, ventricular sensing, or ventricular pacing. It ends after the programmed absolute refractory period following a

ml

ventricular event.

- In AAI or AAT mode, an absolute atrial refractory period starts with atrial sensing or pacing and lasts the programmed absolute refractory period plus 125 ms.

Absolute ventricular refractory period

- In VVI, VVT, DVI, DDI, or DDD mode, an absolute ventricular refractory period starts with ventricular sensing or pacing and lasts the programmed value of the absolute refractory period.

PostVentricular Atrial Refractory Period (PVARP)

The PVARP is a relative refractory period which starts with ventricular sensing or pacing and lasts the programmed value. The PVARP can be used in DDD mode to prevent pacemaker-mediated tachycardias (PMTs⁴) from being initiated by retrograde P waves. However, a long PVARP limits the maximum rate at which atrial activity is synchronized to ventricular activity. Since PMTs are induced by atrioventricular desynchronized activity, Chorus RM automatically lengthens the PVARP to 453 ms for one cycle only after such an activity (see description of Chorus RM response to retrograde waves in this manual). The PVARP then reverts to its programmed value.

Notes :

- 1. The Total Atrial Refractory Period (TARP) is equal to the greater of the (AV delay+PVARP) or (AV delay+absolute refractory period). When the sensed atrial rate is higher than $60,000/TARP$, the pacemaker functions in 2:1 or higher association (see the table below).*
- 2. When the programmed TARP is longer than $60,000/(\text{programmed maximum rate})$, there is no Wenckebach response. The ventricular rate decreases sharply when the atrial rate rises above the programmed maximum rate.*

⁴In this document, PMTs are referred to as endless loop tachycardias (ELTs)

MAXIMUM ACHIEVABLE TRACKING RATES (min⁻¹ or bpm) BEFORE 2:1 BLOCK

	Refractory period (ms)												
	141	156	172	203	234	266	297	328	359	391	422	453	
Total	31									154	142	132	124
AV Delay	47							148	137	128	120		
(ms)	63							153	142	132	124	116	
	78							148	137	128	120	113	
	94						153	142	132	124	116	110	
	109						148	137	128	120	113	107	
	125					153	142	132	124	116	110	104	
	141					147	137	128	120	113	107	101	
	156				154	142	132	124	117	110	104	99	
	172				148	137	128	120	113	107	101	96	
	188			153	142	132	124	116	110	104	98	94	
	203			148	137	128	120	113	107	101	96	91	
	219		154	142	132	124	116	110	104	98	94	89	
	234	154	148	137	128	120	113	107	101	96	91	87	
	250	154	148	142	132	124	116	110	104	98	94	89	85

The total AV delay is the sum of the programmed AV delay (fixed or calculated) and the AV delay hysteresis. The refractory period is the longer period between the absolute refractory period and the PVARP. If the maximum tracking rate is higher than the value indicated in the table, the pacemaker will switch to 2:1 association at the value indicated in the table. If not, the maximum tracking rate corresponds to the maximum pacing rate.

Blanking period

In DVI, DDI, or DDD mode, the blanking period is a short programmable absolute ventricular refractory period which starts with atrial sensing. It prevents ventricular inhibition resulting from atrial output sensing on the ventricular channel (crosstalk).

Committed period

In DVI, DDI, or DDD mode, the committed period is a nonprogrammable 94 ms ventricular relative refractory period which starts with atrial pacing. If a ventricular event is sensed during the committed period, and outside the blanking period, the ventricle is paced at the end of the committed period. The committed period prevents inappropriate ventricular inhibition if crosstalk occurs.

Atrial noise refractory period

The atrial noise refractory period starts at the end of the absolute atrial refractory period and lasts 94 ms. When a signal is sensed in this relative refractory period, an AV delay is initiated and the atrial noise refractory period starts again at the end of the absolute atrial refractory period. If a signal is sensed again in this period, an AV delay is not initiated and another atrial noise refractory period is started. If sensed events occur at a frequency greater than 10 Hz (600 min⁻¹ or bpm), the pacemaker will consider subsequent sensed events as noise and asynchronous atrial pacing will be delivered until the noise subsides.

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Ventricular noise refractory period

A ventricular noise search period starts at the end of the ventricular absolute refractory period and lasts 94 ms. This period protects the ventricular channel of the pacemaker from noise sensing and T wave recycling. When a ventricular signal is sensed during this noise search period, the pacemaker is inhibited and the noise search period is replaced by a noise refractory period for the next three cycles.

When a ventricular signal is sensed in the noise refractory period the pacemaker is not inhibited and another 94 ms ventricular noise refractory period is started as a protection from T wave recycling. If events occurring at a frequency greater than 10 Hz (600 min⁻¹ or bpm) are sensed, the pacemaker will consider subsequent sensed events as noise and asynchronous ventricular pacing will be delivered until the noise subsides. The ventricular noise search period is restored when no sensing has occurred during the noise refractory period for three consecutive cycles.

11.1.9 AV delays

The AV delay is the programmable time interval between atrial pacing or sensing and ventricular pacing.

Basic AV delay

In DOO, DVI, or DDI mode, the AV delay is fixed and equal to the basic programmed AV delay.

Maximum and Minimum AV delays

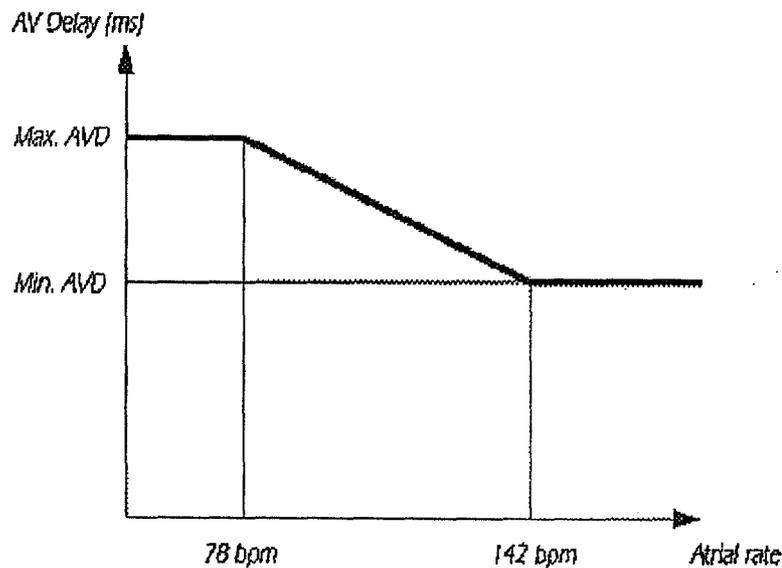
In DDD mode, the maximum AV delay is used for rates less than or equal to 78 min⁻¹ (bpm) and the minimum AV delay is used for rates greater than or equal to 142 min⁻¹ (bpm). Between 78 min⁻¹ (bpm) and 142 min⁻¹ (bpm), the AV delay is automatically calculated so that the AV delay shortens as the rate increases.

Notes :

- 1. The AV delay can be longer than the programmed AV delay if an AV delay hysteresis is programmed or if the pacemaker functions in Wenckebach mode.*
- 2. Chorus RM protection from retrograde P waves modifies the AV delay every second cycle during the eight-cycle confirmation phase.*
- 3. If the minimum AV delay is programmed to a value greater than that of the maximum AV delay, the smaller value (i.e., that of the maximum AV delay) will be used. Thus there will be no rate-adapted AV delay.*
- 4. The AV delay can be shorter than the programmed AV delay if pacing is delivered at the end of the committed period.*

*no channel
limitations
S. 11.1.9*





11.1.10 AV delay hysteresis

In DDD mode, the programmed value of the AV delay hysteresis is added to the AV delay after atrial pacing. The difference between AV and PV intervals compensates for the lag between the atrial stimulus and atrial contraction. This helps to maintain a consistent interval between ventricular and atrial contractions whether AV sequential or P synchronous pacing occurs.

Note : The time from atrial pacing to ventricular pacing (including AV delay hysteresis) is always limited to a maximum of 250 ms.

11.1.11 Hysteresis

Hysteresis allows the patient's natural rhythm to decrease (within a programmed limit) below the escape rate without pacing. After sensing, the pacemaker operates as if the escape rate was reduced by the programmed percentage for hysteresis. For example with an escape rate of 70 min^{-1} (bpm) and a programmed hysteresis of 10%, the lower limit for the natural rate is 63 min^{-1} (bpm). After a sensed event, if no new event has been sensed before 952 ms, which corresponds to 63 min^{-1} (bpm), pacing will be delivered at the programmed basic rate.

Note : If rate response is ON, the lower limit of the programmable basic rate minus the hysteresis is 55 min^{-1} (bpm).

11.2 RATE RESPONSIVE PARAMETERS

Rate responsiveness is based on a linear relationship between heart rate and minute ventilation. This function must rapidly adapt to exercise level and changes in the patient's condition. This is achieved by :

- (1) Initialization which determines the basic parameters of the pacing system when the patient is at rest.
- (2) Calibration, which adapts the system's function to the baseline minute ventilation and to the patient's activity.
- (3) Rapid response to exercise by recalculation of the escape interval every fourth , eighth or twelfth cycle.

11.2.1 Rate responsive mode

The adjustment of the pacing rate to exercise is determined by this parameter. There are three programmable options :

- OFF: Rate responsive pacing does not function. The pacing rate is the programmed basic rate (or smoothed rate if rate smoothing occurs).
- RR: Rate responsive pacing is ON. This can be accessed only if the pacing mode is programmed to SSI, SST, DDI or DDD. Pacing rate is calculated from the measured minute ventilation. This rate may vary between the basic pacing rate and the maximum sensor-driven rate programmed.
- DDD/VVIR Mode Switching: This selection is only available in DDD mode. It activates a switch from DDD to VVIR mode when the pacemaker enters into fallback mode (see Section on "Special functions"). Rate responsive pacing does not function when fallback is not activated.

Notes:

1. *If the pacemaker is programmed to AOO, VOO, DOO or DVI, rate response is automatically programmed to OFF.*
2. *Do not program rate response before implant: the sensor will be initialized and the resulting minute ventilation value will be erroneous. A bipolar atrial lead is required to program rate response.*
3. *If the sensor has not yet been activated, programming rate response to RR or DDD/VVIR mode will start initialization. Rate responsive pacing will only be functional after the 6-minute initialization (see p. 22).*
4. *If DDD/VVIR is programmed, the programmer forces the fallback delay to 50 cycles.*

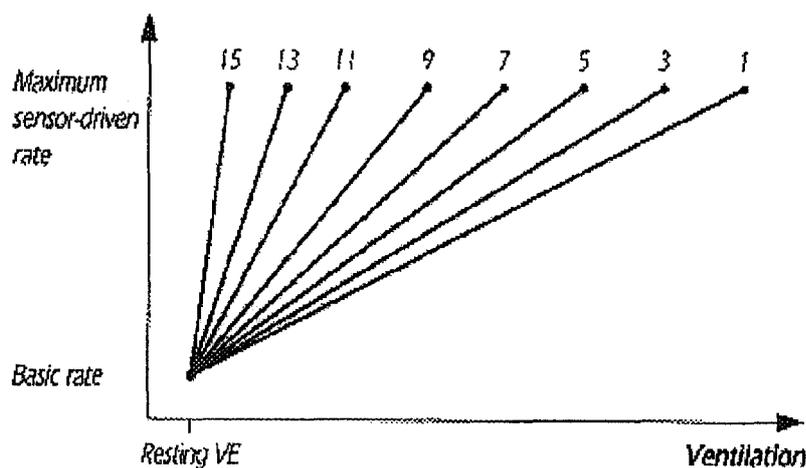
11.2.2 Rate Response Slope Number

The rate response slope number is a programmable parameter which determines the degree to which pacing rate is modified when there is a change in minute ventilation. If the slope number is low, a variation in minute ventilation will only result in a small modification in pacing rate. Contrarily, a high slope number causes larger changes in pacing rate with only a slight variation in measured minute ventilation. The graph shown below illustrates how the pacing rate is allowed to vary according to the measured changes in minute ventilation according to the programmed slope number.

The slope number can be directly programmed by the physician through the programmer from 1 to 15 by steps of 1. Generally, the more active the patient is, the lower the slope number should be. To select a value suited to patient's activity, the simulation tool can be used.

Notes:

- 1. The slope number can be programmed from 1 to 15 by steps of 1 whereas, in automatic calibration the step is 0.1.*
- 2. For high resting minute ventilation values, low slopes cannot be programmed; the resulting exercise minute ventilation will be higher than the technical limit. Programmable slope values are those which respect the exercise minute ventilation limit.*



11.2.3 Initialization

Note : Initialization is available only if the sensor is on, i.e., if the programmed mode is one of the rate responsive modes : SSI, SST, DDI or DDD with rate response programmed to RR or DDD/VVIR or with the AUTO calibration.

Initialization provides the pacemaker with initial values for the patient's minute ventilation at rest and for the rate-response slope. It sets the rest ventilation to the value it measures during the initialization process described below. It sets the slope to 11.

ELA recommends the initialization procedure described below. Caution: Improper initialization can cause inappropriate pacing rates for the patient's activity level, including increased pacing rate with the patient at rest.

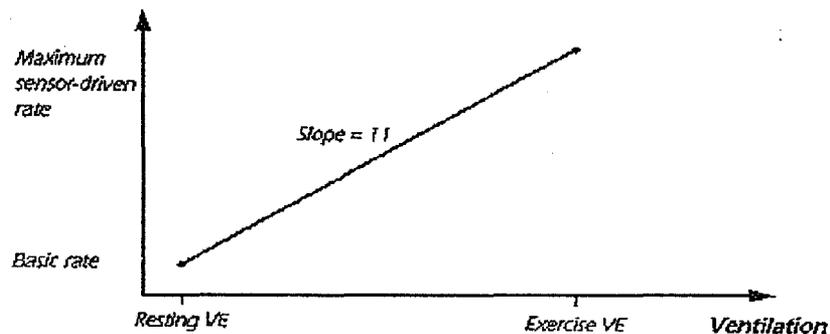
1. Have the patient remain supine and calm throughout initialization. Do not begin initialization until the patient is calm.
2. Begin initialization. The programmer can manually start initialization from the TEST screen provided that calibration is AUTO, or Rate Responsive Mode is RR or DDD/VVIR. Caution: The pacemaker does not provide rate-responsive pacing during initialization.

3. Once initialization starts, move the programming head at least 20 cm away from the patient, and keep it away throughout initialization. Caution: Using the programmer during initialization can abort initialization or falsify results.
4. Initialization takes 6 minutes. The programmer displays time remaining. Caution: The patient must remain supine and calm.
5. Upon completion, the pacemaker starts operation in the programmed Rate Responsive Mode.

ELA recommends verifying initialization with the following procedure:

6. Verify via interrogation that the pacemaker has completed initialization.
7. Program Rate Responsive Mode to RR, if not already set to RR.
8. Insure that the patient is supine and calm, and then begin Simulation (see page 41). Once Simulation starts, move the programming head at least 20 cm away from the patient, and keep it away until step 11 below.
9. Wait for two minutes, with the patient supine and calm.
10. Have the patient stand but remain calm. Wait an additional two minutes.
11. Use the programmer to read and display Simulation data. These must show minute ventilation within 25 % of the line indicating minute ventilation at rest (this corresponds to approximately 4 % of the rate increase that the pacemaker will provide for maximum effort). If not, repeat initialization.

Note: When the initialization phase is started, the programming head must be moved away from the pacemaker.



11.2.4 Calibration

Description:

Calibration adjusts the rate responsive parameters for resting and exercise minute ventilation to the patient's activity. Its purpose is to relate the calculated pacing rate to minute ventilation which corresponds to the patient's work capacities. This adjustment can be performed in two ways:

A

- FIXED programming:

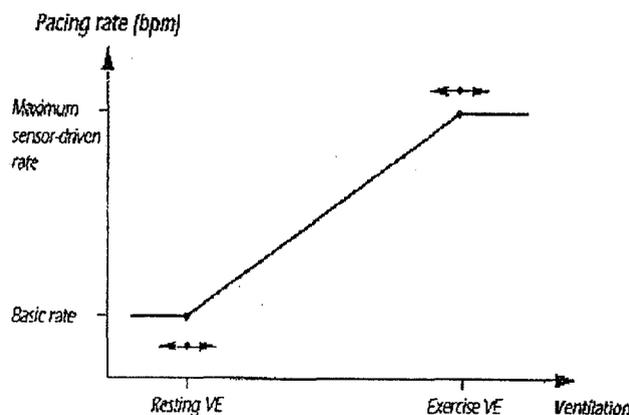
Rate responsive pacing uses the last calibration values to adjust the rate response parameters. These values may be those calculated during exercise testing with AUTO calibration or those corresponding to the programmed slope number. However, they will remain fixed regardless of changes in patient activity.

- AUTO programming:

Calibration of the rate responsive system is determined by the patient's daily activity. The rate responsive escape interval is determined by calibration values which are constantly being recalculated. Thus, the variation in heart rate will be adjusted to the patient's condition whether the patient is tired, sick, or fully active.

Notes:

1. Do not program the automatic calibration before implant as the sensor will be initialized and the resulting resting minute ventilation value will be erroneous. A bipolar atrial lead is required to program the automatic calibration.
2. If the mode is programmed to AOO, VOO, DOO or DVI, calibration is automatically reprogrammed to FIXED.
3. If the pacemaker response is programmed to DDD/VVIR mode, and calibration is programmed to AUTO, calibration values will only be calculated during fallback.
4. If the sensor has not been activated, programming calibration to AUTO will start initialization. Automatic calibration is not operational until after the six-minute initialization.
5. When calibration is programmed to AUTO, the rate response slope number ranges from 1 to 15 by steps of 0.1.
6. If the pacing mode is programmed to SSI, SST, DDI or DDD mode, the rate responsive mode can be programmed to OFF and calibration to AUTO. This is an evaluation phase which finds rate responsive parameters which fit the patient's needs. It also prevents inappropriate rate responsive pacing in the days following implantation.



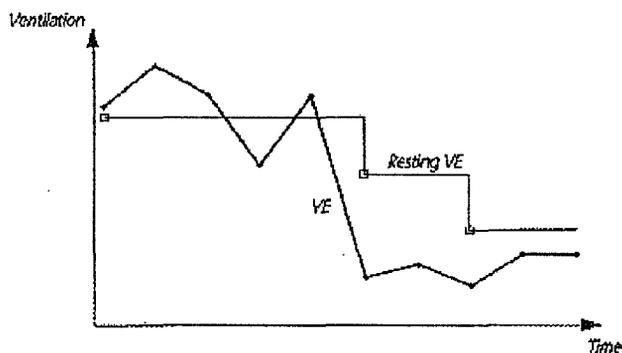
Handwritten signature or initials.

Functioning principle of the AUTOMATIC calibration:

Calibration of the rate-responsive system is based on the measurement of two values of minute ventilation. One is resting ventilation (resting VE), which corresponds to the patient's resting state and, consequently, to the basic rate. The other is exercise ventilation (exercise VE), which corresponds to maximum exercise and, consequently, to the maximum sensor-driven rate.

To determine **resting minute ventilation**, Chorus RM looks at the minimum minute ventilation value and recalculates resting ventilation every 32nd respiratory cycle if a change has occurred. Resting minute ventilation is decreased by 6% if the mean value of minute ventilation calculated for the last 64 respiratory cycles is 6% or more below the present value. Resting minute ventilation is increased by 6% if more than eight mean values of minute ventilation calculated on 64 respiratory cycles are 6% or more above the present value.

However, this increase is limited to 20% of the mean resting minute ventilation recorded the day before. This avoids a significant modification in rate responsive parameters due to prolonged exercise.



To determine **exercise minute ventilation**, Chorus RM looks for the maximum minute ventilation value and recalculates the value of exercise minute ventilation every eighth cycle that a change has occurred. Exercise minute ventilation is increased by a maximum of 6% if the mean value of minute ventilation calculated on eight respiratory cycles is higher than the present value. During sustained exercise, minute ventilation can increase by successive steps several times.

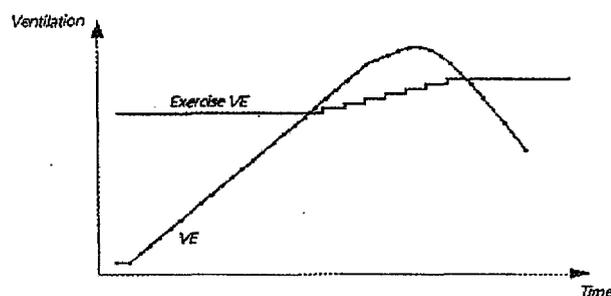
To avoid successive recalibrations, the rate responsive slope number will not be recalculated using the latest exercise minute ventilation until after the end of exercise, that is, when the sensor rate is equal to the basic rate. The new slope number will not be used until the next exercise period.

B

If exercise minute ventilation has not been modified for 24 hours, its value will be decreased by 3%. Thus, when a patient's activity is low, exercise ventilation will decrease progressively and the rate responsive slope number will increase. This means that moderate exercise will bring about a significant increase in heart rate, and could cause the pacemaker to pace at the maximum sensor-driven rate. It is therefore advisable to program a low sensor-driven rate in patients who are not very active.

Notes :

1. When calibration is programmed to AUTO, the rate response slope number range is between 1 and 15 with steps of 0.1. The upper limit of the slope is 15 and cannot be programmed by the physician. Active patients for whom automatic calibration is indicated should not reach this limit and should not be subjected to inappropriately high slopes.
2. Initialization determines the resting minute ventilation and sets the slope number to 11; rate-responsive functions including automatic calibration are then ready to operate.
3. Automatic calibration only modifies the exercise and the resting minute ventilation; consequently, it also modifies the slope number. (Refer to Calibration section for further explanation.)



11.2.5 Maximum sensor-driven rate

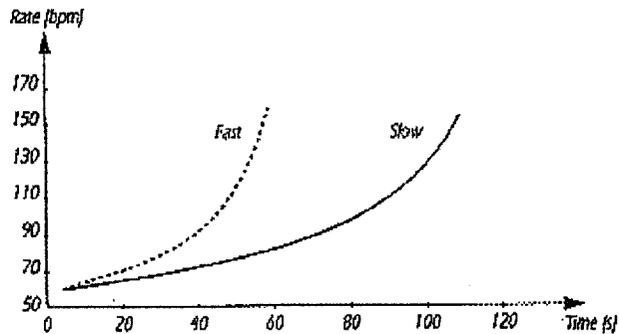
The programmed maximum sensor-driven rate is the fastest pacing rate when the rate responsive function is ON. This sensor-driven rate is lower than or equal to the programmed maximum tracking rate. It corresponds to the maximum heart rate that can be reached by the patient in his everyday life.

11.2.6 Rate acceleration

The programmed value for rate acceleration determines the maximum decrease in the escape interval. It thus determines the maximum acceleration of the corresponding pacing rate during exercise. When acceleration is programmed to fast, there is a 16 ms decrease in the escape interval every fourth cardiac cycle. It allows a more rapid increase in the pacing rate up to the programmed sensor-driven rate, during strenuous exercise. When acceleration is programmed to slow, there is a 16 ms decrease in the escape interval every eighth cardiac cycle. It thus limits the increase in the pacing rate during exercise.

PM

Note : If the pacemaker paces at the basic rate, the first four or eight cycles of rate responsive pacing correspond to an escape interval shortened by 6% depending on whether the device is programmed to fast or slow.



11.2.7 Recovery

The programmed value for recovery determines the maximum increase in the escape interval and thus the maximum deceleration in the pacing rate after exercise, i.e., during the patient's recovery phase. When recovery is programmed to fast, there is a 16 ms increase in the escape interval every eighth cardiac cycle. This brings the pacing rate to the programmed basic rate more rapidly. When recovery is programmed to slow, there is a 16 ms increase in the escape interval every twelfth cardiac cycle. This more slowly decreases the pacing rate at the end of exercise.

Note: The four last recovery cycles (before pacing at basic rate) have an escape interval 6% below the basic rate escape interval.

11.2.8 Other parameters

Other programmable parameters influence the pacemaker behavior during exercise :

* **Basic rate:** This is the pacing rate when the patient is at rest. It should be greater than or equal to 55 min^{-1} (bpm).

* **Maximum tracking rate:** This rate is the upper limit for the programmable maximum sensor-driven rate.

* **Hysteresis:** When hysteresis is programmed, it is applied to the calculated sensor-driven rate. Thus when the sensor-driven rate becomes greater than the sinus rate, there is one cycle of pacing at the hysteresis rate before pacing begins at the sensor-driven rate.

11.3 SPECIAL FEATURES

11.3.1 Protection from retrograde P waves

- **Objective:**

Endless-loop tachycardias (ELTs) induced by retrograde conduction are a well-known risk of dual-chamber pacing. Chorus RM is designed to provide ELT protection at all times and for any rate without reducing atrial sensing capability since long PVARPs are avoided.

- **Indications:**

All patients with permanent retrograde ventriculoatrial conduction.

- **Description:**

Automatic protection (algorithm set to "OFF")

Since most ELTs are initiated by AV dissociations (PVCs) or by asynchronous to synchronous switching (magnet mode, threshold test, noise sensing, and reassociation after fallback), Chorus RM automatically extends the PVARP to 453 ms for one cycle after these events are detected. Since Chorus RM does not initiate an AV delay on a P wave which falls in the PVARP, the PVARP extension avoids most ELTs.

Termination mode (algorithm set to "TERM")

Other undetectable events such as isolated artefacts, loss of capture, or premature atrial contractions (PACs) can induce ELTs. Chorus RM can identify and terminate these ELTs by an algorithm based on the stability of the VP interval (from ventricular paced beat to retrograde P wave). There are three steps:

1) Detection step

Chorus RM suspects an ELT if the following criteria are fulfilled for 16 consecutive cycles :

- Atrial sensing (P) is followed by ventricular pacing (V)
- The ventriculoatrial interval (VP interval) is less than 453 ms
- The VP interval is stable within the programmed limit (max VP variation).

2) Confirmation step

Once an ELT is suspected, Chorus RM attempts to confirm its suspicion by differentiating an ELT from a stable sinus rhythm. During confirmation the AV delay is decreased by the

programmed value (AV delay modulation) every second cycle for eight cycles. If the maximum deviation between the VP intervals measured for these eight cycles is less than the programmed value (VP max. variation), the ELT is confirmed.

3) Termination step

If an ELT is confirmed, Chorus RM extends the PVARP to 453 ms for one cycle to interrupt resynchronization of ventricular pacing to a retrograde P wave.

- Function:

. This algorithm is available in DDD(rate response programmed to RR or DDD/VVIR or OFF) mode

. "As shipped" value : TERM (Terminate)

. It can be used in TERM mode by choosing the AV delay modulation (value of AV delay reduction during the confirmation step) and maximum VP variation (variation tolerance in the retrograde conduction time).

- Programmable settings

. Protection from retrograde P waves : OFF - TERM

. AV delay modulation : 47-63 ms

. Max. VP variation : 16-31 ms

11.3.2 Fallback

- Objective:

This algorithm is designed to limit the time of AV synchrony in Wenckebach mode when the atrial rate is higher than the maximum tracking rate and below the 2:1 rate.

- Indications

Patients at risk for atrial arrhythmias.

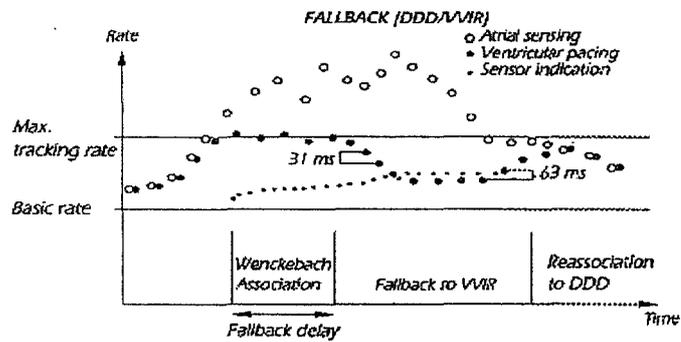
- Description

Non Rate responsive DDD Mode

When the spontaneous atrial rate exceeds the programmed maximum tracking rate, the pacemaker starts functioning in Wenckebach mode. This association mode is allowed for a programmable number of cycles. Then Chorus RM switches to VVI mode while maintaining atrial sensing. This therefore corresponds to VDI mode. The pacing rate is decreased by increasing the pacing interval by 31 ms every eight cycles until it reaches the basic rate. Pacing then remains at the basic rate as long as the patient's atrial rate stays above the programmed maximum tracking rate.

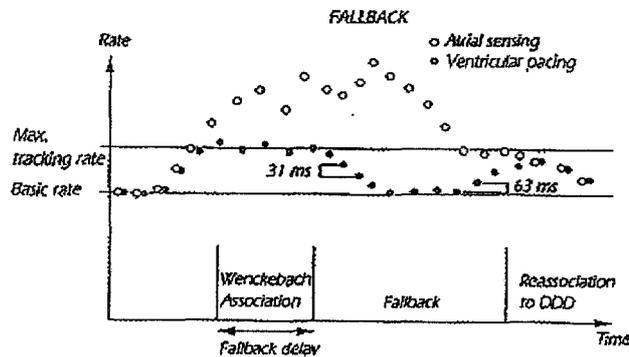
When the atrial rate becomes lower than the maximum tracking rate, the pacing rate is increased by decreasing the pacing interval by 63 ms every eight cycles until it reaches the spontaneous atrial rate. Ventricular pacing is then resynchronized to atrial sensing. During the first resynchronization cycle, the PVARP is lengthened to 453 ms to prevent ELT occurrence. In the following cycle, the PVARP reverts to its programmed value and DDD pacing is delivered at the programmed values.





DDD/VVIR mode (DDD mode and rate response programmed to DDD/VVIR)

In DDD mode with a rate response programmed to DDD/VVIR mode, Chorus RM stays in DDD mode whether ventricular pacing is synchronized to atrial sensing or whether the pacemaker functions in Wenckebach association. However, the sensor is activated as soon as the pacemaker enters Wenckebach association. This association is allowed for a limited programmable number of cycles. As soon as Chorus RM switches to the single chamber mode, the rate is decreased by increasing the escape interval by 31 ms every eighth cycle until the sensor-driven rate is reached. Rate responsive pacing is then triggered and atrial sensing is maintained (VDIR mode). During this period of rate responsive pacing, the values for the rate responsive parameters are the last ones calculated and the automatic calibration will operate if it is programmed ON. As soon as atrial rate becomes lower than the programmed maximum tracking rate, the pacing rate is increased by decreasing the escape interval by 63 ms every eighth cycle until it reaches the spontaneous rate and reassociation is possible. The PVARP is lengthened to 453 ms on the first cycle, after reassociation the sensor is deactivated and the pacemaker functions in non rate responsive DDD mode once again.



DDDR mode, (DDD mode and rate response programmed to RR)

In rate responsive dual-chamber mode (DDDR), fallback is initiated as in DDD mode. After the programmed number of cycles in Wenckebach association, Chorus RM switches to non rate responsive single chamber mode while still sensing the atrium (VDI mode). The rate is decreased by increasing the escape interval by 31 ms every eighth cycle until the sensor-driven rate is reached. Rate responsive pacing is then triggered and atrial sensing is maintained (VDIR mode). As soon as the atrial rate becomes lower than the programmed maximum tracking rate, the pacing

rate is increased by decreasing the escape interval by 63 ms every eighth cycle until reassociation is made possible. The PVARP is lengthened to 453 ms in the first cycle after reassociation and the pacemaker functions in DDDR (DDD mode and rate response programmed to RR) again.

- Function :

- . The fallback algorithm is available in DDD mode (with or without rate response).
- . If the fallback algorithm has been programmed OFF, the pacemaker will use a value of 50 cycles for fallback in the rate responsive DDD/VVIR mode.

- Programmable settings :

Fallback : OFF-10-30-50-100-500-1000-1500-2000 cycles

11.3.3 Rate smoothing

- Objective :

This algorithm is designed to prevent sharp rate decreases in the event of sinus arrest or pause while maintaining atrioventricular synchrony.

- Indications :

Patients with sudden bradycardia episodes.

- Description :

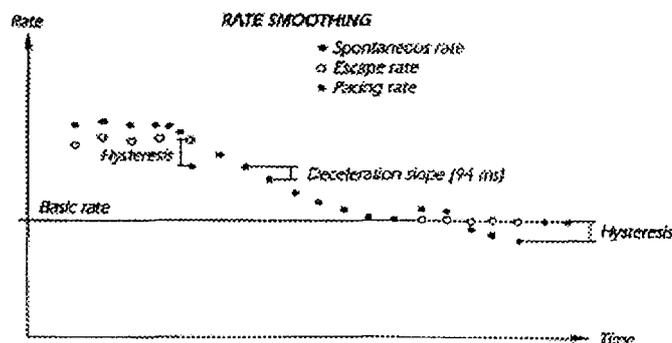
When the rate smoothing algorithm is programmed ON, there are two steps

- . When the patient is in spontaneous rhythm, Chorus RM automatically computes the escape interval based on the value of one spontaneous cycle every eighth beat. If the difference between the present value for the escape interval and the patient's spontaneous interval is greater than 31 ms, a new escape interval is calculated equal to the present stored value for the escape interval minus 31 ms.

As soon as a pause longer than the last escape interval occurs, pacing is delivered at a progressively decreasing rate. This decrease in the pacing rate occurs every eighth cycle (the escape interval is increased by steps of 94 ms). The occurrence of a spontaneous complex stops the process. When the basic rate is reached, the pacing interval remains there until smoothing ends.

- Function :

- . The rate smoothing algorithm can be used with all synchronous modes.



Notes :

1. Programming rate smoothing ON while in a rate responsive mode is not necessary because the rate response provides it's own rate smoothing.
2. In dual-chamber mode, atrioventricular synchrony is preserved.

. If a rate responsive mode is programmed ON and a pause occurs, pacing will be delivered at the higher of the sensor-driven rate and smoothing rate.

. It is advisable to use the hysteresis function together with the rate smoothing function. This avoids initiating rate smoothing on slight variations in the patient's rhythm.

. The smoothed escape interval always lies between the programmed maximum rate interval and the basic rate interval unless hysteresis is programmed. The pacing rate therefore always lies between the programmed maximum tracking rate and basic rate.

- **Programmable settings** :

Rate smoothing : OFF-ON

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11.4 APPLICABLE PARAMETERS

Depending on the mode programmed for the Chorus RM, some parameters are operational and some are disabled. When a parameter which was previously disabled becomes operational after mode reprogramming, its value is either the "as shipped" value or the last value programmed. Refer to the table below for the complete list of applicable parameters for each mode.

<u>Parameters</u>	<u>AOO</u>	<u>VOO</u>	<u>DOO</u>	<u>AAI</u>	<u>VVI</u>	<u>AAT</u>	<u>VVT</u>	<u>DVI</u>	<u>DDI</u>	<u>DDD</u>	
Mode	x	x	x	x	x	x	x	x	x	x	
Basic rate	x	x	x	x	x	x	x	x	x	x	
Maximum rate					Sm	Sm	Sm	Sm	Sm	Sm	x
Hysteresis				x	x	x	x	x	x	x	
Basic AV delay				x					x	x	
Max. AV delay											x
Min. AV delay											x
AVD hysteresis											x
Abs. refr. period				x	x	x	x	x	x	x	x
PVARP										x	x
Blanking period									x	x	x
Rate resp.mode					x	x	x	x		x	x
Max. sensor driven rate					rr	rr	rr	rr		rr	rr
Acceleration				rr	rr	rr	rr		rr	rr	
Recovery				rr	rr	rr	rr		rr	rr	
Slope number				rr	rr	rr	rr		rr	rr	
Calibration				rr	rr	rr	rr		rr	rr	
A pulse ampl. x			x	x		x		x	x	x	
A pulse width x			x	x		x		x	x	x	
A Sensitivity				x		x		x	x	x	
A pac.polarity x			x	x		x		x	x	x	
A sens.polarity					x		x		x	x	x
V pulse ampl.	x	x	x		x		x	x	x	x	
V pulse width	x	x	x		x		x	x	x	x	
V sensitivity					x		x	x	x	x	
V pac.polarity	x	x	x		x		x	x	x	x	
V sens.polarity						x		x	x	x	x
Rate smoothing					x	x	x	x	x	x	x
ELT protection											x
AVD modulation											ELT
Max. VP variation											ELT
Fallback											x

Sm : parameter to program when the smoothing algorithm is programmed

rr : parameters to program in RR or DDD/VVIR mode.

ELT : parameters to program when ELT protection is ON.

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11.5 LONGEVITY INDICATORS

11.5.1 ELECTIVE REPLACEMENT INDICATORS

Elective Replacement Indicators (ERI) correspond to a battery impedance of 10 kOhms. The ERIs are :

- Magnet rate lower than the values displayed by the programmer for ERI magnet rate (approximately $80 \pm 5 \text{ min}^{-1}$ or bpm)
- Battery depletion curve greater than or equal to 10 kOhms.

Atrial and ventricular amplitudes at ERI

programmable	available
1.5 V	1.5 V
2.0 V	2.0 V
2.5 V	2.35 V
3.0 V	3.0 V
3.5 V	3.5 V
4.0 V	4.0 V
5 V	4.1 V

(DDDR mode, 70 min^{-1} (bpm), 0.49 ms, 500 Ohms)

At ERI, 2.5 to 7 months of operation remain before EOL (End Of Life) depending on pacing conditions (see table shown below). The pacemaker should be replaced at ERI.

Programmed amplitude (V)	Estimated longevity at ERI (months)			
	Rate response OFF (1)		Rate response ON (2)	
	500 Ohm	300 Ohm	500 Ohm	300 Ohm
2.5	7	6	5.5	5
3.5	5	3.5	4	3
5	4	3	3	2.5

(1) DDD, 100% pacing, 70 min^{-1} (bpm), 0.49 ms

(2) DDD, 100% pacing, 85 min^{-1} (bpm), 0.49 ms

11.5.2 MAGNET RATE/BATTERY INTERNAL RESISTANCE

Magnet rate is 96.0 ppm at beginning of life (BOL) and 80.0 ± 5 ppm at ERI (exact value provided for each device by the programmer).

Magn.rate(min^{-1})	96.0	93.7	91.4	89.3	87.3	85.3	83.5	81.7	80.0	78.4	76.8	75.3	73.6	72.5	71.1	69.8
Magn.period (ms)	625	640	656	672	687	703	719	734	750	765	781	797	812	828	844	860
Resist.(kOhms)	<5.5	5.5	6.0	6.5	7.0	7.7	8.5	9.3	10.0	11.0	11.7	12.5	13.5	14.5	15.5	>15.5

- Capture test mode

The purpose of this test is to demonstrate that the programmed voltage and pulse width are sufficient to capture. During the capture test, Chorus RM operates as follows:

CAPTURE TEST MODE

Programmed mode	Mode	Pulse amplitude and width	Rate	AV delay
DOO,DVI,DDI,DDD	DOO	as programmed	Magnet	94ms
VOO, VVI, VVT	VOO	as programmed	Magnet	-
AOO,AAI,AAT	AOO	as programmed	Magnet	-

-Rate test mode:

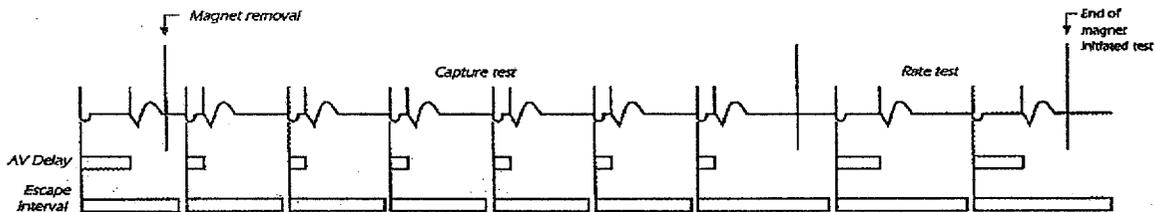
The purpose of this mode is to measure the programmed amplitude and rate and, in dual-chamber pacing, the programmed AV delay. During the rate test, Chorus RM operates as follows :

RATE TEST MODE

Programmed mode	Mode	Pulse amplitude and width	Rate	AV delay
DOO,DVI,DDI,DDD	DOO	as programmed	Basic rate	as programmed
VOO, VVI, VVT	VOO	as programmed	Basic rate	-
AOO,AAI,AAT	AOO	as programmed	Basic rate	-

Notes :

1. If the magnet is reapplied during the capture test or the rate test, Chorus RM reverts to the magnet test.
2. The programmer is not effective during either magnet, capture or rate test.



end of #2

13.2 THRESHOLD TESTS

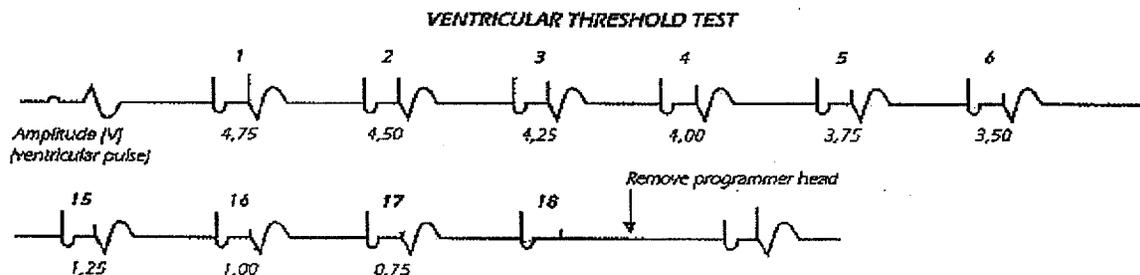
Noninvasive threshold measurements can be performed in both chambers through the pacemaker.

13.2.1 Ventricular threshold test

The ventricular threshold test can be used when Chorus RM is programmed to VOO, VVI, VVT, DOO, DDI, DVI, or DDD mode. The test begins when programmed and lasts for 20 cycles. During the test, ventricular pacing is asynchronous. The first cycle lasts 800 ms (75 min⁻¹ or bpm). During the following nineteen cycles, the pacing rate is the programmed threshold rate. Ventricular pulse width is at the programmed value for the test. The ventricular amplitude (in volts) decreases with each beat as follows :

Cycle	1	2	3	4	5	6	7	8	9	10
Ventr. amplitude	4.75	4.50	4.25	4.00	3.75	3.50	3.25	3.00	2.75	2.50
Cycle	11	12	13	14	15	16	17	18	19	20
Ventr. amplitude	2.25	2.00	1.75	1.50	1.25	1.00	0.75	0.50	0.25	0.00

The beat following the test is delivered asynchronously with the programmed parameters. If the programmed mode is a dual chamber pacing mode, the atrium will be paced asynchronously before the ventricle with a 94 ms AV delay. If a magnet is applied, if the programming head is removed or if any key of the programmer is pressed, the test is immediately stopped.



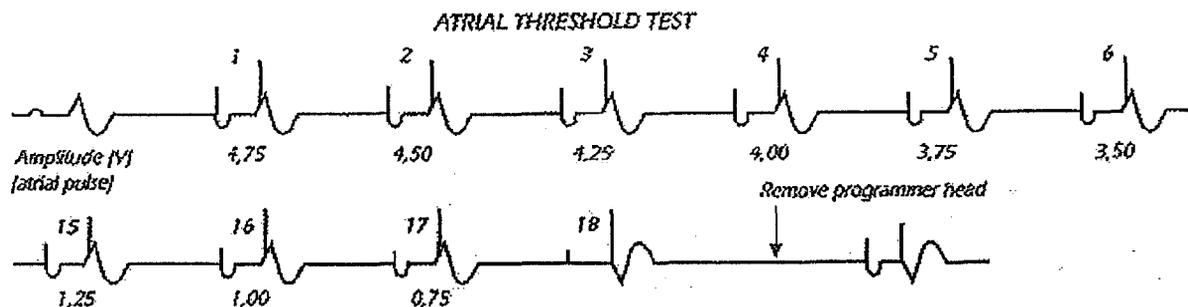
13.2.2 Atrial threshold test

The atrial threshold test can be used when Chorus RM is operating in AOO, AAI, AAT, DOO, DDI, DVI, or DDD mode. The test begins when programmed and lasts for 20 cycles. During the test, atrial pacing is asynchronous. The first cycle lasts 800 ms (75 min⁻¹ or bpm). During the following nineteen cycles, the pacing rate is the programmed threshold rate. Atrial pulse width is at the programmed value for the test. The atrial amplitude (in volts) decreases with each beat as follows:

Cycle	1	2	3	4	5	6	7	8	9	10
Atrial ampl.	4.75	4.50	4.25	4.00	3.75	3.50	3.25	3.00	2.75	2.50
Cycle	11	12	13	14	15	16	17	18	19	20
Atrial ampl.	2.25	2.00	1.75	1.50	1.25	1.00	0.75	0.50	0.25	0.00

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The beat following the test is delivered asynchronously with the programmed parameters. If the programmed mode is a dual chamber pacing mode, the ventricle will be paced asynchronously with a 203 ms delay. If a magnet is applied, if the programming head is removed or if any key of the programmer is pressed, the test is immediately stopped.



13.3 LEAD MEASUREMENTS

The lead measurement test mode allows noninvasive measurements of atrial and ventricular lead characteristics. The lead measurement test mode begins when programmed and lasts two cycles. During these two asynchronous cycles, pulse width is increased to 0.98 ms in the paced chamber(s). The programmer displays the measured averages for voltage, current, impedance and energy.

Parameters	MEASURABLE RANGE			TOLERANCE	
	Min.	Max.	Units		
Voltage		0.50	5.6	V	20 %
Current		0.50	13.00	mA	20 %
Impedance	0.30	3.00		kOhms	30 %
Energy	0.2	50		μ Joules	30 %

13.4 RATE LIMIT OFF

The pacing rate is limited independently in each chamber to 197 min^{-1} (bpm).

It is possible to suppress this limit in one chamber at a time using the programmer. To pace at high rates (electrophysiologic studies), the pacemaker must be programmed to a triggered mode and an external pacemaker which can deliver high-rate pulses must be used; these pulses will be sensed by the implanted pacemaker (AAT or VVT) which will consequently pace at high rates.

If the rate limit is OFF in the atrium, and if the pacemaker is programmed to AAT mode, atrial pacing can be triggered up to 348 min^{-1} (bpm). If the rate limit is OFF in the ventricle, and if the pacemaker is programmed to VVT mode, ventricular pacing can be triggered up to 240 min^{-1}

gs

(bpm). The rate limit reverts to 197 min^{-1} (bpm) as soon as the programming head is removed or any key of the programmer is pressed.

13.5 STATISTICS

Chorus RM automatically stores data via diagnostic counters which can be reset at any time. These counters can be used to check the function of the pacemaker, to optimize programmable values and to evaluate the need for special features.

The different counters are :

- . Number of programmings (255 max)
- . Number of atrial beats :
 - paced (4.3 billion max)
 - sensed (4.3 billion max)
- . Number of ventricular beats :
 - paced (4.3 billion max)
 - sensed (4.3 billion max)
 - paced at the end of the committed period (255 max)
 - PVCs (max 4.3 billion) : sensed ventricular events in DDD mode which have not been preceded by a paced or sensed atrial event within a physiological time interval (between 31 and 250 ms).
- . Total number of cardiac cycles (4.3 billion max)
- . Percentage and number of spontaneous cycles (4.3 billion max)
- . Number and percent of cycles paced at the sensor-driven rate (4.3 billion max)
- . Number of resting ventilation recalculations (255 max)
- . Number of exercise ventilation recalculations (255 max)
- . Number of attempts to terminate ELTs (255 max)
- . Number of fallback starts (255 max)

Chorus RM also stores the following data :

- . Patient's name (maximum of 14 letters)
- . Birth date
- . Pacemaker implant date
- . Implant date of the atrial lead
- . Manufacturer and model of the atrial lead
- . Implant date of the ventricular lead
- . Manufacturer and model of the ventricular lead
- . Atrial and ventricular acute thresholds
- . ECG indications, symptoms and etiology
- . Date and time statistics were reset

13.6 MARKERS

Event markers are particularly useful in the interpretation of dual-chamber pacemaker ECGs. Events are displayed in real time on the same multi-channel ECG recorder as the surface ECG. The different events are marked by pulses of different amplitudes:

Event	marker amplitude
Atrial pacing (including pacing triggered in AAT mode)	+ 10 units
Atrial sensing outside refractory periods	+ 6 units
Atrial sensing during a relative refractory period	+ 3 units
Ventricular pacing (including pacing triggered in VVT)	- 10 units
Ventricular sensing during a relative refractory period	- 3 units
Ventricular sensing outside refractory periods	- 6 units

Chorus RM starts transmitting markers when commanded by the programmer (see programmer manual). A calibration impulse is delivered at the beginning of the sequence. Transmission is ended when the programmer head is removed, a magnet is applied, or any key of the programmer is pressed.

13.7 INTRACARDIAC ECG

Chorus RM provides noninvasive atrial and ventricular intracardiac ECGs, which are essential to evaluate the pacing system. The intracardiac ECG can be used to select pacing and sensing polarities, to reveal possible myopotentials which are not visible on the surface ECG or to measure the retrograde conduction time. Chorus RM starts transmitting intracardiac ECGs when commanded by the programmer (see programmer manual). Transmission is ended when the programmer head is removed, a magnet is applied or, any key of the programmer is pressed.

Note: The programmed sensed polarity determined the intracardiac ECG's polarity displayed on the programmer's screen.

13.8 SIMULATION

Simulation is a feature that is available for programmer software versions CSO 2.46 or higher.

Note : Simulation can only be accessed if the rate responsive mode is programmed to RR.

Simulation is a tool for studying Chorus RM rate responsive parameters. It stores cardiac and respiratory data in the pacemaker memory and then transfers the data to the programmer to simulate the pacemaker behavior based on the programmed rate responsive parameters. The maximum data storage time is approximately 20 minutes. The storage process is stopped when :

- the RAM memory is full
- telemetry is performed
- the stop simulation key is pressed

During the storage process, it is advisable to have the patient exercise (exercise test or daily exercise) to make the minute ventilation vary.

Once data have been stored, a programming simulation makes it possible to modify the basic rate, the maximum sensor-driven rate, the rate response slope number, acceleration and recovery. The simulated pacemaker response can subsequently be displayed with these new parameters. When the simulated pacemaker response is satisfactory, the modified parameters can be directly programmed through the programmer.

Notes:

- 1. During the recording of cardiac and ventilatory data, the programming head does not need to be positioned over the pacemaker.*
- 2. If automatic calibration is programmed and if a recalibration of the slope is necessary, it will be delayed until the end of the simulation procedure.*

13.9 HOLTER FUNCTIONS

Holter functions are useful for assessing the performance of Chorus RM during the patient's daily life. They can be used in conjunction with the statistics function. The large memory capacity of Chorus RM allows the beat-to-beat monitoring of many events for a long period of time. Types of events and periods of time are listed in the description that follows.

13.9.1 Histograms

Note : Histograms are operational only if they are programmed.

- Description :

Three sets of histograms are available on Chorus RM. Each set contains data for one type of event. Each set will have a number of individual histograms. Each individual histogram will have eight cells with programmable boundaries. As Chorus RM collects interval data, it will analyze the interval to determine to which cell it belongs and increment the count for that cell. At the end of a programmed time period, it will begin collecting data for the next successive histogram. The number of individual histograms in the set depends on the length of the programmed time period. If the programmed time period is greater than or equal to 6 hours, a set can contain 14 individual histograms. If the programmed time period is less than 6 hours, a set can contain 30 individual histograms.

- Use:

With the programmer, each set of histograms can be displayed in a table and each histogram can be displayed as a graph. Printouts of tables and/or graphs are easily obtained (refer to the programmer manual).

The programmable parameters are :

* Type of events

A INT : Intervals between two successive atrial paced or sensed events which initiate an AV

delay or recycle the pacemaker. This type of histogram can be used for diagnosis and monitoring of a patient's atrial rhythm profile, hysteresis function, atrial tachycardia, fallback function, 2:1 point setting, or Wenckebach behavior.

A PAUSE : Atrial intervals between an atrial sensed event initiating an AV delay or recycling the pacemaker, and an atrial paced event in the following cycle. This type of histogram can be used for monitoring sinoatrial blocks, rate smoothing, and the hysteresis function.

V INT : Intervals between two successive ventricular paced or sensed events which recycle the pacemaker. This type of histogram can be used with the A INT histogram to obtain a more detailed diagnosis and monitor the ventricular rhythm.

V PAUSE : Ventricular intervals between a ventricular sensed event and a ventricular paced event in the following cycle. This type of histogram can be used for monitoring paroxysmal AV blocks and rate smoothing.

V ASYNCHR : Intervals between the last ventricular event which recycled the pacemaker and the following premature event. A premature ventricular event is a ventricular sensed event occurring after an atrial event within a non physiological time interval (less than 31 ms or more than 250 ms) except during Wenckebach association.

AV INT : Intervals between an atrial event and the following ventricular event. This type of interval allows diagnosis of crosstalk, monitoring the patient's atrioventricular conduction, and monitoring the AV delay behavior.

*** Boundaries :**

Seven programmable boundaries limit the eight cells of the histograms. They should be programmed in increasing order from 31 ms to 3000 ms. They should be chosen according to the other programmed settings such as the basic rate, maximum tracking rate and AV delay.

*** Period :**

This parameter defines the surveillance duration for each histogram. It is programmable from 15 minutes to 1 month.

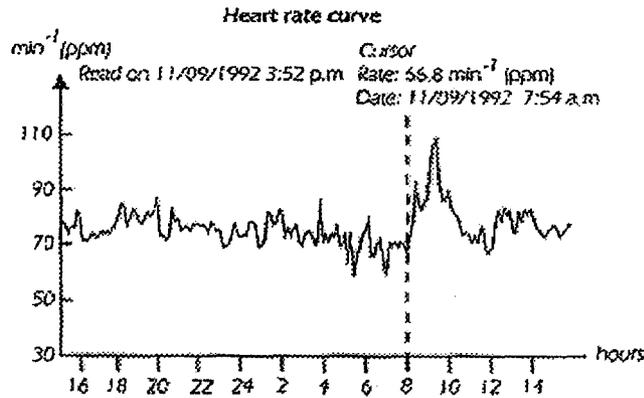
13.9.2 Mean heart rate curve

Note : The mean heart rate curve is operational only if it is programmed.

Description : Chorus RM is capable of recording heart rate variations over a 24-hour or 45-minute period. Chorus RM averages the heart rate every 8.5 minutes for a 24-hour period and every 16 seconds for a 45-minute period. These results are displayed as a mean heart rate curve.

Use : When programmed to dual-chamber or ventricular single-chamber mode, Chorus RM records a ventricular rate curve. When programmed to atrial single-chamber mode, Chorus RM records an atrial rate curve.



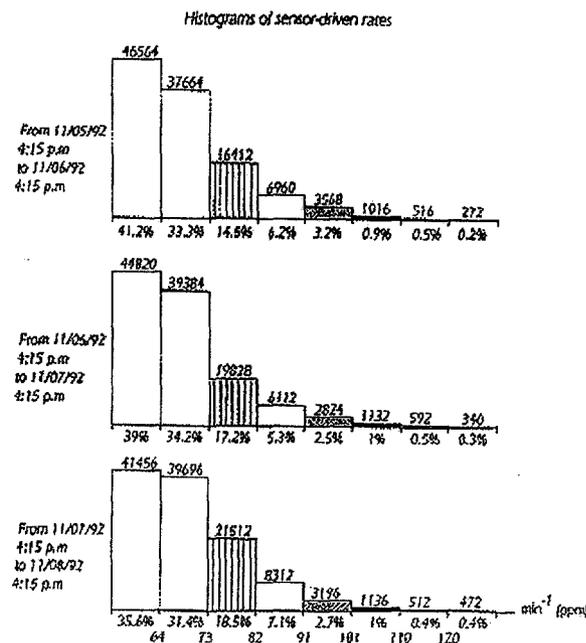


13.9.3 Histograms of the sensor-driven rate

Note : Histograms of the sensor-driven rate function, when the pacemaker is programmed to the RR rate responsive mode.

Description : Chorus RM is capable of recording rates calculated from minute ventilation for the last three days. It collects every rate calculated and records them in three successive histograms of 24 hours each : each histogram consists of eight cells whose limits are automatically set at the programmed basic rate and sensor-driven maximum rate. This makes it possible to display the pacemaker behavior in response to the patient's activity.

Use : Data can be displayed as a graph using the programmer. Data are automatically reset when rate response is programmed to RR.



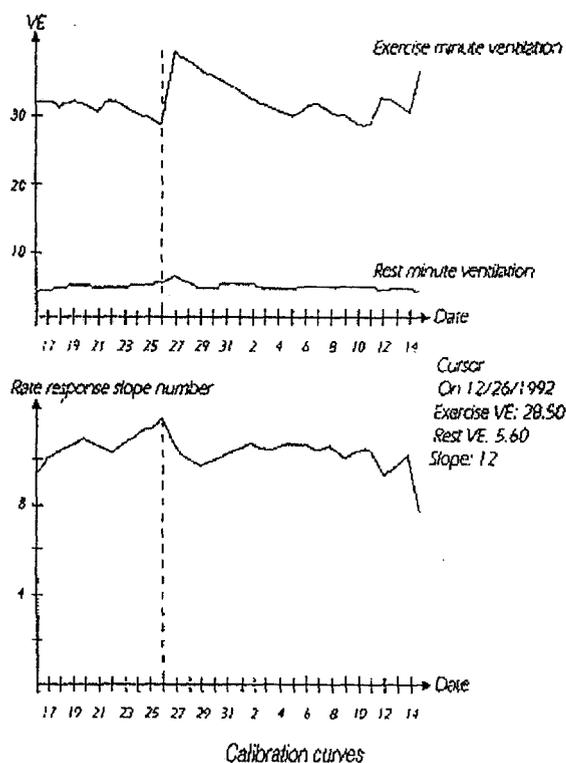
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13.9.4 Curves of calibration parameters

Note : The curves of calibration parameters start functioning as soon as calibration is programmed to AUTO.

Description : Chorus RM is capable of recording the resting and exercise minute ventilation values calculated during calibration. Chorus RM calculates the mean values of resting and of exercise minute ventilation on a daily basis and stores the mean values for the last 30 days. The corresponding rate response slope number is calculated for each day that the calibration is programmed to Auto.

Use : Data can be displayed as three curves corresponding to the resting minute ventilation, exercise minute ventilation, and rate response slope number. To obtain the exact values for a given day, the cursor must be placed on the corresponding day. The values located on the left correspond to those of the activation of the automatic calibration, if recording lasts less than 30 days and the values located on the right corresponds to the current values of resting and exercise VE. These curves are automatically reset when automatic calibration is programmed.



13.9.5 Battery depletion curve

Chorus RM automatically measures the battery (cell) impedance and stores the data, which can then be displayed as a curve of the cell internal impedance versus time.

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APPENDIX 1: PRINCIPLE OF RATE RESPONSE

The purpose of rate response is to adjust the pacing rate to the patient's activity level.

MINUTE VENTILATION AS THE INDICATOR

Minute ventilation is the product of respiratory rate and tidal volume. This physiological indicator closely reflects the metabolic demand during exercise. Minute ventilation is a 2nd order indicator [1]. Resting minute ventilation is approximately 6 l/min and can rise up to 60 l/min during severe exercise. It can even increase to 150 l/min in well-trained athletes during strenuous exercise. Minute ventilation correlates to oxygen consumption and heart rate [2]. Minute ventilation also rapidly increases at the onset of exercise [3].

[1] Rate responsive pacing : biosensor reliability and physiological sensitivity, P. Rossi, PACE, vol 10, 1987.

[2] Normal and abnormal heart rate response to exercise, H.K. Hammond and V.F Froehlicher, Progress in Cardiovascular diseases, Vol 27, No 4, 1985 : 271.

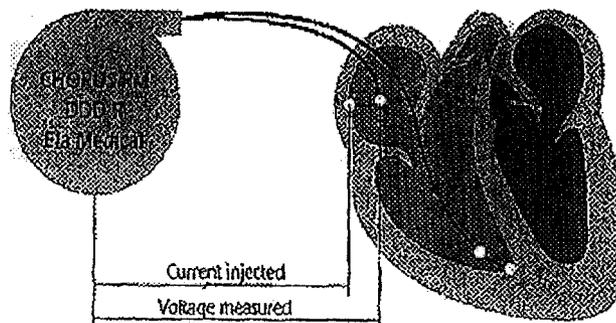
[3] Relationship between heart rate and minute ventilation, tidal volume and respiratory rate during brief and low level exercise, F. Vai, JL. Bonnet, P. Ritter, G. Pioger, PACE, Vol 11, 1988 : 1860

MINUTE VENTILATION SENSOR

Minute ventilation is determined by the measurement of transthoracic impedance. A linear relationship exists between the measured impedance and tidal volume.

An atrial bipolar electrode is necessary for measuring minute ventilation. Low amplitude (400 μ amps) and short duration (15 μ seconds) output pulses are delivered at a 8 Hz frequency to the distal atrial electrode. This probably would not be visible on an ECG strip. Impedance is measured between the proximal electrode of the atrial lead and the pacemaker case (see figure shown below).

Note: Although measuring transthoracic impedance requires a bipolar atrial lead, sensing and pacing in the atrium can be programmed either to unipolar or bipolar mode.



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Impedance increases with inhalation and decreases with exhalation. The signal measured is filtered to allow the detection of respiratory rates between 6 and 45 cycles per minute. The respiration period and amplitude are derived from the detected rates. Ventilation is calculated every respiratory cycle as a function of the Amplitude/Period ratio.

The sensor circuitry has a 3rd order low pass filter with a cut-off frequency of 45 min^{-1} . If the rate of the signal is higher, the signal will be attenuated by the filter.

The effect of this attenuation is to lower the effective minute ventilation respiration used by the pacemaker. Thus, above a respiration rate of 45 per minute, the pacemaker will use a lower effective respiration rate to calculate a minute ventilation value. This lower minute ventilation value will result in a lower rate responsive rate. The higher the respiration rate, the more attenuated the signal. The more attenuated the signal, the lower the effective respiration tidal volume value used to calculate minute ventilation. Thus, depending upon other factors including tidal volume, at some high respiration rate above 45 per minute, the rate responsive rate can equal the basic rate.

The behavior for rate response for high respiration rates is subject to the same constraints as for respiration rates below 45 per minute. The response will be smoothed since minute ventilation is averaged over four respiratory cycles and the change in rate responsive rate cannot be faster than the programmed acceleration and recovery values allow.

RATE RESPONSE : CALCULATION OF THE PACING RATE

Rate response is based on the linear relationship between minute ventilation and heart rate. Minute ventilation is calculated every respiratory cycle and an average is computed over four respiratory cycles. The sensor-driven rate is calculated every fourth, eighth or twelfth cycle from this average. This frequent calculation allows the pacemaker to respond rapidly to changes in the patient's activity.

Different parameters (see Section on "Rate responsive Parameters") allow the appropriate adjustment of the pacemaker response according to the patient need.

APPENDIX 2: TECHNICAL SPECIFICATIONS

PHYSICAL CHARACTERISTICS

Dimensions	Height : 55 mm - Width : 52 mm - Thickness : 8 mm
Weight	46 grams
Volume	18.9 cc
Case coating	Medical grade silicone elastomer
Case material	99.9% pure titanium
Indifferent electrode	case : Surface : 12.5 cm ² Material : titanium shape : part of a disk

ELECTRICAL CHARACTERISTICS

Battery	Manufacturer	Wilson Greatbatch Limited			
	Type	Lithium Iodine			
	Model	WG 8077			
	Usable capacity	BOL : 1.5 Ah ERI : 0.1 Ah			
	Voltage	BOL : 2.8 V ERI : 2.4 V			
Atrial input impedance		unipolar : 15,000 Ohms bipolar : 17,000 Ohms			
Ventricular input impedance		unipolar : 15,000 Ohms bipolar : 17,000 Ohms			
Current drain at BOL (μ A)		5V		2.5V	
		Rate resp. OFF	Rate resp. ON	Rate resp. OFF	Rate resp. ON
Inhibited		16.5	22	16	21.5
DDD (100% pacing) (1)		37.5	43	21	26.5
AAI/VVI (100% pacing)		26.5	32	18	23.5
Current drain at ERI (μ A)		5V		2.5V	
		Rate resp. OFF	Rate resp. ON	Rate resp. OFF	Rate resp. ON
Inhibited		15.5	20	15	19.5
DDD (100% pacing) (1)		34	38.5	20	24.5
AAI/VVI (100% pacing)		24.5	29	17	21.5

(1) 70 min⁻¹ (bpm), 0.49 ms, 500 Ohms on each lead, 37 °C.

DESCRIPTION OF THE CIRCUIT

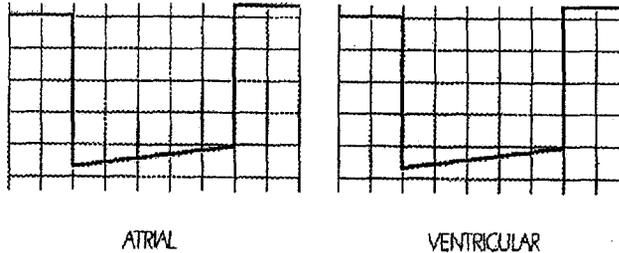
The electronic circuit of Chorus RM combines custom integrated circuits with discrete capacitors, resistors and semi-conductors. The integrated circuits are electrically connected to the substrate with gold wire bonds. They are then hermetically sealed into the pacemaker case. A quartz crystal allows precise interval timing.

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CHARACTERISTICS OF THE PACEMAKER OUTPUT PULSE

Shape of output pulse:

5 V amplitude, 0.49 ms pulse width under 500 Ohms load.



EFFECT OF TEMPERATURE

Chorus RM 's electrical characteristics and parameter values do not vary significantly with temperature. Rate and period variations are less than 1% between 20°C and 43°C.

BIOCOMPATIBILITY

The two materials in contact with the patient are well known for biocompatibility. The case is 99.9% pure titanium. The pacemaker connector is made of medical grade silicone elastomer, a material commonly used in other implantable medical devices.

SPECIAL TESTS

Chorus RM has been subjected to the specific tests of the EN NF 50061 standard, NFC 74346 classification :

- defibrillator discharge
- vibration
- mechanical shock

Chorus RM's characteristics were not affected by these tests.

EXPLANTED PACEMAKERS

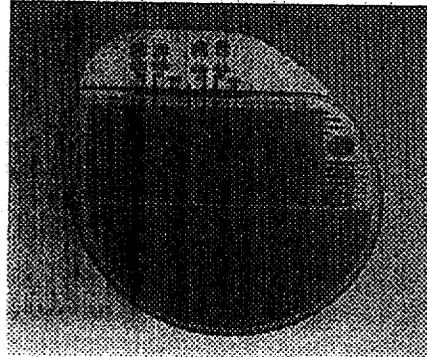
Except stated otherwise, all explanted pulse generators must be returned to ELA Medical . They will be carefully cleaned with all traces of contamination removed. The pulse generator should be cleaned using a solution of hypochlorite containing at least 1% chlorine and should be thoroughly rinsed with clear water. The generator should be returned to the address indicated by your distributor carefully packaged to protect it from mechanical shock and temperature variation.

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PHOTOGRAPHIC IDENTIFICATION



X-RAY IDENTIFICATION



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NONPROGRAMMABLE PARAMETERS

Parameters	Values	Tolerances
Rate limit	197 min ⁻¹ (bpm)	± 6 %
(BOL) magnet rate	96 min ⁻¹ (bpm)	± 3 %
Committed period	94 ms	± 8 ms

PROGRAMMABLE PARAMETERS

This table lists the programmable parameters of Chorus 7034. Ela Medical ships the pacemaker with the "as shipped" values shown below. When emergency VVI (nominal or "Nom") operation is programmed, the parameter values are those marked with an asterisk in the table (*).

Parameters	As shipped	Programmable values	Tolerances
Basic parameters			
Mode (1)	DDD	DDD-DDI-DVI-DOO-VVI*-VVT-VOO AAI-AAT-AOO	
Basic rate (2,3)	60 min ⁻¹	40-45-50-55-60-65-70*-75-80-85-89-96	± 3%
Max. tracking rate(4)	120 min ⁻¹	101-110-120-132-142-154	± 3%
Hysteresis (of rate)	0 %	0*-5-10-20	± 16ms
Basic AV delay (5a)	156 ms	31-47-63-78-94-109-125-141-156-172-188-203-219-234	± 8ms
Maximum AV delay (5b)	156 ms	31-47-63-78-94-109-125-141-156-172-188-203-219-234	± 8ms
Minimum AV delay (5b)	156 ms	31-47-63-78-94-109-125-141-156-172-188-203-219-234	± 8ms
AV delay hysteresis	0 ms	0-16-31-47-63-78-94	± 8 ms
Absolute refract. period	172 ms	141-156-172*-203-234-266-297-328-359	± 16 ms
PVARP	297 ms	141-156-172-203-234-266-297-328-359-391-422-453	± 16 ms
Blanking period	31 ms	31-47	± 8 ms
Rate responsive parameters			
Rate responsive mode (6)	OFF	OFF*-RR-DDD/VVIR	
Max.sensor-driven rate(7)	120	101-110-120-132-142-154 min ⁻¹	± 3%
Acceleration (8)	Slow	Slow-Fast	
Recovery (8)	Slow	Slow-Fast	
Slope number		1 to 15 (steps of 1)	
Calibration(6)	Fixed	Fixed-Auto	
Atrial parameters			
Pulse amplitude (9,11,16)	5 V	1.5-2-2.5-3-3.5-4-5	± 15 %
Pulse width (10)	0.37 ms	0.12-0.24-0.37-0.49-0.61-0.73-0.85-0.98	± 0.05ms
Sensitivity (12,15)	1 mV	0.4-0.6	± 0.2 mV
		0.8-1.0-1.2-1.5-1.8-2.0-2.2-2.5-2.7	± 0.4 mV
		3.0-3.5-4.0	± 0.8 mV
Sensing polarity (13)	UNI	UNI-BI	
Pacing polarity (13)	UNI	UNI-BI	

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Ventricular parameters

Pulse amplitude (9,11,16)	5 V	1.5-2-2.5*-3-3.5-4-5	± 15 %
Pulse width (10)	0.37 ms	0.12-0.24-0.37-0.49*-0.61-0.73-0.85-0.98	±0.05ms
Sensitivity (12,14)	2.2 mV	1.2-1.5-1.8-2.0-2.2*-2.5-2.7	± 0.4mV
		3.0-3.5-4.0-4.5-5.0	± 0.8 mV
Sensing polarity (13)	UNI	UNI*-BI	
Pacing polarity(13)	UNI	UNI*-BI	

Note: the unit for rate is min-1 or bpm.

Parameters	As shipped	Programmable values	Tolerances
Special features			
Rate Smoothing(17,18)	OFF	ON-OFF*	
ELT protection	TERMIN	OFF-TERMIN	
AV delay modulation	47 ms	47-63	± 8 ms
Max. VP variation	16 ms	16-31	± 8 ms
Fallback	OFF	OFF-10-30-50-100-500-1000-1500-2000 cycles	

(1) Only DDD, DDI, VVI, VVT, AAI, AAT modes may be used for rate responsive pacing (see section on rate responsive parameters)

(2) The corresponding basic periods and escape intervals (hysteresis =0) are the following :

1500-1333-1200-1091-1000-923-857-800-750-706-674-625 ms ± 3 %

(3) Rates below 55 min⁻¹ (bpm) are not available in rate responsive mode

(4) The maximum tracking rate is the fastest rate at which consecutively paced ventricular complexes maintain AV synchrony with atrial sensed events.

(5a) This parameter is available only in DDI, DVI or DOO mode.

(5b) DDD Mode only.

(6) Do not program the rate responsive function or the automatic calibration before implant; the sensor will be initialized and the resulting resting ventilation value will be erroneous. A bipolar atrial lead is required to program the rate responsive function or the automatic calibration.

(7) Only values less than or equal to the programmed maximum tracking rate can be programmed.

(8) For the acceleration, "Slow" corresponds to a 16 ms change in the escape interval every 8 cardiac cycles, and "Fast" to a 16 ms change in the escape interval every 4 cardiac cycles. For recovery, "Slow" corresponds to a 16 ms change in the escape interval every 12 cardiac cycles and "Fast" to a 16 ms change every 8 cardiac cycles.

(9) Only 1.5-2-3-3.5-4 V are regulated values.

(10) Measured at 1/3 of the maximum amplitude.

(11) Measurement of the peak amplitude.

(12) Sensitivity is measured by injecting a negative triangular signal of 10 ms.

(13) The pacemaker cannot be programmed to bipolar configuration if the impedance of the bipolar lead connected is not satisfactory.

(14) Correspondance between the programmable values of ventricular sensitivity and measurements using an injected positive and negative triangular signal of 2/13 ms.

Prog. ventr. sens.(mV) 1.2 1.5 1.8 2.0 2.2 2.5 2.7 3.0 3.5 4.0 4.5 5.0

2/13 neg. triangle (mV) 1.1 1.4 1.7 1.8 2.0 2.2 2.4 2.7 3.2 3.6 4.0 4.5

Neg. tolérance (mV) ±0.4 ±0.4 ±0.4 ±0.4 ±0.4 ±0.4 ±0.4 ±0.8 ±0.8 ±0.8 ±0.8 ±0.8

2/13 pos. triangle (mV) 2.1 2.7 3.2 3.6 3.9 4.5 4.9 5.4 6.3 7.2 8.1 9.0

Pos. tolérance (mV) ±0.8 ±0.8 ±0.8 ±0.8 ±0.8 ±0.8 ±0.8 ±1.5 ±1.5 ±1.5 ±1.5 ±1.5

(15) Correspondance between the programmable values of atrial sensitivity and measurements using an injected positive and negative triangular signal of 2/13 ms.

Prog. atr. sens. (mV) 0.4 0.6 0.8 1.0 1.2 1.5 1.8 2.0 2.2 2.5 2.7 3.0 3.5 4.0

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2/13 neg. triangle (mV)	0.4	0.5	0.7	0.9	1.1	1.3	1.6	1.8	2.0	2.2	2.4	2.7	3.1	3.6
Neg. tolérance (mV)	±0.2	±0.2	±0.4	±0.4	±0.4	±0.4	±0.6	±0.6	±0.6	±0.6	±0.8	±0.8	±0.8	
2/13 pos. triangle (mV)	0.7	1.1	1.4	1.8	2.1	2.7	3.2	3.6	3.9	4.5	4.9	5.4	6.3	7.2
Pos. tolérance (mV)	±0.4	±0.4	±0.8	±0.8	±0.8	±0.8	±1.2	±1.2	±1.2	±1.5	±1.5	±1.5	±1.5	

(16) Correspondance between the programmed amplitude and the mean value measured..

Atrial or ventricular pulse amplitude

Programmed value (V)	1.5	2.0	2.5	3.0	3.5	4.0	5.0
Mean value measured (V)	1.4	1.9	2.4	2.8	3.2	3.7	4.7
Tolerance (%)	±10	±10	±10	±10	±10	±10	±10

(17) Do not program rate smoothing prior to implant. The pacemaker may sense noise and pace at a rate higher than the programmed basic rate but lower than the programmed maximum tracking rate.

(18) The acceleration slope is 31 ms, the deceleration slope is 94 ms.

TELEMETRY FUNCTIONS

Type	As shipped	Description	Tolerances
Administrative data		Magnet rate Model, serial number Patient's name and birth date Indications for implant Pacemaker implant date Manufacturer, model, threshold, implant date of atrial lead Manufacturer, model, threshold, implant date of ventricular lead	
Measured data		Lead impedance (A and V) Pulse amplitude (A and V) Pulse current (A and V) Pulse energy (A and V)	20% 10% 10% 30%
Sensor		Sensor re-initialization Simulation	
Threshold tests		Atrial and ventricular	
- Threshold test rate	101	80 - 89 - 101* - 110 - 120 min ⁻¹	± 3%
Rate limit off		Atrial and ventricular	
Real time data transmission			
-Intracardiac ECG		Atrial and ventricular	
- Marker pulses		3 levels (A and V)	

STATISTICS

	Type	Max. recordable
- Programmings	Number of programmings	255
- Ventricular events	Paced, sensed, PVCs	4.3 billion
	End of the committed period	65535
- Atrial events	Paced, sensed	4.3 billion
- Cardiac activity	Total number of cardiac cycles (100%)	4.3 billion
- Spontaneous activity	Number and % of sensed cycles	4.3 billion
- RM paced cycles	Number and % of cycles paced at sensor driven rate	4.3 billion
- Exercise VE calibration	Number of exercise VE recalculations	255
- Resting VE calibration	Number of resting VE recalculations	255
- ELT termination	Number of attempts	255

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- Fallback

Number of starts

255

HOLTER FUNCTIONS

Type	As shipped	Values
EVENT HISTOGRAMS		Read - Reset
- Event type	STANDBY	V INT- V PAUSES - A INT - A PAUSES AV INT - V ASYNC - STANDBY
- Recording period	1 day	15 min - 1h - 3h - 6h - 12h - 1 day - 2 days - 1 week - 1mth
- Limits ms)	391 to 1328 ms	Programmable from 31 to 3000 ms (steps of 16)

HISTOGRAMS OF SENSOR-DRIVEN RATES
MEAN HEART RATE CURVE
CURVE OF CALIBRATION PARAMETERS
BATTERY DEPLETION CURVE

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Opus RM 4534

Single Chamber Rate Responsive Pacemaker System

Caution: Federal Law restricts this device to sale by or on the order of a physician (or properly licensed practitioner).

1. DEVICE DESCRIPTION

Opus RM (Model 4534) is a single chamber, bipolar, rate responsive, pulse generator which uses a minute ventilation sensor. It is powered by a lithium-iodine cell, and encapsulated in a hermetically sealed titanium case. The Opus RM can be programmed and interrogated via bi-directional telemetry using an IBM PC compatible microcomputer (programming software CSO 2.46 or higher and operating system configured and furnished by ELA Medical with that software) connected to a CPR1 programming head. The Model 4534 is fitted with one IS-1 standard 3.2 mm connectors (ISO/DP 5841-3).

2. INDICATIONS

The Opus RM pacemaker system is indicated for:

Rate adaptive pacing in patients who may benefit from increased pacing rates concurrent with increases in minute ventilation; and

The accepted patient conditions warranting chronic cardiac pacing which include:

- Symptomatic paroxysmal or permanent second or third-degree AV block;
- Symptomatic bilateral bundle branch block;
- Symptomatic paroxysmal or transient sinus node dysfunctions with or without associated AV conduction disorders;
- Bradycardia-tachycardia syndrome to prevent symptomatic bradycardia or some forms of symptomatic tachyarrhythmias; and
- Vaso-vagal syndromes or hypersensitive carotid sinus syndromes.

3. CONTRAINDICATIONS

- This device is contraindicated in patients with an implanted cardioverter-defibrillator (ICD) because the pulses used in the measurement of minute ventilation may cause unwanted delivery of ICD therapy.
- Single-chamber atrial pacing is contraindicated in patients with impaired AV nodal conduction.
- Single-chamber atrial pacing is contraindicated in patients with chronic refractory atrial tachyarrhythmias.

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4. WARNINGS

- **Rate adaptive pacing** should be used with care in patients unable to tolerate increased pacing rates.
- **Minute ventilation rate response pacing** may be inappropriate for patients who can achieve respiratory cycles shorter than 1.33 seconds (greater than 45 breaths per minute). Higher respiratory rates attenuate the impedance signal which diminishes the MV rate response, i.e., the pacing rate will drop toward the programmed basic rate.
- **Asynchronous pacing (VOO/AOO)** is contraindicated in the presence (or likelihood) of competition between paced and intrinsic rhythms.
- **Single chamber ventricular pacing** should be used with care in patients who may develop pacemaker syndrome or who may have a need for maximum atrial contribution.
- **Magnetic resonance imaging** of pacemaker patients has resulted in significant adverse effects (see PRECAUTIONS)
- **Therapeutic diathermy** can induce current in the pacing leads and may cause fibrillation, burning of the myocardium, and irreversible damage to the pulse generator.

5. PRECAUTIONS

5.1 Programming

- **Rate response or autocalibration** should not be enabled before implantation because the sensor will be incorrectly initialized resulting in inappropriate rates.
- During **automated threshold testing**, the programming head must be removed when capture ceases, to restore preprogrammed pulse amplitude, otherwise the pacemaker will continue the threshold test for the 20 cycles of the test without pacing the patient.

5.2 Storage and sterilization

- Store the device between 5°C and 50°C because temperatures outside this range can damage components.
- A device should not be implanted if sterility is not assured:
 - ⇒ If its sterility indicator within the inner package is not green, it might not have been sterilized;
 - ⇒ If its storage package has been pierced or altered, this could have rendered it non-

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sterile.

- Do not implant a device when:
 - ⇒ It has been dropped after it has been removed from its sterile packaging;
 - ⇒ Its “use before” date has expired, because this can adversely affect pulse generator longevity.
- Do not resterilize devices. Return unimplanted devices in their storage packages to ELA Medical for resterilization.

5.3 Lead Evaluation and Lead Connection

- Do not use a unipolar atrial lead if rate response is required, because the device’s rate response function will only operate with a bipolar lead.
- Do not use any lead with this pulse generator without first verifying IS-1 compatibility, because use with other leads can damage the connector or result in a leaking or intermittent connection.
- Do not use as-shipped pulse generator values for pacing amplitude and sensitivity without verifying that they are appropriate for the patient because this may result in shortened battery longevity or improper sensing.
- Consider lead maturation in choice of pacing amplitude and sensitivity because:
 - ⇒ acute pacing thresholds > 1 V or 2 mA or chronic pacing thresholds > 3 V or 6 mA can result in loss of capture because thresholds increase after implantation.
 - ⇒ R wave amplitude < 5 mV can result in undersensing because R-wave sensed amplitude decreases after implantation
- Exercise extreme caution if testing leads using line-powered equipment, because leakage current exceeding 10 microA can induce ventricular fibrillation.
- Do not insert a lead in the pacemaker connector without first visually verifying that the setscrews are sufficiently retracted to allow insertion.
- Do not insert a lead or setscrew wrench in the pacemaker connector without first lubricating the lead connector body or the wrench tip with silicone lubricant, because failure to do so can damage the connector.
- Do not tighten the setscrews with no lead connector inserted. This can damage the connector block.

5.4 Environmental and Medical Therapy Hazards

Patients should exercise reasonable caution in avoidance of devices which generate a strong electric or magnetic field. If a pulse generator should inhibit or revert to asynchronous operation at the programmed pacing rate or at the magnet rate while in the presence of EMI, moving away

from the source or turning it off will allow the pulse generator to return to its normal mode of operation.

5.4.1 Hospital and Medical Environments

- **Mechanical ventilators** may cause pacing rate changes. Program the pacemaker to a non-rate responsive mode during ventilation.
- **Electrosurgical cautery** could induce ventricular arrhythmias and/or fibrillation, or may cause asynchronous or inhibited pulse generator operation or operation in standby mode. If use of electrocautery is necessary, the current path and ground plate should be kept as far away from the pulse generator and leads as possible. (see Section 12)
- **Magnetic Resonance Imaging (MRI)** among pacemaker patients has been contraindicated by MRI manufacturers. Clinicians should carefully weigh the decision to use MRI with pacemaker patients.
 - ⇒ Magnetic and radio-frequency (RF) fields produced by MRI may: increase ventricular pacing beyond the rate limit, result in total inhibition of pacing output, result in pacing at random rates, or result in synchronous pacing.
 - ⇒ Magnetic fields may activate magnet mode operation and cause asynchronous pacing.¹
 - ⇒ Pacemaker patients treated with MRI should be closely monitored and programmed parameters should be verified upon cessation of MRI
- **Lithotripsy** may damage the pulse generator. If lithotripsy must be used, do not focus the beam near the pulse generator. (see Section 12)
- **External defibrillation** may damage the pulse generator. Attempt to minimize current flowing through the pulse generator and lead system by following these precautions (see Section 12)
 - ⇒ Position defibrillation paddles as far from the pulse generator as possible. Attempt to minimize current flowing through the pulse generator and leads by positioning the defibrillation paddles perpendicular to the implanted pulse generator/lead system.
 - ⇒ Use the lowest clinically appropriate energy output (watt seconds).
 - ⇒ Confirm pacemaker function following any internal or external defibrillation.
- **Transcutaneous electrical nerve stimulation (TENS)** may interfere with pacemaker function. If necessary, the following measures may reduce the possibility of interference:
 - ⇒ Place the TENS electrodes as close to each other as possible.
 - ⇒ Place the TENS electrodes as far from the pulse generator/lead system as possible.
 - ⇒ Monitor cardiac activity during TENS use.

¹ Holmes, Hayes, Gray, et al. The effects of magnetic resonance imaging on implantable pulse generators. PACE 1986: 9(3): 360-70.

- **High radiation sources** such as cobalt 60 or gamma radiation should not be directed at the pulse generator. If a patient requires radiation therapy in the vicinity of the pulse generator, place lead shielding over the device to prevent radiation damage. (see Section 12).

5.4.2 Home and Occupational Environments

- **High voltage power transmission lines** may generate enough EMI to interfere with pulse generator operation if approached too closely. (see Section 12)
- **Communication equipment** such as microwave transmitters, linear power amplifiers, or high-power amateur transmitters may generate enough EMI to interfere with pulse generator operation if approached too closely. (see Section 12)
- **Commercial electrical equipment** such as arc welders, induction furnaces, or resistance welders may generate enough EMI to interfere with pulse generator operation if approached too closely. (see Section 12)
- **Home appliances** which are in good working order and properly grounded do not usually produce enough EMI to interfere with pulse generator operation. There are reports of pacemaker disturbances caused by electric hand-tools or electric razors used directly over the skin over the pulse generator (see Section 12)

5.4.3 Cellular Phones

Recent studies have indicated there may be a potential interaction between cellular phones and pacemaker operation. Potential effects may be due to either the radio frequency signal or the magnet within the phone and could include inhibition or asynchronous pacing.

Based on testing to date, effects resulting from an interaction between cellular phones and the implanted pacemakers have been temporary. Simply moving the phone away from the implanted device will return it to its previous state of operation. Because of the great variety of cellular phones and the wide variance in patient physiology, an absolute recommendation to cover all patients cannot be made.

Patients having an implanted pacemaker who operate a cellular phone should:

- Maintain a minimum separation of 6 inches (15 centimeters) between a hand-held personal cellular phone and the implanted device. Portable and mobile cellular phones generally transmit at higher power levels compared to hand held models. For phones transmitting above 3 watts, maintain a minimum separation of 12 inches (30 centimeters) between the antenna and the implanted device.
- Patients should hold the phone to the ear opposite the side of the implanted device. Patients should not carry the phone in a breast pocket or on a belt within 6 inches (15 centimeters) of the implanted device as some phones emit signals when they are turned ON but not in use (i.e., in the listen or standby mode). Storing the phone in a location opposite the side of implant is recommended.

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5.5 Pulse Generator Disposal

- Do not incinerate pacemakers, because they can explode if subjected to incineration or cremation temperatures.
- Return all explanted pacemakers to ELA Medical for analysis and safe disposal.
- Do not implant an explanted pacemaker in another patient because sterility, functionality, and reliability cannot be assured.

6. ADVERSE EVENTS

The Opus RM was evaluated in a clinical study involving 74 devices implanted in 74 patients. As of June 17, 1996, total device exposure was 513 device months, and individual patient exposure averaged 7 months (ranging from 0.1 to 18.2 months). A total of 8 patients died during the study. None of these deaths were judged related to the device.

6.1 Observed Adverse Events

Table 1 reports the adverse events on a per patient and a per patient-month basis in descending order of frequency by category.

Table 1. Adverse Events Reported in > 1 Study Patient

(n=74 patients, 513 device months)

Adverse Event	# of Patients	% of Patients	# of Patients	Events per device year
<i>Observations</i> ¹				
<i>Ventricular loss of sensing</i>	3	4.1%	3	0.6%

¹ Observations are adverse events which are correctable by noninvasive measures, e.g., reprogramming.

6.2 Potential Adverse Effects

Adverse events (including those reported in Table 1) associated with pacing systems based on historical implant experience include:

- Cardiac perforation
- Cardiac tamponade
- Transvenous lead-related thrombosis
- Elevated thresholds
- Erosion through the skin
- Pulse generator migration
- Body rejection phenomena
- Hematoma/seroma
- Nerve and muscle stimulation
- Myopotential sensing
- Local tissue reaction
- Fibrotic tissue formation

7. CLINICAL STUDIES

The Opus RM was evaluated in a multi-center prospective study of the rate response in calibrated symptom-limited treadmill testing.

Objectives: Evaluate oxygen consumption rate, peak heart rate, proportionality of rate increase, correlation with a literature standard², and correlation with intrinsic rates.

Methods: Oxygen consumption and peak heart rate were obtained in a single-blind, randomized crossover design using paired exercise testing, comparing Opus RM in VVIR mode to VVI mode. Proportionality and correlation were evaluated from the device's sensor-determined rate, patient intrinsic rate, and elapsed time during exercise. These effectiveness data were obtained at approximately one month post-implant.

Study subjects were selected from candidates for single chamber pacing, able to perform treadmill exercise tests, in each investigator's general patient population. They were further required to have been diagnosed with chronotropic incompetence (CI), defined as the inability to achieve heart rates greater than 75% of the maximum predicted heart rate (MPHR = 220 - age). Although this diagnosis was a requirement for participation in paired exercise testing, only eight of the eleven tested patients in fact exhibited chronotropic incompetence.

Results: Table 2 summarizes the results of exercise testing. The devices demonstrated a linear increase in sensor rates with exercise level, an appropriate response for a rate responsive pacemaker. The slope of increase (3.79 ± 0.14) was comparable to a literature standard² (3.48 ± 0.46). The slope of the regression of sensor-indicated rates versus a literature standard was 0.96 which was not significantly different statistically from 1.0. A slope of 1.0 would indicate identical performance to predicted values.

Table 2. Rate sensor proportionality during exercise testing
(n= 8 patients exhibiting chronotropic incompetence)

Parameter	# of Patients	Correlation Coefficient [95% confidence interval]
Sensor indicated rates vs. exercise time	8	0.99 [.973, .999]
Sensor indicated rate vs. method of Kay	8	0.93 [.708, .986]

² Kay GN: Quantitation of chronotropic response: Comparison of methods for rate-modulating permanent pacemakers. J Am Coll Cardiol 1992; 20:1533.

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8. STORAGE AND STERILIZATION

Opus RM and its accessories are sterilized with ethylene oxide gas and are hermetically sealed in a dual plastic package in accordance with international standard. Sterility is ensured if:

- the sterility indicator within the inner container is green, and
- the external packaging is neither pierced nor altered

8.1 Shelf Life

The "use before" date on the storage package is calculated twelve months from the time of manufacture. Pacemakers not implanted before the "use before" date should be returned to ELA Medical.

8.2 Resterilization

If the pulse generator needs to be resterilized, it is advisable to return it in its storage package to ELA Medical.

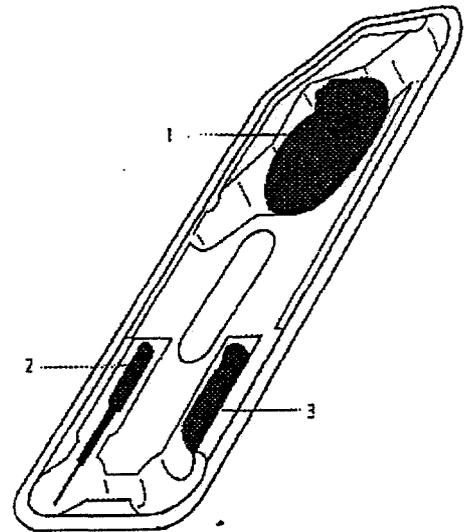
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9. IMPLANT INFORMATION

9.1 STERILE PACKAGE DESCRIPTION AND HANDLING

The sterile inner package contains the following items :

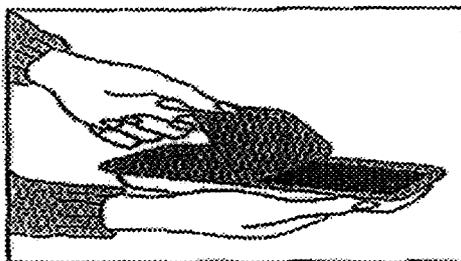
1. Opus RM pulse generator
2. Hexagonal screwdrivers
3. Bottle of silicone lubricant



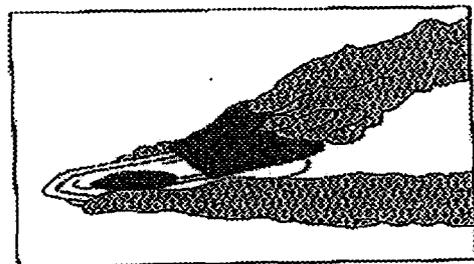
The non-sterile cardboard package also contains the following items :

- Physician's manual
- Patient ID card
- Individual technical data sheet
- Warranty form

Before opening the package, examine the label to verify that the package contains the desired pacemaker. Inspect the package to make sure that (1) the "use before" date has not been exceeded and (2) the sterile trays are still intact and have not been opened, pierced or broken.



Open the first plastic package and present it to the sterile field.



The physician takes the internal package and opens it as shown above.

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9.2 THRESHOLD TESTS AT IMPLANT

9.2.1 External pulse generator

Pacing thresholds as well as the amplitude of intracardiac events should be measured at implant. A battery-powered external pulse generator or a pacing system analyzer should be used for this purpose. Slew rates can also be measured using the external system.

9.2.2 Measuring pacing thresholds

- Set the rate of the external pulse generator higher than the patient's spontaneous rate
- Program the external pacer's pulse width to the value desired for the pulse generator to be implanted
- Program the external pacer's output to 7.5 V and/or 15 mA
- Connect the implanted leads to the external pulse generator following the manufacturer's instructions.
- Gradually decrease the external pulse generator amplitude while observing the ECG for loss of capture. The lowest amplitude at which capture is reacquired after it has been lost is the pacing threshold. Acute thresholds should be less than 1 V or 2 mA. Chronic thresholds should be less than 3 V or 6 mA.

9.2.3 Measuring sensing thresholds

Follow the external generator manufacturer's instructions to measure the recorded amplitude of intracardiac events. The minimum amplitude of intracardiac events that can be sensed by Opus RM depends on the slew rate and the lead impedance.

The slew rate usually lies between 0.5 and 1.5 V/s in the atrium and 1.6 and 2.2 V/s in the ventricle. In most cases, an R wave greater than 5 mV during acute threshold measurement will be adequate with Opus RM programmed to a ventricular sensitivity of 2.2 or 2.5 mV. In most cases, a P wave with an amplitude greater than 2 mV during acute measurement will be adequate with Opus RM programmed to an atrial sensitivity of 1.0 mV. The programming of 0.7 mV sensitivity should be used only for lower amplitude P waves because such settings enhance the pacemaker's sensitivity to interference.

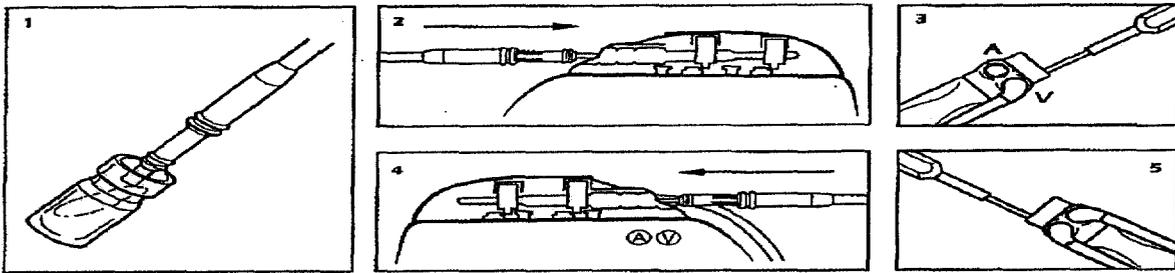
9.3 LEAD CONNECTION

It is imperative that each lead be properly connected to the corresponding pacemaker connector. Ensure that the pre-inserted setscrews are sufficiently retracted to allow insertion of the lead connector into the pacemaker connector.

1. Apply a small amount of silicone lubricant to the silicone rubber body of the connector.
2. Insert the lead connector into the port. The lead pin must be visible through the opposite end of the connector block.

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Lead pin should
be visible here



10. PACEMAKER INTERROGATION

Opus RM can be interrogated and programmed via telemetry using a CPR1 programming head connected to a microcomputer. Refer to the computer software (CSO) manual supplied with the programmer for details concerning its use.

11. PACEMAKER PROGRAMMING

11.1 BASIC PARAMETERS

11.1.1 Mode and Pacing Mode Selection

Three programmable modes are available on Opus RM. Two of them can be associated with rate responsive pacing :

- SOO mode : asynchronous pacing

Pacing is provided at the programmed rate regardless of the patient's intrinsic rhythm.

Use for: Diagnostic evaluation

Avoid use in:

- atrial pacing: AV block, conduction system disease, atrial flutter, atrial fibrillation, supraventricular tachyarrhythmia, competitive intrinsic rhythm
- ventricular pacing: competitive intrinsic rhythm and pacemaker syndrome.

- SSI(R) mode : inhibited pacing

Pacing is provided at the programmed rate (SSI) or at the sensor-driven rate (SSIR) in the absence of intrinsic activity. A sensed cardiac event inhibits pacing.

Use for:

- atrial pacing: Sick sinus syndrome with symptoms

- ventricular pacing: Bradycardia with chronic atrial fibrillation or severe physical disability or other diseases with a short prognosis.

Avoid use in :

- atrial pacing: AV block, conduction system disease, supraventricular tachyarrhythmia
- ventricular pacing: pacemaker syndrome and need for maximum atrial contribution.

- SST(R) mode : triggered pacing

Pacing is provided at the programmed rate (SST) or at the sensor-driven rate (SSTR) in the absence of intrinsic activity. Any sensed cardiac event triggers pacing.

Use for: Diagnostic evaluation³

Avoid use in:

- atrial pacing: AV block, conduction system disease, atrial flutter, atrial fibrillation, supraventricular tachyarrhythmia
- ventricular pacing: pacemaker syndrome.

11.1.2 Basic rate

The programmed basic rate is the programmable lower limit for the pacing rate in the absence of sensed events . The programmed basic rate minus the programmed hysteresis is the intrinsic lower limit. If the patient's intrinsic rate falls below this limit, the pacemaker starts pacing.

Notes :

- 1. In special test modes, such as during the magnet or threshold tests, the pacing rate is independent of the programmed basic rate.*
- 2. If rate smoothing or the rate responsive function is ON, the escape rate can be higher than the programmed basic rate.*
- 3. If rate responsive pacing is ON, the lower limit of the programmable pacing rate is 55 bpm.*

11.1.3 Upper rate limit

When the smoothing algorithm is ON, the pacing rate cannot exceed the programmed upper rate limit.

Note : The upper rate limit is the highest limit of the programmable maximum sensor-driven rate.

11.1.4 Pulse amplitude

The programmed pulse amplitude determines the voltage applied to the heart while pacing. Use the "as shipped" pulse amplitude immediately after implant to avoid loss of capture due to the early rise in threshold. This acute threshold level can be up to five times the implant threshold level. After threshold stabilization, a setting which provides a suitable safety margin (twice the

³Allows diagnostic evaluation without having to reinitialize the device to rate response.

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chronic threshold) and saves pacemaker battery can be found.

11.1.5 Pulse width

The pulse width is the duration the programmed pulse amplitude is applied to the heart during pacing. Pulse width can be used to adjust pacemaker output.

11.1.6 Sensitivity

The pacemaker sensing circuit is designed to sense any cardiac event. If the pacemaker does not correctly sense the intrinsic signal, a higher sensitivity (lower value) may be programmed. However, extracardiac signals should not be sensed. If the pacemaker senses signals other than intrinsic cardiac signals, a lower sensitivity (higher value) can be programmed as long as a sufficient safety margin of two to four times the amplitude of the recorded signal is maintained.

11.1.7 Polarity

Although mechanically configured like a bipolar pulse generator, Opus RM may be programmed either to unipolar or bipolar configuration. Pacing and sensing polarity configuration can be programmed independently. The pacemaker is shipped with unipolar sensing and pacing configuration programmed for each channel. To avoid programming the pacemaker to bipolar configuration when connected to a unipolar lead, the lead impedance is measured during programming to bipolar configuration.

Notes:

- 1. Due to this protection, the pacemaker cannot be programmed to a bipolar configuration while it is still in the storage package. It must be connected to a bipolar lead with an appropriate impedance.*
- 2. Polarity is programmed independently of the rate-response function.*

Pacing polarity

In unipolar pacing configuration, the anode (positive pole) is the pacemaker's titanium case and the distal electrode is the cathode (negative pole). In bipolar pacing configuration, the proximal electrode is the anode (positive pole) and the distal electrode is the cathode (negative pole). One of the advantages of bipolar pacing is to avoid nerve and muscle stimulation. One of the advantages of unipolar pacing is a larger pacing pulse, which can be more visible on a surface ECG.

Sensing polarity

In unipolar sensing configuration, the potential difference is measured between the pacemaker titanium case and the distal tip of the lead.

In bipolar sensing configuration, the potential difference is measured between the proximal ring and the distal tip of the lead. One advantage of bipolar sensing is a lower susceptibility to detection of myopotentials and electromagnetic interference. In unipolar sensing configuration,

patient's activity.

(3) Rapid response to exercise by recalculation of the escape interval every fourth , eighth or twelfth cycle.

11.2.1 Rate responsive mode

The adjustment of the pacing rate to exercise is determined by this parameter. There are three programmable options :

- OFF : Rate responsive pacing does not function. The pacing rate is the programmed basic rate (or smoothed rate if rate smoothing occurs).
- RR : Rate responsive pacing is ON. This can be accessed only if the pacing mode is programmed to SSI, or SST. Pacing rate is calculated from the measured minute ventilation. This rate may vary between the basic pacing rate and the maximum sensor-driven rate programmed.

Notes :

1. *Do not program rate response before implant: the sensor will be initialized and the resulting minute ventilaiton value will be erroneous.*
2. *A bipolar lead is required to program rate response.*
3. *If the pacemaker is programmed to SOO, rate response is automatically programmed to OFF.*
3. *If the sensor has not yet been activated, programming rate response to RR mode will start initialization. Rate responsive pacing will only be functional after the 6-minute initialization .*

11.2.2 Rate Response Slope Number

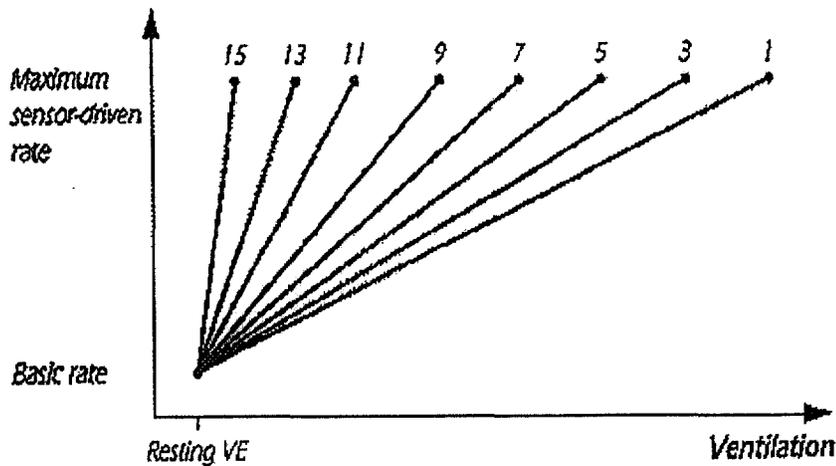
The rate response slope number is a programmable parameter which determines the degree to which pacing rate is modified when there is a change in minute ventilation. If the slope number is low, a variation in minute ventilation will only result in a small modification in pacing rate. Contrarily, a high slope number causes larger changes in pacing rate with only a slight variation in measured minute ventilation. The graph shown below illustrates how the pacing rate is allowed to vary according to the measured changes in minute ventilation according to the programmed slope number.

The slope number can be directly programmed by the physician through the programmer from 1 to 15 by steps of 1. Generally, the more active the patient is, the lower the slope number should be. To select a value suited to patient's activity, the simulation tool can be used.

Notes:

1. *If calibration is programmed to AUTOMATIC, the slope number programmed by the physician is ineffective. The pacemaker will automatically calculate a new slope number ranging from 1 to 15.*
2. *For high resting minute ventilation values, low slopes cannot be programmed; the resulting exercise minute ventilation will be higher than the technical limit. Programmable slope values are those which respect the exercise minute ventilation limit.*

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11.2.3 Initialization

Note : Initialization is available only if the sensor is ON, i.e., if the programmed mode is one of the rate responsive modes : (SSI or SST) with rate response programmed to RR or with the AUTO calibration.

Initialization provides the pacemaker with initial values for the patient's minute ventilation at rest and for the rate-response slope. It sets the rest ventilation to the value it measures during the initialization process described below. It sets the slope to 11.

ELA recommends the initialization procedure described below. Caution: Improper initialization can cause inappropriate pacing rates for the patient's activity level, including increased pacing rate with the patient at rest.

1. Have the patient remain supine and calm throughout initialization. Do not begin initialization until the patient is calm.
2. Begin initialization. The programmer can manually start initialization from the TEST screen provided that calibration is AUTO, or Rate Responsive Mode is RR. Caution: The pacemaker does not provide rate-responsive pacing during initialization.
3. Once initialization starts, move the programming head at least 20 cm away from the patient, and keep it away throughout initialization. Caution: Using the programmer during initialization can abort initialization or falsify results.
4. Initialization takes 6 minutes. The programmer displays time remaining. Caution: The patient must remain supine and calm.
5. Upon completion, the pacemaker starts operation in the programmed Rate Responsive Mode.

ELA recommends verifying initialization with the following procedure:

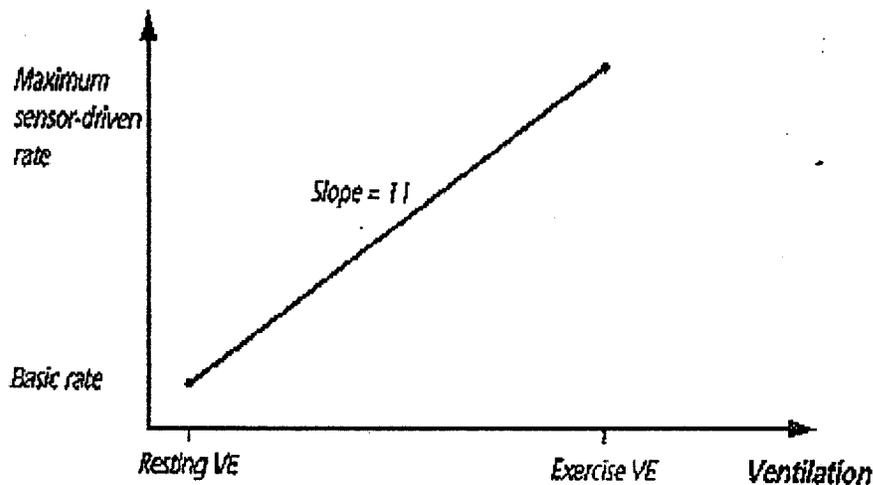
6. Verify via interrogation that the pacemaker has completed initialization.
7. Program Rate Responsive Mode to RR, if not already set to RR.
8. Insure that the patient is supine and calm, and then begin Simulation . Once Simulation

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starts, move the programming head at least 20 cm away from the patient, and keep it away until step 11 below.

9. Wait for two minutes, with the patient supine and calm.
10. Have the patient stand but remain calm. Wait an additional two minutes.
11. Use the programmer to read and display Simulation data. These must show minute ventilation within 25 % of the line indicating minute ventilation at rest (this corresponds to approximately 4 % of the rate increase that the pacemaker will provide for maximum effort). If not, repeat initialization.

Note: When the initialization phase is started, the programming head must be moved away from the pacemaker.



11.2.4 Calibration

Description :

Calibration adjusts the rate responsive parameters for resting and exercise minute ventilation to the patient's activity. Its purpose is to relate the calculated pacing rate to minute ventilation which corresponds to the patient's work capacities. This adjustment can be performed in two ways :

- FIXED programming :

Rate responsive pacing uses the last calibration values to adjust the rate response parameters. These values may be those calculated during exercise testing with AUTO calibration or those corresponding to the programmed slope number. However, they will remain fixed regardless of changes in patient activity.

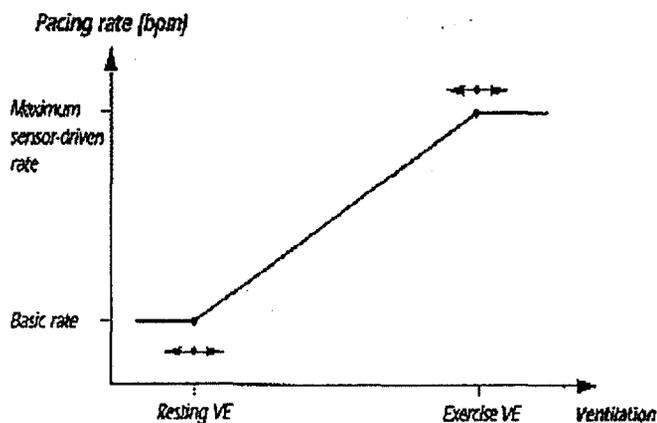
- AUTO programming

Calibration of the rate responsive system is determined by the patient's daily activity. The rate

responsive escape interval is determined by calibration values which are constantly being recalculated. Thus, the variation in heart rate will be adjusted to the patient's condition whether the patient is tired, sick, or fully active.

Notes :

- 1. Do not program the automatic calibration before implant as the sensor will be initialized and the resulting resting minute ventilation value will be erroneous.*
- 2. Program the automatic calibration only if the lead is bipolar.*
- 3. If the mode is programmed to SOO, calibration is automatically reprogrammed to FIXED.*
- 4 If the sensor has not yet been activated, programming calibration to AUTO will start initialization. Automatic calibration is not operational until after the six-minute initialization.*
- 5. When calibration is programmed to AUTO, the rate response slope number ranges from 1 to 15 by steps of 0.1.*
- 6. If the pacing mode is programmed to SSI or SST, mode, the rate responsive mode can be programmed to OFF and calibration to AUTO. This is an evaluation phase which finds rate responsive parameters which fit the patient's needs. It also prevents inappropriate rate responsive pacing in the days following implantation.*



Functioning principle of the AUTOMATIC calibration :

Calibration of the rate-responsive system is based on the measurement of two values of minute ventilation. One is resting ventilation (resting VE), which corresponds to the patient's resting state and, consequently, to the basic rate. The other is exercise ventilation (exercise VE), which corresponds to maximum exercise and, consequently, to the maximum sensor-driven rate.

To determine **resting minute ventilation**, Opus RM looks at the minimum minute ventilation value and recalculates resting ventilation every 32nd respiratory cycle if a change has occurred. Resting minute ventilation is decreased by 6% if the mean value of minute ventilation calculated for the last 64 respiratory cycles is 6% or more below the present value. Resting minute ventilation is increased by 6% if more than eight mean values of minute ventilation calculated on

64 respiratory cycles are 6% or more above the present value.

However, this increase is limited to 20% of the mean resting minute ventilation recorded the day before. This avoids a significant modification in rate responsive parameters due to prolonged exercise.

To determine **exercise minute ventilation**, Opus RM looks for the maximum minute ventilation value and recalculates the value of exercise minute ventilation every eighth cycle that a change has occurred.

Exercise minute ventilation is increased by a maximum of 6% if the mean value of minute ventilation calculated on eight respiratory cycles is higher than the present value. During sustained exercise, minute ventilation can increase by successive steps several times.

To avoid successive recalibrations, the rate responsive slope number will not be recalculated using the latest exercise minute ventilation until after the end of exercise, that is, when the sensor rate is equal to the basic rate. The new slope number will not be used until the next exercise period.

If exercise minute ventilation has not been modified for 24 hours, its value will be decreased by 3%. Thus, when a patient's activity is low, exercise ventilation will decrease progressively and the rate responsive slope number will increase. This means that moderate exercise will bring about a significant increase in heart rate, and could cause the pacemaker to pace at the maximum sensor-driven rate. It is therefore advisable to program a low sensor-driven rate in patients who are not very active.

Notes :

1. When calibration is programmed to AUTO, the rate response slope number range is between 1 and 15 with steps of 0.1.
2. The upper limit of the slope is 15 and cannot be programmed by the physician. Active patients for whom automatic calibration is indicated should not reach this limit and should not be subjected to inappropriately high slopes.
3. Initialization determines the resting minute ventilation and sets the slope number to 11; rate-responsive functions including automatic calibration are then ready to operate.
4. Automatic calibration only modifies the exercise and the resting minute ventilation; consequently, it also modifies the slope number. Refer to calibration section for further explanation.

11.2.5 Maximum sensor-driven rate

The programmed maximum sensor-driven rate is the fastest pacing rate when the rate responsive function is ON. This sensor-driven rate is lower than or equal to the programmed maximum tracking rate. It corresponds to the maximum heart rate that can be reached by the patient in his everyday life.

Note: It is therefore advisable to program a low sensor-driven rate in patients who are not very

active.

11.2.6 Rate acceleration

The programmed value for rate acceleration determines the maximum decrease in the escape interval. It thus determines the maximum acceleration of the corresponding pacing rate during exercise. When acceleration is programmed to fast, there is a 16 ms decrease in the escape interval every fourth cardiac cycle. It allows a more rapid increase in the pacing rate up to the programmed sensor-driven rate, during strenuous exercise. When acceleration is programmed to slow, there is a 16 ms decrease in the escape interval every eighth cardiac cycle. It thus limits the increase in the pacing rate during exercise.

Note : If the pacemaker paces at the basic rate, the first four or eight cycles of rate responsive pacing correspond to an escape interval shortened by 6% depending on whether the device is programmed to fast or slow.

11.2.7 Recovery

The programmed value for recovery determines the maximum increase in the escape interval and thus the maximum deceleration in the pacing rate after exercise, i.e., during the patient's recovery phase. When recovery is programmed to fast, there is a 16 ms increase in the escape interval every eighth cardiac cycle. This brings the pacing rate to the programmed basic rate more rapidly. When recovery is programmed to slow, there is a 16 ms increase in the escape interval every twelfth cardiac cycle. This more slowly decreases the pacing rate at the end of exercise.

Note : The four last recovery cycles (before pacing at basic rate) have an escape interval 6% below the basic rate escape interval.

11.2.8 Other parameters

Other programmable parameters influence the pacemaker behavior during exercise :

- * **Basic rate** : This is the pacing rate when the patient is at rest. It should be greater than or equal to 55 min⁻¹ (bpm).
- * **Upper rate limit** : This rate is the upper limit for the programmable maximum sensor-driven rate.
- * **Hysteresis** : When hysteresis is programmed, it is applied to the calculated sensor-driven rate. Thus when the sensor-driven rate becomes greater than the sinus rate, there is one cycle of pacing at the hysteresis rate before pacing begins at the sensor-driven rate.

11.2.9 Rate smoothing

-Objective :

This algorithm is designed to prevent the pacing rate from decreasing abruptly to the programmed basic rate when pacing is triggered upon sensing of a cardiac pause or cessation of the spontaneous rhythm.

- **Indications :**

Patients with sudden bradycardia episodes.

- **Description :**

When the rate smoothing algorithm is programmed ON, there are two steps

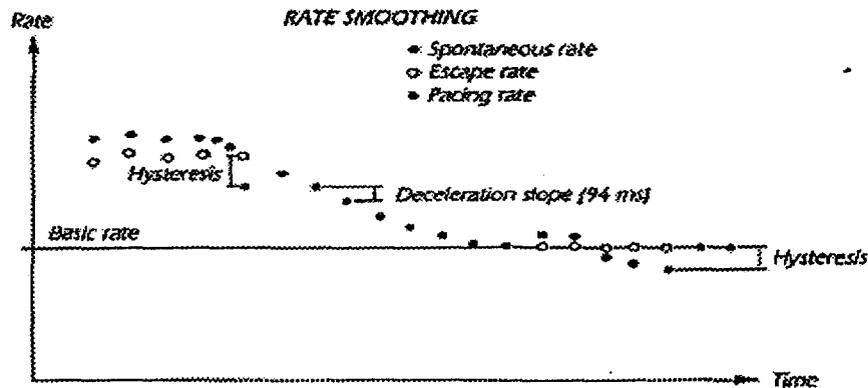
. When the patient is in spontaneous rhythm, Opus RM automatically computes the escape interval based on the value of one spontaneous cycle every eighth beat.

If the difference between the present value for the escape interval and the patient's spontaneous interval is greater than 31 ms, a new escape interval is calculated equal to the present stored value for the escape interval minus 31 ms.

. As soon as a pause longer than the last escape interval occurs, pacing is delivered at a progressively decreasing rate. This decrease in the pacing rate occurs every eighth cycle (the escape interval is increased by steps of 94 ms).

The occurrence of a spontaneous complex stops the process.

When the basic rate is reached, the pacing interval remains there until smoothing ends.



- **Function :**

. The rate smoothing algorithm can be used with all synchronous modes. Programming rate smoothing ON, while in a rate responsive mode, is not recommended since rate responsive pacing already has a rate smoothing function.

. If a rate responsive parameter is programmed ON and a pause occurs, pacing will be delivered at the higher of the sensor-driven rate and smoothing rate.

. It is advisable to use the hysteresis function together with the rate smoothing function. This avoids initiating rate smoothing on slight variations in the patient's rhythm.

. The smoothed escape interval always lies between the programmed maximum rate interval and the basic rate interval unless hysteresis is programmed. The pacing rate therefore, always lies between the programmed upper rate limit and basic rate.

- **Programmable settings :**

Rate smoothing : OFF-ON

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11.3 APPLICABLE PARAMETERS

Depending on the mode programmed for the Opus RM, some parameters are operational and some are disabled. When a parameter which was previously disabled becomes operational after mode reprogramming, its value is either the "as shipped" value or the last value programmed. Refer to the table below for the complete list of applicable parameters for each mode.

Parameters	SOO	SSI	SST
Basic rate	x	x	x
Upper rate limit		x	x
Hysteresis		x	x
Abs. refr. period		x	x
Rate resp.mode		x	x
Max. sensor driven rate		x	x
Acceleration		x	x
Recovery		x	x
Slope number		x	x
Calibration		x	x
Pulse ampl.	x	x	x
Pulse width	x	x	x
Sensitivity		x	x
Pac.polarity	x	x	x
Sens.polarity		x	x
Rate smoothing		x	x

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11.4 LONGEVITY INDICATIONS

11.4.1 ELECTIVE REPLACEMENT INDICATORS

Elective Replacement Indicators (ERI) correspond to a battery impedance of 10 kOhms. The ERIs are :

- Magnet rate lower than the values displayed by the programmer for ERI magnet rate (approximately $80 \pm 5 \text{ min}^{-1}$ or bpm)
- Battery depletion curve greater than or equal to 10 kOhms.

Amplitudes at ERI :	programmable	available
	1.5 V	1.5 V
	2.0 V	2.0 V
	2.5 V	2.4 V
	3.0 V	3.0 V
	3.5 V	3.5 V
	4.0 V	4.0 V
	5 V	4.5 V

(SSI mode, 70 min^{-1} (bpm), 0.49 ms, 500 Ohms)

At ERI, 4.5 to 8 months of operation remain before EOL (End Of Life) depending on pacing conditions (see table shown below). The pacemaker should be replaced at ERI.

Programmed amplitude (V)	Estimated longevity at ERI (months)			
	Rate response OFF (1)		Rate response ON (2)	
	500 Ohm	300 Ohm	500 Ohm	300 Ohm
2.5	8	7.5	6.5	6
3.5	6.5	5.5	5	4.5
5	6	4.5	4.5	4

(1)SSI, 100% pacing, 70 min^{-1} (bpm), 0.49 ms

(2)SSI, 100% pacing, 85 min^{-1} (bpm), 0.49 ms

11.4.2 MAGNET RATE/BATTERY INTERNAL RESISTANCE

Magnet rate is 96.0 ppm at beginning of life (BOL) and 80.0 ± 5 ppm at ERI (exact value provided for each device by the programmer).

Magn.rate(min^{-1})	96.0	93.7	91.4	89.3	87.3	85.3	83.5	81.7	80.0	78.4	76.8	75.3	73.6	72.5	71.1	69.8
Magn.period (ms)	625	640	656	672	687	703	719	734	750	765	781	797	812	828	844	860
Resist.(kOhms)	<5.5	5.5	6.0	6.5	7.0	7.7	8.5	9.3	10.0	11.0	11.7	12.5	13.5	14.5	15.5	>15.5

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11.4.3 LONGEVITY PROJECTION

Longevity estimates have been made for a range of programmed settings. The following table provides the estimated time in months until ERI after 12 months of shelf storage with "as-shipped" parameter values. The calculation assumes SSI pacing at 70 min⁻¹ (bpm), with a 0.49 ms pulse width and a lead resistance of 500 Ohms.

Ampl. (V)	LONGEVITY (months)							
	RATE RESPONSE ON				RATE RESPONSE OFF			
	100% pacing		50% pacing		100% pacing		50% pacing	
	mean	-3SD	mean	-3SD	mean	-3SD	mean	-3SD
1.5	81	74.5	83	76.5	106	97.5	109	100
2.0	79	73	82	75.5	103	95	107	98.5
2.5	78	72	81	74.5	100	92	106	97.5
3.0	66	61	75	69	83	76.5	96	88
3.5	64	59	73	67	79	73	93	85.5
4.0	61	56	71	65	75	69	90	83
5.0	57	52.5	68	62.5	68	62.5	85	78

Note : Continuous use of the Holter function could result in approximately a 4% reduction in longevity.

The following table provides the effect on longevity of pacing into a low impedance load. The calculation assumes SSI pacing at 70 min⁻¹, 0.49 ms, 5 V .

Lead resistance	RATE RESPONSE ON		RATE RESPONSE OFF	
	mean value	-3SD	mean value	-3SD
500 Ohm	57	52.5	68	62.5
300 Ohm	46	42.5	54	49.5

11.4.4 BEHAVIOR OF RATE-MODULATED FUNCTION AT ERI

If the rate responsive circuit is supplied with a voltage lower than 2.1 V for five consecutive cycles, rate responsive pacing can no longer function and patient will then be paced at the basic rate.

12. STANDBY MODE

If the internal pacemaker circuitry does not function properly, the pacemaker automatically switches to a safety mode, called standby mode. In standby mode, Opus RM functions as follows:

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Mode	SSI	Absolute refr. period	172 ms
Basic rate	70 min ⁻¹ (bpm)	Test modes	Non available
Hysteresis	0%	Statistics	Not available
Pulse amplitude	5 V	Rate smoothing	No
Pulse width	0.49 ms	Rate limit	Yes
Sensitivity	2.2 mV	Rate responsive pacing	No
(Pacing or sensing) polarity	UNI		

When in standby mode, the pacemaker can be interrogated, but the programmer will display the message "CAUTION STANDBY MODE". Programming cannot be performed, test modes, including magnet mode, are disabled and statistics are not incremented.

To restore normal pacemaker function, reset the pacemaker by pressing the function key INITIALization when the "CAUTION STANDBY MODE" is displayed on the programmer screen. The different programming and test functions will then be reactivated.

13. MEDICAL FOLLOWUP

13.1 MAGNET TEST

The magnet test gives an indication of the cell capacity, capture, amplitude and basic rate programmed without using the programmer. Application of a magnet over Opus RM makes the pulse generator operate in a simple safety mode.

13.1.1 Magnet on

When a magnet is applied over Opus RM, the pulse generator finishes the cycle in progress and then reverts to the magnet test mode described below :

Mode:	SOO
Pulse width:	0.49 ms (or value programmed if this value is higher than 0.49 ms)
Pulse amplitude:	5V
Rate:	Magnet

13.1.2 Magnet off

When the magnet is removed, the pulse generator finishes the cycle in progress and then reverts to the capture test for six cycles, then to the rate test for two cycles.

- Capture test mode

The purpose of this test is to demonstrate that the programmed voltage and pulse width are sufficient to capture. During the capture test, Opus RM operates as follows:

Mode:	SOO
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Pulse amplitude
and width: as programmed
Rate: Magnet

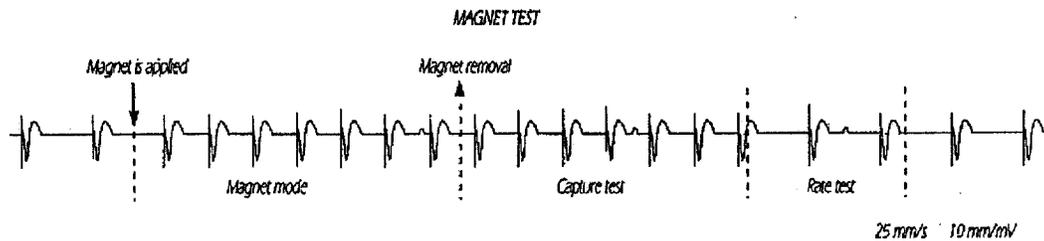
-Rate test mode:

The purpose of this mode is to measure the programmed amplitude and rate and to verify capture. During the rate test, Opus RM operates as follows :

Mode: SOO
Pulse amplitude and width: as programmed
Rate: Basic Rate

Notes :

1. *If the magnet is reapplied during the capture test or the rate test, Opus RM reverts to the magnet test.*
2. *Programming is not effective during either magnet, capture or rate test.*



13.2 THRESHOLD TESTS

Noninvasive threshold measurements can be performed through the pacemaker.

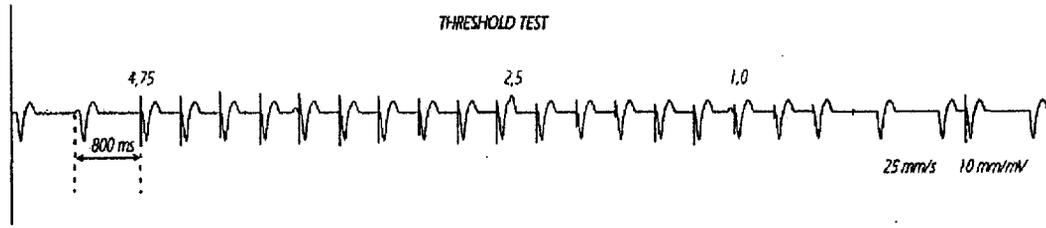
The test begins when programmed and lasts for 20 cycles. During the test, ventricular pacing is asynchronous. During the test, pacing is asynchronous. The first cycle lasts 800 ms (75 min^{-1} or bpm). During the following nineteen cycles, the pacing rate is the programmed threshold rate. Pulse width is at the programmed value for the test. The amplitude (in volts) decreases with each beat as follows :

Cycle	1	2	3	4	5	6	7	8	9
10									
Amplitude	4.75	4.50	4.25	4.00	3.75	3.50	3.25	3.00	2.75
2.50									
Cycle	11	12	13	14	15	16	17	18	19
20									
Amplitude	2.25	2.00	1.75	1.50	1.25	1.00	0.75	0.50	0.25
0.00									

The beat following the test is delivered asynchronously with the programmed parameters. If a magnet is applied, if the programming head is removed or if any key of the programmer is

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pressed, the test is immediately stopped.



13.3 LEAD MEASUREMENTS

The lead measurement test mode allows noninvasive measurements of lead characteristics. The lead measurement test mode begins when programmed and lasts two cycles. During these two asynchronous cycles, pulse width is increased to 0.98 ms. The programmer displays the measured averages for voltage, current, impedance and energy

Parameters	MEASURABLE RANGE			TOLERANCE
	Min.	Max.	Units	
<i>Voltage</i>	0.20	8.4	V	10 %
<i>Current</i>	0.00	28.00	mA	10 %
<i>Impedance</i>	0.30	3.00	kOhms	20 %
<i>Energy</i>	2	18.7	μJoules	30 %

13.4 RATE LIMIT OFF

The pacing rate is limited to 179 min⁻¹ (bpm). It is possible to suppress this limit through the programmer. To pace at high rates (electrophysiologic studies), the pacemaker must be programmed to a triggered mode (SST) and an external pacemaker which can deliver high-rate pulses must be used; these pulses will be sensed by the implanted pacemaker (SST) which will consequently pace at high rates.

If the rate limit is OFF, and if the pacemaker is programmed to SST mode, pacing can be triggered up to 213 min⁻¹ (bpm).

The rate limit reverts to 179 min⁻¹ (bpm) as soon as the programming head is removed or any key of the programmer is pressed.

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13.5 STATISTICS

Opus RM automatically stores data via diagnostic counters which can be reset at any time. These counters can be used to check the function of the pacemaker, to optimize programmable values and to evaluate the need for special features.

The different counters are :

- . Number of programmings (255 max)
- . Number of beats :
 - paced (4.3 billion max)
 - sensed (4.3 billion max)
- . Total number of cardiac cycles (4.3 billion max)
- . Percentage and number of spontaneous cycles (4.3 billion max)
- . Number and percent of cycles paced at the sensor-driven rate (4.3 billion max)
- . Number of resting ventilation recalculations (255 max)
- . Number of exercise ventilation recalculations (255 max)

Opus RM also stores the following data :

- . Patient's name (maximum of 14 letters)
- . Birth date
- . Pacemaker implant date
- . Implant date of the lead
- . Manufacturer and model of the lead
- . Acute thresholds
- . ECG indications, symptoms and etiology
- . Date and time statistics were reset

13.6 MARKERS

Event markers are particularly useful in the interpretation of pacemaker ECGs. Events are displayed in real time on the same multi-channel ECG recorder as the surface ECG. The different events are marked by pulses of different amplitudes :

Event	marker amplitude
Sensed events	- 6 units
Paced events (including paced events triggered in SST mode)	- 10 units

Opus RM starts transmitting markers when commanded by the programmer (see programmer manual). A calibration impulse is delivered at the beginning of the sequence. Transmission is ended when the programmer head is removed, a magnet is applied, or any key of the programmer is pressed.

13.7 INTRACARDIAC ECG

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Opus RM provides noninvasive atrial and ventricular intracardiac ECGs, which are essential to evaluate the pacing system. The intracardiac ECG can be used to select pacing and sensing polarities, to reveal possible myopotentials which are not visible on the surface ECG. The intracardiac ECG has the same polarity as the sensing. Opus RM starts transmitting intracardiac ECGs when commanded by the programmer (see programmer manual). Transmission is ended when the programmer head is removed, a magnet is applied or, any key of the programmer is pressed.

13.8 SIMULATION

Note : Simulation can only be accessed if the rate responsive mode is programmed to RR.

Simulation is a tool for studying Opus RM rate responsive parameters. It stores cardiac and respiratory data in the pacemaker memory and then transfers the data to the programmer to simulate the pacemaker behavior based on the programmed rate responsive parameters.

The maximum data storage time is approximately 20 minutes. The storage process is stopped when :

- the RAM memory is full
- telemetry is performed
- the stop simulation key is pressed

During the storage process, it is advisable to have the patient exercise (exercise test or daily exercise) to make the minute ventilation vary.

Once data have been stored, a programming simulation makes it possible to modify the basic rate, the maximum sensor-driven rate, the rate response slope number, acceleration and recovery. The simulated pacemaker response can subsequently be displayed with these new parameters.

When the simulated pacemaker response is satisfactory, the modified parameters can be directly programmed through the programmer.

Note: If automatic calibration is programmed and if a recalibration of the slope is necessary, it will be delayed until the end of the simulation procedure.

13.9 HOLTER FUNCTIONS

Holter functions are useful for assessing the performance of Opus RM during the patient's daily life. They can be used in conjunction with the statistics function. The large memory capacity of Opus RM allows the beat-to-beat monitoring of many events for a long period of time. Types of events and period of time are listed in the description that follows.

13.9.1 Histograms

Note : Histograms are operational only if they are programmed.

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- Description :

Three sets of histograms are available on Opus RM. Each set contains data for one type of event. Each set will have a number of individual histograms. Each individual histogram will have eight cells with programmable boundaries. As Opus RM collects interval data, it will analyze the interval to determine to which cell it belongs and increment the count for that cell. At the end of a programmed time period, it will begin collecting data for the next successive histogram. The number of individual histograms in the set depends on the length of the programmed time period. If the programmed time period is greater than or equal to 6 hours, a set can contain 14 individual histograms. If the programmed time period is less than 6 hours, a set can contain 30 individual histograms.

- Use

With the programmer, each set of histograms can be displayed in a table and each histogram can be displayed as a graph. Printouts of tables and/or graphs are easily obtained (refer to the programmer manual).

The programmable parameters are :

*** Type of events**

INT : Intervals between two successive paced or sensed events which recycle the pacemaker. This type of histogram can be used for diagnosis and monitoring of a patient's rhythm profile, hysteresis function.

PAUSE : Intervals between a sensed event recycling the pacemaker, and a paced event in the following cycle. This type of histogram can be used for monitoring rate smoothing, and the hysteresis function.

*** Boundaries :**

Seven programmable boundaries limit the eight cells of the histograms. They should be programmed in increasing order and chosen according to the other programmed settings such as the basic rate, upper rate limit and hysteresis.

*** Period :**

This parameter defines the surveillance duration for each histogram. It is programmable from 15 minutes to 1 month.

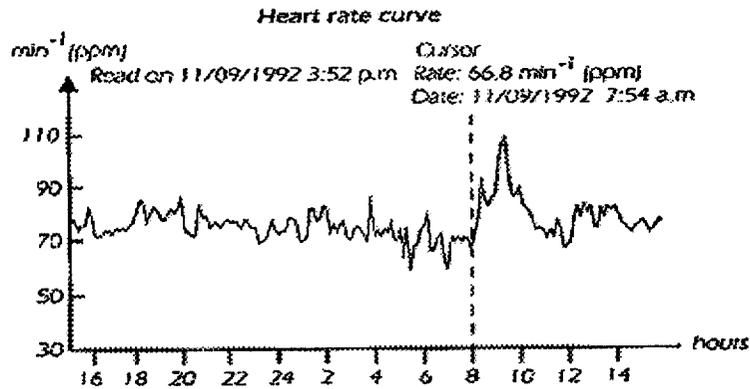
13.9.2 Mean heart rate curve

Note : The mean heart rate curve is operational only if it is programmed.

Description :

Opus RM is capable of recording heart rate variations over a 24-hour or 45-minute period. Opus RM averages the heart rate every 8.5 minutes for a 24-hour period and every 16 seconds for a 45-minute period. These results are displayed as a mean heart rate curve.

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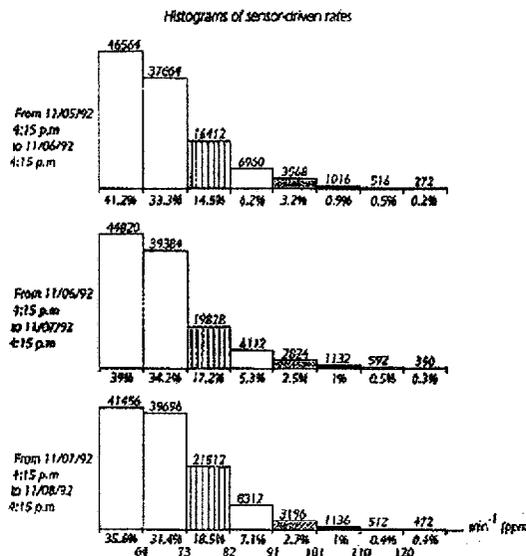
13.9.3 Histograms of the sensor-driven rate

Note : Histograms of the sensor-driven rate function, when the pacemaker is programmed to the RR rate responsive mode.

Description :

Opus RM is capable of recording rates calculated from minute ventilation for the last three days. It collects every rate calculated and records them in three successive histograms of 24 hours each : each histogram consists of eight cells whose limits are automatically set at the programmed basic rate and sensor-driven maximum rate. This makes it possible to display the pacemaker behavior in response to the patient's activity.

Use : Data can be displayed as a graph using the programmer. Data are automatically reset when rate response is programmed to RR, basic rate or maximum sensor-driven rate are changed.



Handwritten signature or initials.

13.9.4 Curves of calibration parameters

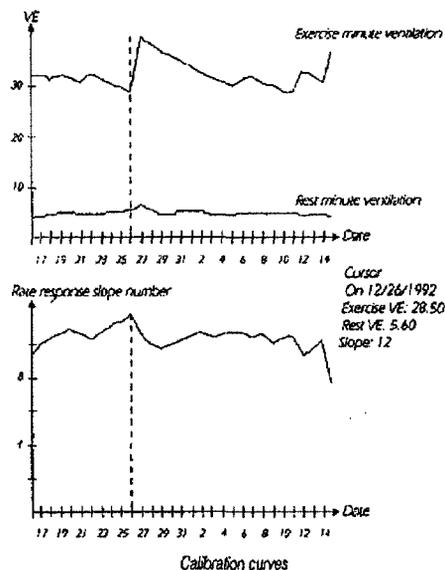
Note : The curves of calibration parameters start functioning as soon as calibration is programmed to AUTO.

Description :

Opus RM is capable of recording the resting and exercise minute ventilation values calculated during calibration. Opus RM calculates the mean values of resting and of exercise minute ventilation on a daily basis and stores the mean values for the last 30 days. The corresponding rate response slope number is calculated for each day that the calibration is programmed to Auto.

Use :

Data can be displayed as three curves corresponding to the resting minute ventilation, exercise minute ventilation, and rate response slope number. To obtain the exact values for a given day, the cursor must be placed on the corresponding day. The values located on the left correspond to those of the activation of the automatic calibration, if recording lasts less than 30 days and the values located on the right corresponds to the current values of resting and exercise VE. These curves are automatically reset when automatic calibration is programmed.



13.9.5 Battery depletion curve

Opus RM automatically measures the battery (cell) impedance and stores the data, which can then be displayed as a curve of the cell internal impedance versus time.

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APPENDIX 1 : PRINCIPLE OF RATE RESPONSE

The purpose of rate response is to adjust the pacing rate to the patient's activity level.

MINUTE VENTILATION AS THE INDICATOR

Minute ventilation is the product of respiratory rate and tidal volume. This physiological indicator closely reflects the metabolic demand during exercise. Minute ventilation is a 2nd order indicator [1]. Resting minute ventilation is approximately 6 l/min and can rise up to 60 l/min during severe exercise. It can even increase to 150 l/min in well-trained athletes during strenuous exercise. Minute ventilation correlates to oxygen consumption and heart rate [2]. Minute ventilation also rapidly increases at the onset of exercise [3].

[1] Rate responsive pacing : biosensor reliability and physiological sensitivity, P. Rossi, PACE, vol 10, 1987.

[2] Normal and abnormal heart rate response to exercise, H.K. Hammond and V.F Froehlicher, Progress in Cardiovascular diseases, Vol 27, No 4, 1985 : 271.

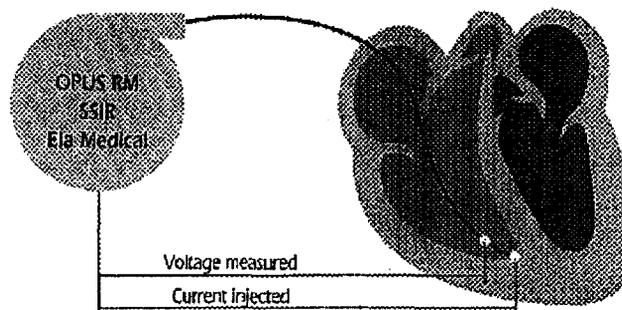
[3] Relationship between heart rate and minute ventilation, tidal volume and respiratory rate during brief and low level exercise, F. Vai, JL. Bonnet, P. Ritter, G. Pioger, PACE, Vol 11, 1988 : 1860

MINUTE VENTILATION SENSOR

Minute ventilation is determined by the measurement of transthoracic impedance. A linear relationship exists between the measured impedance and tidal volume.

A bipolar electrode is necessary for measuring minute ventilation. Low amplitude (400 μ amps) and short duration (15 μ seconds) output pulses are delivered at a 8 Hz frequency to the distal electrode. This probably would not be visible on an ECG. Impedance is measured between the proximal electrode of the lead and the pacemaker case (see figure shown below).

Note: Although measuring transthoracic impedance requires a bipolar lead, sensing and pacing polarities can be programmed either to unipolar or bipolar mode.



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Impedance increases with inhalation and decreases with exhalation. The signal measured is filtered to allow the detection of respiratory rates between 6 and 45 cycles per minute. The respiration period and amplitude are derived from the detected rates. Ventilation is calculated every respiratory cycle as a function of the Amplitude/Period ratio.

The sensor circuitry has a 3rd order low pass filter with a cut-off frequency of 45 min^{-1} . If the rate of the signal is higher, the signal will be attenuated by the filter.

The effect of this attenuation is to lower the effective respiration minute ventilation used by the pacemaker. Thus, above a respiration rate of 45 per minute, the pacemaker will use a lower effective respiration rate to calculate a minute ventilation value. This lower minute ventilation value will result in a lower rate responsive rate. The higher the respiration rate, the more attenuated the signal. The more attenuated the signal, the lower the effective respiration tidal volume value used to calculate minute ventilation. Thus, depending upon other factors including tidal volume, at some high respiration rate above 45 per minute, the rate responsive rate can equal the basic rate.

The behavior for rate response for high respiration rates is subject to the same constraints as for respiration rates below 45 per minute. The response will be smoothed since minute ventilation is averaged over four respiratory cycles and the change in rate responsive rate cannot be faster than the programmed acceleration and recovery values allow.

RATE RESPONSE : CALCULATION OF THE PACING RATE

Rate response is based on the linear relationship between minute ventilation and heart rate. Minute ventilation is calculated every respiratory cycle and an average is computed over four respiratory cycles. The sensor-driven rate is calculated every fourth, eighth or twelfth cycle from this average. This frequent calculation allows the pacemaker to respond rapidly to changes in the patient's activity. Different parameters (see Section on "Rate responsive Parameters") allow the appropriate adjustment of the pacemaker response according to the patient need.

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APPENDIX 2 : TECHNICAL SPECIFICATIONS

PHYSICAL CHARACTERISTICS

Dimensions	Height : 55 mm - Width : 52 mm - Thickness : 8 mm
Weight	43 grams
Volume	18.9 cc
Case coating	Medical grade silicone elastomer
Case material	99.9% pure titanium
Indifferent electrode	case : Surface : 12.5 cm ² Material : titanium shape : part of a disk

ELECTRICAL CHARACTERISTICS

Battery	Manufacturer	Wilson Greatbatch Limited
	Type	Lithium Iodine
	Model	WG 8077
	Usable capacity	BOL : 1.5 Ah ERI : 0.1 Ah
	Voltage	BOL : 2.8 V ERI : 2.45 V

Input impedance	unipolar : 15,000 Ohms bipolar : 17,000 Ohms
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Current drain at BOL (μ A)	5V	2.5V
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	Rate resp. OFF	Rate resp. ON	Rate resp. OFF	Rate resp. ON
Inhibited	16	21.5	16	20.5
SSI (100% pacing) (1)	26.5	32	18	23.5

Current drain at ERI (μ A)	5V	2.5V
---------------------------------	----	------

	Rate resp. OFF	Rate resp. ON	Rate resp. OFF	Rate resp. ON
Inhibited	15	19.5	15	19.5
SSI (100% pacing) (1)	24.5	29	17	21.5

(1) 70 min⁻¹ (bpm), 0.49 ms, 500 Ohms on each lead, 37 °C.

DESCRIPTION OF THE CIRCUIT

The electronic circuit of Opus RM combines custom integrated circuits with discrete capacitors, resistors and semi-conductors. The integrated circuits are electrically connected to the substrate with gold wire bonds. They are then hermetically sealed into the pacemaker case. A quartz crystal

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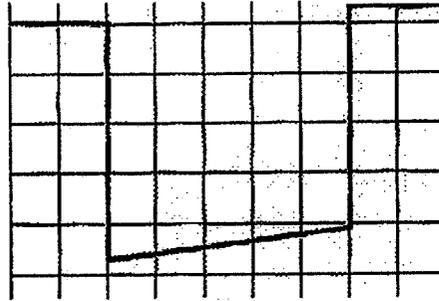
allows precise interval timing.

CHARACTERISTICS OF THE PACEMAKER OUTPUT PULSE

Shape of output pulse:

5 V amplitude, 0.49
500 Ohms load.

ms pulse width under



EFFECT OF TEMPERATURE

Opus RM 's electrical characteristics and parameter values do not vary significantly with temperature. Rate and period variations are less than 1% between 20°C and 43°C.

BIOCOMPATIBILITY

The two materials in contact with the patient are well known for biocompatibility. The case is 99.9% pure titanium. The pacemaker connector is made of medical grade silicone elastomer, a material commonly used in other implantable medical devices.

SPECIAL TESTS

Opus RM has been subjected to the specific tests of the EN NF 50061 standard, NFC 74346 classification :

- defibrillator discharge
- vibration
- mechanical shock

Opus RM's characteristics were not affected by these tests.

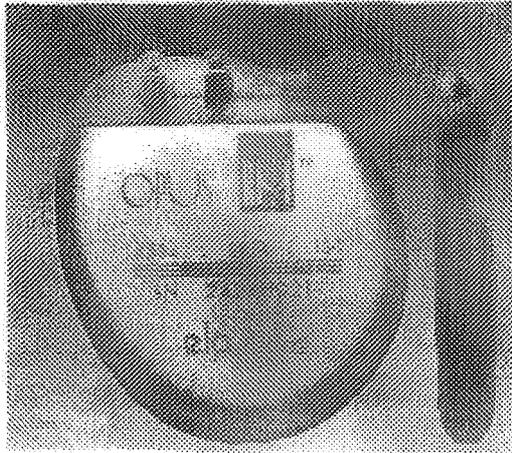
EXPLANTED PACEMAKERS

Except stated otherwise, all explanted pulse generators must be returned to ELA Medical

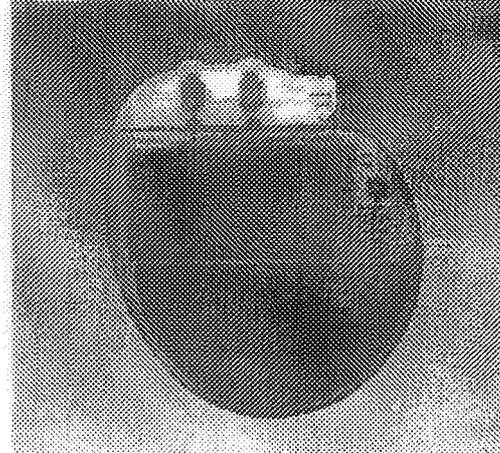
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thoroughly cleaned with all traces of contamination removed. The pulse generator should be cleaned using a solution of hypochlorite containing at least 1% chlorine and should be thoroughly rinsed with clear water. The generator should be returned to the address indicated by your distributor carefully packaged to protect it from mechanical shock and temperature variation.

PHOTOGRAPHIC IDENTIFICATION



X-RAY IDENTIFICATION



Handwritten signature or initials.

NONPROGRAMMABLE PARAMETERS

Parameters	Values	Tolerances
Rate limit	179 min ⁻¹ (bpm)	± 6 %
(BOL) magnet rate	96 min ⁻¹ (bpm)	± 3 %

PROGRAMMABLE PARAMETERS

This table lists the programmable parameters of Opus RM 4534. Ela Medical ships the pacemaker with the "as shipped" values shown below. When emergency SSI (nominal or "Nom") operation is programmed, the parameter values are those marked with an asterisk in the table (*).

Parameters	As shipped	Programmable values	Tolerances
Basic parameters			
Mode (1)	SSI	SSI*-SST-SOO	
Basic rate (2,3)	70min ⁻¹	40-45-50-55-60-65-70*-75-80-85-89-96	± 3%
Upper rate limit	120 min ⁻¹	101-110-120-132-142-154	± 3%
Hysteresis (%of rate)	0 %	0*-5-10-20	± 16 ms
Absolute refract. period	172 ms	141-156-172*-203-234-266-297-328-359	± 16 ms
Rate responsive parameters			
Rate responsive mode (4)	OFF	OFF*-RR	
Max.sensor-driven rate(5)	120	101-110-120-132-142-154 min ⁻¹	± 3%
Acceleration (6)	Slow	Slow-Fast	
Recovery (6)	Slow	Slow-Fast	
Slope number	1 to 15 (steps of 1)		
Calibration(4)	Fixed	Fixed-Auto	
Output pulse parameters			
Pulse amplitude (7,8)	5 V	1.5-2-2.5-3-3.5-4-5	± 15 %
Pulse width (9)	0.37 ms	0.12-0.24-0.37-0.49-0.61-0.73-0.85-0.98	± 0.05 ms
Sensitivity (10,11)	1 mV	0.7-1.0-1.2-1.5-1.8-2.0-2.2-2.5-2.7 3.0-3.5-4.0-4.5-5.0	± 0.4 mV ± 0.8 mV
Sensing polarity (12,13)	UNI	UNI-BI	
Pacing polarity (12,13)	UNI	UNI-BI	
Rate Smoothing(14,15)	OFF	ON-OFF*	

Note: the unit for rate is min-1 or bpm.

(1) Only SSI and SST modes may be used for rate responsive pacing (see section on rate responsive parameters)

(2) The corresponding basic periods and escape intervals (hysteresis =0) are the following :

1500-1333-1200-1091-1000-923-857-800-750-706-674-625 ms \pm 3 %

(3) Rates below 55 min⁻¹ (bpm) are not available in rate responsive mode

(4) Do not program the rate responsive function or the automatic calibration before implant; the sensor will be initialized and the resulting resting ventilation value will be erroneous. A bipolar atrial lead is required to program the rate responsive function or the automatic calibration.

(5) Only values less than or equal to the programmed upper rate limit rate can be programmed.

(6) For the acceleration, "Slow" corresponds to a 16 ms change in the escape interval every 8 cardiac cycles, and "Fast" to a 16 ms change in the escape interval every 4 cardiac cycles. For recovery, "Slow" corresponds to a 16 ms change in the escape interval every 12 cardiac cycles and "Fast" to a 16 ms change every 8 cardiac cycles.

(7) Measurement of the peak amplitude.

(8) Correspondance between the programmed amplitude and the mean value measured

Programmed pulse amplitude (V)	1.5	2.0	2.5	3.0	3.5	4.0	5.0
Mean value measured (V)	1.4	1.9	2.4	2.8	3.2	3.7	4.7
Tolerance (%)	10	10	10	10	10	10	10

(9) Measured at 1/3 of the maximum amplitude.

(10) Sensitivity is measured by injecting a negative triangular signal of 10 ms.

(11) Correspondance between the programmable sensitivity and measurements using an injected positive and negative triangular signal of 2/13 ms.

Prog. ventr. sens.(mV)	0.7	1.0	1.2	1.5	1.8	2.0	2.2	2.5	2.7	3.0	3.5	4.0	4.5	5.0
2/13 neg. triangle (mV)	0.6	0.9	1.1	1.4	1.7	1.8	2.0	2.2	2.4	2.7	3.2	3.6	4.0	4.5
Neg. tolérance (mV)	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.8	0.8	0.8	0.8	0.8
2/13 pos. triangle (mV)	1.3	1.8	2.1	2.7	3.2	3.6	3.9	4.5	4.9	5.4	6.3	7.2	8.1	9.0
Pos. tolérance (mV)	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	1.5	1.5	1.5	1.5	1.5

(12) The pacemaker cannot be programmed to bipolar configuration if the impedance of the bipolar lead is not satisfactory.

(13) Polarity is programmed independently of the rate response function.

(17) Do not program rate smoothing prior to implant. The pacemaker may sense noise and pace at a rate higher than the programmed basic rate but lower than the programmed upper rate limit.

(18) The acceleration slope is 31 ms/8 cycles, the deceleration slope is 94 ms/8 cycles.

TELEMETRY FUNCTIONS

Type	As shipped	Description	Tolerances
Administrative data		Magnet rate	
		Model, serial number	
		Patient's name and birth date	
		Indications for implant	
		Pacemaker implant date	
		Manufacturer, model, threshold, implant date of lead	

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Measured data	Lead impedance	20%
	Pulse amplitude	10%
	Pulse current	10%
	Pulse energy	30%
Sensor	Sensor re-initialization	
	Simulation	
Threshold tests		
- Threshold test rate	80 - 89 - 101* - 110 - 120 min ⁻¹	± 3%
Rate limit off		
Real time data transmission		
-Intracardiac ECG		
- Marker pulses	2 levels	

STATISTICS	Type	Max. recordable
- Programmings	Number of programmings	255
- Cardiac events	Paced, sensed	4.3 billion
- Cardiac activity	Total number of cardiac cycles (100%)	4.3 billion
- Spontaneous activity	Number and % of sensed cycles	4.3 billion
- RM paced cycles	Number and % of cycles paced at sensor driven rate	4.3 billion
- Exercise VE calibration	Number of exercise VE recalculations	255
- Resting VE calibration	Number of resting VE recalculations	255

HOLTER FUNCTIONS

Type	As shipped	Values
EVENT	HISTOGRAMS	Read - Reset
- Event type	STANDBY	INT- PAUSES- OFF
- Recording period	1 day	15 min - 1h - 3h - 6h - 12h - 1 day - 2 days - 1 week - 1mth
- Limits	406 to 906 ms	Programmable from 172 to 3000 ms(steps of 16 ms)

HISTOGRAMS OF SENSOR-DRIVEN RATES

MEAN HEART RATE CURVE

CURVE OF CALIBRATION PARAMETERS

BATTERY DEPLETION CURVE

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