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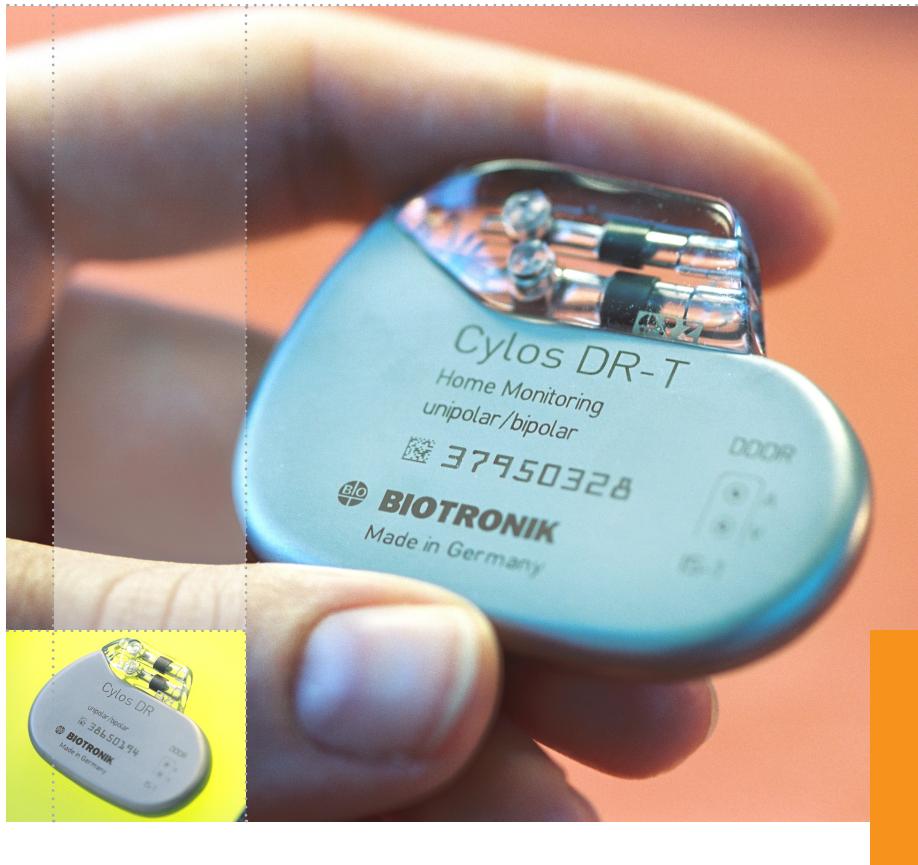
BIOTRONIK

Cylos Pulse Generators

Technical Manual



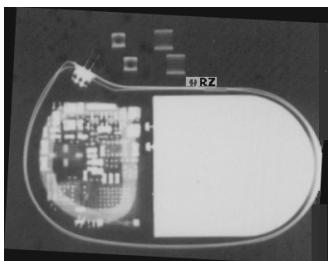
Cylos Family of Pulse Generators



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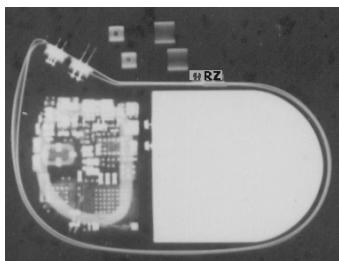
Cylos

Implantable Pulse Generators



Cylos DR

X-Ray identification



Cylos DR-T

X-Ray identification

Radiopaque Identification

A radiopaque identification code is visible on standard x-ray, and identifies the pulse generator:

Cylos DR, DR-T and VR



CAUTION

Because of the numerous available 3.2-mm configurations (e.g., the IS-1 and VS-1 standards), lead/pulse generator compatibility should be confirmed with the pulse generator and/or lead manufacturer prior to the implantation of a pacing system.

IS-1, wherever stated in this manual, refers to the international standard, whereby leads and generators from different manufacturers are assured a basic fit.

[Reference ISO 5841-3:1992(E)].

CAUTION

Federal (U.S.A.) law restricts this device to sale by or on the order of, a physician (or properly licensed practitioner).

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1. Device Description

Cylos is a multi-programmable, dual chamber pulse generator with rate-adaptive pacing. The Cylos family of pulse generators is BIOTRONIK's state of the art pacing system with two methods of rate-adaptation. Rate-adaptation is achieved through programming of either the unique principle of closed-loop stimulation (CLS) or by motion-based pacing via a capacitive accelerometer.

The basic function of CLS involves the translation of myocardial contractility into patient-specific pacing rates. Specifically, the pulse generator monitors and processes the intracardiac impedance signals associated with myocardial contraction dynamics. Changes in the waveform of this impedance signal are associated with changes in the contraction dynamics of the patient's heart due to the heart's inotropic response to exercise and acute mental stress. By monitoring these changes, the pulse generator can provide a pacing rate that is appropriate and specific to the patient's individual physiologic demands due to exercise and acute mental stress.

For standard motion-based rate-adaptation, the Cylos is equipped with an accelerometer located within the pulse generator. This sensor produces an electric signal during physical activity of the patient. If a rate-adaptive (R) mode is programmed, then the accelerometer sensor signal controls the stimulation rate.

Cylos also employs Home Monitoring™ technology, which is an automatic, wireless, remote monitoring system for management of patients with pulse generators. With Home Monitoring, physicians can review data about the patient's cardiac status and pulse generator's functionality between regular follow-up visits, allowing the physician to optimize the therapy process.

BIOTRONIK conducted the TRUST study to evaluate the safety and effectiveness of Home Monitoring. Refer to [Section 6.4](#) for details regarding the study design and results. With the TRUST study, BIOTRONIK was able to show the following with regards to Home Monitoring:

- BIOTRONIK Home Monitoring information may be used as a replacement for device interrogation during in-office follow-up visits.

- A strategy of care using BIOTRONIK Home Monitoring with office visits when needed has been shown to extend the time between routine, scheduled in-office follow-ups of BIOTRONIK implantable devices in many patients. Home Monitoring data is helpful in determining the need for additional in-office follow-up.
- BIOTRONIK Home Monitoring-patients—who are followed remotely with office visits when needed—have been shown to have similar numbers of strokes, invasive procedures and deaths as patients followed with conventional in-office follow ups.
- BIOTRONIK Home Monitoring provides early detection of arrhythmias.
- BIOTRONIK Home Monitoring provides early detection of silent, asymptomatic arrhythmias.
- Automatic early detection of arrhythmias and device system anomalies by BIOTRONIK Home Monitoring allows for earlier intervention than conventional in-office follow-ups.
- BIOTRONIK Home Monitoring allows for improved access to patient device data compared to conventional in-office follow ups since device interrogation is automatically scheduled at regular intervals.

The Cylos provides single and dual chamber pacing in a variety of rate-adaptive and non-rate adaptive pacing modes. Pacing capability is supported by a sophisticated diagnostic set.

The device is designed and recommended for use with atrial and ventricular unipolar or bipolar leads having IS-1 compatible connectors. (Note that IS-1 refers to the International Standard whereby leads and generators from different manufacturers are assured a basic fit [Reference ISO 5841-3:1992]) The pulse generator is powered by a lithium-iodine cell and is hermetically contained in a titanium case.

Cylos is designed to meet all indications for bradycardia therapy as exhibited in a wide variety of patients. The family is comprised of three pulse generators that are designed to handle a multitude of situations. The three pulse generators include:

Cylos DR	Dual chamber, rate-adaptive, unipolar/bipolar
Cylos VR	Single chamber (ventricle only), rate-adaptive, unipolar/bipolar
Cylos DR-T	Dual chamber, rate-adaptive, unipolar/bipolar, with Home Monitoring

Throughout this manual, specific feature and function descriptions may only be applicable to certain pulse generators of the Cylos family. If specified as dual chamber configurations, the descriptions are specifically referring to Cylos DR and Cylos DR-T. If specified as single chamber configurations, the descriptions are specifically referring to Cylos VR.

2. Indications

Rate-adaptive pacing with Cylos pulse generators is indicated for patients exhibiting chronotropic incompetence and who would benefit from increased pacing rates concurrent with physical activity.

Generally accepted indications for long-term cardiac pacing include, but are not limited to: sick sinus syndrome (i.e., bradycardia-tachycardia syndrome, sinus arrest, sinus bradycardia), sino-atrial (SA) block, second- and third-degree AV block, and carotid sinus syndrome.

Patients who demonstrate hemodynamic benefit through maintenance of AV synchrony should be considered for one of the dual chamber or atrial pacing modes. Dual chamber modes are specifically indicated for treatment of conduction disorders that require both restoration of rate and AV synchrony such as AV nodal disease, diminished cardiac output or congestive heart failure associated with conduction disturbances, and tachyarrhythmias that are suppressed by chronic pacing.

3. Contraindications

Use of Cylos pulse generators is contraindicated for the following patients:

- Unipolar pacing is contraindicated for patients with an implanted cardioverter-defibrillator (ICD) because it may cause unwanted delivery or inhibition of ICD therapy.
- Single chamber atrial pacing is contraindicated for patients with impaired AV nodal conduction.
- Dual chamber and single chamber atrial pacing is contraindicated for patients with chronic refractory atrial tachyarrhythmias.

For a complete discussion of mode-specific contraindications, please refer to [Appendix A](#) of this manual.

4. Warnings and Precautions

Certain therapeutic and diagnostic procedures may cause undetected damage to a pulse generator, resulting in malfunction or failure at a later time. Please note the following warnings and precautions:

Magnetic Resonance Imaging (MRI)—Avoid use of magnetic resonance imaging as it has been shown to cause movement of the pulse generator within the subcutaneous pocket and may cause pain and injury to the patient and damage to the pulse generator. If the procedure must be used, constant monitoring is recommended, including monitoring the peripheral pulse.

Rate-Adaptive Pacing—Use rate-adaptive pacing with care in patients unable to tolerate increased pacing rates.

High Output Settings—High output settings combined with extremely low lead impedance may reduce the life expectancy of the pulse generator to less than 1 year. Programming of pulse amplitudes, higher than 4.8 V, in combination with long pulse widths and/or high pacing rates may lead to premature activation of the replacement indicator.

4.1 Medical Therapy

Before applying one of the following procedures, a detailed analysis of the advantages and risks should be made. Cardiac activity during one of these procedures should be confirmed by continuous monitoring of peripheral pulse or blood pressure. Following the procedures, pulse generator function and stimulation threshold must be checked.

Therapeutic Diathermy Equipment—Use of therapeutic diathermy equipment is to be avoided for pacemaker patients due to possible heating effects of the pulse generator and at the implant site. If diathermy therapy must be used, it should not be applied in the immediate vicinity of the pulse generator/lead. The patient's peripheral pulse should be monitored continuously during the treatment.

Transcutaneous Electrical Nerve Stimulation (TENS)—Transcutaneous electrical nerve stimulation may interfere with pulse generator 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.

Defibrillation—The following precautions are recommended to minimize the inherent risk of pulse generator operation being adversely affected by defibrillation:

- The paddles should be placed anterior-posterior or along a line perpendicular to the axis formed by the pulse generator and the implanted lead.
- The energy setting should not be higher than required to achieve defibrillation.
- The distance between the paddles and the pacer/electrode(s) should not be less than 10 cm (4 inches).

Radiation—Pulse generator electronics may be damaged by exposure to radiation during radiotherapy. To minimize this risk when using such therapy, the pulse generator should be protected with local radiation shielding.

Lithotripsy—Lithotripsy treatment should be avoided for pacemaker patients since electrical and/or mechanical interference with the pulse generator is possible. If this procedure must be used, the greatest possible distance from the point of electrical and mechanical strain should be chosen in order to minimize a potential interference with the pulse generator.

Electrocautery—Electrocautery should never be performed within 15 cm (6 inches) of an implanted pulse generator or lead because of the danger of introducing fibrillatory currents into the heart and/or damaging the pulse generator. Pacing should be asynchronous and above the patient's intrinsic rate to prevent inhibition by interference signals generated by the cautery. When possible, a bipolar electrocautery system should be used.

For transurethral resection of the prostate, it is recommended that the cautery ground plate be placed under the buttocks or around the thigh, but not in the thoracic area where the current pathway could pass through or near the pacing system.

4.2 Storage and Sterilization

Storage (temperature)—Recommended storage temperature range is 5° to 55°C (41°-131°F). Exposure to temperatures outside this range may result in pulse generator malfunction (see [Section 10.1](#)).

Low Temperatures—Exposure to low temperatures (below 0°C) may cause a false elective replacement indication to be present. If this occurs, warm the device to room temperature and reset the ERI with magnet application (see [Section 10.1](#)).

Handling—Do not drop. If an unpackaged pulse generator is dropped onto a hard surface, return it to BIOTRONIK (see [Section 10.1](#)).

FOR SINGLE USE ONLY—Do not resterilize the pulse generator or accessories packaged with the pulse generator; they are intended for one-time use.

Device Packaging—Do not use the device if the packaging is wet, punctured, opened or damaged because the integrity of the sterile packaging may be compromised. Return the device to BIOTRONIK.

Storage (magnets)—Store the device in a clean area, away from magnets, kits containing magnets, and sources of electromagnetic interference (EMI) to avoid damage to the device.

Temperature Stabilization—Allow the device to reach room temperature before programming or implanting the device. Temperature extremes may affect the initial device function.

Use Before Date—Do not implant the device after the USE BEFORE DATE because the device may have reduced longevity.

4.3 Lead Connection and Evaluation

The pulse generator requires atrial and ventricular leads with IS-1 compatible connectors. There are no requirements specific to the atrial lead. It is required to use a low polarization ventricular lead for activation of Active Capture Control.

Active Capture Control—The Active Capture Control feature should be programmed OFF before lead connection. The feature is designed to measure thresholds and will automatically reprogram the ventricular pulse amplitude. In the absence of a connected lead, the feature will not be able to perform these measurements and set the output to an appropriate value.

Lead Check—Care should be taken when programming Cylos pulse generators with Lead Check ON as the device may switch from bipolar to unipolar pacing and sensing without warning. This situation may be inappropriate for patients with an Implantable Cardioverter Defibrillator (ICD). The following associated message appears when programming this feature: “Lead check may result in a switch to unipolar pacing and sensing, which may be inappropriate for patients with an ICD.”

Additionally, Lead Check should be programmed OFF before lead connection as the feature will automatically reprogram the device to unipolar in the absence of a lead.

Lead/pulse Generator Compatibility—Because of the numerous available 3.2-mm configurations (e.g., the IS-1 and VS-1 standards), lead/pulse generator compatibility should be confirmed with the pulse generator and/or lead manufacturer prior to the implantation of a pacing system.

IS-1, wherever stated in this manual, refers to the international standard, whereby leads and generators from different manufacturers are assured a basic fit. [Reference ISO 5841-3:1992(E)].

Lead Configuration—Lead configuration determines proper programming of the pulse generator. Pacing will not occur with a unipolar lead if the lead configuration is programmed to bipolar (see **Section 11**).

Setscrew Adjustment—**Back-off the setscrew(s)** prior to insertion of lead connector(s) as failure to do so may result in damage to the lead(s), and/or difficulty connecting lead(s).

Cross Threading Setscrew(s)—**To prevent cross threading** the setscrew(s), do not back the setscrew(s) completely out of the threaded hole. Leave the torque wrench in the slot of the setscrew(s) while the lead is inserted.

Tightening Setscrew(s)—**Do not overtighten** the setscrew(s). Use only the BIOTRONIK supplied torque wrench.

Sealing System—**Be sure to properly insert the torque wrench** into the perforation at an angle perpendicular to the connector receptacle. Failure to do so may result in damage to the plug and its self-sealing properties.

4.4 Programming and Operation

Negative AV delay Hysteresis—This feature insures ventricular pacing, a technique which has been used in patients with hypertrophic obstructive cardiomyopathy (HOCM) with normal AV conduction in order to replace intrinsic ventricular activation. No clinical study was conducted to evaluate this feature, and there is conflicting evidence regarding the potential benefit of ventricular pacing therapy for HOCM patients. In addition, there is evidence with other patient groups to suggest that inhibiting the intrinsic ventricular activation sequence by right ventricular pacing may impair hemodynamic function and/or survival.

Programming ACC—If the SQC/CTS sequence is not successful, program the ACC to OFF and program the pacing pulse amplitude manually.

NIPS—Life threatening ventricular arrhythmias can be induced by stimulation in the ventricle. Ensure that an external cardiac defibrillator is easily accessible. Only physicians trained and experienced in tachycardia induction and reversion protocols should use non-invasive programmed stimulation (NIPS).

Unipolar/Bipolar—All Cylos models can be used with either unipolar or bipolar IS-1 leads.

If the pacing or sensing function is to be programmed to **bipolar**, it must be verified that **bipolar leads** have been implanted in that chamber. If either of the leads is **unipolar**, **unipolar** sensing and pacing functions must be programmed in that chamber. Failure to program the appropriate lead configuration could result in entrance and/or exit block.

In addition, if the lead polarity setting within the Patient Data Memory has been set to **bipolar**, the polarity of the corresponding implanted lead(s) must be confirmed to be **bipolar**.

Programmers—Use only appropriate BIOTRONIK programmers equipped with appropriate software to program Cylos pulse generators. Do not use programmers from other manufacturers.

Pulse Amplitude—Programming of pulse amplitudes, higher than 4.8 V, in combination with long pulse widths and/or high pacing rates can lead to premature activation of the replacement indicator. If a pulse amplitude of 7.2 V or higher is programmed and high pacing rates are reached, output amplitudes may differ from programmed values.

Pacing Thresholds—When decreasing programmed output (pulse amplitude and/or pulse width), the pacing threshold must first be accurately assessed to provide a 2:1 safety margin. When using the Active Capture Control feature, the device will automatically set the output to the measured threshold plus the programmed Safety Margin. A new threshold search will occur at scheduled intervals or upon loss of capture.

EMI—Computerized systems are subject to EMI or “noise.” In the presence of such interference, telemetry communication may be interrupted and prevent programming.

Programming Modifications—Extreme programming changes should only be made after careful clinical assessment. Clinical judgment should be used when programming permanent pacing rates below 40 ppm or above 100 ppm.

Short Pacing Intervals—Use of short pacing intervals (high pacing rates) with long atrial and/or ventricular refractory periods may result in intermittent asynchronous pacing and, therefore, may be contraindicated in some patients.

OFF Mode—Use of the OFF mode should be avoided in pacemaker dependent patients. The OFF mode can be transmitted as a temporary program only to permit evaluation of the patient's spontaneous rhythm.

Myopotential Sensing—The filter characteristics of BIOTRONIK pulse generators have been optimized to sense electrical potentials generated by cardiac activity and to reduce the possibility of sensing skeletal myopotentials. However, the risk of pulse generator operation being affected by myopotentials cannot be eliminated, particularly in unipolar systems. Myopotentials may resemble cardiac activity, resulting in pulse generator pulse inhibition, triggering and/or emission of asynchronous pacing pulses, depending on the pacing mode and the interference pattern. Certain follow-up procedures, such as monitoring pulse generator performance while the patient is doing exercises involving the use of pectoral muscles, as well as Holter monitoring, have been recommended to check for interference caused by myopotentials. If sensing of myopotentials is encountered, corrective actions may include selection of a different pacing mode or sensitivity.

Muscle or Nerve Stimulation—Inappropriate muscle or nerve stimulation may occur with unipolar pacing when using a non-coated pulse generator.

Atrial Sensitivity—In dual chamber systems, the atrial sensitivity of 0.1 mV should only be programmed in conjunction with a bipolar lead configuration.

CLS Rate-Adaptation—Under certain circumstances (e.g., EMI, lead dislodgment), the Cylos device may not be able to obtain a useable impedance measurement as required for CLS rate-adaptive pacing. At this point, CLS rate-adaptation will be inactive until the situation is corrected. Rate-adaptation may be programmed to switch to motion based adaptation.

Programmed to Triggered Modes—When programmed to triggered modes, pacing rates up to the programmed upper limit may occur in the presence of either muscle or external interference.

Triggered Modes—While the triggered modes (DDT, DVT, DDTR/A, DDTR/V, DDI/T, VDT, VVT, and AAT) can be programmed permanently, the use of these modes is intended as a temporary setting in situations where maintaining the programming head in place would be impossible or impractical (i.e., during exercise testing or extended Holter monitoring) or as a short term solution to pulse generator inhibition by extracardiac interference. To avoid the potential for early battery depletion, it is important that the triggered modes are not used for long term therapy, and that the pulse generator is returned to a non-triggered permanent program.

4.5 Home Monitoring

BIOTRONIK's Home Monitoring system is designed to notify clinicians in less than 24 hours of changes to the patient's condition or status of the implanted device. Updated data may not be available if:

- The patient's CardioMessenger is off or damaged and is not able to connect to the Home Monitoring system through an active telephone link
- The CardioMessenger cannot establish a connection to the implanted device
- The telephone and/or Internet connection do not operate properly
- The Home Monitoring Service Center is off-line (upgrades are typically completed in less than 24 hours)

Patient's Ability—Use of the Home Monitoring system requires the patient and/or caregiver to follow the system instructions and cooperate fully when transmitting data.

If the patient cannot understand or follow the instructions because of physical or mental challenges, another adult who can follow the instructions will be necessary for proper transmission.

Electromagnetic Interference (EMI)—Precautions for EMI interference with the Cylos DR-T pulse generator are provided in [Section 4.6](#). Sources of EMI including cellular telephones, electronic article surveillance systems, and others are discussed therein.

Use in Cellular Phone Restricted Areas—The mobile patient device (transmitter/receiver) should not be utilized in areas where cellular phones are restricted or prohibited (i.e., commercial aircraft).

Patient-Activated Report—The magnet effect must be programmed “synchronous” if the [Patient Report] function is activated.

Magnet Effect—The magnet effect must be programmed “synchronous” if the attending physician enables the patient to transmit messages.

4.6 Electromagnetic Interference (EMI)

The operation of any implanted pulse generator may be affected by certain environmental sources generating signals that resemble cardiac activity. This may result in pulse generator pulse inhibition and/or triggering or in asynchronous pacing depending on the pacing mode and the interference pattern. In some cases (i.e., diagnostic or therapeutic medical procedures), the interference sources may couple sufficient energy into a pacing system to damage the pulse generator and/or cardiac tissue adjacent to the electrodes.

BIOTRONIK pulse generators have been designed to significantly reduce susceptibility to electromagnetic interference (EMI). However, due to the variety and complexity of sources creating interference, there is no absolute protection against EMI. Generally, it is assumed that EMI produces only minor effects, if any, in pacemaker patients. If the patient presumably will be exposed to one of the following environmental conditions, then the patient should be given the appropriate warnings.

4.6.1 Home and Occupational Environments

The following equipment (and similar devices) may affect normal pulse generator operation: electric arc welders, electric melting furnaces, radio/television and radar transmitters, power-generating facilities, high-voltage transmission lines, electrical ignition systems (also of gasoline-powered devices) if protective hoods, shrouds, etc., are removed, electrical tools, anti-theft devices of shopping centers and electrical appliances, if not in proper condition or not correctly grounded and encased.

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

High Voltage Power Transmission Lines—High voltage power transmission lines may generate enough EMI to interfere with pulse generator operation if approached too closely.

Home Appliances—Home appliances normally do not affect pulse generator operation if the appliances are in proper condition and correctly grounded and encased. There are reports of pulse generator disturbances caused by electrical tools and by electric razors that have touched the skin directly over the pulse generator.

Communication Equipment—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—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.

Electrical Appliances—Electric hand-tools and electric razors (used directly over the skin of the pulse generator) have been reported to cause pulse generator disturbances. Home appliances that are in good working order and properly grounded do not usually produce enough EMI to interfere with pulse generator operation.

Electronic Article Surveillance (EAS)—Equipment such as retail theft prevention systems may interact with the pulse generators. Patients should be advised to walk directly through and not to remain near an EAS system longer than necessary.

4.6.2 Cellular Phones

Recent studies have indicated there may be a potential interaction between cellular phones and pulse generator 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 when the phone is within close proximity (within 6 inches [15 centimeters]) to the pulse generator.

Based on testing to date, effects resulting from an interaction between cellular phones and the implanted pulse generators 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 pulse generator 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 over or 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). Store the phone in a location opposite the side of implant.

4.6.3 Hospital and Medical Environments

Electrosurgical Cautery—Electrosurgical cautery could induce ventricular arrhythmias and/or fibrillation, or may cause asynchronous or inhibited pulse generator operation. If use of electrocautery is necessary, the current path (ground plate) should be kept as far away from the pulse generator and leads as possible.

Lithotripsy—Lithotripsy may damage the pulse generator. If lithotripsy must be used, do not focus the beam near the pulse generator.

External Defibrillation—External defibrillation may damage the pulse generator. Attempt to minimize current flowing through the pulse generator and lead system by following the precautions.

High Radiation Sources—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.

4.7 Pulse Generator Explant and Disposal

Device Incineration—Never incinerate a pulse generator. Be sure the pulse generator is explanted before a patient who has died is cremated. (see [Section 14](#))

Explanted Devices—Return all explanted devices to BIOTRONIK.

5. Adverse Events

NOTE:

The Cylos family of pulse generators is a successor to the BIOTRONIK's Dromos, Philos, Inos and Protos families of pulse generators. Therefore, data from the clinical studies of these earlier generations are used to support the safety and efficacy of the Cylos family of pulse generators.

5.1 Observed Adverse Events

5.1.1 Dromos DR Clinical Study

The Dromos DR Clinical Study involved 273 patients with cumulative implant duration of 1418 months (mean implant duration 5.2 months). Eleven patients died during the course of the trial; none of the deaths was judged to be device-related. One Dromos DR pulse generator was explanted during the trial, secondary to infection.

Table 1 reports the adverse events (AE) on a per patient and a per patient-month basis. The last column gives the expected time (in months) between events; i.e., the reciprocal of the AE/patient-month rate.

Table 1: Adverse Events Reported in > 1 Patient

Category	# pts (n=273)	% of pts	# of AEs	AE/pt-mo (n=1418)	Pt-mos between AEs
Observations [†] (total)	79*	28.9%	86	0.0606	16
Atrial Loss of Sensing	10	3.7%	10	0.0071	142
Atrial Loss of Capture	8	2.9%	8	0.0056	177
Pacemaker Mediated Tachycardia	11	4.0%	12	0.0085	118
Premature AV Stimulation	4	1.5%	4	0.0028	355
Arrhythmias	34	12.5%	36	0.0254	39
Muscle/Diaphragmatic Stimulation	3	1.1%	3	0.0021	473
Unexplained Syncope	3	1.1%	3	0.0021	473
Complications [‡] (total)	14*	5.1%	14	0.0099	101
Atrial Lead Dislodgment	6	2.2%	6	0.0042	236
Ventricular Lead Dislodgment	4	1.5%	4	0.0028	355

All Dromos DR Patients (N=273), Number and % of Patients, Events/Patient Mo., and Pt-Mos. between Events

The Dromos SR Clinical Study involved 91 patients with a cumulative implant duration of 327 months (mean implant duration 3.6 months). Three patients died during the course of the trial; none of the deaths was judged to be device-related. During this clinical study, there were 3 ventricular lead dislodgments requiring invasive lead repositioning resulting in 0.0092 AE/patient-month and a mean patient-month between adverse events of 109. There were 2 observations having only one occurrence each.

* Not included in the table are 6 observations and 4 complications each having only one occurrence.

** Observations are adverse events, which are correctable by non-invasive measures, e.g., reprogramming.

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

NOTE:

The Dromos family of pulse generators is an earlier generation of BIOTRONIK devices. The Cylos family of pulse generators is based upon the Dromos pulse generators.

5.1.2 PACC Clinical Study

The multi-center Philos DR ACC Clinical Study involved 152 devices in 151 patients with a cumulative implant duration of 764.1 months (average implant duration of 5.1 ± 0.3 months). A total of 109 patients had an implant duration of greater than 90 days.

There were two patient deaths reported. Both deaths were not pacemaker-related. Two pulse generators were explanted. One explant was due to a pocket infection and the second explant was due to infection and sepsis. The second patient was subsequently implanted with another Philos DR ACC device.

Table 2 provides a summary of adverse events that were reported during the clinical study regardless of whether or not the events were related to the pacemaker system. A complication was defined as a clinical event that resulted in additional invasive intervention. An observation was defined as a clinical event that did not result in additional invasive intervention. Note that the number of patients and events in each individual category are not mutually exclusive; certain patients may have had more than one event reported within a category.

Table 2: Adverse Events

Category	# of Patients with AEs	% of Patients with AEs	# of AEs	AEs / pt-yr
Complications - Total	14	9.3%	16	0.25
Lead Repositioning	11	7.3%	12	0.19
Medical	3	2.0%	4	0.06
Device-Related Events	0	0.0%	0	0.00
Observations - Total	42	27.8%	54	0.85
Sensing & Pacing	17	11.3%	20	0.31
Holter Evaluation	15	9.9%	15	0.23
Medical	11	7.3%	12	0.19
Arrhythmias	4	2.6%	4	0.06
B-KAC.V.U Software	3	2.0%	3	0.05

Number of Patients=151, Number of Patient-Years=63.7

5.1.3 Inos²⁺ CLS Clinical Study

The adverse events reported below are from the Inos²⁺ CLS clinical study which investigated the principle of Closed Loop Stimulation (CLS) and its regulation of heart rate. Additionally, the Protos AxVx Clinical Evaluation study investigated the safety and effectiveness of the AxVx algorithm in patients with a high percentage of ventricular sensing (80% or more).

NOTE:

The Inos and Protos families of pulse generators are earlier generations of BIOTRONIK devices. The CLS portion of the Cylos family of pulse generators is based upon the Inos and Protos pulse generators.

The Inos Clinical Study involved 130 devices implanted in 129 patients with cumulative implant duration of over 1600 months (mean implant duration 12.4 months).

There were a total of 15 deaths during the course of the trial; none of which was judged by the clinical study investigators to be device related. Two devices were explanted during the trial. One device was explanted secondary to pocket erosion. The patient was subsequently implanted with another Inos device. The other device was explanted because the patient needed ICD therapy.

Table 3 provides a summary of adverse events that were reported during the clinical study regardless of whether or not the event was related to the pacemaker system. A complication was defined as a clinical event that resulted in additional invasive intervention. An observation was defined as a clinical event that did not result in additional invasive intervention.

Table 3: Reported Adverse Events

Category	# of Patients with AEs	% of Patients with AEs	# of AEs	AEs/ pt-yrs
Complications Total	13	10.08%	15	0.11
Lead repositioning	10	7.75%	11	0.08
Medical	4	3.10%	4	0.03

The Protos AxVx Clinical Evaluation study involved 21 patients. There were no complications during the course of the study.

5.2 Potential Adverse Events

The following possible adverse events may occur with this type of device based on implant experience including:

- Cardiac tamponade
- Air embolism
- Infection
- Lead dislodgment
- Body rejection phenomena
- Elevated pacing thresholds
- Myopotential sensing
- Pulse generator migration
- Cardiac perforation
- Pocket erosion
- Lead fracture/insulation damage
- Lead-related thrombosis
- Muscle or nerve stimulation
- Pocket hematoma
- Local tissue reaction/fibrotic tissue formation
- Pacemaker-mediated tachycardia (dual chamber modes only)
- Undersensing of intrinsic signals

6. Clinical Study

6.1 Dromos DR

Primary Objectives

To evaluate the safety and effectiveness of the Dromos DR pulse generator and the utility of the DDDR pacing mode in patients with chronotropic incompetence (CI) in a crossover, double-blind trial. CI was defined as the inability to achieve a heart rate of a) 60% of their age predicted maximum (220-age), or b) 100 bpm.

Patients, Methods and Results

A total of 273 patients were implanted with the Dromos DR pulse generator between July 21, 1995 and July 31, 1996, at 34 investigational centers (32 in the US, 1 France, and 1 Mexico). Mean patient age was 71 years with a range of 31 to 95, and 145 of 273 (53%) were male. Pre-implantation clinical symptomatology was: bradycardia in 44% of the patients, dizziness in 31%, syncope in 25%, ECG indications were: Sick Sinus Syndrome in 46%, heart block in 40%, and atrial fibrillation/atrial flutter in 13% of the patients. The mean implant duration was 5.2 months (range = 0 to 16 months) with a total implant experience of 1418 months. At the one-month follow-up, 212 patients (91%) were programmed to a rate-adaptive mode according to the sensor parameter optimization procedure. Of the 63 patients completing a DDD exercise test (CAEP protocol) at one-month, 25 were found to be CI, and 21 completed the paired exercise testing at six-weeks. Patients performed the exercise tests, including metabolic measurements, in both the DDD and DDDR modes in randomized order.

Table 4: Dromos DR Metabolic Exercise Testing at 6 Weeks

Endpoints	DDDR Mode	DDD Mode	Difference (CI)
Maximum VO ₂ (mL/kg/minute)	20.4 ± 8.0	17.8 ± 6.2	2.67* ± 2.77 [1.5, 3.8]
VO ₂ @ AT (mL/kg/minute)	14.6 ± 3.6	13.1 ± 4.0	1.5* ± 2.71 [0.33, 2.6]
Total exercise time (minutes)	9.2 ± 3.0	8.2 ± 3.3	0.92* ± 1.08 [0.45,1.4]
Exercise time to AT (minutes)	6.3 ± 2.4	5.7 ± 2.8	0.69* ± 1.43 [0.04, 1.3]
Heart rate @AT (bpm)	113 ± 16	84 ± 16.5	29* ± 18 [21,37]

All chronotropically incompetent patients tested; n = 21, Mean ± SD and [95% confidence interval]; 95% confidence interval = mean difference ± 1.96 SEM

There were no pulse generator-related deaths or unusual rates of observations or complications (see [Section 5](#), Adverse Events).

Conclusions

No unusual safety concerns were raised by the results of the clinical study. The accelerometer-based motion sensor provided the patients with appropriate rate-adaptation when programmed according to the sensor parameter optimization procedure. Additionally, the DDDR mode provided statistically significant improvement in metabolic measures during paired exercise testing of CI patients at 6 weeks.

6.2 Active Capture Control

The clinical study involved 151 patients, of which 72 were male (47.7%) and 79 were female (52.3%) with a mean age of 72 years (range: 30-93 years). The majority of patients presented with an abnormal sinoatrial node (85%) and an abnormal conduction system (57%) at implant.

* Difference statistically significant, p<0.05 by paired t-test

6.2.1 Primary Objectives

The multi-center, non-randomized clinical investigation was designed to demonstrate the safety and effectiveness of the Philos DR Active Capture Control pulse generator in patients with standard pacemaker indications. The specific predefined objectives of the investigation included 3 primary endpoints.

1. Appropriate ACC Performance - Safety
2. ACC Algorithm Performance - Effectiveness
3. ACC Threshold Comparison - Effectiveness

6.2.2 Methods

The prospective, multi-center, controlled Philos DR ACC Clinical Study involved 151 patients with a cumulative implant duration of 764.1 months (average implant duration of 5.1 ± 0.3 months). The investigation was conducted at 14 centers.

The patients selected for participation were from the investigator's general patient population meeting the indications for use of the Philos DR ACC pulse generator. The average patient was a 72 year-old female, with indications for a pacemaker of Sinus Bradycardia.

Each patient was followed at hospital discharge and at one, three and six month post-implant and every 6 months thereafter. 24 hour Holter recordings were performed at the one month follow-up.

6.2.3 Results

The cumulative implant duration was 761.4 months with an average implant duration of 5.1 ± 0.3 months. A total of 109 patients had an implant duration of greater than 90 days as of November 29, 2002. The patient follow-up compliance rate was 99.6% out of 549 required follow-ups.

Table 5 provides an overview of the results of the study group for the predefined endpoints.

Table 5: Clinical Study Results

Description	Result
Safety: ventricular capture success rate	100% (104/104) [Lower CI = 97.2%]
Efficacy: pauses observed during 24 hour Holter	0% [0/3189 non captures] [Upper CI = 0.1%]
Efficacy: ACC threshold comparison to manual threshold	N=140 Mean difference \pm Stdev = 0.06 ± 0.03 volts

Appropriate ACC Performance - Safety

The objective was to evaluate the chronic safety of the ACC feature through an analysis of the rate of loss of capture caused by inappropriate functioning of the ACC feature at all scheduled follow-ups for patients with a 90 day implant duration.

There were 104 patients with an implant duration of greater than 90 days who had an evaluable ECG tracing demonstrating 100% ventricular pacing with appropriate ventricular capture. The exact 95% lower confidence interval (one-sided) for the rates of successful ventricular capture exceeded 95% from pre-discharge through > 3-month follow-up visits and the overall per patient success rate. There were an additional 33 patients that had less than 90-days implant duration that demonstrated a 100% ventricular capture success rate. In total, 137 patients, regardless of implant duration, demonstrated a 100% ventricular capture success rate.

The data clearly demonstrates the ACC algorithm performs safely when activated.

ACC Algorithm Performance - Effectiveness

The objective was to evaluate the effectiveness of the ACC feature through an analysis of the number of pauses during 24-hour Holter recordings. A pause is defined as a ventricular rate interval longer than the previous rate interval plus 400 ms in the normal tracking mode. The two types of pauses are defined as:

- Case 5 - Ventricular pacing with loss of capture that is not recognized by the algorithm

- Case 6 - Ventricular pacing with loss of capture and delivery of back-up pacing with loss of capture but with no escape beat within 400 ms of the initial ventricular pacing pulse

The ACC feature demonstrated efficacy as evidenced by the absence of documented case 5 or 6 pauses in 41 Holter recordings. For every loss of capture recorded by the Holters, the ACC algorithm recognized the loss of capture and delivered an appropriate back-up pulse. A total of 3189 non-captured events were documented on the Holter recordings and analyzed on a beat-to-beat basis. The Holter recordings documented that 3189 back-up pulses were delivered appropriately by the Philos DR ACC in response to the non-capture events. With 41 evaluable Holter recordings, there were 82.5% ventricular paced events, demonstrating an adequate sample of paced events to provide the necessary analysis of the ACC feature. Overall, the percentage of Case 5 or 6 pauses was 0.0%, with an exact lower confidence interval of 0.1%, which supports the effectiveness of the ACC algorithm.

The 24 hour Holter recordings clearly demonstrate the effectiveness of the ACC feature to recognize loss of capture and provide safety back-up pulses with ventricular capture.

ACC Threshold Comparison - Effectiveness

The objective was to evaluate the effectiveness of the ACC feature by comparing the ACC threshold with the manual threshold measurement.

The ACC feature provided an absolute mean difference between the ACC threshold and the manual threshold of 0.10 volt in 382 paired evaluations within 140 patients.

A total of 87.1% (122/140) of the patients enrolled in the PACC study had individual average absolute differences between manual and ACC thresholds of 0.2 volts or less. There were 18 of the 140 patients (13%) that had an average difference higher than 0.2 volts. Of these 18 patients, 16 patients had average absolute differences between 0.22 and 0.67 volts, one patient had an average absolute difference of 1.4 volts and one patient had a single reading difference of 3.3 volts.

Out of a total number of 382 paired evaluations, 42 (11%) had threshold differences that were higher than 0.2 volts. In 4 patients, a threshold difference of 2.0 volts or more was observed between the manual and ACC pacing thresholds at a single follow-up. One discrepancy occurred at implant and three others occurred at pre-discharge follow-up (within 2 days of implant). All subsequent follow-ups (after lead maturation) for these four patients showed a difference of less than 0.5 volts between

the ACC and manual pacing threshold. All differences of 0.5 volts or higher were recorded at instances where the ACC threshold was higher than the manual threshold. There is little risk of non-capture or safety concerns because the ACC programmed output would be set to the ACC threshold plus the safety margin (0.5V), providing a much higher effective safety margin. Also, it is important to note that 96.4 % of the patients enrolled in the PACC study had an absolute difference lower than the actual 0.5 volt safety margin. There were no ACC thresholds more than 0.4 volts lower than the manual threshold. Therefore, the use of a nominal safety margin of 0.5 volts is adequate to provide patient safety.

Figure 1 below provides a distribution of the mean absolute differences per patient.

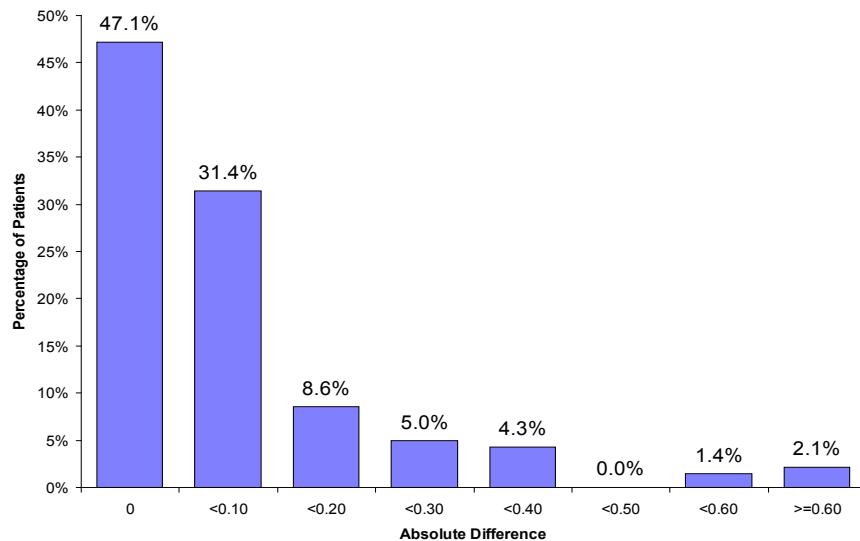


Figure 1. Absolute Ventricular Threshold Comparison

To further outline the threshold comparison trends, the mean threshold difference was 0.06 volts in 382 paired evaluations within 140 patients. The mean absolute threshold comparison yielded a slightly larger difference than mean difference.

It is concluded that the automatic ventricular pacing threshold is equivalent within 0.2 volts to the manual determination. The threshold measurement analysis clearly demonstrates the ACC algorithm is able to accurately perform threshold measurements in both acute and chronic conditions.

Additional Results

The study evaluated the evolution of the successful activation of the ACC feature at the scheduled follow-ups.

Figure 2 provides a comparison of the ACC activation rates at the pre-discharge and three-month follow-ups. The reasons for failed ACC activation are non-capture or high polarization artifact.

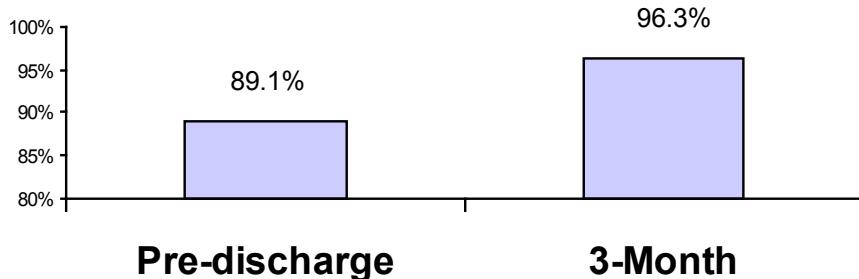


Figure 2. ACC Activation Rates

During the one-month follow-up, the ACC algorithm was tested to determine the highest maximum ACC amplitude setting (from 2.4V to 6.4V) for which ACC can be successfully activated. **Table 6** provides the distribution of the highest maximum ACC amplitudes successfully activated at the one-month follow-up visit. A high percentage (88.9%) of patients can be safely programmed at or above 4.8V where ACC remains activated.

Table 6: Highest Maximum ACC Amplitude Setting

Testing of Maximum ACC Amplitude	Result
Number of tests completed	99
Highest Functional Maximum ACC Amplitude	
2.4 Volts	4 (4.0%)
3.6 Volts	7 (7.1%)
4.8 Volts	15 (15.2%)
6.4 Volts	73 (73.7%)

6.2.4 Clinical Study Conclusions

The clinical data support the following conclusions regarding the safety and efficacy of the ACC feature.

The Philos DR ACC Pacing System is safe and effective for use in patients that are indicated for pacing therapy. The Philos DR ACC Clinical Study fulfilled the predefined primary safety and efficacy endpoints. These endpoints included safety and effectiveness of the ACC feature.

The gender distribution in this clinical investigation is consistent with other clinical studies and includes a representative proportion of female participants. There were also no significant differences found between high and low volume implant centers in either the safety or effectiveness endpoints.

In accordance with the above conclusions, the clinical data provides assurance that the ACC feature is safe and effective for the treatment of conditions requiring chronic cardiac pacing as specified in Section 2, Indications for Use.

6.3 Closed Loop Stimulation (CLS)

Three clinical studies were utilized to support the safety and effectiveness determination of the CLS portion of the Cylos family of pulse generators:

1. The Protos DR/CLS ER study provides information on the response of CLS to acute mental stress ([Section 6.3.1](#)).
2. The Protos DR/CLS AxVx study provides information on the response of CLS to physical activity using the most current version of CLS rate-adaptation ([Section 6.3.2](#)).
3. The Inos family of pulse generators is an earlier generation of BIOTRONIK devices. The CLS AxVp portion of the Protos family of pulse generators is based upon a study of the Inos pulse generators that focused on response to physical activity ([Section 6.3.3](#)).

6.3.1 Protos DR/CLS Response to Mental Stress

6.3.1.1 Primary Objectives

Demonstrate that CLS exhibits an appropriate heart rate response to acute mental stress. This hypothesis was based on administration of the ER Test© which was designed to elicit an increase in heart rate by means other than physical activity.

6.3.1.2 Methods

Overview

Prospective, single arm acute study prospectively assessing the heart rate response of chronotropic incompetent patients implanted with Protos DR/CLS pacemakers while being challenged with emotional stress such as during the ER Test©.

The primary objective of this study was to compare each patient's own heart rate response during emotional stresses evoked by the ER Test© in both the CLS and Accelerometer rate responsive modes. The comparison used each patient as their own control, and the heart rate response was measured as the difference between the maximum heart rate recorded during the ER Test© and the resting heart rate.

Procedure

This study was accomplished by having the patient view a computer slide show presentation. The first part of the presentation was aimed at relaxation to obtain a resting baseline for the patient's heart rate. The second half of the presentation was to challenge the patient by asking questions regarding colors / word association and mathematical equations.

For the color word test (CWT) portion, the patient viewed slides with a color word (e.g. PURPLE) with the corresponding letters in the same color. The patient was asked to write down what color they saw. As this portion of the test progressed, the color of the letters may or may not match the verbal description (i.e., the word PURPLE may appear with red letters) and the time allowed for each response decreased. The intent was to cause intellectual or emotional ambivalence as to what color they were actually seeing and thus potentially elicit an increase in heart rate.

The arithmetic challenge testing (ART) portion was similar to the CWT in that the patient was asked to write down an answer to simple math equations that became increasingly difficult while allowing the patient less time to respond. Again, the goal was to elicit an increase in heart rate.

6.3.1.3 Results

Primary Endpoint: Effectiveness of the CLS Algorithm during Emotional Stressors

H_0 : The average observed sensor driven peak heart rate during emotional stress testing does not significantly exceed the average observed resting heart rate for the tested patient population.

H_a : The average observed sensor driven peak heart rate during emotional stress testing significantly exceeds the average observed resting heart rate for the tested patient population.

As shown in **Figure 3**, for these 40 subjects, the average heart rate increased from 64.27 ± 4.8 bpm to 71.26 ± 5.4 bpm when the pacemaker was programmed to an accelerometer pacing mode during the ER Test[©]. For the same test, the average heart rate increased from 65.24 ± 4.0 bpm to 83.90 ± 7.5 bpm when the pacemaker was programmed to the CLS pacing mode.

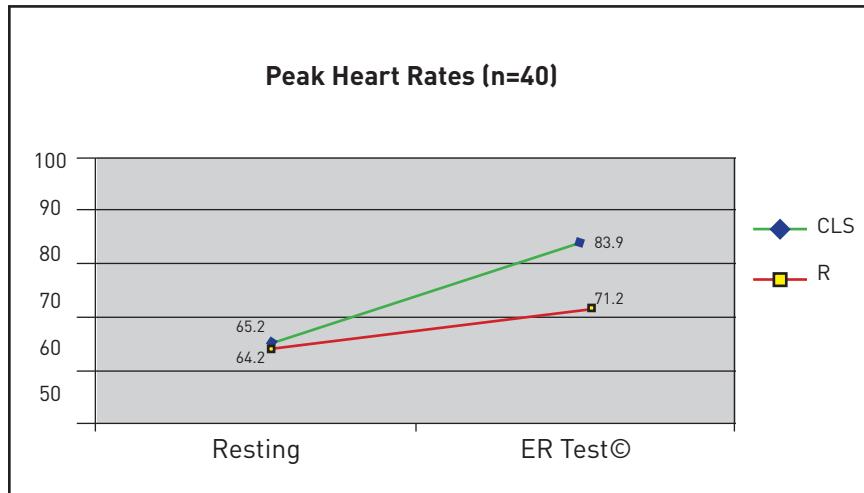


Figure 3: Average Heart Rates at Baseline and during ER Test©

The increase in heart rate in CLS mode was 18.65 ± 5.77 bpm compared to 6.99 ± 3.22 bpm in the accelerometer mode. Using the paired Student's t-test, the p value was less than 0.001. The null hypothesis was rejected.

6.3.1.4 Summary and Conclusions

- A total of 74 patients were enrolled at 16 medical centers.
- The study analysis included forty (40) of those 74 patients who met the predefined criteria of at least 80% sensor driven heart rates during the ER Test©.
- During the ER Test©, the average sensor driven heart rate increase for CLS mode was 18.65 ± 5.77 bpm versus 6.99 ± 3.22 bpm while in accelerometer mode, $p < 0.001$.
- The mean heart rate increase from baseline associated with the ER Test© for age group 40-60 years was 16.14 ± 1.15 bpm and the age group 60+ years was 18.79 ± 5.89 bpm. The rate response provided by CLS is consistent with those age matched healthy subjects in the literature.
- CLS demonstrated an appropriate response to myocardial contractility changes due to acute mental stress.
- All 40 patients (100%) showed a higher peak heart rate in the CLS pacing mode compared to the accelerometer pacing mode.
- In conclusion, BIOTRONIK has shown the effectiveness of the Protos DR/CLS pacemaker for providing appropriate rate response as tested during an acute mental stress test, the ER Test©, for patients exhibiting a high percentage of sensor-driven pacing.

6.3.2 Protos DR/CLS with AxVx

6.3.2.1 Primary Objectives

The clinical study included evaluation of the safety and effectiveness of the device in patients with a high percentage of ventricular sensing (80% or more) to demonstrate that the AxVx version of CLS functions appropriately for this type of patients.

Effectiveness

The analysis was based on the simple linear regression ($y = m + ax$) of the obtained rate-adaptive pacing rate versus the expected heart rate during a CAEP treadmill test with the device in patients with a high percentage of ventricular sensing (80% or more).

Safety

This endpoint was based on the analysis of adverse events (complications and observations) caused by the Protos CLS devices during this acute study.

6.3.2.2 Methods

A total of 21 patients with previously implanted legally marketed Protos DR/CLS pulse generators were enrolled in a controlled, prospective study. The investigation was conducted at 5 centers. The average patient was a 70 year-old male, with sinus bradycardia.

During a follow-up visit, the pacemakers were downloaded with the AxVx investigational software. At a second follow-up, the patient performed a symptom limited CAEP treadmill test. Following the treadmill testing with the investigational AxVx algorithm, the pacemaker was downloaded with legally marketed AxVp software for routine follow-up care.

6.3.2.3 Results

Effectiveness

A total of 13 treadmills were included for the analysis of the rate response slope. The mean rate response slope during the CAEP treadmill test was 0.66 with standard deviation of 0.23 and a 95% confidence interval of [0.52, 0.80].

The number and percentages of patients who met the predefined performance criteria are presented in [Table 7](#).

Table 7: Percentages of Patients Meeting Success Criteria

Criteria	% Patients
Slope > 0.650	53.8% (7/13)
Within 20 bpm of MCLR*	69.2% (9/13)
Achieved MCLR	46.2% (6/13)

[Figure 4](#) shows the obtained heart rate versus the expected heart rate during the CAEP treadmill test for all patients completing at least 3 stages of exercise ($n = 13$).

* MCLR = Maximum Closed Loop Rate

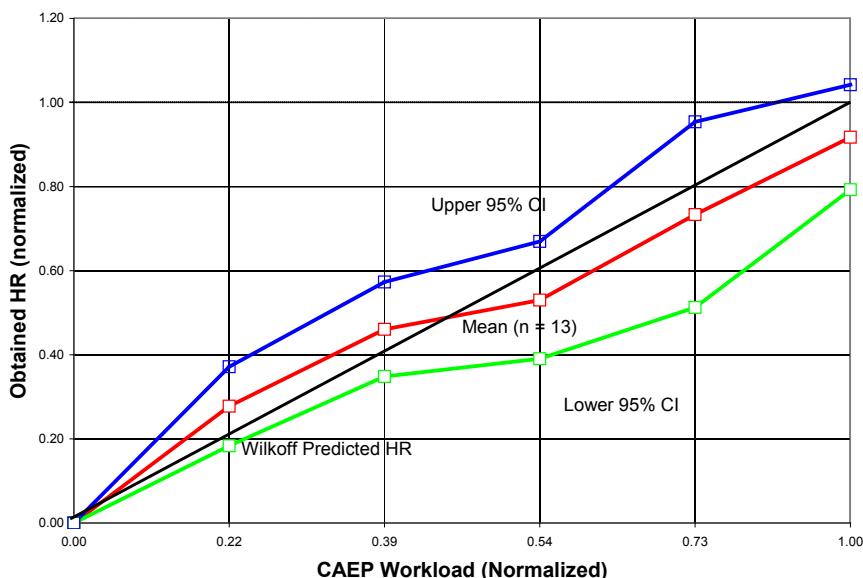


Figure 4. Obtained vs. Expected Heart Rate during CAEP

Safety

There were no complications reported and there was only 1 observation reported. One patient reported feeling fatigued since the reprogramming of his Protos pulse generator to AxVx. The patient performed well during the CAEP treadmill, resulting in a slope of 0.7. After the CAEP treadmill testing, his pacemaker was reprogrammed to the settings before the AxVx download. The calculated rate for observations is 0.05 observations per patient which is within the clinically acceptable rate. This clinical study demonstrates the overall safety profile of the AxVx algorithm.

6.3.2.4 Clinical Study Conclusions

BIOTRONIK has shown that the Protos DR/CLS AxVx rate-adaptive algorithm provides appropriate rate response as tested during a symptom limited CAEP treadmill test for patients exhibiting a high percentage of ventricular sensing (99.1% for 13 patients meeting the pre-defined analysis criteria).

6.3.3 Inos²⁺ CLS

6.3.3.1 Primary Objectives

The clinical study included evaluation of the safety and effectiveness of the device.

6.3.3.2 Methods

A total of 129 patients were implanted with the Inos pulse generator in a controlled, prospective study. The investigation was conducted at 15 centers. The average patient was a 73 year-old male, with a NYHA Classification of I and Sinus Bradycardia.

Each patient was followed at hospital discharge and at one, three and six month post-implant and every 6 months thereafter. At the one month follow-up a Chronotropic Assessment Exercise Protocol (CAEP) treadmill test and a 24 hour Holter recording were performed.

6.3.3.3 Results

Safety

The clinical study complication rate was 10.08% (13 out of 129 patients) versus the acceptance criterion of 11.5% (15 out of 129 patients). The clinical investigation did not classify any of these complications as being related to the pulse generator.

Effectiveness

A total of 52 treadmills were included for the analysis of the rate response slope. The mean rate response slope during the CAEP treadmill test was 0.82 with a 95% confidence interval of [0.75, 0.89]. These values meet the acceptance criterion for this objective.

Table 8 compares several predicted heart rates to the obtained rates as estimated by linear regression of the treadmill data. This table shows that overall the patients reached about 95% of the programmed maximum closed loop rate (MCLR) in the last stages of exercise.

Table 8: Estimated Heart Rates

Predicted Heart Rate (bpm)	Obtained Heart Rate (bpm)	Ratio of Obtained to Predicted (%)
60	68.13	113.6%
80	84.53	105.7%
100	100.93	100.9%
120	117.33	97.8%
140	133.73	95.5%
160	150.13	93.8%

The number and percentages of patients who met certain performance criteria are presented in **Table 9**.

Table 9: Percentages of Patients Meeting Success Criteria

Criteria	% Patients
Slope > 0.825	53.8% (28/52)
Slope > 0.650	78.8% (41/52)
Within 20 bpm of MCLR	80.8% (42/52)
Achieved MCLR	46.2% (24/52)

Figure 5 shows the obtained heart rate versus the expected heart rate during the CAEP treadmill test for all patients completing at least 4 stages of exercise (n = 52).

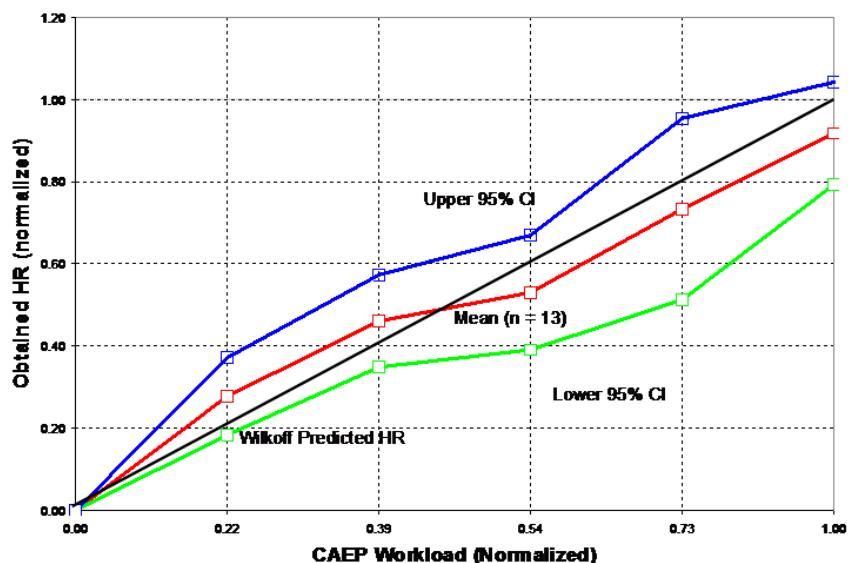


Figure 5. Obtained vs. Expected Heart Rate during CAEP

In addition to slope analysis, the treadmill performance was evaluated by quantitatively comparing the obtained rates to the predicted heart rate for each stage. In forty-six patients (88.5%) the heart rate obtained at the different CAEP stages was nearly equivalent to the predicted heart rate for each of the stages. The average slope for this group was 0.83. Two patients (3.8%) obtained heart rates at the different CAEP stages that were significantly (15%) lower than the predicted heart rates in three or more stages. The average slope for this group was 0.13. Four patients (7.7%) obtained heart rates at the different CAEP stages that were significantly (15%) higher than the predicted heart rate in three or more stages. The average slope for this group was 0.96.

6.3.3.4 Clinical Study Conclusions

The clinical data support that the Inos pacing system is safe and effective for use in patients that are indicated for rate-adaptive pacing. The Inos Clinical Study fulfilled the predefined primary safety and efficacy endpoints. These endpoints included appropriate obtained heart rates during exercise and complication-free rate.

6.4 TRUST Clinical Study

6.4.1 Study Overview

The TRUST study is a multi-center, prospective and randomized trial. The purpose of the study was to demonstrate that the use of the BIOTRONIK Home Monitoring system (HM) can safely reduce the number of regularly scheduled office follow up visits, compared to the conventional method of ICD follow-up. The assessment consists of comparing the number of in-office follow-ups for patients with HM (HM group) versus patients without HM (Control group). With the use of HM, the number of in-office follow up visits per year could be reduced from an expected five scheduled office follow up visits (3, 6, 9, 12 and 15 months) to two visits (3 and 15 months). Additionally, the time from onset to evaluation of arrhythmias in both groups was compared. It was expected that evaluation of cardiac events in the HM arm would occur earlier than those in the Control group.

6.4.2 Methods

All enrolled patients received a BIOTRONIK ICD with Home Monitoring/ IEGM-Online® technology and were randomized to either Group 1 (Home Monitoring (HM)) or Group 2 (No Home Monitoring (Control)) using a randomization ratio of 2:1.

Group 1 (HM)

Device evaluations for scheduled follow-ups, patient-initiated inquiries and event triggered notifications were performed with HM/IEGM Online. Patients were scheduled for office device interrogations only at the 3 month and 15 month follow-up points (following the HM online check). At 6, 9 and 12 months, a HM check was performed first. Investigators may then elect to perform an office device interrogation if they determine that it is necessary after reviewing the HM data.

Group 2 (Control)

Patients were evaluated using conventional, calendar-based office visits at 3, 6, 9, 12 and 15 months post-implant. Interim visits were made according to physician discretion (e.g. following any ICD discharges or symptoms). Home Monitoring was programmed OFF for the duration of the study.

HM Event Triggered Device Evaluations

Investigators with patients in Group 1 (HM) may receive HM notifications in response to pre-programmed events such as VT1 detected and SVT detected. Upon the receipt of a HM Event Notification, investigators reviewed the notification and the associated information on the HM/IEGM-Online website and recorded the type of event and what type of action, if any, was taken as a result of this notification.

Patient-Initiated Device Evaluations

Investigators may be contacted by the patient for device/arrhythmia-related care (e.g. perceived device discharge, symptoms). For patients in Group 1 (HM), investigators triaged the complaint using the Home Monitoring website. Investigators recorded if the information from Home Monitoring was sufficient. For patients in Group 2 (Control), the complaint was assessed per standard of care or normal clinic procedures.

Primary Endpoints

The purpose of primary endpoint 1 (HM efficacy) was to compare the number of in-office ICD follow-ups for patients in Group 1 (HM) to the conventional, calendar-based method of ICD follow-up as in Group 2 (Control).

The purpose of the primary endpoint 2 (safety) was to compare the Safety Event Rate (SER), which includes death, incidence of strokes and events requiring surgical interventions (e.g. device explants or lead revision) between the two groups.

Secondary Endpoints

The purpose of secondary endpoint 1 was to compare AF, VT and VF events between Group 1 and Group 2 in terms of the number, categories, and detection time relative to onset.

Inclusion Criteria

To support the objectives of this investigation, the inclusion criteria at the time of patient enrollment for this investigational study included the following requirements:

- Implanted within the last 45 days or being considered for implant with a BIOTRONIK ICD with Home Monitoring/IEGM-Online technology

- Able to utilize the HM system throughout the study
- Ability to give informed consent
- Geographically stable and able to return for regular follow-ups for fifteen (15) months
- At least 18 years old

Exclusion Criteria

To support the objectives of this investigation, the exclusion criteria at the time of patient enrollment included the following requirements:

- Patients who do not fulfill all inclusion criteria
- Patients who are pacemaker dependent
- Currently enrolled in any other cardiac clinical investigation.

Clinical Events Committee

The Clinical Events Committee (CEC) is an advisory review board comprised of three physicians that are not participating in the TRUST Study who reviewed and adjudicated all deaths, strokes, surgical interventions, and cardiac adverse events that occur during the study. The CEC also reviewed all divergent classifications of actionable vs. non-actionable office follow up visits between the physician and BIOTRONIK, and reviewed a random sampling of 1% of office follow up visits in which there is no disputed classification.

6.4.3 Summary of Clinical Results

The study involved 1443 patients (1038 males, 71.9%), with a mean age of 63.5 years (range: 20-95). The cumulative enrollment duration is 18,367 months with mean enrollment duration of 12.7 months. The patient follow-up compliance rate for all enrolled patients is 87.5% in Group 1 and 78.8% in Group 2.

6.4.3.1 Primary Endpoint 1: Home Monitoring Effectiveness

The purpose of primary endpoint 1 (HM efficacy) was to compare the number of in-office ICD follow-ups for patients in Group 1 (HM) to the conventional, calendar-based method of ICD follow up as in Group 2 (Control).

Detailed primary endpoint 1 results are presented in [Table 10](#).

Table 10: Primary Endpoint Group 1 vs. Group 2

	No. of Pts**	Office Follow-up Visits		
		Scheduled	Unscheduled	Total
Group 1 (HM)	898	n = 991 1.3 ± 1.0 per pt yr 13.1% actionable	n = 401 0.6 ± 1.7 per pt yr 29.7% actionable	1.9 ± 1.9 per pt yr
Group 2 (Control)	414	n = 1110 3.0 ± 1.1 per pt yr 10.7% actionable	n = 117 0.4 ± 1.4 per pt yr 29.1% actionable	3.4 ± 1.7 per pt yr
p value		< 0.001	0.032	< 0.001

Analysis

The comparison of the number of 3, 6, 9, and 12 month and unscheduled office follow-up visits in Group 1 versus Group 2 showed that there was an average number of 1.9 office follow-up visits on a per year basis in Group 1 (HM) and an average number of 3.4 office follow-up visits on a per year basis in Group 2 (Control). Therefore, the null hypothesis (H_0) can be rejected, indicating that the average number of office visits per year is statistically significantly less in the HM group than in the Control group ($p < 0.001$). The primary effectiveness endpoint was met.

6.4.3.2 Primary Endpoint 2: Safety Event Rate

The purpose of the primary endpoint 2 was to compare the Safety Event Rate (SER), which includes death, incidence of strokes and events requiring surgical interventions (e.g. device explants or lead revision) between the two groups.

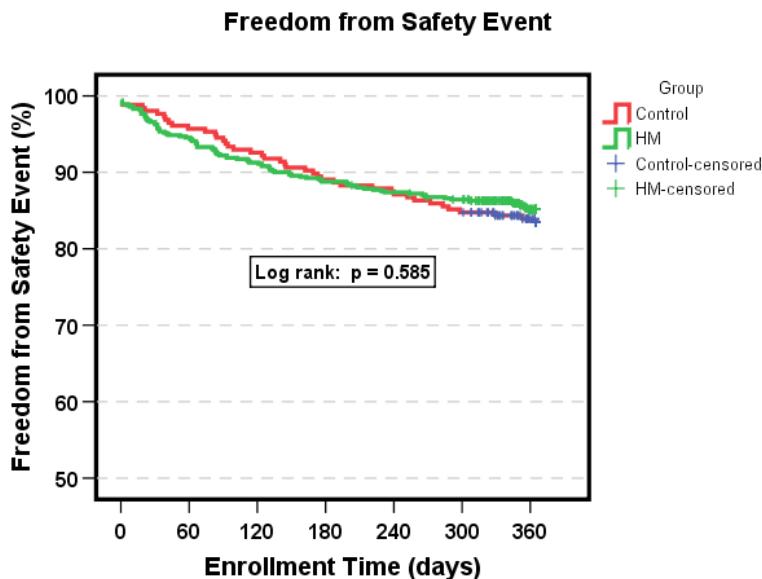
[Table 11](#) summarizes the Safety Event Rate for the study patients for 12 months post-enrollment. [Figure 6](#) shows these data in a Kaplan-Meier analysis.

* Up to and including 12 month follow-up data

** Number of patients that have contributed at least 1 follow-up

Table 11: Safety Event Rate Comparison

Safety Event Rate*	Group 1	Group 2	p value**
Type of Event			
Death	36 / 608 (5.9%)	18 / 245 (7.3%)	0.440
Stroke	2 / 574 (0.3%)	3 / 227(1.3%)	0.141
Surgical intervention	57 / 605 (9.4%)	22 / 239 (9.2%)	1.000
Any Event	95 / 643 (14.8%)	42 / 256 (16.4%)	0.539

**Figure 6: Safety Event Rate Kaplan Meier**

Analysis

The safety event rate for a 12-month duration was 14.8% for Group 1 (HM) and 16.4% for Group 2 (Control), with a non inferiority p-value of 0.005. Therefore, the safety event rate for HM Group was non-inferior to the safety event rate for the Control Group within 5%. The upper, one sided 95% confidence bound for the difference was 2.7%.

* Only includes events occurring within 12 months of enrollment

** 2-sided Fisher Exact test

A rejection of the null hypothesis indicates that the safety event rate for Group 1 (HM) is equivalent (non-inferior) to that of Group 2 (Control).

6.4.3.3 Secondary Endpoint 1: Early Detection of Cardiac Events (AF, VT & VF)

The purpose of secondary endpoint 1 was to compare AF, VT and VF events between Group 1 and Group 2 in terms of the number, categories, and detection time relative to onset.

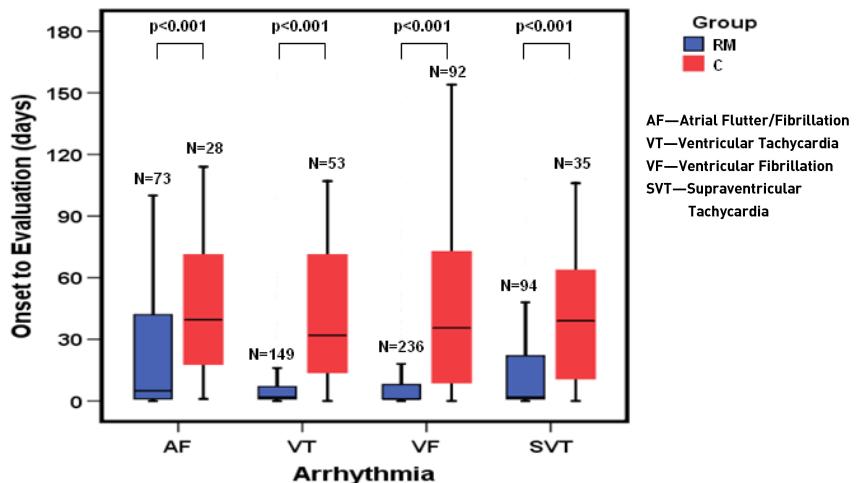
Table 12 compares the time from onset to evaluation of the first AF, VT and VF events for each patient that have occurred in each group, as well as the first of any type of event for each patient in each group. **Figure 7** illustrates the time from onset to evaluation of arrhythmic events in a boxplot graph.

Table 12: Time from First Event Onset to Evaluation

Time from Event Onset to Evaluation of First Event/ Patient	Group 1 N=972	Group 2 N=471	p value
AF			
Median	5.0	39.5	p < 0.001 p = 0.005
Mean ± SD (days)	25.2 +/- 34.2	46.8 +/- 33.7	
Min	0	1	
Max	171	114	
# of patients with events	73 (7.5%)	28 (5.9%)	
VT1 & VT2			
Median	2.0	32.0	p < 0.001 p < 0.001
Mean ± SD (days)	12.9 +/- 33.8	46.6 +/- 46.9	
Min	0	0	
Max	256	245	
# of patients with events	149 (15.3%)	53 (11.2%)	

Table 12: Time from First Event Onset to Evaluation

Time from Event Onset to Evaluation of First Event/ Patient	Group 1 N=972	Group 2 N=471	p value
VF			
Median	1.0	35.5	p < 0.001 p < 0.001
Mean ± SD (days)	10.5 +/- 22.2	45.0 +/- 47.0	
Min	0	0	
Max	145	287	
# of patients with events	236 [24.3%]	92 [19.5%]	
SVT			
Median	2.0	39.0	p < 0.001 p < 0.001
Mean ± SD (days)	16.6 ± 27.4	42.1 ± 35.6	
Min	0	0	
Max	108	157	
# of patients with events	94 [9.7%]	35 [7.4%]	

**Figure 7: Median Time from Onset to Evaluation of Arrhythmic Events**

Analysis

The mean time from onset to evaluation of first AF, VT, and VF events in Group 2 is greater than the mean time from onset to evaluation of first AF, VT, or VF events in Group 1. A rejection of the null hypothesis for AF, VT and VF event types indicates that the mean time from onset to evaluation of the first AF, VT and VF events in Group 1 is significantly less than the mean time from onset to evaluation of the first AF, VT and VF events in Group 2. P-values are =0.005, <0.001 and <0.001 respectively.

6.4.4 Conclusions

- Use of HM in Group 1 resulted in an average of 1.9 office visits per patient year in the 12 months post-implant, versus an average of 3.4 office visits per patient year in Group 2, a 44% reduction in office visits. The average number of office visits is significantly less in the HM group than in the Control group ($p < 0.001$).
- The safety event rate for a 12 month duration for Group 1 (HM) was non-inferior to the safety event rate for Group 2 (Control) within 5% ($p = 0.005$). The upper, one-sided 95% confidence bound for the difference was 2.7%.
- The mean time from onset to evaluation of AF, VT and VF events indicates that those events for Group 1 patients are evaluated in significantly less time when compared to Group 2 patients (AF $p = 0.005$, VT $p < 0.001$, VF $p < 0.001$).

7. Programmable Parameters

For a complete list of programmable parameters and the available settings, see [Section 15.](#)

7.1 Pacing Modes

For a complete list of pacing modes available in each Cylos configuration, see [Section 15.1.](#)

NOTE:

Active Capture Control is only available with the following pacing modes: DDD-CLS, VVI-CLS, DDDR, VDDR, VVIR, DDD, VDD, VVI, DDTR/A, DDTR/V, DDT/A, and DDT/V.

7.1.1 Motion Based Rate-Adaptive Modes

The motion based rate-adaptive modes are designated with a “R” in the fourth position of the NBG pacemaker code on the programmer screen. The rate-adaptive modes function identically to the corresponding non-rate-adaptive modes, except that the basic rate increases when physical activity is detected by the motion sensor.

In demand modes (DDDR, DDIR, DVIR, VDDR, VVIR, AAIR), it is possible that the atrial and/or ventricular refractory period can comprise a major portion of the basic interval at high sensor-modulated rates. This may limit the detection of spontaneous events or even exclude their recognition altogether. Further details of this potential occurrence are provided in [Section 7.5.1.](#)

7.1.2 CLS Modes

As explained in the device description, Cylos also can be programmed to use a unique rate-adaptive principle called Closed Loop Stimulation (CLS) to adapt the patient’s pacing rate.

The Cylos measures electrical impedance by injecting a small AC current between the pulse generator case and the ventricular electrode tip. The induced voltage (which is proportional to the intracardiac impedance) is also measured between pulse generator case and ventricular electrode tip.

CAUTION

Rate-Adaptive Pacing – Use rate-adaptive pacing with care in patients unable to tolerate increased pacing rates.

CLS Rate Adaptation – Under certain circumstances (e.g., EMI, lead dislodgment), the Cylos device may not be able to obtain a useable impedance measurement as required for CLS rate-adaptive pacing. At this point, CLS rate-adaptation will be inactive until the situation is corrected. Rate-adaptation may be programmed to switch to motion based adaptation.

The DDD-CLS and VVI-CLS mode is functionally equivalent to the DDDR and VVIR pacing modes, respectively. However these modes use the CLS concept to determine the pacing rate variations that are mediated by the body's own cardiovascular control. In these modes, the atrial and/or ventricular refractory periods may comprise a major portion of the basic interval at high rates. This could limit the detection of spontaneous events or even exclude their recognition altogether. However, this phenomenon will not limit the functionality of the mode switch.

Motion based rate adaptive pacing will take over if the CLS pacing algorithm switches into a passive mode.

7.1.3 Non-Rate-Adaptive Modes

Non-rate-adaptive modes that are programmable with the Cylos pacemaker perform similarly to earlier generations of BIOTRONIK pulse generators (i.e., Philos II DR and Dromos DR).

7.1.4 Mode Conversion and Mode Switching

Cylos provides two options to change pacing modes as a result of atrial tachycardias. The two available options are Automatic Mode Conversion and Mode Switching, which are designed to avoid tracking of non-physiologic atrial rates due to paroxysmal atrial tachycardias (PATs). Automatic Mode Conversion and Mode Switching are only available in atrial tracking modes DDD(R) and VDD(R).

Mode Switching

The Mode Switching algorithm causes the pulse generator to change pacing modes when a programmed number of atrial intervals (X) out of 8 consecutive atrial intervals (p-p) are faster than the programmed mode switch intervention rate (X out of 8). X is programmable from

3 to 8. The rate at which an atrial interval is determined to signify an atrial tachyarrhythmia is called the mode switch intervention rate. The mode switch intervention rate is programmable from 100 to 250 bpm. A Mode Switch Basic Rate can be programmed to allow for a higher basic rate during an active Mode Switch, in order to diminish undesirable hemodynamic behaviors.

The mode switch occurs from atrial tracking to non-atrial tracking pacing modes (e.g. DDDR to DDIR) as described in [**Table 13**](#).

Reversion back to the programmed pacing mode occurs in a similarly programmable manner. If a programmable number of atrial intervals (Z) out of 8 consecutive atrial intervals (p-p) are slower than the programmed mode switch intervention rate (Z out of 8), the device will revert back to the permanently programmed parameters. Z is programmable from 3 to 8. The device will also revert back to the permanent program if no atrial paced or sensed events have occurred for at least 2 seconds.

The occurrence of a Mode Switch activates a Far Field Blanking period after every ventricular event. The purpose of the Far Field Blanking period is to keep far field R-waves from being considered. The Far Field Blanking parameter is programmable to 32, 40, 48, 56, 72, 100... (25)...200ms. Additionally, during DDI(R), the AV-delay is set to 100 ms.

Mode Switch Events are recorded in memory and are available to the user through the following diagnostics:

- IEGM Recordings Screen
- Tachy Episode Trends
 - Mode Switch Trends
 - Mode Switch Histogram
 - Mode Switch Counter

If the pulse generator does not Mode Switch during an atrial tachycardia as programmed, an extension of Mode Switch (2:1 Lock-In Management) can be programmed. 2:1 Lock-In Management, which is described in [**Section 7.8**](#), will detect and confirm a tachycardia, thereby triggering a Mode Switch.

Mode Switching is temporarily suspended during magnet application and is inactive during ERI. Mode Switching occurs as described in [**Table 13**](#).

Table 13: Programmable Mode Switches

Programmed Pacing Mode	Programmable Mode Switch Pacing Modes	
	Rate-Adaptive	Non-Rate-Adaptive
DDDR and DDD-CLS	DDIR	DDI
DDTR/A	DDIR	DDI
DDTR/V	DDIR	DDI
VDDR	VDIR	VDI
DDD	DDIR	DDI
DTT/A	DDIR	DDI
DTT/V	DDIR	DDI
VDD	VDIR	VDI

NOTE:

If the programmed target pacing mode during Mode Switch is rate adaptive (e.g., DDIR), the device-determined rate adaptive pacing rate during mode switch may be lower than the programmed value. When the target pacing mode is programmed to a rate adaptive mode, the maximum sensor indicated rate may be as low as 101 ppm (standard settings).

Automatic Mode Conversion

With Automatic Mode Conversion OFF in the DDD(R) or VDD(R) mode, atrial sensing within the refractory period does not retrigger the atrial refractory period interval. Mode Conversion does not function in CLS mode.

With Automatic Mode Conversion ON in DDD(R) or VDD(R) mode, atrial sensing within the refractory period restarts the atrial refractory period. If the interval between successive P-waves becomes shorter than the atrial refractory period (i.e., during periods of tachycardia), the atrial refractory period will be re-started continuously. Thus, the period is extended through the entire basic interval. At the end of the basic interval, an atrial pulse is emitted asynchronously and the AV delay is started. As a result, the pulse generator performs as if it were placed in the DVI(R) or VVI(R) mode and ventricular pacing triggered by P-wave tracking is prevented.

Referring to **Figure 8**, “ A_S ,” “[A_S]” and “ A_P ” indicate atrial sensed events, unused atrial sensed events (inside refractory), and atrial paced events, respectively. In the top diagram, every other P-wave triggers ventricular pacing during an atrial arrhythmia. In the lower diagram, P-waves falling within the atrial refractory period (ARP) retrigger the ARP without resetting the lower rate timer during the atrial arrhythmia.

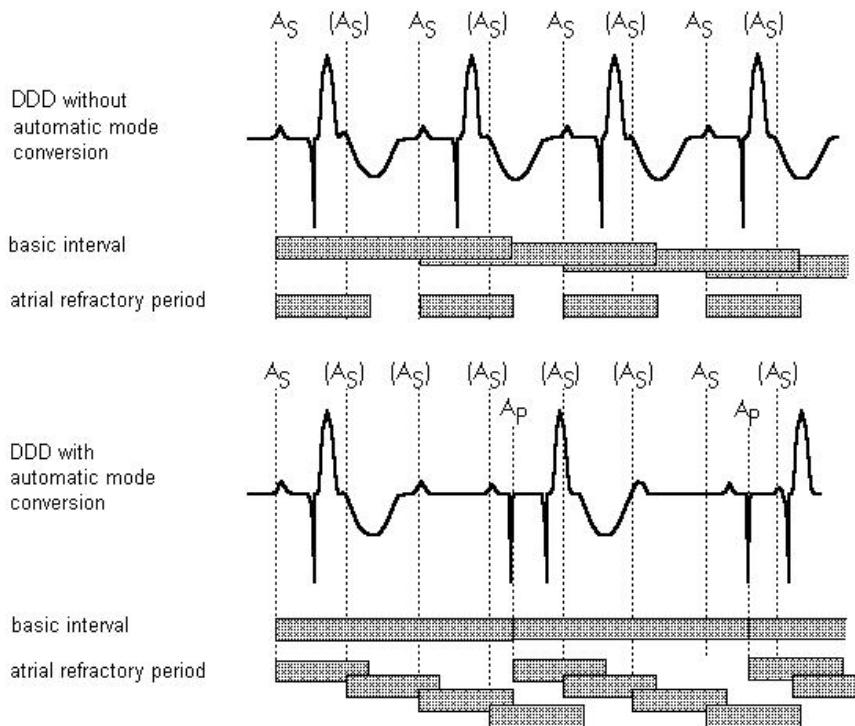


Figure 8. DDD with Automatic Mode Conversion inactive (upper panel) and active (lower panel)

Automatic Mode Conversion differs in the DDD/VDD mode from the DDD(R)/VDD(R) mode in that pacing occurs at the lower rate (DDD/VDD), whereas in the DDD(R)/VDD(R) mode pacing occurs at the sensor-indicated rate.

7.1.5 Pacing Modes with Triggered Response

Pacing modes with triggered response correspond to their respective demand pacing modes, except that a sensed event will not inhibit but

will rather trigger a pacing pulse, simultaneously with the sensed event, into the same chamber where sensing has occurred. The demand and corresponding triggered pacing modes are:

Demand:	DDD	DDI	DDDR	DVI	VDD	VVI	AAI
Triggered:	DDT	DDI/T	DDTR/A (DDTR/V)	DVT	VDT	VVT	AAT

The triggered pacing modes DDT, DVT and DDI/T limit the AV delay to a maximum of 150 ms and do not provide a safety AV delay.

Lower rate timing in the pacing modes DDI/T and DVT differs from that of the corresponding demand pacing modes DDI and DVI with respect to ventricular sense events occurring during the AV delay. In the demand pacing modes, they reset the lower rate interval, while in the triggered pacing modes they do not.

The triggered pacing modes DDTR/A and DDTR/V are similar to the triggered pacing mode DDT with the addition of rate adaption. However, only the chamber designated by the reference following the slash (i.e., A or V) will result in a sensed event triggering a pacing pulse in the same chamber where sensing has occurred. A sensed event in the chamber not selected will inhibit a pacing pulse.

Pacing modes with triggered response may be indicated in the presence of interference signals to prevent inappropriate pulse inhibition. They may also have diagnostic application for ECG identification of sense events as an alternative to marker signals. Triggered pacing may also be used for hemodynamic as well as electrophysiologic studies and for termination of tachycardias by non-invasive triggering of pulse generator pulses with chest wall stimuli generated by an external pulse generator.

CAUTION

Programmed to Triggered Modes—When programmed to triggered modes, pacing rates up to the programmed upper limit may occur in the presence of either muscle or external interference.

Triggered Modes—While the triggered modes (DDT, DVT, DDTR/A, DDTR/V, DDI/T, VDT, VVT, and AAT) can be programmed permanently, the use of these modes is intended as a temporary setting in situations where maintaining the programming head in place would be impossible or impractical (i.e., during exercise testing or extended Holter monitoring) or as a short term solution to pulse generator inhibition by extracardiac interference. To avoid the potential for early battery depletion, it is important that the triggered modes are not used for long term therapy, and that the pulse generator is returned to a non-triggered permanent program.

7.2 Rate Related Functions

The availability of parameters and parameter values is determined by the software used for programming/interrogating the pulse generator.

7.2.1 Basic Rate

The basic rate is the pacing rate in the absence of a spontaneous rhythm and is programmable up to 180 ppm.

CAUTION

Programming Modifications—Extreme programming changes should only be made after careful clinical assessment. Clinical judgment should be used when programming permanent pacing rates below 40 ppm or above 100 ppm.

7.2.2 Rate Hysteresis

Hysteresis can be programmed OFF or to values as low as -80 bpm. The Hysteresis rate is based on the lower rate and the value of the programmable parameter. Hysteresis is initiated by a sensed event. The resulting Hysteresis rate is always less than the lower rate. A conflict symbol (>>) will appear and transmission will be prohibited for Hysteresis rates which are less than 30 bpm. The ability to decrease the effective lower rate through Hysteresis is intended to preserve a spontaneous rhythm. The pulse generator operates by waiting for a

sensed event throughout the effective lower rate interval (Hysteresis interval). If no sensed event occurs, a pacing pulse is emitted following the Hysteresis interval.

NOTE:

If rate adaptation is active, the Hysteresis rate is based on the current sensor-indicated rate and the value of the programmable parameter.

Hysteresis is not available in CLS or DVI, DVIR, DDIT, DDIR, DVT and DVTR modes.

If Hysteresis is used in the DDI mode, the AV delay must be programmed shorter than the spontaneous AV conduction time. Otherwise, stimulation in the absence of spontaneous activity occurs at the hysteresis rate instead of the lower rate.

Hysteresis is suspended during the Night Mode activated time. Programming conflicts arise when the total decrease in rate is below 30 ppm. Care should be exercised to avoid programming a Night Mode rate and hysteresis that is below what is appropriate and may be tolerated by the individual patient.

7.2.3 Scan Hysteresis

Scan hysteresis is expanded programmability of the Hysteresis feature. Scan hysteresis searches for an underlying intrinsic cardiac rhythm, which may exist slightly below the programmed lower rate (or sensor-indicated rate) of the pulse generator. Following 180 consecutive paced events, the stimulation rate is temporarily decreased to the hysteresis rate for a programmed number of beats. If a cardiac rhythm is not detected within the programmed number of beats at the hysteresis rate, the stimulation rate returns back to the original lower rate (or sensor-indicated rate). Several programmable beat intervals are available to allow a greater probability of detecting a spontaneous rhythm.

If an intrinsic cardiac rhythm is detected within the programmed number of beats between the hysteresis rate and the lower rate, the intrinsic rhythm is allowed and the pulse generator inhibits.

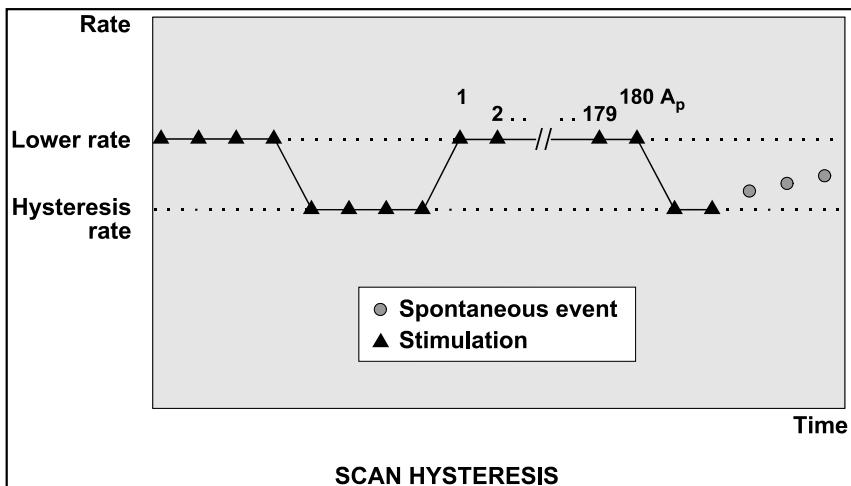


Figure 9. Scan Hysteresis

Scan hysteresis has been incorporated to promote intrinsic cardiac rhythm and may reduce pulse generator energy consumption.

NOTE:

Scan Hysteresis is not active during the programmed Night Mode.

Scan Hysteresis is only available when Hysteresis is selected ON.

Magnet application (closing of reed switch) suspends the 180 consecutive event counter independent of the magnet effect.

7.2.4 Repetitive Hysteresis

Repetitive hysteresis is expanded programmability of the Hysteresis feature. Repetitive hysteresis searches for an underlying intrinsic cardiac rhythm, which may exist slightly below the programmed lower rate (or sensor-indicated rate) of the patient. Following 180 consecutive sensed events, this feature allows the intrinsic rhythm to drop to or below the hysteresis rate. During the time when the intrinsic rate is at or below the hysteresis rate, pacing occurs at the hysteresis rate for the programmed number of beats (up to 10). Should the number of programmed beats be exceeded, the stimulation rate returns to the lower rate (or sensor-indicated rate).

If an intrinsic cardiac rhythm is detected within the programmed number of beats between the hysteresis rate and the lower rate, the intrinsic rhythm is allowed and inhibits the pulse generator.

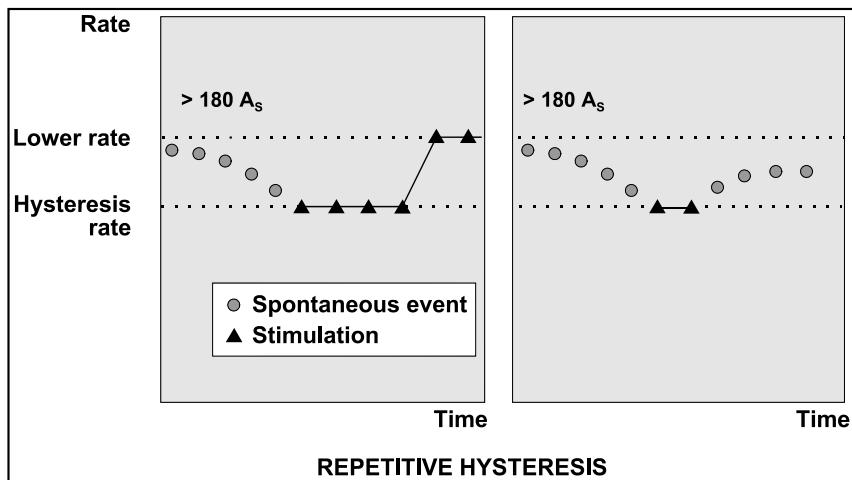


Figure 10. Repetitive Hysteresis

Repetitive hysteresis has been incorporated to promote spontaneous cardiac rhythm and may reduce pulse generator energy consumption.

NOTE:

Repetitive Hysteresis is not active during the programmed Night Mode.

Repetitive Hysteresis is only available when Hysteresis is selected ON.

Magnet application (closing of reed switch) suspends the 180 consecutive event counter independent of synchronous or asynchronous magnet effect.

There is one Standard Hysteresis interval which occurs before the programmable number of Repetitive Hysteresis occur.

7.2.5 Night Mode

Programmable Night Time Begin and End in 10 minute steps.

The Night Mode feature allows a temporary reduction of the base rate during normal sleeping hours. If selected, the base rate is gradually and temporarily reduced to the programmed night pacing rate. At the end of night mode, the base rate gradually returns to the original values.

The Night Mode feature has been incorporated to allow the patient's spontaneous night rhythm and may reduce pulse generator energy consumption.

NOTE:

When Night Mode and Active Capture Control are programmed ON simultaneously in VVI(R), the rate during the night may drop below the programmed night mode due to application of the ACC underdrive rate.

Over time, the pulse generator's internal time-of-day clock will exhibit a discrepancy with the actual time (less than 1 hour per year). This will cause a corresponding discrepancy between the programmed bed and wake times and the actual times that the system changes the rate.

The programmer automatically updates the pulse generator time-of-day clock each time the pulse generator is programmed.

The actual time when the respective increase or decrease in rate occurs may begin up to 4 minutes after the programmed time because of internal pulse generator timing.

7.2.6 Rate Fading

Rate Fading is intended to prevent a sudden drop in heart rate when the pulse generator transitions from tracking an intrinsic rhythm to pacing due to an abrupt decrease in the intrinsic rate, in order to prevent potential reactions such as dizziness, light headedness, lack of energy and fainting.

With Rate Fading enabled, the pulse generator calculates the Fading Rate, which is a four beat average of the intrinsic rate reduced by 10 ppm. When the intrinsic rate drops considerably (below the Fading Rate), the pacing rate begins at the RF rate and then decreases gradually by the programmable Decay Rate to the Sensor Indicated Rate or Basic Rate. This behavior is illustrated in [Figure 11](#).

NOTE:

The Fading Rate cannot exceed the programmed Maximum Activity Rate and cannot increase faster than the RF Rate Increase (programmable in ppm/cycle).

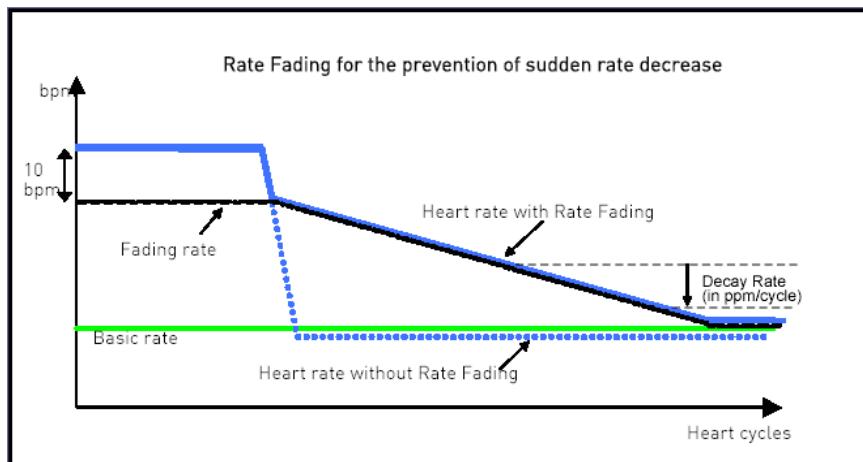


Figure 11: Rate Fading

The Rate Fading feature is suspended while in magnet mode and disabled at ERI and in backup mode.

7.3 Pulse Specific Features

Features related to the pacing pulse.

7.3.1 Pulse Amplitude

The programmed pulse amplitude determines the voltage applied to the heart during each pacing pulse. The pulse amplitude is independently programmable for the atrial and ventricular channels up to 8.4 volts. The pulse amplitude remains consistent throughout the service life of the pulse generator. The pacing safety margin is therefore not reduced by a decrease in the pulse generator's battery voltage.

NOTE:

When ACC is programmed to ON or ATM, the pulse amplitude can not be programmed by the user to a value higher than the programmed Maximum ACC Amplitude (Max. Ampl.). When ACC is programmed to ON, the pulse amplitude will be set by the device to the threshold plus the programmed Safety Margin, but never lower than the Minimum ACC Amplitude (Min. Ampl.).

CAUTION

Pulse Amplitude – Programming of pulse amplitudes, higher than 4.8 V, in combination with long pulse widths and/or high pacing rates can lead to premature activation of the replacement indicator. If a pulse amplitude of 7.2 V or higher is programmed and high pacing rates are reached, output amplitudes may differ from programmed values.

Programming Modifications – **Extreme programming changes** should only be made after careful clinical assessment. Clinical judgment should be used when programming permanent pacing rates below 40 ppm or above 100 ppm.

7.3.2 Pulse Width

The selected pulse width determines the duration for which the programmed pulse amplitude will be applied to the heart. The pulse width is independently programmable (up to 1.5 ms) for the atrial and ventricular channels. Pulse width remains constant throughout the service life of the pulse generator.

NOTE:

When ACC is programmed to ON or ATM, the pulse width cannot be programmed to a value higher than 0.4 ms.

7.4 Sensitivity

The parameter “sensitivity” is used to set the pulse generator’s threshold for detecting intracardiac signals. The lower the programmed sensitivity values the higher the device’s sensitivity.

If intracardiac signals are of low amplitude, a change to a higher sensitivity (lower value) may be indicated. Conversely, if the sensing amplifier is responding to extraneous signals, such as artifacts or interference, a change to a lower sensitivity (higher value) may resolve the difficulty. In dual chamber sensing modes, the sensitivity values for the atrial and ventricular channels are independently programmable. With Unipolar programming, the highest possible sensitivity setting is 0.5 mV.

7.5 Timing Features

Features related to pulse generator timing cycles.

7.5.1 Refractory Period

Immediately upon sensing or pacing, the pulse generator starts a refractory period in the same channel. During the refractory period, intracardiac signals are ignored. This prevents the pulse generator from responding to the depolarization signal or the repolarization signal (T-wave) that might otherwise result in inappropriate inhibition or triggering.

If the pulse generator is programmed to dual chamber sensing, the refractory periods are independently programmable for each sensing channel. The atrial refractory period is always initiated by a sensed or paced atrial event or a sensed ventricular event outside of the AV delay (e.g., PVC). The pulse generator's ventricular refractory period is always initiated by a sensed or paced ventricular event.

Under certain circumstances (i.e., Automatic Mode Conversion) (DDD-CLS, DDD(R), VDD(R)) additional sensed events will re-trigger the atrial refractory period. Refer to the appropriate section of the manual for details.

CAUTION

Short Pacing Intervals – Use of short pacing intervals (high pacing rates) with long atrial and/or ventricular refractory periods may result in intermittent asynchronous pacing and, therefore, may be contraindicated in some patients.

7.5.2 Atrial Refractory Period Extension (ARPE)

The ARPE applies to DDD-CLS, DDD(R), VDD(R), DDT(R), and VDT(R). To prevent the initiation of a pacemaker mediated tachycardia (PMT) by a ventricular depolarization not preceded by an atrial depolarization, the ARP will be extended by the ARPE if the ARP:

- Was started by a ventricular sense event outside of the AV delay (e.g., PVC) in DDD, DDT, VDD and VDT, or
- Was reset by a ventricular pulse not triggered by an atrial sense event in VDD and VDT.

In these instances, the ARP will usually be long enough to prevent sensing of retrograde P-waves. Programming to an ARPE other than 0 ms may rarely be required but could provide additional protection if the ARP is limited or the retrograde conduction time extended.

7.5.3 AV delay

7.5.3.1 Dynamic AV delay

The AV delay defines the interval between an atrial paced or sensed event and the ventricular pacing pulse. If the pulse generator is programmed to a dual chamber sensing mode, an intrinsic ventricular event falling within the AV delay will inhibit the ventricular pacing pulse. If not contraindicated, a longer AV delay can be selected to increase the probability of ventricular output pulse inhibition. Short AV delays are available for testing purposes or if ventricular pre-excitation is desired (i.e., hemodynamic considerations).

Dynamic AV delay provides independent selection of AV delays from five rate ranges at pre-set AV delay values. In addition, the AV delay after atrial pace events can be differentiated from the AV interval after atrial sense events for dual chamber pacing modes. Dynamic AV delay is programmable within the following atrial rate ranges at the values specified in [Table 14](#).

Table 14: Dynamic AV delay settings

Rate Ranges	LOW	MEDIUM	HIGH
Non-CLS Modes			
below 70 bpm	180 ms	180 ms	180 ms
70-90 bpm	170 ms	160 ms	150 ms
91-110 bpm	160 ms	140 ms	120 ms
111-130 bpm	150 ms	120 ms	100 ms
above 130 bpm	140 ms	100 ms	75 ms
CLS Modes			
below 70 bpm	150 ms	150 ms	150 ms
70-90 bpm	140 ms	130 ms	120 ms
91-110 bpm	130 ms	120 ms	100 ms
111-130 bpm	120 ms	100 ms	75 ms
above 130 bpm	120 ms	75 ms	50 ms

In addition the Dynamic AV delays may be programmed individually for each rate range or a fixed AV delay may be programmed for all ranges.

The AV delay feature includes an AV shortening option (sensed compensation) for dual chamber pacing modes. The sense compensation can be programmed to -15 ... (-15) ... -120 ms. When selected, the AV delay after an atrial sense event is the AV delay after an atrial pace minus the sense compensation.

The Dynamic AV delay is intended to mimic the physiologic, catecholamine-induced shortening of the AV delay with increasing rate. It also serves for automatic prevention/termination of “circus movement” pacemaker mediated tachycardia and for prevention of reentrant supraventricular tachycardia (see PMT Management section).

7.5.3.2 AV Hysteresis

AV Hysteresis allows a user-programmable change in AV delay that is designed to encourage normal conduction of intrinsic signals from the atrium into the ventricles. An AV hysteresis interval can be programmed to low, middle, or high setting as defined in [**Table 15**](#) to promote intrinsic AV conduction. With AV hysteresis enabled, the AV delay is extended by a defined time value after sensing a ventricular event. The long AV interval is used as long as intrinsic ventricular activity is detected. The programmed short AV delay interval resumes after a ventricular paced event.

Table 15: AV Hysteresis Settings

AV Setting	Low (1.15x)	Medium (1.3x)	High (1.5x)
15ms	15ms	15ms	15ms
50ms	50ms	50ms	50ms
75ms	75ms	75ms	100ms
100ms	120ms	130ms	150ms
120ms	140ms	160ms	170ms
130ms	150ms	170ms	180ms
140ms	160ms	180ms	190ms
150ms	170ms	190ms	200ms
160ms	180ms	200ms	225ms
170ms	190ms	225ms	225ms
180ms	200ms	225ms	250ms
190ms	225ms	250ms	250ms
200ms	225ms	250ms	300ms
225ms	250ms	300ms	300ms
250ms	300ms	300ms	300ms
300ms	300ms	300ms	300ms

7.5.3.3 AV Repetitive Hysteresis

With AV Repetitive Hysteresis, the AV delay is extended by a defined hysteresis value after sensing an intrinsic ventricular event. When a ventricular stimulated event occurs, a long AV delay is used for the programmed number of cycles. (1 ... 6). If an intrinsic rhythm occurs during one of the repetitive cycles, the long duration AV delay interval remains in effect. If an intrinsic rhythm does not occur during the repetitive cycles, the original AV delay interval resumes.

7.5.3.4 AV Scan Hysteresis

With AV Scan Hysteresis enabled, after 180 consecutive pacing cycles, the AV delay is extended for the programmed number of pacing cycles. (1 ... 6). If an intrinsic rhythm is detected within the extended AV delay, the longer AV delay remains in effect. If an intrinsic rhythm is not detected within the number of scan cycles, the original AV delay value resumes.

7.5.3.5 Negative AV delay Hysteresis

With Negative AV delay Hysteresis, the AV delay is decreased by a defined value after a ventricular event is sensed, thereby promoting ventricular pacing. The Negative AV delay Hysteresis value corresponds to the programmed AV delay ([Table 16](#)).

Table 16: Negative AV delay Hysteresis Values

AV delay (Standard)	AV delay (Negative Hysteresis ON)
100 ms	100 ms
120 ms	100 ms
130 ms	100 ms
140 ms	100 ms
150 ms	100 ms
160 ms	120 ms
170 ms	120 ms
180 ms	130 ms
190 ms	140 ms
200 ms	150 ms
225 ms	170 ms
250 ms	180 ms
300 ms	200 ms

The normal AV delay resumes after the programmed number of consecutive ventricular paced events (Repetitive Negative AV delay Hysteresis) elapses.

CAUTION

Negative AV delay Hysteresis—This feature insures ventricular pacing, a technique which has been used in patients with hypertrophic obstructive cardiomyopathy (HOCM) with normal AV conduction in order to replace intrinsic ventricular activation. No clinical study was conducted to evaluate this feature, and there is conflicting evidence regarding the potential benefit of ventricular pacing therapy for HOCM patients. In addition, there is evidence with other patient groups to suggest that inhibiting the intrinsic ventricular activation sequence by right ventricular pacing may impair hemodynamic function and/or survival.

7.5.3.6 I-Opt

The I-Opt function serves to support the intrinsic rhythm of the heart. It activates all of the AV hysteresis function parameters in a single step. Subsequent to switching I-Opt on, the range of values is pre-configured as follows:

Table 17: I-Opt Parameters

Function	I-Opt	Standard Program
AV Hysteresis	300 ms	OFF
AV Scan Hysteresis	5	--
Repetitive AV Hysteresis	5	--

NOTE:

Activate PMT Protection to prevent pacemaker mediated tachycardia.

7.5.4 Ventricular Blanking Period

The ventricular blanking time is the period after an atrial pacing pulse during which ventricular sensing is deactivated. It is intended to prevent ventricular sensing of the atrial pacing pulse ("crosstalk").

The blanking time shall be as short as possible in order to provide ventricular sensing when a ventricular depolarization could occur.

Crosstalk may be encountered if a shorter blanking time, unipolar ventricular sensing, a higher ventricular sensitivity (lower value) and/or a high atrial pulse amplitude and pulse width are programmed.

7.5.5 Atrial Blanking Period

The atrial blanking period is the time after a ventricular pacing pulse is delivered during which atrial sensing is deactivated. It is intended to prevent atrial sensing of the ventricular pacing pulse (“crosstalk”).

The blanking time shall be as short as possible in order to provide atrial sensing when an atrial depolarization could occur.

Far-field blanking

Far-field blanking affects the atrial channel for both sensed and paced events to prevent inappropriate mode switching. The blanking interval begins with a ventricular paced / sensed event. The device recognizes the paced / sensed far-field event on the atrial channel but does not use the event in the mode switch criterion or use the event to restart pacemaker timing cycles.

Furthermore, a short far-field blanking period is beneficial when programming this parameter in conjunction with the 2:1 Lock-In Management feature ([Section 7.8.1](#)), as the pulse generator is completely blinded in the atrial channel for a shorter amount of time. As a result, the 2:1 Lock-In Management feature has a greater chance of recognizing a 2:1 situation. Likewise, a longer far-field blanking period can be programmed in order to conceal continuous far-field sensing so that such sensing does not constantly trigger the 2:1 Lock-In Management feature.

7.5.6 Safety AV delay

The safety AV delay (set at 100 ms) applies to the pacing modes DDD-CLS, DDD(R), DVI(R) and DDI(R).

To prevent ventricular pulse inhibition in the presence of crosstalk, a ventricular pulse will be emitted at the end of the safety AV delay ([Figure 12](#)). When pacing is AV sequential at the pre-set safety AV delay, the presence of crosstalk should be considered and appropriate reprogramming performed (lengthen the ventricular blanking time, lower ventricular sensitivity, bipolar configuration, and/or lower atrial pulse energy).

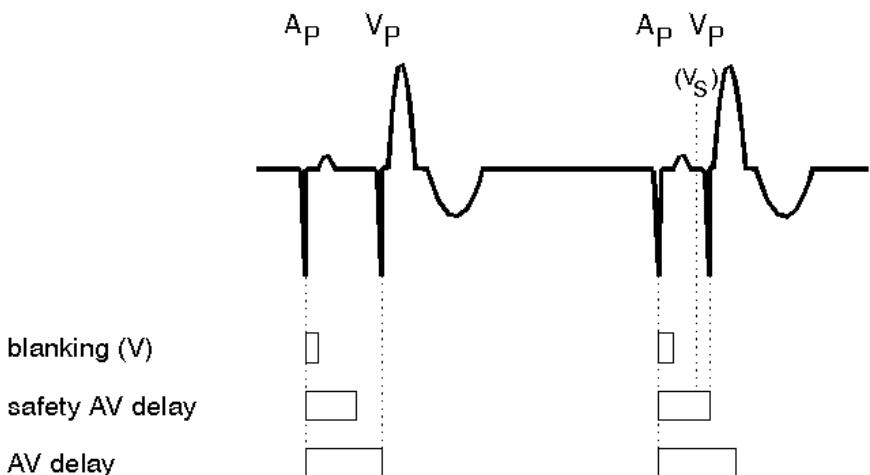


Figure 12. Ventricular blanking time and safety AV delay (Dual chamber)

7.5.7 Upper Rate and UTR Response

The upper rate is programmable (up to 185 ppm) for the dual chamber sensing modes [DDD-CLS, DDD(R), VDD(R)], and for all triggered modes (single and dual chamber). The ventricular pacing rate will never exceed the programmed upper rate regardless of the patient's atrial rate.

NOTE:

Select the upper rate based upon the patient's tolerance for the rate. The upper rate limit determines the minimal interval between a sense or pace event and the subsequent atrial or ventricular pacing event. A shortening of the pacing interval to the upper rate interval may also be initiated at rest (e.g., by detection of muscle potentials). Therefore, for patients with increased vulnerability a lower programmed upper rate is recommended.

UTR response : 2:1, WRL (Automatic Selection)

The UTR response will automatically toggle between 2:1 and WRL (Wenkebach Rate Limiting) depending on the relative programmed values for upper rate and atrial refractory period.

If the UTR is less than the maximum sensed atrial rate, defined by the atrial refractory period (60,000/ARP), the WRL response is utilized. Atrial rates exceeding the selected upper rate will result in a

* Dual chamber

Wenckebach-type pacing pattern. This is accomplished by progressively lengthening the AV delay to keep the ventricular pacing rate at the upper rate. Lengthening of the AV interval is interrupted as soon as: 1) a P-wave falls within the atrial blanking period and is not detected; or 2) a succeeding P-wave is detected before the end of the AV delay previously started. In the second case, the corresponding ventricular pacing pulse is suppressed. If the atrial rate is just above the upper rate, a low degree (i.e., 6:5) block results. Higher atrial rates result in higher degrees of AV block until the intrinsic atrial cycle length violates the programmed atrial refractory period causing a 2:1 or greater block.

The 2:1 response is utilized when the rate defined by the atrial refractory period is less than the upper rate and Automatic Mode Conversion is OFF. In such a case, the maximum pacing rate is regulated by the inability to respond to P-waves falling within the atrial refractory period.

If the resulting length of the spontaneous atrial cycle is shorter than the atrial refractory period in a rate-adaptive mode, the resulting pacing rate will depend on whether the 2:1 rate has been exceeded. If this is the case, the pulse generator will use the sensor rate as the pacing rate. If the 2:1 rate is not exceeded, the pulse generator will use a rate that lies between the sensor rate and the rate determined by the atrial refractory period.

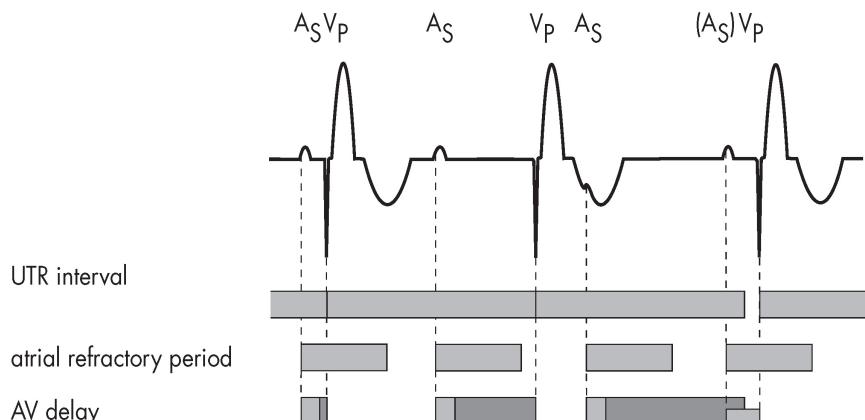


Figure 13. Wenckebach-type pacing pattern (Dual chamber)

7.6 Lead Polarity

The programmed lead polarity determines whether the pulse generator senses or paces in a unipolar or bipolar configuration. Lead polarity can be programmed separately for sensing and pacing in both chambers.

CAUTION

Atrial Sensitivity—In dual chamber systems, the **atrial sensitivity** of 0.1 mV should only be programmed in conjunction with a **bipolar** lead configuration.

If a bipolar lead is connected to the pulse generator, unipolar or bipolar configuration can be programmed for pacing and sensing. As compared to bipolar pacing, the unipolar pacing pulse has the advantage of being clearly identifiable on the ECG. Unipolar pacing occasionally results in muscle stimulation in the pulse generator pocket or diaphragm.

Bipolar sensing offers an improved “signal-to-noise” ratio due to the decreased susceptibility to interference signals like skeletal myopotentials or EMI, and, therefore, permits programming of higher sensitivities (lower values).

WARNING

Unipolar/Bipolar—All Cylos models can be used with either unipolar or bipolar IS-1 leads.

7.7 Parameters for Rate-Adaptive Pacing

The Cylos pulse generator achieves rate adaption through programming of either standard motion-based pacing via a capacitive accelerometer or by the means of the principle of closed loop stimulation (CLS) which involves the translation of myocardial contractility into patient-specific pacing rates.

For standard motion-based rate adaption, the pulse generator is equipped with an accelerometer located on the hybrid circuit of the pulse generator. This sensor produces an electric signal during physical activity of the patient. If a rate-adaptive mode is programmed, then the sensor signal controls the stimulation rate. Sensing and inhibition remains in effect during sensor controlled operation. In the case of high pacing rates, however, the refractory periods may cover a majority of the lower rate interval, resulting in asynchronous operation.

When in CLS mode, the pulse generator monitors and processes the intracardiac impedance signal associated with myocardial contraction dynamics. Changes in the waveform of this impedance signal are associated with changes in the contraction dynamics of the patient's

heart due to the heart's inotropic response to exercise. By monitoring these changes, the pulse generator can provide a pacing rate that is appropriate and specific to the patient's physiologic demands.

For a complete list of rate-adaptive pacing modes available in the Cylos, see [Section 15.1](#).

The following functions are available for tailoring the motion based rate adaptation to the individual patient except for the maximum closed loop rate, which is relevant to CLS.

7.7.1 Sensor Gain

The sensor gain defines the slope of the linear function between exertion and pacing rate. It designates a factor by which the electric signal of the sensor is amplified prior to the signal processing stages. The programmable amplification permits adaptation of the individually programmed sensor gain to the desired rate response. The optimum setting is achieved when the desired maximum pacing rate during exertion is reached during maximum exercise levels. The rate increase, rate decrease and maximum sensor rate settings must be checked for their suitability with respect to the individual patient before adjusting the sensor gain.

If the sensor-driven rate is not sufficient at high levels of exertion the sensor gain setting should be increased. The sensor gain should be reduced if high pacing rates are obtained at low levels of exertion.

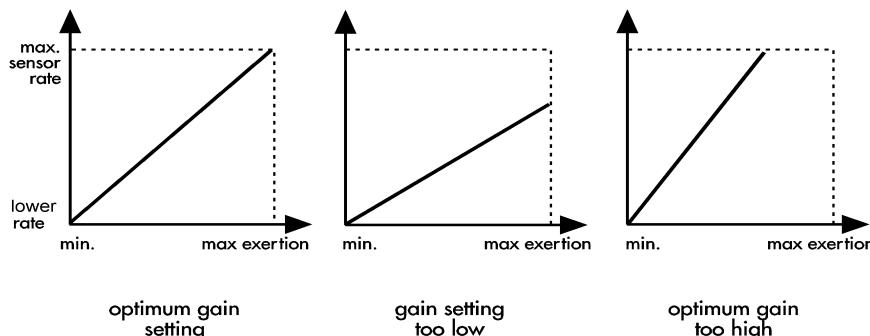


Figure 14. Influence of sensor gain on the rate response

NOTE:

When programmed to DDD-CLS or VVI-CLS, it is recommended to program the Sensor Gain to 10. Note that the programming of the Sensor Gain is only available when Mode Switching is activated.

7.7.2 Automatic Sensor Gain

Cylos pulse generators offer an Automatic Sensor Gain setting, which allows the physician to have the Sensor Gain parameter adjusted automatically.

When the Automatic Sensor Gain is activated, the pulse generator samples the sensor-indicated rate. The sensor gain will be increased by 10%, if the activity rate does not reach or exceed the programmed activity rate (fixed to 90% of maximum sensor rate) for one hour each day over 7 consecutive days. An increase in gain cannot occur more often than every 7 days. If, during the 24 hour period beginning at midnight, the activity rate reaches or exceeds the programmed activity rate (90% of maximum sensor rate) for one hour, the sensor gain setting is reduced by 10%. A change in the sensor gain only occurs at midnight.

NOTE:

If the reed switch is closed, the accumulated time at maximum sensor rate is reset to zero, and the sensor indicated rate measurement resumes for the period that remains in that day.

The Automatic Sensor Gain function is primarily influenced by the Maximum Sensor Rate setting. Therefore the Maximum Sensor Rate must be appropriately selected.

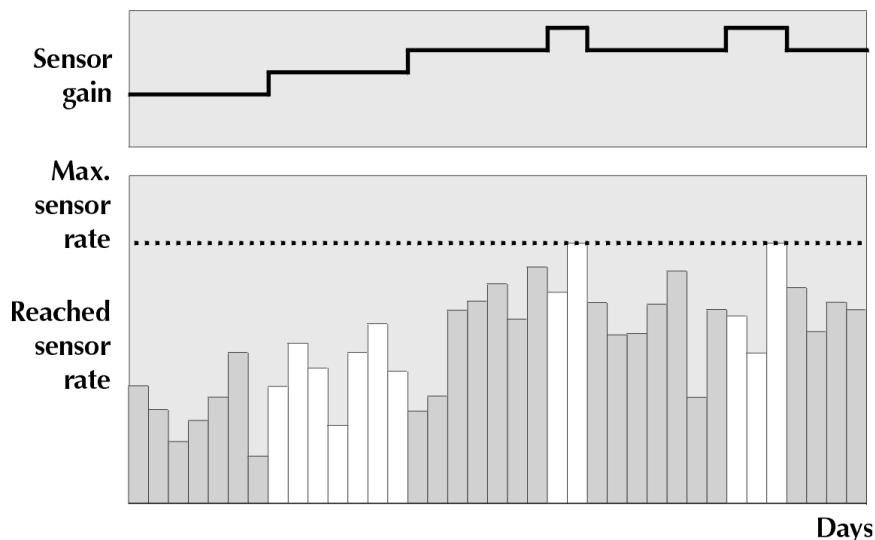


Figure 15. Automatic Sensor Gain

7.7.3 Sensor Threshold

The effects of rate adaptation are limited to sensor signals exceeding the programmable sensor threshold. Sensor signals below this threshold do not affect rate response ([Figure 16](#)). The programmable sensor threshold ensures that a stable rate at rest can be achieved by ignoring sensor signals of low amplitude that are not related to exertion.

If the pacing rate at rest is unstable, or tends to stay above the lower rate without activity, the sensor threshold should be increased. The sensor threshold should be reduced if a sufficient rate increase is not observed at a given level of exertion.

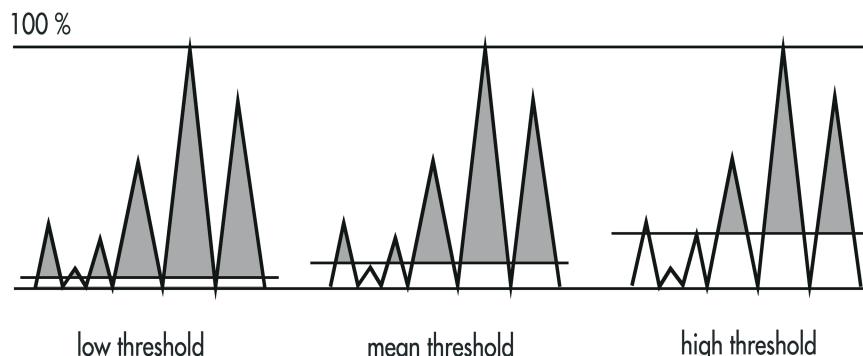


Figure 16. Effect of sensor threshold

7.7.4 Rate Increase

The rate increase parameter determines the maximum rate of change in the pacing rate if the sensor signal indicates increasing exertion ([Figure 17](#)). In DDDR, VDDR, DOOR, VVIR, VOOR, AAIR and AOOR, a rate increase setting of 2 ppm per second increase in pacing rate would take 45 seconds to change from a pacing rate of 60 ppm to 150 ppm.

Table 18: Rate Increase

Increase in Rate (ppm/s)	Time to Increase Rate (seconds)
1	90
2	45
4	23
8	11

In DDIR and DVIR, the rate increase is slightly slower than indicated here (depending on the programmed AV interval). The programmed rate increase setting applies only to the increase in pacing rate during sensor-driven operation and does not affect the pacing rate during atrial triggered ventricular pacing.

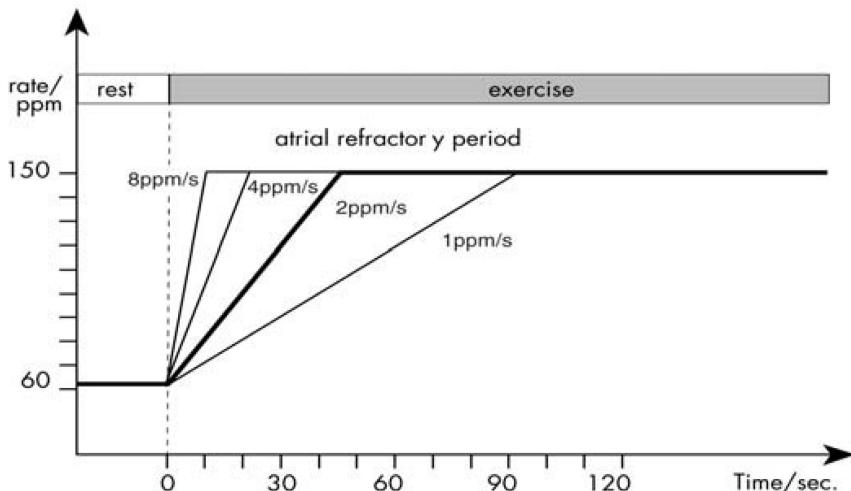


Figure 17. Rate increase during exercise

7.7.5 Maximum Sensor Rate

Regardless of the sensor signal strength, the pacing rate during sensor-driven operation will never exceed the programmed maximum sensor rate. The maximum sensor rate only limits the pacing rate during sensor-driven operation and is independent of the rate limit. The maximum sensor rate (programmable up to 180 ppm) must be less than or equal to the programmed UTR.

CAUTION

Programming Modifications—Extreme programming changes should only be made after careful clinical assessment. Clinical judgment should be used when programming permanent pacing rates below 40 ppm or above 100 ppm.

NOTE:

In the DDIR and DVIR modes, lower maximum sensor rates result, depending on the selected AV interval. The actual values are displayed on the programmer screen. Short AV intervals result in high maximum sensor rates.

7.7.6 Maximum Closed Loop Rate

With the Cylos pulse generator programmed to CLS rate adaptation, the pacing rate during CLS-driven operation will never exceed the programmed maximum closed loop rate. The maximum closed loop rate only limits the pacing rate during sensor-driven operation and is independent of the rate limit. The maximum closed loop (programmable up to 160 ppm) must be less than or equal to the programmed UTR.

CAUTION

Programming Modifications—Extreme programming changes should only be made after careful clinical assessment. Clinical judgment should be used when programming permanent pacing rates below 40 ppm or above 100 ppm.

7.7.7 Rate Decrease

The rate decrease parameter determines the maximum rate of change in the pacing rate, if the sensor signal indicates decreasing exertion ([Figure 18](#)). In DDDR, VDDR, DOOR, WVIR, VOOR, AAIR, and AOOR, the rate decrease setting of 0.4 ppm per second decrease in pacing rate would take 225 seconds to change from 150 ppm to 60 ppm.

Table 19: Rate Decrease

Decrease in Rate (ppm/s)	Time to Decrease Rate (seconds)
0.1	900
0.2	450
0.4	225
0.8	112

In DDIR and DVIR, the rate decrease is slightly slower than indicated here (partly depending on the programmed AV interval).

The programmed rate decrease setting applies only to the decrease in pacing rate during sensor-driven operation and does not affect the pacing rate during atrial triggered ventricular pacing.

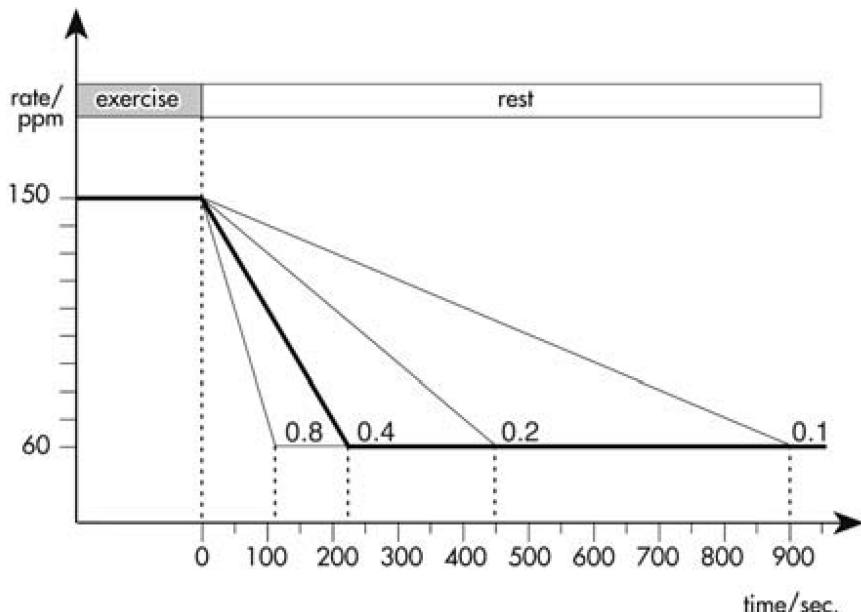


Figure 18. Rate decrease after exercise

7.8 Management of Specific Scenarios

7.8.1 2:1 Lock-In Management

2:1 Lock-In Management is an expansion to the Mode Switch feature. If the AV delay and far-field blanking periods are programmed such that every second intrinsic atrial event falls within the blanking period and the pulse generator detects an atrial rate that is half of the actual rate, the pulse generator does not Mode Switch during an atrial tachycardia as programmed. With 2:1 Lock-In Management, the tachycardia is detected and confirmed, thereby triggering a Mode Switch.

The 2:1 Lock-In Management feature consists of suspicion, confirmation and termination phases, which are described below:

Suspicion

The pulse generator suspects 2:1 Lock-In when the following criteria are met:

- 8 successive V-pace – A-sense (VpAs) sequences have occurred with an average length shorter than the 2:1 Lock-In VA Length Criterion. This VA Length Criterion is based on the AV delay (AsVp) and far-field blanking period (FFB).
- The mean deviation of these 8 VpAs intervals is less than the 2:1 Lock-In Stability Criterion, defined as 40ms.

Confirmation

When the suspicion criteria have been met, the AV delay is increased by the programmed far-field blanking period (up to a maximum of 300 ms) and the Minimum PVARP is set to ON for one cycle. If an atrial event is detected within the AV delay and the detected atrial rate is less than the programmed Mode Switch Detection rate, a 2:1 Lock-In is confirmed.

Otherwise, 2:1 Lock-In is not confirmed, and the AV delay is gradually decreased to the programmed value. The 2:1 Lock-In Management feature is suspended for 120 seconds.

Termination

The pulse generator will immediately mode switch to a non-atrial tracking mode (e.g., DDDR to DDIR) when the confirmation criteria have been met, and then the 2:1 Lock-In Management feature is suspended until the pulse generator mode switches back to the programmed pacing mode.

In order to optimize the programmability of the 2:1 Lock-In Management feature, the atrial blanking period is programmable to allow the physician to ensure that the blanking period is sufficient to recognize cases where a 2:1 Lock-In is likely to occur. Refer to [**Section 7.5.5**](#) for recommendations for programming the atrial blanking period in conjunction with the 2:1 Lock-In Management feature.

7.8.2 PMT Management

A PMT is defined as a tachycardia caused by inadvertently tracking retrograde P-waves. The PMT management feature includes PMT Protection/Termination and a programmable PMT detection and termination algorithm.

7.8.2.1 Protection

PMT protection is accomplished by the following mechanisms:

- Upon detection of a ventricular extrasystole (VES), the lower rate interval and the atrial refractory period (ARP) are reset. Additionally, in VDD mode, the atrial refractory period is initiated with a ventricular pacing pulse that has not been triggered by atrial detection. This prevents a retrograde P-wave with a VA conduction time shorter than the ARP from being sensed and thus from triggering a ventricular pacing pulse. This provides an automatic PMT protection.
- A programmable atrial refractory period extension (ARPE) is available in the DDD, VDD, DDT and VDT modes. To prevent the initiation of a pacemaker mediated tachycardia (PMT) by a ventricular depolarization not preceded by an atrial depolarization, the ARP will be extended by the ARPE if the ARP was:
 - started by a ventricular sense event outside of the AV delay (e.g., PVC) in DDD, DDT, VDD and VDT, or
 - reset by a ventricular pulse not triggered by an atrial sense event in VDD and VDT.

In these instances, the ARP will usually be long enough to prevent sensing of retrograde P-waves. Programming to an ARPE other than 0 ms may rarely be required but could provide additional protection if the ARP is limited or the retrograde conduction time extended.

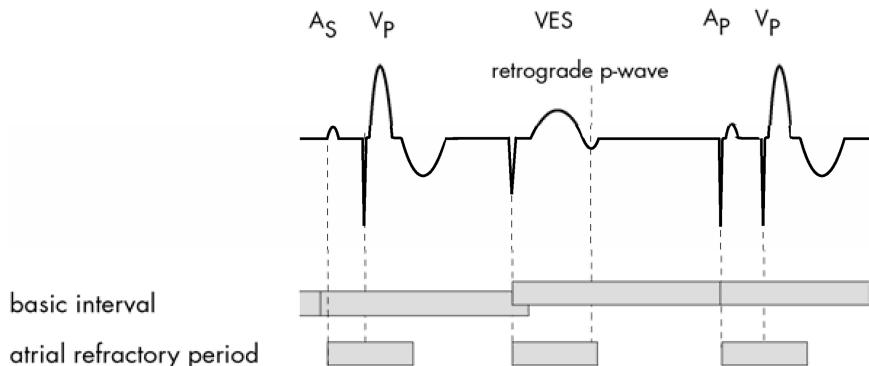


Figure 19. Prevention of PMT by VES starting ARP (DDD)

7.8.2.2 Termination

PMT termination can be accomplished by the following mechanism:

The programmable dynamic AV delay in combination with a fixed TARP (i.e., modulated PVARP) can act as a 'passive' termination of a PMT. Because a PMT is generally at higher rates, the AV delay will be relatively short. This causes the PVARP to be prolonged, which then increases the chance that a retrograde conducted atrial depolarization falls in the PVARP and thus will be inhibited, terminating the PMT.

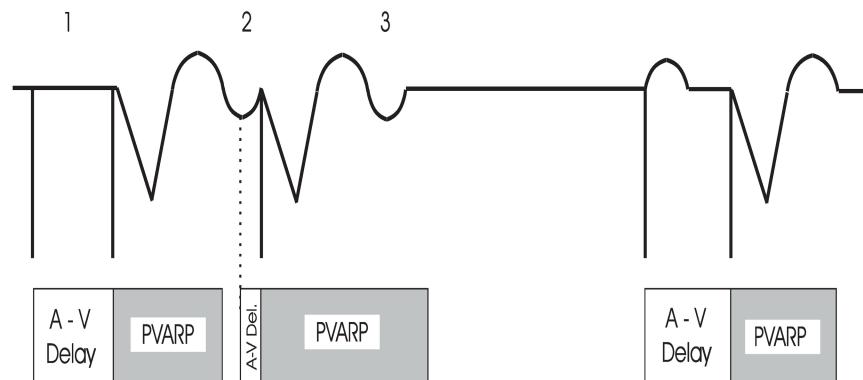


Figure 20. Dynamic AV delay for PMT termination

7.8.2.3 PMT Detection and Termination

In addition to PMT prevention, Cylos contains a programmable PMT detection and termination algorithm. The termination feature will take action in case the prevention was not effective and a PMT is detected. The PMT detection constantly monitors for the presence of a PMT.

The Cylos PMT detection/termination algorithm consists of suspicion, confirmation and termination components and is described as follows.

Suspicion

A PMT is suspected when two criteria are met:

- 8 successive V_p-A_s sense sequences have occurred with a length shorter than the VA criterion. This VA criterion is programmable between 250 and 500 ms.
- The mean deviation of these 8 V_p-A_s intervals is less than the Stability criterion parameter, defined as less than 25 ms.

Confirmation

When the suspicion criterion has been met, the Cylos slightly modifies the AV delay interval (+ or - 50 ms) or the upper tracking rate (+50ms) for one cardiac cycle. If the Vp-As interval remains stable, a PMT is confirmed. Otherwise, a PMT is not confirmed and the algorithm restarts. Once the PMT algorithm has confirmed a PMT, the cycle is broken as follows:

Termination

Cylos extends TARP (Total Atrial Refractory Period) for one cycle to equal the V-V interval + 50 ms.

7.8.3 VES Lock-In Termination

VES Lock-In Termination can benefit patients with first degree AV block, in which case, it is possible for the P-wave to systematically fall in the pulse generator's atrial refractory period after the occurrence of a VES. As a result, the following ventricular event will also be classified as a VES. The VES Lock-In Termination feature breaks through the cyclical misclassification of ventricular events with an atrial pacing pulse.

Circumstances under which the VES Lock-In feature would be programmed include: patients with frequent VES's or patients with occasional atrial undersensing. Under these circumstances, there is a

risk for VES Lock-In caused by the PVARP extension and subsequent atrial event falling in the extended PVARP, which in turn can lead to the classification of a conducted ventricular sensed event as a VES. This VES Lock-In situation can result in a lack of AV synchrony (i.e., long AV delays in case of first degree AV block).

The physician should determine the minimum number of cycles that the pulse generator patient can be exposed to AV dissynchrony and program the number of VES Lock-In cycles to correspond with this minimum.

When the programmed number of consecutive atrial refractory sensed (A_{rs}) – VES sequences (VES Lock-In Detection Count) are detected (programmable to 4, 6, and 12 cycles), an atrial paced event will be delivered following an atrial sensed event that is timed directly after the far-field blanking within the atrial refractory period. As a result, the pulse generator will be resynchronized to the heart's intrinsic rhythm.

The VES Lock-In Termination feature is suspended while in magnet mode and is disabled at Elective Replacement Indication (ERI).

7.9 Active Capture Control (ACC)

7.9.1 Feature Description

The ACC feature periodically measures the capture threshold, and automatically adjusts the pacing output (with a programmable safety margin). Additionally, the feature continuously assesses ventricular pacing capture on a beat-to-beat basis and responds to any loss of capture with a safety back-up pulse. During the clinical evaluation of the Active Capture Control algorithm, it was demonstrated that use of Active Capture Control can increase device longevity (as compared to standard programming).

Differences in the signal morphology between the polarization artifact and the evoked response signal are used to distinguish capture events from non-capture events. The polarization artifact is the signal caused by the pacing pulse between the pacing electrode and the cardiac tissue. The evoked response signal is the intracardiac signal measured during electrical activation of the myocardium.

Figure 21 shows an example of an evoked response signal and a polarization artifact. After an effective blanking period of 20 ms, the signal is evaluated over the next 60 ms. Several characteristics of the signal falling into this window are evaluated in order to discriminate the evoked response (capture) from polarization artifact (possible non-capture).

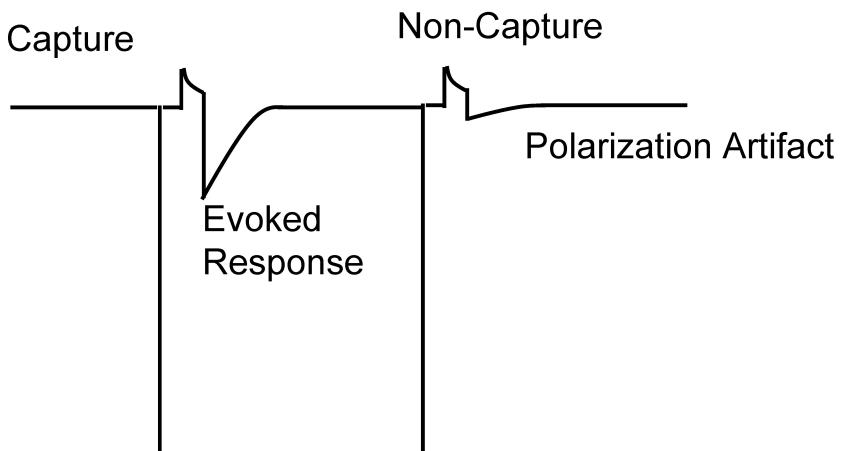


Figure 21. Example of a Capture and a Non-Capture beat

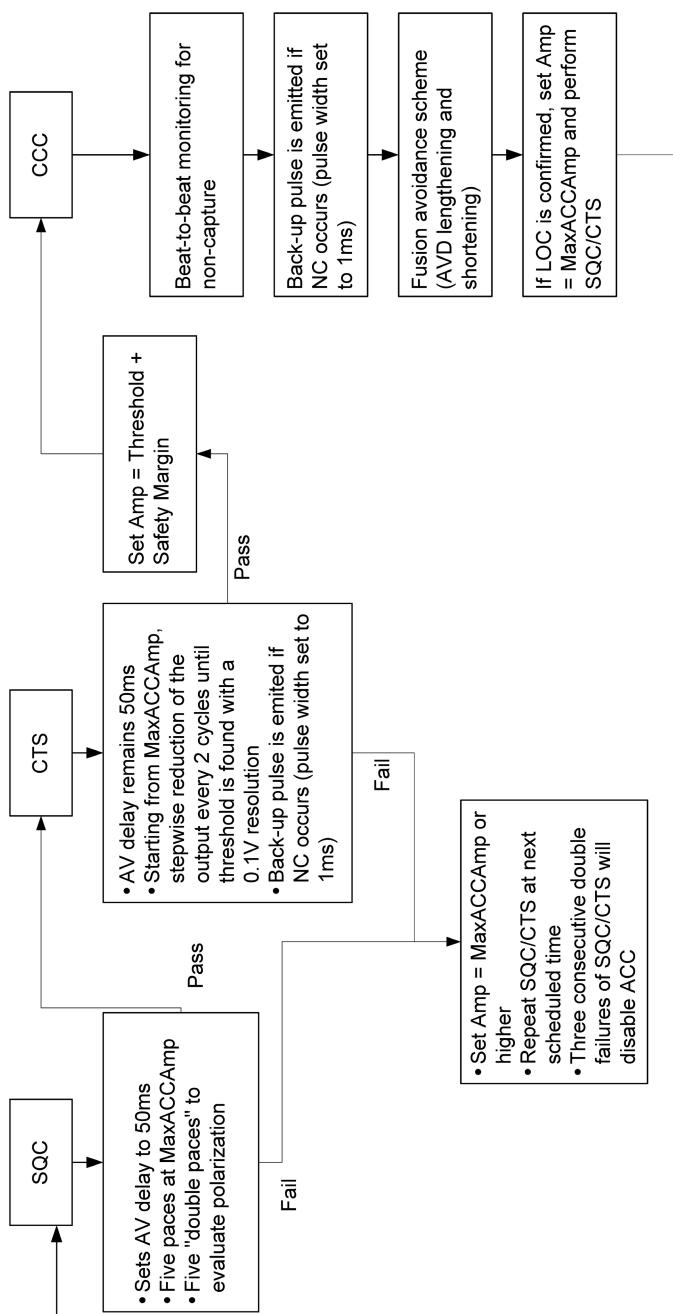
Table 20 contains a list and description of the acronyms and terms pertaining to the ACC feature used in this manual.

Table 20: Acronyms and Terms

Term	Definition
CCC	Continuous Capture Confirmation —A component of the ACC feature that provides beat-to-beat classification of capture and non-capture.
CTS	Capture Threshold Search —A component of the ACC feature that periodically measures the ventricular pacing threshold. CTS can only occur after a successful SQC.
Evoked Response	The intracardiac signal measured during electrical activation of the cardiac tissue.
LOC	Loss-of-Capture —The ACC feature classifies loss of capture when a series of ventricular pacing pulses at varying AV delays did not capture (with a maximum of 3 consecutive NC's).
MaxACCAmp	Maximum ACC Amplitude —This programmable parameter is the maximum voltage setting that ACC will set after a successful CTS.

Table 20: Acronyms and Terms

Term	Definition
NC	Non-Capture —The ACC feature identifies a non-capture as a single ventricular pacing pulse without capture.
Polarization Artifact	The signal or noise caused by the pacing pulse between the pacing electrode and the cardiac tissue.
Safety Margin	The safety margin is the difference between the pacing threshold and the programmed pacing amplitude.
SQC	Signal Quality Check —A component of the ACC feature that periodically determines whether evoked responses are appropriately detected and that pacing artifact is sufficiently small in amplitude. If the SQC determines that the signal is not acceptable, then the other portions of the ACC feature cannot be activated.

**Figure 22. ACC flow chart**

The feature includes three primary components: Signal Quality Check, Capture Threshold Search, and Continuous Capture Confirmation. The following paragraphs describe the operation of these three components (SQC, CTS and CCC) of ACC while active in DDD(R) pacing mode. In the other modes (VDD(R) and VVI(R)), there are slight variations in the operation of ACC. **Figure 22** provides a flow chart of the ACC operation.

Signal Quality Check (SQC)

A polarization artifact that is too large may disturb the cardiac signal following the pacing pulse and result in misclassification of the event. Conversely, the evoked response signal may be too small or may not meet the capture criteria, which again may lead to misclassification of the event. Therefore, the SQC analyzes the evoked response and the amplitude of the polarization artifact. A successful SQC must always be completed before the Capture Threshold Search or the activation of Continuous Capture Confirmation.

1. SQC is performed in two separate phases. In both phases, the AV delay is shortened to 50 ms after a paced atrial event and to 15 ms after a sensed atrial event to ensure ventricular pacing. First, five ventricular pacing pulses are delivered at MaxACCAmp, which is the programmable maximum voltage setting (2.4, 3.6, 4.8 or 6.4 V). If non-capture is detected at the maximum voltage setting, the second phase of the SQC is aborted and the test is classified as unsuccessful. In the next phase, five “double” pacing pulses (one pacing pulse followed by another pacing pulse 100 ms later, in the absolute refractory period) are delivered. These pulses are used to verify that the polarization artifact is small enough to distinguish capture from non-capture. If the artifact following the second pacing pulse is higher than a certain limit, then SQC is classified as unsuccessful. If necessary, this test can be repeated at a lower maximum voltage setting.
2. If the first SQC after activating ACC is not completed successfully, ACC is immediately disabled, and the pacing amplitude is programmed to MaxACCAmp. ACC then requires manual reactivation of the feature with the programmer.

3. If the first SQC after activating ACC is completed successfully, but subsequent SQC's are not completed successfully, then ACC is suspended, and the pacing amplitude is programmed to the last measured threshold plus the safety margin or higher. The SQC will be attempted up to three times. After the 3rd failure, ACC is disabled, and the pacing amplitude is programmed to the MaxACCAmp plus the Safety Margin of 1.2V. ACC then requires manual reactivation of the feature with the programmer.

Capture Threshold Search (CTS)

1. The Capture Threshold Search is the component of the ACC feature that measures the ventricular pacing threshold by stepping down the output until non-capture occurs.
2. The CTS occurs over a series of cardiac cycles and begins at the programmed MaxACCAmp (2.4, 3.6, 4.8 or 6.4 V) that decreases until capture is lost. AV delay is shortened to 50 ms after a paced atrial event and to 15 ms after a sensed atrial event to ensure ventricular pacing.
3. The pacing amplitude decrements every 2 paced beats by one eighth of the current pulse amplitude. Once the pacing output is less than 1.2 V, the voltage decrements 0.1 V every 2 paced beats.
4. If a single non-capture is detected on the second pace when the voltage decrement is 0.1 V, the pacing amplitude is set to the sum of the pacing threshold voltage and the programmed safety margin. If a single non-capture is detected on the first pace when the voltage decrement is 0.1 V, the pacing amplitude that is set is increased by 0.1 V. If a single non-capture is detected when the voltage decrements are greater than 0.1 V, the pacing amplitude is set to the previous amplitude minus 0.1 V and then the amplitude decrements by 0.1 V until the pacing threshold is determined. When another single non-capture is detected, the previous voltage setting is the pacing threshold.
5. The pacing amplitude is then set to the pacing threshold plus a programmable safety margin (0.3 V through 1.2 V in steps of 0.1 V).

6. In addition to performing the threshold search after a loss of capture, the search is also conducted at a programmable interval or at 2 specific times during the day to provide an accurate safety margin even with gradual changes in the pacing threshold. Note that a CTS initiated by spontaneous loss of capture will reset the timer that triggers the next periodic measurement if the search is programmed to interval.

Continuous Capture Confirmation (CCC)

The Continuous Capture Confirmation function is the component of the ACC feature that provides beat-to-beat capture verification. (Not available in the ATM mode).

1. If ACC determines that capture has been maintained, then the pulse amplitude remains at that current setting and no action is required.
2. If ACC determines that non-capture (NC) occurred, then a safety back-up pacing pulse is delivered at an increased energy (same output voltage and pulse width extended to 1.0 ms) within 130 ms after the non-captured pacing pulse. The back-up pulse restarts the pacing interval timer, i.e., the next timing cycle is lengthened by approximately 130 ms.
3. If a series of ventricular pacing pulses at varying AV delays result in loss-of-capture, a Signal Quality Check (SQC) and Capture Threshold Search (CTS) are initiated to determine the current pacing threshold.

4. The algorithm is designed to respond appropriately to fusion beats. In order to discriminate non-capture from fusion, a capture confirmation algorithm varies the AV delay after detection of non-capture in the dual chamber pacing modes. First, fusion is diminished by extending the AV delay. If a second non-capture is detected, the AV delay is returned to the programmed AV delay. If a third consecutive non-capture is detected, loss of capture is confirmed and a Signal Quality Check and Capture Threshold Search are initiated. If the first event was truly fusion, the extended AV delay could allow intrinsic conduction. The AV delay will not return to the normal programmed value until ventricular pacing is required. In case the capture confirmation continues to detect non-captures without detecting 3 consecutive non-captures, the algorithm shortens the AV delay (50 ms after an atrial paced event and 15 ms after an atrial sensed event for up to 2 paced cycles) to confirm the occurrence of non-capture. When ACC and CLS are both enabled, the AV delay is extended after detection of non-capture and then capture confirmation is temporarily disabled while CLS performs an AV Hysteresis Scan.

7.9.1.1 Algorithm Suspension, Abort and Disabling

The ACC feature is inactive until the first SQC and CTS after programming is completed successfully. The SQC/CTS sequence is unsuccessful when the SQC or CTS fail or are aborted. In addition, an SQC/CTS sequence can be postponed and CCC can be temporarily suspended.

The SQC/CTS sequence will fail when the following events occur:

- Non-capture during SQC: non-capture occurs twice in the second through fifth cycles of the SQC (at the maximum voltage amplitude setting).
- High polarization artifact during SQC: the polarization artifact measured during the SQC is too high.
- No non-capture during CTS: the threshold search decreases the output to 0.1 V without detecting non-capture.

An ongoing SQC/CTS sequence will abort when the following events occur:

- Mode Switch: Mode switch has a higher priority than the SQC/CTS. If Mode switch aborts an SQC/CTS, the device will be set to high output. After reversion back to the programmed mode, a new SQC/CTS will be initiated.

- Programmer Wand application: An ongoing SQC/CTS aborts when a magnet (programmer wand) is applied and the device is then set to high output. After removal of the magnet, a new SQC/CTS is started.
- Search timer expiration (120 seconds): if the SQC/CTS takes longer than 120 seconds to be completed (e.g. due to sensing), the SQC/CTS will be aborted and the device will be set to high output.
- Noise detection: if excessive noise is detected, the initial SQC/CTS will be aborted and the device will be set to high output.

A SQC/CTS sequence will be postponed when the following events occur:

- Mode switch is ongoing: If Mode switch is ongoing when an SQC/CTS is scheduled, the SQC/CTS will be postponed until reversion back to the programmed mode.
- The presence of a magnet is detected: A scheduled SQC/CTS is postponed when a magnet (programmer wand) is detected. After removal of the magnet, the SQC/CTS is started.
- The ventricular rate is higher than 100 bpm: A scheduled SQC/CTS is postponed when the ventricular rate is higher than 100 bpm. When the ventricular rate drops below 100 bpm, the SQC/CTS is started.

The continuous capture control (CCC) will be suspended and the ventricular pacing amplitude is set to high output when the following events occur:

- The ventricular rate is higher than 110 bpm: CCC is suspended while the ventricular rate is higher than 110 bpm. When the ventricular rate drops below 110 bpm, CCC is resumed.
- Mode Switch: CCC is suspended and the device is set to high output until reversion back to the programmed mode.

The ACC feature will be automatically turned OFF when the following events occur:

- The initial SQC/CTS sequence after activating ACC failed
- Three subsequent and consecutive failed SQC attempts
- The occurrence of 25 Losses of Capture between two consecutive days
- ERI: the device will be set to ERI mode with ACC OFF

The occurrence of these unsuccessful, aborted or postponed SQC/CTS sequences and disabling of the ACC feature are being reported in the Status log in the ACC statistics.

7.9.2 Active Capture Control Programming

ACC is programmable to ON, Active Threshold Monitoring (ATM) modes, and OFF. **Table 21** provides details about the ACC programmability.

Table 21: ACC Programmability

ACC Components	Programmable Modes for ACC	
	ON	ATM
Pulse width programmability		≤0.4 ms
SQC and Capture Threshold searches	Yes	Yes
Set output to threshold + safety margin	Yes	No
Continuous Capture Confirmation (CCC)	Yes	No

When programmed to ON, the device will continuously monitor the cardiac signal following the pacing pulse to verify that a depolarization occurred as a result of the pulse. Upon detection of non-capture, the device will issue a back-up pulse at a higher output (pulse width increased to 1 ms) within 130 ms. If loss-of-capture (LOC) occurs, the device will immediately increase the pacing amplitude to the maximum ACC amplitude (MaxACCAmpl) plus the Safety Margin (1.2 V) for two cycles and then initiate an SQC/CTS. Additionally, the device will perform regular threshold searches at the programmed interval or at two programmable times per day. After a successful threshold search, the device will program the pulse amplitude to the threshold plus the programmed Safety Margin. The device will never set the amplitude lower than the programmed Minimum ACC Amplitude (Min Ampl.).

NOTE:

After programming the Active Capture Control feature to ON or ATM, the device will perform a signal quality check and a capture threshold search. This sequence can take up to 2 minutes.

7.10 Home Monitoring (Cylos DR-T)

Home Monitoring enables the exchange of information about a patient's cardiac status from the implant to the physician. Home Monitoring can be used to provide the physician with advance reports from the implant and can process them into graphical and tabular format called a Cardio Report. This information helps the physician optimize the therapy process, as it allows the patient to be scheduled for additional clinical appointments between regular follow-up visits if necessary.

BIOTRONIK conducted the TRUST study to evaluate the safety and effectiveness of Home Monitoring. Refer to [**Section 6.4**](#) for details regarding the study design and results. With the TRUST study, BIOTRONIK was able to show the following with regards to Home Monitoring:

- BIOTRONIK Home Monitoring information may be used as a replacement for device interrogation during in-office follow-up visits.
- A strategy of care using BIOTRONIK Home Monitoring with office visits when needed has been shown to extend the time between routine, scheduled in-office follow-ups of BIOTRONIK implantable devices in many patients. Home Monitoring data is helpful in determining the need for additional in-office follow-up.
- BIOTRONIK Home Monitoring-patients—who are followed remotely with office visits when needed—have been shown to have similar numbers of strokes, invasive procedures and deaths as patients followed with conventional in-office follow ups.
- BIOTRONIK Home Monitoring provides early detection of arrhythmias.
- BIOTRONIK Home Monitoring provides early detection of silent, asymptomatic arrhythmias.
- Automatic early detection of arrhythmias and device system anomalies by BIOTRONIK Home Monitoring allows for earlier intervention than conventional in-office follow-ups.
- BIOTRONIK Home Monitoring allows for improved access to patient device data compared to conventional in-office follow ups since device interrogation is automatically scheduled at regular intervals.

The implant's Home Monitoring function can be used for the entire operational life of the implant (prior to ERI) or for shorter periods, such as several weeks or months.

Home Monitoring can be utilized as a functional replacement for in-office follow-up visits and allows the time between routine, scheduled, in-office follow-ups of BIOTRONIK implantable devices to be extended to twelve months or more. Home Monitoring evaluation of implanted devices and patient status is as safe as conventional in-office follow-ups. BIOTRONIK's Home Monitoring system provides early detection of arrhythmic events and of silent, asymptomatic events. Automatic

early detection of clinical events by Home Monitoring leads to earlier intervention than conventional in-office follow-ups and improves adherence to scheduled follow-ups.

NOTE:

When ERI mode is reached, this status is transmitted. Further measurements and transmissions of Home Monitoring data are no longer possible.

7.10.1 Transmission of Information

The implant transmits information with a small transmitter, which has a range of about 6 feet (2 meters). The patient's implant data are sent to the corresponding patient device in configurable periodic intervals. The transmissions may also be activated by the patient with the application of a magnet over the implant and by certain cardiac events, as programmed. The types of transmissions are discussed in Section 4.

The minimal distance between the implant and the patient device must be 6 inches (15 cm).

7.10.2 Patient Device

The patient device ([Figure 23](#)) is designed for use in or away from the home and is comprised of the mobile unit and the associated charging station. The patient can carry the mobile unit during his or her occupational and leisure activities. The patient device is rechargeable, allowing for an approximate operational time of 24 hours. It receives information from the implant and forwards it via the cellular mobile network or the standard telephone system to a BIOTRONIK Service Center.

For additional information about the patient device, please refer to its manual.

7.10.3 Transmitting Data

The implant's information is digitally formatted by the BIOTRONIK Service Center and processed into a concise report called a Cardio Report. The Cardio Report, which is adjusted to the individual needs of the patient, contains current and previous implant data. The Cardio Report is sent to the attending physician via fax or is available on the Internet, which is selected during registration of the patient. For more information on registering for Home Monitoring, contact your BIOTRONIK sales representative.

The password protected BIOTRONIK Home Monitoring website can be accessed at the following URL:

www.biotronik-homemonitoring.com

An online help menu is available in order to assist with the use of the Home Monitoring website.

Use of the Internet for reviewing Home Monitoring data must be in conjunction with the system requirements listed in **Table 22**. Additionally, **Table 22** provides system specifications that are recommended for optimizing usage of the Internet.

Table 22: System Requirements / Recommendations

	System Requirements	System Recommendations (for Optimal Usage)
Screen Resolution	1024 x 768	≥ 1280 x 1024
Internet Bandwidth	56 kB/sec	≥ 128 kB/sec (DSL, cable modem)
PC	800 MHz Pentium processor, 128 MB RAM	N/A
Internet Browser	MS Internet Explorer 5.5 - or - ≥ Mozilla 1.8 (Firefox ≥ 2.0)	≥ MS Internet Explorer 5.5 - or - ≥ Mozilla 1.8 (Firefox ≥ 2.0)
Acrobat Reader	Version 6.1	Version 6.1 or higher
Communication Channel	Fax (G3) or e-mail	Fax (G3), e-mail or mobile phone

Additionally, the attending physician may register to be informed of the occurrence of an Event Triggered Message through email or SMS (i.e., mobile phone) with a brief text message. If registered for Internet availability, the patient's detailed implant data can then be viewed by logging onto the Home Monitoring website.



Figure 23: Example of Patient Device with Charging Stand

7.10.4 Types of Report Transmissions

When the Home Monitoring function is activated, the transmission of a report (Cardio Report) from the implant can be triggered as follows:

- Trend report – the time period (daily) initiates the report
- Event report – the pulse generator detects certain events, which initiate a report
- Patient report – the patient initiates the report

7.10.4.1 Trend Report

The time of the report transmission is programmable. For periodic messages, the time can be set anywhere between 0:00 and 23:59 hours. It is recommended to select a time between 0:00 and 4:00.

The length of the time interval (monitoring interval) is preset to “daily”. For each monitoring interval, a data set is generated in the implant and the transmission is initiated at the designated time.

7.10.4.2 Event Report

When certain cardiac and technical events are detected by the implant, a report transmission is automatically triggered. This is described as an “event message”.

The following clinical and technical events initiate a Home Monitoring message transmission:

- Atrial Lead Check < 300 and > 3000 Ohm
- Ventricular Lead Check < 300 and > 3000 Ohm
- ACC Disabled
- Low P-wave Amplitude (<50% safety margin)
- Low R-wave Amplitude (<50% safety margin)
- Ventricular Threshold >4.8 volts

NOTE:

The attending physician must notify the BIOTRONIK Service Center about which of these events he/she wishes to be informed.

7.10.4.3 Patient Report

It is possible to trigger a transmission through magnet application over the pacemaker. The attending physician must inform the patient in detail about operating the device and about the physical symptoms which would warrant a magnet application by the patient.

WARNING

The magnet effect must be programmed “synchronous” if the [Patient Report] function is activated. Otherwise, this function will not be available.

* Examples: The programmed sensitivity is 1.0 mV.

- Average of the measured P/R-Wave amplitudes is 2.6 mV. Therefore, measured value is greater than 100% of the safety margin. Event report is not triggered.
- Average of the measured P/R-Wave amplitudes is 1.9 mV. Therefore, measured value is less than 100%, but greater than 50% of the safety margin. Event report is not triggered.
- Average of the measured P/R-Wave amplitudes is 1.4 mV. Therefore, measured value is smaller than 50% of the safety margin. As a result, an event report is triggered.

7.10.5 Description of Transmitted Data

The following data are transmitted by the Home Monitoring system, when activated. In addition to the medical data, the serial number of the implant is also transmitted.

The Monitoring Interval

The monitoring interval is considered the time period since the last periodic message was transmitted. In a periodic report, the monitoring interval since the previous periodic report would be 24 hours. For an event or patient report, the monitoring interval would be less than 24 hours, since these reports are sent after the programmed transmission time of the periodic report.

Heart Rate

- Average ventricular heart rate (bpm)
- Maximum ventricular heart rate (bpm)
- Duration of maximum ventricular heart rate (sec)

Atrial Rhythm

- Number of Mode Switch events
- Duration of Mode Switching (%)
- Number of Atrial Fibrillation / 24hours
- Number of Atrial Flutter / 24hours
- Number of Atrial Tachycardia / 24hours

Ventricular Rhythm

- Intrinsic rhythm (Vs/ Vx) (%)
- Ventricular rate at Mode Switching (bpm)
- Number of ventricular runs (4...8 sequential VES)
- Number of ventricular events (more than 8 sequential VES), defined as a ventricular tachycardia (VT)
- Maximum VES / hour

Sensing / Pacing

- Mean P-Wave amplitude / programmed sensitivity (%)
- Mean R-Wave amplitude / programmed sensitivity (%)

System Status

- Atrial lead check
- Ventricular lead check
- Active Capture Control (ACC) status
- Ventricular Threshold
- Battery status

8. Statistics

8.1 Statistics Overview

Cylos pulse generators can store a variety of statistical information. The various statistics consist of such features as rate histograms, event counters, sensor trends, VES statistics, and activity reports, which are described in the following sections.

8.1.1 Timing

- Event Counters
- Special Events
 - AV Scan Hysteresis. Successful
 - Mode Switching
 - PMT Termination
 - VES Lock-In Termination Counter
- A / V Rate Histogram
- A / V Rate Trend
- Intrinsic A / V Conduction Histogram
- Far-Field Histogram

8.1.2 Arrhythmia

- Tachy Episode Trend
 - Mode Switch Histogram
 - Mode Switch Trend
 - Tachy Episode Counter
 - 1st Tachy Episode
- AT Histogram
- AES Trend
- AES vs. Atrial Rate
- AES Coupling Intervals
- VES Classification
- VES vs. Ventricular Rate
- VES Coupling Intervals

8.1.3 Sensor

- Rate / Sensor Trend
- Sensor Histogram
- Activity Report
- Sensor Gain Trend

8.1.4 Sensing

- P-wave Trends
- R-wave Trends

8.1.5 Pacing

- A / V Impedance Trends
- Ventricular Pacing Amplitude Trend
- Ventricular Pacing Amplitude Histogram
- Ventricular Threshold Trend
- ACC Status

8.1.6 General Statistical Information

- The Cylos pulse generators statistics modes are always in operation and cannot be selected OFF.
- The counters within the statistic features do not operate when a magnet is applied to the pulse generator.
- The counters within the statistic features are reset each time the pulse generator is permanently programmed.
- The histogram bars are standardized to a rate class width of 10 ppm to avoid distortion of the rate distribution that would be caused by varying rate class widths. The formula is:

percentage of total events occurring represented by the
events counted in this class x 10

Bar Length = _____

rate width of this class

8.2 Timing Statistics

8.2.1 Event Counter

The event counter can record the following events and event sequences:

Events

- A_s = atrial sense
- A_p = atrial pace
- A_{rs} = atrial refractory sense
- V_s = ventricular sense
- V_p = ventricular pace
- V_{rs} = ventricular refractory sense

Event sequences

- $A_s - V_s$
- $A_s - V_p$
- $A_p - V_s$
- $A_p - V_p$
- $V - V$
(ventricular extrasystole = VES)

Upon interrogation, the total number of events as well as the relative number with respect to all events counted (expressed as a percentage) in each category are displayed.

NOTE:

Upon magnet application, the recording of events and event sequences is interrupted temporarily, regardless of the selected magnet effect.

Any reprogramming will clear the counters in the pulse generator. Premature ventricular contractions (PVCs) are counted both as PVCs and as ventricular sense events.

When Event Counters exceed 8 digits, they are presented in exponential form. Heart Rate and Sensor Rate Histograms will switch to exponential form when the Counters exceed 6 digits (e.g., 1,000,000 events will appear as 1.0E+06).

8.2.2 Heart Rate Histogram

A heart rate histogram is available for both atrial and ventricular events. This function records the number of heart sense and pace events within certain rate ranges. The rate range is subdivided into 16 rate classes from 40 bpm to 180 bpm, including bins for rates <40 bpm and rates >180 bpm. The percentage and total number of sensed and paced events occurring within a rate class is displayed. Recording stops when the

memory available for recording the heart rates is full. Recordings can be stored for several years. The frequency distribution of the heart rates can be displayed on the programmer as a diagram during follow-up examinations.

NOTE:

The bars of the histogram are standardized to a rate class width of 10 ppm to avoid distortion of the rate distribution.

When Event Counters exceed 8 digits, they are presented in exponential form. Heart Rate and Sensor Rate Histograms will switch to exponential form when the Counters exceed 6 digits (e.g., 1,000,000 events will appear as 1.0E + 06).

8.2.3 A/V Rate Trend

This feature permits recording of the atrial and ventricular heart rate (sense and pace) from the last 24 hours to show the percentage of pacing events ([Figure 24](#)). The duration of the averaging intervals is 16 minutes for a 24-hour recording period. For a recording period less than 24 hours, the resolution is automatically increased (for example 30 seconds for a 30 minute recording period). The shorter the recording interval, the higher the resolution. Therefore, it is possible to document rate changes very accurately, for example, during exercise tests.

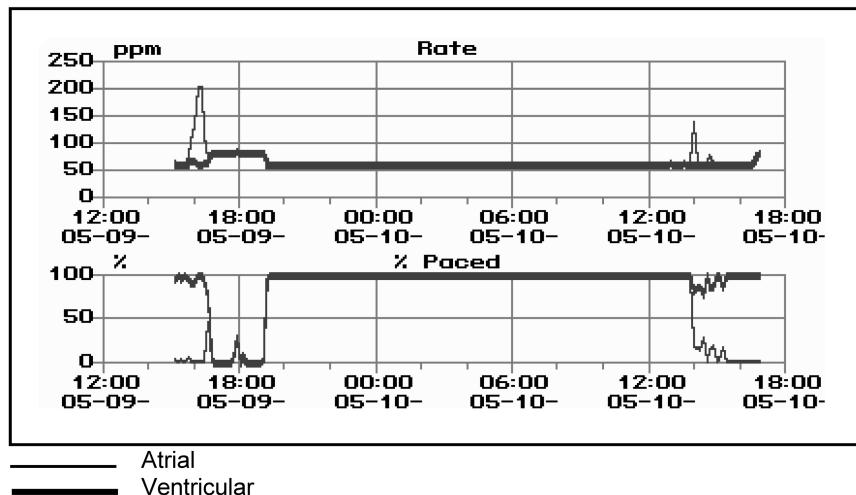


Figure 24. A/V Rate Trend

8.2.4 Intrinsic AV Conduction Histogram

This diagnostic records the distribution of intrinsic AV conduction for several rate bins in bar graph format ([Figure 25](#)). The rate bins used for the AV Conduction Histogram are the same as those used for programming the Dynamic AV delay settings. This diagnostic aids in optimizing the programmed AV delay with the patient's intrinsic AV conduction over a range of heart rates.

Intrinsic AV conduction

— AV delay
- - - AV hysteresis

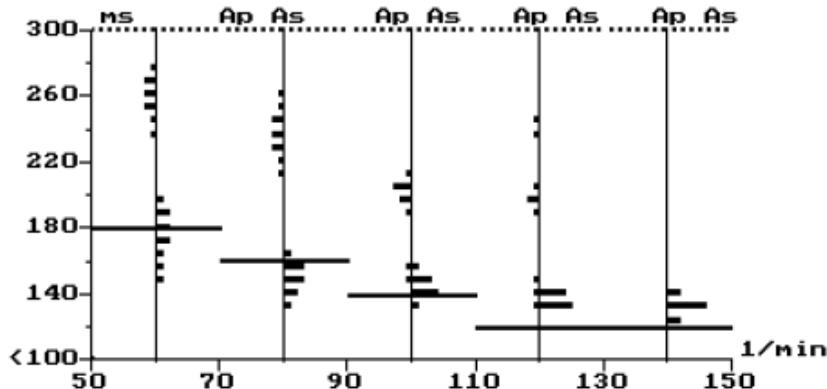


Figure 25. Intrinsic AV Conduction Histogram

8.3 Arrhythmia Statistics

8.3.1 Tachy Episode Trend

The Tachy Episode trend can only be selected when Mode Switching has been programmed ON. The following information is available when the Tachy Episode Trend is enabled.

NOTE:

One tachycardia episode may contain multiple mode switches within the same trend.

Mode Switch Histogram—A histogram indicates the percentage of time the atrial rate was above the mode switch intervention rate.

Tachy Episode Counter—A counter reports the number of mode switches that occurred since the last follow-up visit.

Mode Switch Trend (Tachy Episode Protocol)—The trend records up to 64 atrial tachycardia episodes that result in a mode switch. The trends are available as a rolling trend and therefore contain information about the most recent events. The atrial tachycardia episodes are displayed graphically as a function of time on the programmer screen.

Mode Switch Report (Tachy Episode Protocol)—The printout of the stored diagnostics includes a Mode Switch Report entitled Tachy Episode Protocol. This report includes a list of the 64 stored atrial tachycardia episodes detailing the date/time stamp and the duration of each episode.

8.3.2 AES Statistics

This function enables long-term recording and analysis of atrial extrasystoles (AES events). An atrial event is classified as an atrial extra systole (AES) if it falls in the AES window. This AES window begins after the absolute atrial refractory period and ends at a programmable Atrial Prematurity percentage of the average of the last four P-P intervals.

AES Histogram

The pulse generator classifies AES events that occur according to their complexity. The following information is available when AES statistics are enabled.

Class	Corresponding to Additional Criteria
AF	Atrial Fibrillation unstable rate and x out of 8 criteria
AFl	Atrial Flutter stable rate
AT	Atrial Tachycardia sudden onset

Additionally, the following accelerations between zones are reported.

AFl to AF	AT to AFL
AT to AF	SR to AT

The AES events are classified according to their complexity in one of the following classes.

Class	Event Sequence
Single AES	A-AES
Couplets	A-AES-AES

Class	Event Sequence
Triplets	A-AES-AES-AES

The average number of AES per hour is also reported.

AES vs. Atrial Rate

Information about the number of AES events as a function of the atrial rate can be found in the AES vs Atrial Rate Histograms.

This histogram has 16 rate bins with 10 bpm/bin resolution. The data in every bin contains the percentage of the total number of events and the number of counts falling into that bin.

AES Coupling Interval

The AES coupling interval shows the time interval between the regular atrial event and the subsequent AES in the form of a histogram.

This histogram has 16 rate bins at approximately 100ms/bin. The data in every bin contains the percentage of the total number of events and the number of counts falling in that bin.

8.3.3 VES Statistics

This function enables long-term recording and analysis of ventricular extrasystoles (VES events). VES events are defined as ventricular events that have not been preceded by an atrial sensed or pacing event.

VES Classification

VES events are classified according to their prematurity and their complexity.

The VES prematurity histogram consists of 3 bins (0-25%, 25-50%, 50-100%). The data in every bin contains the percentage of the total number of events and the number of counts falling in that bin. The VES prematurity is defined as the time at which the VES events occur prior to the expected regular ventricular event as a percentage of the normal V-V interval.

Additionally, the pulse generator classifies VES events that occur according to their complexity. The following information is available when VES statistics are enabled.

Class	Event sequence
Single VES	V- VES
Couplets	V-VES-VES
Triplets	V-VES-VES-VES
Runs (4...8)	V-VES-VES-...
#VT Episodes	More than 8 consecutive VES

The maximum number of VES per hour is also reported.

NOTE:

If in DDD(R) and atrial undersensing occurs, spontaneously conducted ventricular events are evaluated as VES events. For this reason, we recommend using the VES analysis in DDD(R) mode only in conjunction with bipolar sensing and an appropriately high atrial sensitivity.

The interval between two consecutive VES events must be shorter than 500 ms (i.e., over 120 ppm) for them to be counted. Otherwise, the second VES will be ignored and the sequence interpreted or terminated. This predominantly eliminates the possibility of VES events being miscounted as a result of atrial undersensing.

VES Coupling Interval

The VES coupling interval shows the time interval between the regular ventricular event and the subsequent VES in the form of a histogram. This histogram includes 16 bins at approximately 60 ms/bin. The data in every bin contains a percentage of the total number of events and the number of counts falling in that bin.

VES vs. Ventricular Rate

The number of VES events as a function of the ventricular rate is recorded into a histogram with 16 rate bins at 10 bpm/bin. The data in every bin contains the percentage of the total number of events and the number of counts falling in that bin.

8.4 Sensor Statistics

8.4.1 Rate/Sensor Trend

The sensor rate forecast may be used to optimize the rate adaptation parameters without repeated exercise tests. The pulse generator records the sensor rate over a period of 12 minutes to develop a sensor rate curve. The trend contains a forecast feature that can assist in sensor optimization as described in [Section 12.8](#) – Optimizing Rate Adaptation.

8.4.2 Sensor Histogram

This function records how often the sensor rate is within certain ranges. The rate range is subdivided into 16 rate classes going from 40 to 180, including bins for rates < 40 bpm and rates >180 bpm. The percentage and total number of sensed and paced events occurring within a rate class is displayed.

Sensor rate recording is independent of the effectiveness of the respective pacing rate, and it is not influenced by inhibition of pacing due to spontaneous events. Rate data are also recorded in non-rate-adaptive modes.

Recording stops when the memory available for recording the sensor rates is full. Recordings can be stored for several years. The frequency distribution of the sensor rates can be displayed as a diagram during follow-up examinations.

NOTE:

When Event Counters exceed 8 digits, they are presented in exponential form. Heart Rate and Sensor Rate Histograms will switch to exponential form when the Counters exceed 6 digits (e.g., 1,000,000 events will appear as 1.0E + 06).

8.4.3 Activity Chart

This feature operates by recording characteristic pulse generator data related to patient activity.

- No Activity
- Activity
- MAR (Maximum Activity Rate)

This data can assist in the analysis of heart and sensor activity. For example, a high value for the activity may indicate that the sensor gain is set too high. In contrast, an extremely low value for activity may indicate that the sensor gain is too low.

8.4.4 Sensor Gain Trend

The sensor gain trend is available as a rolling trend and therefore contains information about the most recent events. The sensor gain can be recorded up to 180 days with a time resolution of 2 seconds to 24 hours, depending on the recording duration.

8.5 ACC Statistics

8.5.1 Ventricular Pacing Amplitude Histogram

This function records how often the ventricular pulse amplitude is within specific ranges. The rate range is subdivided into 10 categories ranging from 0.5 V to 4.4 V, including bins for the values less than 0.5 V and higher than 4.4 V. The ventricular pacing amplitude is sampled at 2 second intervals and entered in the histogram. The percentage and total number of 2 second intervals occurring within an amplitude class is displayed.

Recording stops when ACC is disabled between follow-ups or if the memory available for recording the ventricular amplitude is full. Data may be recorded for several years. The frequency distribution of the sensor rates can also be displayed as a diagram during follow-up examinations.

8.5.2 Ventricular Pacing Amplitude Trend

This trend records the ventricular pulse amplitude in the range of 0.0 to 10V. The ventricular pulse amplitude can be recorded up to 180 days.

8.5.3 Pacing Threshold Trend

This trend records the ventricular pacing threshold measured during SQC/CTS sequences. The trend automatically and progressively decreases resolution as the time period for the trend increases. A threshold sample is measured every 2 seconds and averaged over the required time interval for the current resolution. For example, the trend will average the pacing threshold over 16 minute intervals for a 24-hour trend. The maximum trend duration is approximately 136 days with an averaged sampling interval of approximately 18 hours.

The pacing threshold sampled is always the most recent measured threshold. In other words, the logged pacing threshold is unaffected by ACC algorithm failures or aborts.

8.5.4 ACC Status

The ACC Status displays the status, threshold last value (including time and date), current pacing amplitude, and reason for ACC being disabled (if applicable).

8.6 Sensing Statistics

P- and R-wave Trends

Cylos pulse generators periodically perform P- and R-wave amplitude measurements to be displayed later as trend data. The P- and R-wave trends are available as a long-term and short-term trend up to 180 days and 33 hours, respectively. After the initial timeframe has elapsed, the first data stored is overwritten with new data; therefore, the most recent data are available for review.

8.7 Pacing Statistics

A/V Impedance Trends with Lead Check

Cylos pulse generators can perform lead impedance measurements for both atrial and ventricular leads. These measurements are stored in memory for use in lead impedance trend data as a function of time. The pace current and voltage is measured in order to determine the lead impedance.

Every 90 minutes, the lead impedance measurements are taken and are available for diagnostic trend display. The programmer will display two impedance trends: a short-term trend of the previous 33 hours and a long-term trend of 180 days.

Impedance trends are always recorded. When the Lead Check feature is programmed ON, the lead impedance measurements are used to determine if a lead failure has occurred. The range for normal lead impedance is from 200 to 3000 ohms. The Lead Check feature is available with pacing voltages between 1.4 and 5.8 volts.

If the Cylos pulse generator detects a bipolar lead failure while Lead Check is ON, the lead polarity for the respective lead will automatically be changed to unipolar configuration. A bipolar lead failure is verified if the lead impedance measurement falls outside of the acceptable range

for three consecutive readings. When a lead failure has been detected, a message is displayed on the programmer screen at the next follow-up visit in order to notify the physician of the change.

Lead Check also may be activated with unipolar leads. The pass-fail criterion remains the same as with bipolar leads. In the event that a lead failure occurs, the Lead Check feature is disabled and a message is displayed on the programmer screen at the next follow-up visit to notify the physician of the lead status.

CAUTION

Lead Check—Care should be taken when programming Cylos pulse generators with Lead Check ON as the device may switch from bipolar to unipolar pacing and sensing without warning. This situation may be inappropriate for patients with an Implantable Cardioverter Defibrillator (ICD). The following associated message appears when programming this feature: “Lead check may result in a switch to unipolar pacing and sensing, which may be inappropriate for patients with an ICD.”

Additionally, Lead Check should be programmed OFF before lead connection as the feature will automatically reprogram the device to unipolar in the absence of a lead.

Lead Check is temporarily suspended during magnet application and is inactive during ERI.

8.8 IEGM Snapshots

Cylos pulse generators can provide IEGM Snapshots, which are stored intracardiac events based on programmable triggers for later display and review via the programmer screen. The intracardiac events are represented on the programmer screen by event markers. Recordings may be triggered by the following events:

- High atrial rates
- Mode Switch
- High ventricular rates
- Pacemaker Mediated Tachycardia Terminations (PMTs)
- Patient activation (by applying a magnet)

Cylos pulse generators can be programmed to store an IEGM on any or all of the events listed above. However, the programmability of the High Atrial Rate and Mode Switch triggers are linked such that only one trigger can be activated at a time.

By applying a magnet over the pulse generator for approximately 2 seconds, the current heart rhythm will be instantly recorded. However, Cylos commits the recording to memory only when the magnet has been removed.

The following intracardiac events are stored with each IEGM:

- Type of IEGM snapshot
- Date and time of IEGM snapshot
- Duration of episode (for Mode Switch and High ventricular rates only)
- Maximum ventricular rate during episode
- Atrial IEGM markers (i.e., atrial paced events, atrial sensed events, atrial unused or refractory sensed events)
- Ventricular IEGM markers (i.e., ventricular paced events, ventricular sensed events, ventricular unused or refractory sensed events)
- Atrial IEGM
- Ventricular IEGM

Cylos pulse generators allow a maximum of twenty separate IEGM recordings that each include approximately 10 seconds per event.

Upon interrogation of the Cylos pulse generator containing stored IEGMs, a list of the stored IEGMs (with date and time stamp) is displayed under the Tests... screen. If the number of events triggering a snapshot is greater than the available memory, the oldest IEGM will be overwritten according to an internal priority list.

An IEGM is not recorded when the programming wand is placed over the pulse generator. However, a patient triggered IEGM will be recorded when a magnet is placed over the pulse generator with normal transtelephonic monitoring.

9. Other Functions/Features

Cylos pulse generators offer many additional functions and features to assist the physician in the care of the pacemaker patient.

9.1 Safe Program Settings

Activating the preset values for the Safe Program is a quick and convenient way to provide VVI pacing at a high output setting in urgent situations. Listed in **Table 23** are the Safe Program settings for Cylos pulse generators.

Table 23: Safe Program Settings

Parameter	Dual chamber	Single chamber
Mode	VVI	VVI
Pacing Rate	70 ppm	70 ppm
Amplitude	4.8 V (ventricle)	4.8 V
Pulse Width	1.0 ms	1.0 ms
Sensitivity	2.5 mV	2.5 mV (ventricle)
Ventricular Refractory Period	300 ms	300 ms
Pacing Polarity	Unipolar	Unipolar
Single Chamber Hysteresis	OFF	OFF

9.2 Magnet Effect

Automatic Magnet Effect

After magnet application the pulse generator paces at 90 ppm for 10 cycles asynchronously. Thereafter, the pulse generator paces synchronously at the programmed basic rate. During asynchronous pacing, the AV interval is reduced to 100 ms.

Asynchronous Magnet Effect

When programmed to asynchronous operation, magnet application results in asynchronous pacing. The pulse generator paces asynchronously at 90 ppm as long as the magnet is over the pulse generator. Upon magnet removal, the current basic interval is completed before the pulse generator reverts to its original operating mode.

If the magnet effect is set to asynchronous, the AV delay is reduced to 100 ms (or the programmed AV delay, whichever is shorter). Shortening of the AV delay to 100 ms during asynchronous AV sequential stimulation is provided to avoid ventricular fusion beats in the presence of intact AV conduction. This allows efficient diagnosis of ventricular capture or failure to capture.

Synchronous Magnet Effect

If the magnet effect is programmed to synchronous operation, magnet application does not affect timing and sensing behavior of the pulse generator. Synchronous operation is of particular importance during follow-up, if sensing and inhibition functions are desired during magnet application.

Trend monitor and event counter operation is interrupted during any magnet application.

9.3 Temporary Programming

CAUTION

OFF Mode—Use of the OFF mode should be avoided in pacemaker dependent patients. The OFF mode can be transmitted as a temporary program only to permit evaluation of the patient's spontaneous rhythm.

A temporary program is a pacing program which remains activated while the programming head is positioned over the pulse generator. Upon removal of the programming head (at least 15 cm away from the pulse generator), the temporary program will be automatically deactivated and the permanent program will again be in effect.

Generally, every pacing program displayed on the programmer screen may be transmitted as a temporary program by pressing the key designated on the programmer keyboard. With few exceptions, this also applies to pacing programs containing a parameter conflict, which cannot be programmed as permanent programs. Temporary programming facilitates follow-up and enhances patient safety. Test programs affecting patient safety, like pacing threshold measurements in a pacemaker-dependent patient, should be activated as a temporary program only.

When interrogating the pulse generator, the permanent program will always be displayed and documented, even though a temporary program was activated during the interrogation.

During temporary program activation, the rate adaptation, trend monitor, and the event counter are always inactive.

9.4 Patient Data Memory

Individual patient data can be stored in the pulse generator's memory. The stored data is automatically displayed upon each interrogation. The amount of data stored is determined by the software version being used. The patient data memory contains the following data categories:

- Patient Index (Code)
- Patient Name
- Date of Birth
- Symptom
- Etiology
- ECG Indication
- Implantation Date
- Lead Polarity (A / V)
- Lead Type
- Lead Manufacturer

The lead polarity setting has an added safety feature that prevents the programming of bipolar configuration unless bipolar leads have been documented within the patient data memory.

WARNING

Unipolar/Bipolar—All Cylos models can be used with either unipolar or bipolar IS-1 leads.

If the pacing or sensing function is to be programmed to **bipolar**, it must be verified that **bipolar leads** have been implanted in that chamber. If either of the leads is **unipolar**, **unipolar** sensing and pacing functions must be programmed in that chamber. Failure to program the appropriate lead configuration could result in entrance and/or exit block.

Symptom, etiology and ECG indication are specified using the European PASSPORT code system. The PASSPORT code is an identification system of two character codes that represent specific conditions. A listing of the codes available with definitions is displayed on the screen of the programmer when patient data is selected. When the patient data screen is entered symptom, etiology, or ECG indication may be entered, and can be accessed following interrogation to check code definition.

When the patient data screen is printed, the date of last follow-up is automatically given on the print-out.

9.5 Position Indicator

The position indicator facilitates positioning of the programmer head. The programmer optically and acoustically indicates whether the programmer head is in communication with the pulse generator.

9.6 Pacing When Exposed to Interference

CAUTION

EMI—Computerized systems are subject to EMI or “noise”. In the presence of such interference, telemetry communication may be interrupted and prevent programming.

A sensed event occurring during the interference interval will continuously reset that interval for the corresponding chamber without resetting the basic interval. Depending upon whether the interference (electromagnetic interference, muscle potentials, etc.) is detected by the atrial and/or ventricular channel, atrial and/or ventricular asynchronous pacing at the programmed timing intervals will result for the duration of the interference. The interference interval has a duration of 125 ms. If the detected rate exceeds 480/min (8 Hz), then the interference interval remains refractory during the entire basic interval.

Depending on the programmed pacing mode and the channel in which electromagnetic interference (EMI) occurs, **Table 24** details the resulting pacing modes for the duration of exposure to EMI.

Table 24: Response to EMI

MODE	EMI* (A)	EMI* (V)	EMI* (A+V)
DDD-CLS	DVDR	DADR	DOOR
VVI-CLS	---	VOOR	---
DDD(R)	DVD(R)	DAD(R)	DOO(R)
DDI(R)	DVI(R)	DAI(R)	DOO(R)
DVI(R)	---	DOO(R)	---
VDD(R)	VVI(R)	VAT(R)	VOO(R)
VVI(R)	---	VOO(R)	---
AAI(R)	AOO(R)	---	---
DDT	DVT	DAT	DOO
DDI/T	DVT	DAT	DOO
DVT	---	DOO	---
VDT	VVT	VAT	VOO
VDI	VVT	VOO	VOO
VVT	---	VOO	---
AAT	AO0	---	---

* EMI = Electromagnetic Interference

10. Product Storage and Handling

10.1 Sterilization and Storage

The pulse generator is shipped in a cardboard box, equipped with a quality control seal and product information label. The label contains the model specifications, technical data, serial number, expiration date, and sterilization and storage information of the pulse generator. The box contains a double container with the pulse generator and product documentation.

The pulse generator and its accessories have been sealed in a container and gas sterilized with ethylene oxide. To assure sterility, the container should be checked for integrity prior to opening. If a breach of sterility is suspected, return the pulse generator to BIOTRONIK.

CAUTION

Storage (temperature)—Recommended storage temperature range is 5° to 55°C (41°-131°F). Exposure to temperatures outside this range may result in pulse generator malfunction.

Low Temperatures—Exposure to **low temperatures** (below 0°C) may cause a false elective replacement indication to be present. If this occurs, warm the device to room temperature and reset the ERI with magnet application.

Handling—Do not drop. If an unpackaged pulse generator is dropped onto a hard surface, return it to BIOTRONIK.

CAUTION

FOR SINGLE USE ONLY—Do not resterilize the pulse generator or accessories packaged with the pulse generator, they are intended for one-time use.

Device Packaging—Do not use the device if the packaging is wet, punctured, opened or damaged because the integrity of the sterile packaging may be compromised. Return the device to BIOTRONIK.

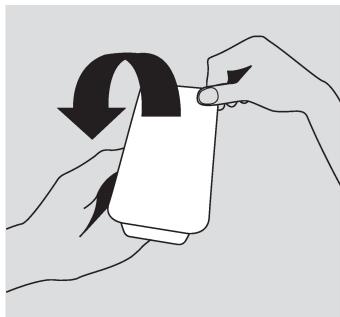
Storage (magnets)—Store the device in a clean area, away from magnets, kits containing magnets, and sources of electromagnetic interference (EMI) to avoid damage to the device.

Use Before Date—Do not implant the device after the USE BEFORE DATE because the device may have reduced longevity.

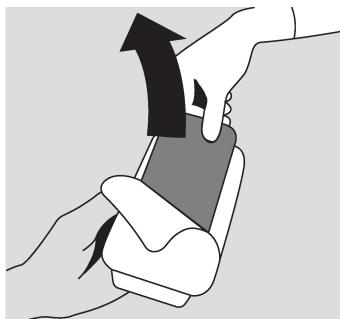
If a replacement pulse generator is needed, contact your local BIOTRONIK representative.

10.2 Opening the Sterile Container

The pulse generator is packaged in two plastic containers, one within the other. Each is individually sealed and then sterilized with ethylene oxide. Due to the double packing, the outside of the inner container is sterile and can be removed using standard aseptic technique and placed on the sterile field.



Peel off the sealing paper of the outer container as indicated by the arrow.



Take out the inner sterile container by the gripping tab and open it by peeling the sealing paper as indicated by the arrow.

A torque wrench is included within the blister package of each Cylos pulse generator.

10.3 Pulse Generator Orientation

The pulse generator may be used in either the left or right side pectoral implants. Either side of the pulse generator can face the skin to facilitate excess lead wrap.

11. Lead Connection

Cylos pulse generators have been designed and are recommended for use with bipolar or unipolar leads having an IS-1 connector. The IS-1 configured leads may be placed in one or both chambers of the heart, depending upon model selected.

WARNING

Unipolar/Bipolar—All Cylos models can be used with either unipolar or bipolar IS-1 leads.

If the pacing or sensing function is to be programmed to **bipolar**, it must be verified that **bipolar leads** have been implanted in that chamber. If either of the leads is **unipolar**, **unipolar** sensing and pacing functions must be programmed in that chamber. Failure to do program the appropriate lead configuration could result in entrance and/or exit block.

NOTE:

Connecting systems with a 3.2 mm configuration that do not expressly claim to agree with the IS-1 dimensions generally have to be regarded as incompatible with IS-1 connectors and can only be used with BIOTRONIK products together with an appropriate adapter. For questions regarding lead-generator compatibility, consult your BIOTRONIK representative.

In case of pulse generator replacement, make sure that the existing lead connector and lead are not damaged.

CAUTION

Lead/Pulse Generator Compatibility—Because of the numerous available 3.2-mm configurations (e.g., the IS-1 and VS-1 standards), lead/pulse generator compatibility should be confirmed with the pulse generator and/or lead manufacturer prior to the implantation of a pacing system.

IS-1, wherever stated in this manual, refers to the international standard, whereby leads and generators from different manufacturers are assured a basic fit. [Reference ISO 5841-3:1992(E)].

BIOTRONIK recommends the use of bipolar pacing leads with new implants so that all of the programmable parameters of Cylos pulse generators are available for use. Cylos pulse generators have a self-sealing header. Refer to the following steps when connecting a lead(s) to the pulse generator.

First, confirm that the setscrew(s) is not protruding into the connector receptacle. To retract a setscrew, insert the enclosed torque wrench through the perforation in the self-sealing plug at an angle perpendicular to the lead connector until it is firmly placed in the setscrew.

CAUTION

Setscrew Adjustment—Back-off the setscrew(s) prior to insertion of lead connector(s) as failure to do so may result in damage to the lead(s), and/or difficulty connecting lead(s).

Cross Threading Setscrew(s)—To prevent cross threading the setscrew(s), do not back the setscrew(s) completely out of the threaded hole. Leave the torque wrench in the slot of the setscrew(s) while the lead is inserted.

Rotate the wrench counterclockwise until the receptacle is clear of obstruction. Then connect the pacing leads as described below.

Insert the lead connector pin into the connector receptacle of the pulse generator without bending the lead until the connector pin becomes visible behind the setscrew. Hold the connector in this position.

1. Insert the enclosed torque wrench through the perforation in the self-sealing plug at an angle perpendicular to the lead connector until it is firmly placed in the setscrew.

CAUTION

Tightening Setscrew(s)—Do not overtighten the setscrew(s). Use only the BIOTRONIK supplied torque wrench.

Sealing System—Be sure to properly insert the torque wrench into the perforation at an angle perpendicular to the connector receptacle. Failure to do so may result in damage to the plug and its self-sealing properties.

2. Securely tighten the setscrew of the connector clockwise with the torque wrench until torque transmission is limited by the wrench.

3. After retracting the torque wrench, the perforation will self-seal. The proximal electrode of bipolar leads is automatically connected. Connect the second lead as described above.
4. Pass non-absorbable ligature through the hole in the connector receptacle to secure the pulse generator in the pocket.

NOTE:

Do not lubricate the grommets.

11.1 Auto Initialization

Auto Initialization detects when a pacing lead is connected to the pulse generator at implantation as well as the polarity of the lead detected. Upon successful detection, the pulse generator automatically initiates several key features. Auto Initialization consists of four phases, which are described below.

1. Lead detection

In order to detect a lead, the Cylos pulse generator continuously paces unipolar in both the ventricle and the atrium at the factory programmed amplitude after battery connection. Intrinsic events trigger a pacing pulse in the chamber in which the event was detected. The Cylos pulse generator measures the lead impedance at each paced event and considers a lead "detected" when the measured impedance is from 200 to 3000 Ohms.

2. Detection and Configuration of the Lead Polarity

The Cylos pulse generator switches the polarity to bipolar pacing immediately after a bipolar lead is detected. If the lead impedance measured is between 200 and 3000 Ohms, the lead connected is classified as bipolar and the sense and pace polarities are set appropriately. The device switches back to unipolar if the lead impedance falls outside this range.

3. 30-Minute Confirmation Phase

A 30-minute confirmation phase is initiated after detection of the lead and its polarity. The lead impedance is again measured at each paced event and lead detection is confirmed when all impedance measurements taken during the confirmation phase fall within the range of 200 to 3000 ohms.

A lead impedance measurement outside this range restarts the lead detection process described above. If the pulse generator is inhibited by intrinsic events during the confirmation phase, a triggered pace is delivered in the both chambers every three minutes to force a measurement.

Interrogation of the pulse generator during the confirmation phase results in a message that lead detection is activate. The auto initialization feature is deactivated if the pulse generator is reprogrammed during this time. At the next pulse generator interrogation, the physician is informed that lead detection was not successfully completed.

4. Activation of Pulse Generator Features

The following pulse generator features are activated after the confirmation phase has been successfully completed:

- Mode Switching (in dual chamber pulse generators only)
- PMT Management (in dual chamber pulse generators only)
- ACC's Active Threshold Monitoring (ATM) mode
- Statistics
- Collection of patient-specific impedance waveform characteristics for adapting the CLS algorithm to the patient (data does not control the pacing rate until CLS is programmed on)

12. Follow-up Procedures

12.1 General Considerations

The pacemaker follow-up serves to verify appropriate function of the pacing system, and to optimize the parameter settings.

In most instances, pacing system malfunction attributed to causes such as chronic threshold can be corrected by reprogramming the pulse generator. The follow-up intervals are, therefore, primarily determined by medical judgment, taking possible pacemaker dependency into consideration.

The following notes are meant to stress certain product features, which are of importance for follow-up visit. For detailed information on follow-up procedures and medical aspects, please refer to the pertinent medical literature.

NOTE:

In order to enable full device functionality, including statistics functions and ERI detection, transmit a permanent program after implantation by pressing the **[Transmit/Program]** button.

CAUTION

Programming Modifications—Extreme programming changes should only be made after careful clinical assessment. Clinical judgment should be used when programming permanent pacing rates below 40 ppm or above 100 ppm.

12.2 Battery and Lead Telemetry

Non-invasive measurements of battery and lead pulse parameters are available with these pulse generator models. Measurement tests are performed asynchronously at the magnet rate. In the dual chamber models, lead data are available for both the atrial and ventricular channels. The parameters measured and displayed by the programmer are shown in [Table 25](#).

Table 25: Battery and Lead Telemetry Parameters

Parameter	Measurement Units
Battery voltage	V
Battery impedance	kOhm
Battery current	uA
Lead pulse voltage	V
Lead pulse current	mA
Lead pulse charge	uC
Lead pulse energy	uJ
Lead impedance	Ohm

See **Section 13** - Elective Replacement Indication (ERI) to determine battery depletion by means of the magnet rate.

12.3 Threshold Test

The pulse generator models are equipped with a high-precision threshold test with a resolution of 0.1 V ranging from 0.1 V to 4.8 V. The threshold test is activated as a temporary program whose specific operation is defined by the applicable software version. The threshold is determined by observing the ECG. Likewise, all determinations of threshold or threshold margin, by any means, should only be performed by use of temporary programming to permit immediate reactivation of the permanent program in case of loss of capture. Removal of the programmer head immediately stops the test and reactivates the permanent program.

The threshold test should be performed with the pulse width programmed to the same value as that selected for the permanent program. To ensure pacing, the pacing rate of the threshold test program should exceed the patient's intrinsic rate.

To determine the threshold, the ECG must be observed continuously. Based on the measured threshold, the pulse amplitude for the permanent program should be adjusted. Please consult the pertinent medical literature for specific recommendations regarding necessary safety margins.

In addition to the manual ventricular threshold test, the threshold test can be performed automatically, requiring no user interaction. The automatic threshold test uses the ACC function to determine the threshold. Once the threshold is determined, ACC is deactivated if the feature is not programmed ON in the permanent program.

12.4 P/R Measurement

The pulse generators provide a P-/R-wave test for measuring the amplitude of intrinsic events during follow-up examination. The test determines the minimum, mean and maximum amplitude values over a programmable period of time. In addition, these values may be printed out.

To permit evaluation of the sensing function, the pacing rate must be lower than the patient's intrinsic rate. In demand pacing, the proper sensing function can be recognized if the interval between intrinsic events and the following pacing pulse equals the basic interval (if no Hysteresis is programmed).

For evaluation of the sensing function, the pulse generator features an intracardiac electrogram (IEGM) with marker signals to indicate sensed and paced events. In addition, triggered pacing modes can be selected which, synchronously to the detection of an intrinsic event, emit a pacing pulse and mark the sensed event and its timing on the ECG.

Especially with unipolar sensing functions, the selected sensitivity level should be checked for possible interference from skeletal myopotentials. If oversensing is observed, the programming of a lower sensitivity (higher value), or bipolar sensing function, if the implanted lead is bipolar, should be evaluated.

12.5 Testing for Retrograde Conduction

Retrograde conduction from the ventricle to the atrium can be assumed when a 1:1 relationship between the ventricular stimulation and atrial depolarization has been obtained with a constant coupling interval during ventricular stimulation. The pulse generator features a test for measuring retrograde conduction time. During operation of this test, the patient is paced at an increased ventricular rate over several cycles while the retrograde conduction time is measured.

Both the programmer display and printout provide measured retrograde conduction times (minimum, mean and maximum). The duration of time that the test is conducted may be selected.

To prevent retrograde P-waves from triggering ventricular pulses, thereby mediating a “re-entry” tachycardia (pacemaker mediated tachycardia, PMT), the programmed post-ventricular atrial refractory period must be longer than the retrograde conduction time.

12.6 Real-time IEGM Transmission

The pulse generators provide real time transmission of the unfiltered intracardiac electrogram (IEGM) to the programmer. During dual chamber operation, IEGMs from the atrium and ventricle can be simultaneously recorded with a bandwidth of 0.5 to 200 Hz. The IEGMs may be transmitted to the programmer via the programming head positioned over the implanted pulse generator. They are then displayed together with surface ECG and markers on the programmer screen and printed on the ECG recorder. Likewise, intracardiac signals and markers identifying atrial/ventricular paced and sensed events are received via the programming head, and may be displayed on the programmer screen and printed on the ECG recorder.

To determine the amplitudes of intracardiac signals (P-/R-waves) the automatic P/R-wave measurement function may be used.

12.7 Non-Invasive Programmed Stimulation (NIPS)

WARNING

NIPS—Life threatening ventricular arrhythmias can be induced by stimulation in the ventricle. Ensure that an external cardiac defibrillator is easily accessible. Only physicians trained and experienced in tachycardia induction and reversion protocols should use non-invasive programmed stimulation (NIPS).

12.7.1 Description

The implanted pulse generator/lead system may be used in conjunction with the programmer to generate externally controlled pacing pulses. Burst Stimulation or Programmed Stimulation may be selected with up to four extra stimuli at pacing rates to 800 ppm.

12.7.2 Burst Stimulation

Burst Stimulation offers a burst of pacing pulses to either atrium or ventricle when the programming wand is placed directly over the pulse generator. The duration of the burst is as long as the burst key on the

programmer is touched. When the burst key is no longer touched, the program reverts to the backup program. Should the wand be removed, the pulse generator reverts to the permanent program.

Burst Stimulation may be stepped up or down from the nominal value to user-defined high or low limits as long as the selection is touched on the touchscreen. When the **Step Up** or **Step Down** key is touched, NIPS is invoked starting at the nominal burst rate and then steps up or down respectively in 25 ppm steps. As soon as the step up or step down key is released, NIPS terminates. Subsequent inductions resume at the initially programmed burst rate.

12.7.3 Programmed Stimulation

Programmed Stimulation offers burst pacing at specifically defined intervals that are user defined. Programmed stimulation offers S1-S1, S1-S2, S2-S3, S3-S4, S4-S5 individual intervals. In addition, up to 7 cycles are available containing a programmable pause of up to 50 seconds. The last selected interval decrements in 0 to 100 ms steps. As with Burst Stimulation, the pacing mode switches to the permanent program when the wand is removed.

12.7.4 Back up Pacing

The back up pacing program remains active once NIPS has been selected and remains active during burst or programmed burst stimulation and within this menu. This program remains active until the **Stop** touchkey is pressed.

CAUTION

Short Pacing Intervals—Use of short pacing intervals (high pacing rates) with long atrial and/or ventricular refractory periods may result in intermittent asynchronous pacing and, therefore, may be contraindicated in some patients.

12.7.5 NIPS Safety Features

The BIOTRONIK offers the following safety features during NIPS sessions.

- Before the NIPS feature can be used, NIPS must be specifically selected and then is released through user acknowledgment. In addition, before NIPS is performed in the Ventricle, the user must acknowledge that delivering NIPS into the Ventricle may induce dangerous arrhythmias.

- When the battery voltage has reached the Elective Replacement Indicator point (ERI), the NIPS feature is no longer available.
- Ventricular pacing support is available to pacemaker dependent patients during burst or programmed burst stimulation through the back up pacing program as long as the wand is within 15 cm of the pulse generator. Removing the programmer wand or placement to distance greater than 15 cm from the pulse generator returns the pulse generator to its permanent program.
- NIPS may only be programmed temporarily.

NOTE:

High pacing rates and pulse amplitudes together with wide pulse widths may temporarily decrease the amplitude of the pacing pulse. The pacing pulse must be continuously verified with an ECG to assure effectiveness.

To perform NIPS function, the programmer wand must be placed directly over the pulse generator to enable continuous telemetry.

12.8 Optimizing Rate Adaptation

It is recommended to check the parameters controlling rate adaptation during each follow-up for their individual therapeutic suitability. Any intermediate change in the patient's general well being and cardiac performance since the last follow-up should be taken into consideration. It must be assured that in all cases, the settings for sensor gain, maximum sensor rate, rate increase and rate decrease are well tolerated by the patient.

WARNING

Rate-Adaptive Pacing—Use rate-adaptive pacing with care in patients unable to tolerate increased pacing rates.

Use of the diagnostic functions for recording the pacing and/or intrinsic rate during follow-up and during daily activities facilitates evaluation of the parameter settings for rate adaptation. The rolling mode of the A/V rate trend is particularly useful during follow-up since the time period immediately preceding the follow-up may be evaluated.

When in doubt about the suitability of particular sensor settings for a certain patient, the sensor rate forecast can be utilized to observe the sensor response without the sensor actually controlling the pacing rate. The simulation of the sensor activity can be recorded using the sensor optimization feature.

12.8.1 Rate/Sensor Trend

The sensor rate forecast may be used to optimize the rate adaptation parameters without repeated exercise tests. The pulse generator records the sensor rate over a period of 12 minutes. During this time, the pulse generator develops a sensor rate curve. This curve is used to forecast optimal parameters such as the sensor gain, threshold, and maximum sensor rate.

12.8.2 Adjusting the Sensor Gain

The sensor gain controls the change in stimulation rate for a certain change in workload detected by the sensor. An exercise test is recommended in order to achieve a rate response proportional to work load by optimizing the sensor gain. If the pacing rate tends to be too high for the specific amount of work load or if the selected maximum sensor rate is achieved at too low of an exercise level, the sensor gain should be reduced by selecting a lower gain setting. If, on the other hand, rate adaptation is insufficient for a specific amount of workload, selection of a higher gain setting may be indicated. The memory functions can be used to record the pacing rate during exercise.

The sensor rate forecast function facilitates optimization of the rate-adaptive parameters.

12.8.3 Adjusting the Sensor Threshold

The sensor threshold controls the (motion) signal level that has to be exceeded to cause a rate increase. This parameter is meant to assure a stable pacing rate at rest and to prevent rate increases at signal levels not consistent with physical exertion. The sensor gain should be optimized prior to adjusting the sensor threshold. Otherwise, changing of the gain setting will cause changes in the effective threshold.

If rate increase is caused by low level activities, when no rate-adaption is desired, the sensor threshold setting should be increased by selecting the next higher setting (e.g., low to mean). If, on the other hand, the pulse generator tends to respond only at higher levels of work, a reduction of the sensor threshold may be indicated (e.g., high reduced

to mean). It may be useful to record a sensor test trend for evaluation of sensor response. The sensor rate forecast may also be used to tailor the sensor threshold to the patient.

12.9 Analog Telemetry

The pulse generator provides the capability to transmit non-invasive analog data. In addition to the intracardiac electrogram with marker signals, the measured battery voltage, lead impedance, and current consumption in the selected pacing programs can be displayed and documented via the programmer. By measuring the current consumption, the most energy conserving combination of pulse amplitude and pulse width can be determined. The analog telemetry provides additional information that can be utilized for the interest of patient safety and, therefore, should be used at every follow-up.

13. Elective Replacement Indication (ERI)

The service time of Cylos pulse generators vary based on several factors, including battery properties, storage time, lead system impedance, programmed parameters, amount of pacing and sensing required, and circuit operating characteristics. Service time is the time from beginning of service (BOS) to the end of service (EOS). To assist the physician in determining the optimum time for pulse generator replacement, an elective replacement indicator is provided that is activated when the battery cell capacity drops to a predetermined level. The following table defines the different service cycles (at standard settings, 37°C, and with a lead impedance of 500 ohms). The beginning of the replacement cycle is displayed on the programmer after pulse generator interrogation and appears on the printout.

Table 26: Service Cycle Definitions

Abbreviation	Service Cycle	Definition
BOS	Beginning of Service	Normal service cycle; battery in good condition
ERI	Elective Replacement Indication	Identifies the time of elective replacement indication. The rate occurring at ERI depends upon the programmed mode and magnet application.
EOS	End of Service	Identifies the end of the elective replacement indication period.

The pulse generator indicates the need for replacement by a defined decrease in the programmed rate without a magnet applied. The rate change is dependent on the programmed pacing mode.

The pacing rate decreases by 11% when programmed to DDD(R), DDT(R), D00(R), VDD(R), VDI(R), VDT(R), VVI(R), VVT(R), AAI(R), AAT(R), or A00(R).

In DDI(R), DDI/T(R), DVI(R), and DVT(R) modes, only the V-A delay is extended by 11%. This reduces the pacing rate by 4.5-11%, depending on the programmed AV delay.

The pulse generator indicates the need for replacement by a defined decrease of its rate after magnet application and the programmer displays it upon interrogation of the pulse generator programmed parameters. The magnet rate in all modes decreases as shown in **Table 27**.

Table 27: Pulse Generator Behavior After Reaching ERI

Magnet Mode	Cycles 1-10 after magnet application	After Cycle 10
Automatic	Asynchronous, basic rate at 80 ppm	Synchronized with basic rate reduced by 4.5 - 11%
Asynchronous	Asynchronous, basic rate at 80 ppm	Asynchronous with basic rate at 80
Synchronous	Synchronized with basic rate reduced by 4.5 - 11%	Synchronized with basic rate reduced by 4.5 - 11%

If the pulse generator is programmed to dual chamber pacing, it will switch to single chamber pacing when it reaches the elective replacement indication. The “ERI mode” varies according to the programmed pacing mode and is indicated by the pulse generator.

CAUTION

High output settings combined with very low lead impedance may reduce the life expectancy of the pulse generator to less than 1 year. Programming of pulse amplitudes, higher than 4.8 V, in combination with long pulse widths and/or high pacing rates can lead to premature activation of the replacement indicator

Table 28 shows the expected longevity (in months) from BOS to ERI at standard program for Cylos pulse generators. The programmer software for the Cylos pulse generators provides an estimated time to ERI in months and years that is updated each time the device is reprogrammed. This estimation allows the physician to understand the longevity effects of modifying programmed parameters.

Table 28: Nominal Pulse Generator Longevity

Pulse Generator	Standard* (BOS - ERI) in Months
Cylos DR, Cylos DR-T	65
Cylos VR	86

During the clinical evaluation of the Active Capture Control algorithm, it was demonstrated that use of Active Capture Control can increase device longevity (as compared to Standard programming).

* Standard: 60 ppm, 3.6 V, 0.4 ms

The mean expected time intervals from ERI to EOS at standard program for Cylos pulse generators is 6 months. All service intervals, including the above-cited nominal pulse generator longevity, are based on considerations that consider the battery discharge behavior and the hybrid circuit properties including current consumption and replacement indicator. The statistical calculations are based on a 500 ohm load, 100% pacing, and data supplied by the battery manufacturer. With a 300-ohm load, the service times stated below are decreased by a maximum of 30%.

* 50% of all pacemakers reach or exceed the given value

14. Explantation

Explanted pulse generators or explanted accessories may not be reused. Explanted pulse generators can be sent either to the local BIOTRONIK representative or the BIOTRONIK home office for expert disposal. If possible, the explanted pulse generator should be cleaned with a sodium-hyperchlorine solution of at least 1% chlorine and, thereafter, washed with water prior to shipping.

The pulse generator should be explanted before the cremation of a deceased patient.

CAUTION

Device Incineration - Never incinerate a pulse generator. Be sure the pulse generator is explanted before a patient who has died is cremated.

Explanted Devices – Return all explanted devices to BIOTRONIK.

14.1 Common Reasons to Explant a Pulse Generator

A pulse generator may be explanted emergently or at a physician's discretion at any time subsequent to an implant procedure. Reasons for explant include, but are not limited to: patient death; no output/intermittent output; loss of capture/ sensing; inability to program/interrogate the pulse generator; infection, EOS (normal or premature); system upgrade; physician preference for another pulse generator model; and/or other reason(s) which may or may not be known to the pulse generator manufacturer. Complications related to other portions of the pacing system (i.e., lead, patient) may also result in pulse generator explant. [Table 29](#) summarizes some of the more common reasons for pulse generator explant.

Table 29: Common Reasons to Explant a Pulse Generator

Source	Cause	Possible Effect
Battery	Premature depletion due to high programmed output or other cause(s) resulting in excessive battery current drain.	Output voltage decrease; rate decrease; loss of capture; increased pulse width; inability to program/interrogate; sensing difficulty.
Circuitry	Electrical parameter changes due to shorts, opens, or component parametric drift Electromagnetic Interference (EMI) from large power tools, industrial equipment, electrocautery, defibrillation, radiation therapy, RF ablation therapy, etc.	No output; rate increase, rate decrease; reversion to asynchronous mode; loss of capture and/or sensing Permanent or temporary loss of output; output inhibition; reversion to asynchronous mode with rate change or instability; pacing synchronized to interference; reversion to "Elective Replacement" or electrical reset parameters; inability to program/interrogate; other damage to circuit components resulting in permanent or temporary parameter changes.
Connector, Setscrew, etc.	Poor connection, intrusion of body fluid.	Excessive current drain; early battery depletion; intermittent or continuous loss of capture and/ or sensing.

Table 29: Common Reasons to Explant a Pulse Generator

Source	Cause	Possible Effect
Leads	Displacement, fracture, loss of insulation integrity.	Intermittent or continuous loss of capture and/or sensing; excessive current drain; early battery depletion.
	Cardiac perforation	The above plus cardiac tampon-ade; muscle or nerve stimulation.
	Myocardial irritability at time of insertion, e.g., from an acute myocardial infarction	Fibrillation
Patient	Threshold Elevation	Loss of capture and/or sensing.
	Normal medical complication	Infection
	Body rejection phenomena	Fluid accumulation; migration; erosion.
Misc.	Unipolar pacing systems	Inhibition of pulse generator due to sensing of skeletal muscle activity.
	Physician preference	Upgrade to bipolar, dual chamber, rate-adaptive pulse generator, etc.
	Introducer caused	Air embolism or pneumothorax.

15. Technical Data

15.1 Modes

Modes	DR	VR	DR-T*
DDD-CLS	X		X
VVI-CLS	X	X	X
DDDR	X		X
DDIR	X		X
DVIR	X		
VDDR	X		X
VVIR	X	X	X
AAIR	X		
VDIR	X		X
DDIR/T	X		X
VDTR	X		X
VVTR	X	X	
DVTR	X		
DDTR	X		X
DDTR/A	X		X
DDTR/V	X		X
AATR	X		
DOOR	X		
VOOR	X	X	
AOOR	X		

Modes	DR	VR	DR-T*
DDD	X		X
DDI	X		X
DVI	X		
VDD	X		X
VVI	X	X	X
VDI	X		X
AAI	X		
DOO	X		
VOO	X	X	
AOO	X		
DDT	X		X
DDI/T	X		X
DVT	X		
VDT	X		X
VVT	X	X	
AAT	X		
DDT/A	X		X
DDT/V	X		X
OFF	X	X	

NOTE:

Programmability dependent on programmer software utilized.

Bold parameters indicate factory settings.

Parameters specified at 37° C, with a lead impedance of 500 ohms.

* The Home Monitoring function is available for the following pacing modes. With Home Monitoring deactivated, all Cylos DR pacing modes are available.

15.2 Pulse- and Control Parameters

Basic rate

30...(1)...**60**...(1)...88...(2)...122...(3)...140...(5)...180 ppm

(30 – 34 ppm are for temporary programs only)

Night rate

Off, 30...(1)...60...(1)...88...(2)...122...(3)...140...(5)...180 ppm

(30 – 34 ppm are for temporary programs only)

Rate Hysteresis

Off; -5...(5)...-80 bpm

Repetitive Hysteresis

Off; 1...(1)...10

Scan Hysteresis

Off; 1...(1)...10

Upper Rate

100; 110; 120; **130**; 140; 160; 185 ppm

UTR Response

2:1; WRL (automatic selection)

Rate Limitation , ,

190...220 ppm

Dynamic AV delay (Dual chamber only)

Off; **low**; medium; high (individual or fixed)

* The corresponding intervals t correlate with the rates f by the formula $t = 60.000 / f$ [t in ms, f in ppm].

** In the event of electronic defect.

*** Rate Limitation changes as the Pacemaker approaches End of Service. The Rate Limitation is nominally 190 ppm at Beginning of Service (BOS) and can reach 220 ppm at End of Service (EOS) due to battery depletion.

AV delay Values (Dual chamber only)

15; 50; 75; 100; 120...{10}...200; 225; 250; 300 ms

(Programmable in 5 ranges)

AV delay Hysteresis (Dual chamber only)

Off; low; medium; high; negative

AV Repetitive Hysteresis (Dual chamber only)

Off; 1...{1}...6

AV Scan Hysteresis (Dual chamber only)

Off; 1...{1}...6

Repetitive AV delay Hysteresis (Negative AV Hysteresis)

1...{1}...10...{3}...100...{10}...180

I-Opt

Off; On (If I-Opt is activated, the parameters are as follows)

AV Hysteresis: 300 ms

AV Scan Hysteresis: 5

Repetitive AV Hysteresis: 5

AV safety delay (Dual chamber only)

100 ms

Sense Compensation

Off; -15...{15}...**45**...{15}...-120 ms

Far Field Blanking

32, 40, 48, **56**, 72, 100, 125, 150, 175, 200 ms

Atrial Blanking Time

32; 40; 48; **56**; 72 ms

Ventricular Blanking Time

16; 24; **32**; 40; 48; 56; 72 ms

Magnet effect

Automatic; asynchronous; synchronous

Asynchronous Magnet Effect: paces at 90 ppm.

Automatic Magnet Effect; 10 cycles at 90 ppm asynchronous; thereafter synchronous with the programmed basic rate

Synchronous Magnet Effect; synchronous with programmed basic rate

Pulse amplitude

A 0.1...[0.1]...**3.6**...[0.1]...4.8...[0.6]...8.4 V

V 0.1...[0.1]...**3.6**...[0.1]...4.8...[0.2]...8.4 V

Pulse width

A 0.1; 0.2; 0.3; **0.4**; 0.5; 0.75; 1.0; 1.5 ms

V 0.1; 0.2; 0.3; **0.4**; 0.5; 0.75; 1.0; 1.5 ms

Sensitivity

A 0.1...[0.1]...**1.0**...[0.1]...1.5...[0.5]...7.5 mV

V 0.5...[0.5]...**2.5**...[0.5]...7.5 mV

Refractory period

A 200...[25]...**425**...[25]...775 ms

V 170, 195, 220, **250**; 300; 350; 400 ms

PVARP (minimum)

Off, dependent on TARP and AV delay settings

ARP Extension

0...[50]...350 ms

Lead Check

Off; On

* In the DDIR, VVIR and VOOR modes, lower maximum sensor rates result than indicated here (partly depending on the selected AV interval). The correct values are indicated by the programmer.

Automatic Mode Conversion

Off; On

Mode Switch (X out of Y)

Off; On

X = 3...{1}...8

Z = 3...{1}...8

Intervention Rate

110...(10)...**160**...(10)...250 ppm

Mode Switch Basic Rate

+5...(5)...**+10**...(5)...+30

2:1 Lock-In Protection

Off; On

VES Lock-In Protection

Off; On

VES Lock-In Detection Count

4, 6, and 12 cycles

Lead Polarity

Pace: A **unipolar**; bipolar

V **unipolar**; bipolar

Sense: A **unipolar**; bipolar

V **unipolar**; bipolar

15.2.1 Rate Adaptation

Sensor gain

1.0, 1.1, 1.3, 1.4, 1.6, 1.8, 2.0, 2.2, 2.6, 3.0, 3.3, 3.7, 4.0, 4.5, 5.0, 6.0, 7.0, 8.0, 8.5, 10, 11, 12, 14, 16, 18, 20, 22, 24, 28, 32, 35, 40

* Philos DR-A/SR-B polarity is limited to **unipolar** only.

Sensor threshold

very low; low; mean; high; very high

Rate increase

1, 2, 4, 8 ppm/cycle

Maximum sensor rate

80...[5]...180 ppm

Rate decrease

0.1, 0.2, 0.5, 1.0 ppm/cycle

Automatic Sensor Gain

Off; On

15.2.2 Active Capture Control (ACC)

Active Capture Control

Off, On, **ATM**

Minimum ACC Amplitude

0.1 ... **0.7** ... MaxACCAmp minus safety margin

Maximum ACC Amplitude

2.4, **3.6**, 4.8, 6.4 V

Safety Margin

OFF, 0.3...[0.1]...**0.5**...[0.1]... 1.2V

Search Scheduling

Interval, Time of Day

Interval

0.1, 0.3, 1, 3, 6, **12**, 24 hours

1st Time of Day

0:00 ... 23:15 in 15 minute increments, nominal **02:00**

2nd Time of Day

0:00 ... 23:15 in 15 minute increments, nominal **14:00**

15.2.3 Home Monitoring Parameters

Home Monitoring

Off, On

Monitoring Interval

1 day

Time of the Trend Report Transmission

0:00...(10)...23:50 hours

Event Report

Off, On

Patient Report

Off, On

15.2.4 Additional Functions

NOTE:

Availability of the following functions is dependent upon pulse generator configuration.

- Temporary Program Activation
- High Precision Threshold test in the range of 0.1 up to 4.8 V with 0.1 V resolution
- PAC (pulse amplitude control) system produces consistent pulses
- Analog Telemetry with measuring of battery, pulse and lead data
- Two channel Real Time IEGM Transmission with markers
- Patient Data Memory
- Sensor Simulation
- Position Indicator for the programmer head
- 24 hour Trend
- Heart Rate Histogram

- Sensor Rate Histogram
- Sensor Test Trend with complete Rate Forecast
- Automatic Sensor Gain with Trend Monitor
- VES Analysis
- AES Analysis
- Retrograde Conduction Test
- Automatic Mode Conversion
- Mode Switching
- Activity Report
- Event counter
- P-/R-wave Tests with Trend Data
- External Pulse Control up to 800 ppm
- Night Program
- IEGM Recordings
- Lead Impedance Trends
- Lead Check
- Rate Fading

15.2.5 NIPS Specifications

Burst Mode	Burst Chamber	Atrium, Ventricle
Burst stimulation	Coupling Interval / ms	None... 2000
	Burst Type	Pushbutton, Ramp
	Burst Range / ppm	30...800
Programmed Stimulation	S1-S1	S1-S2, S2-S3, S3-S4, S4-S5
	Cycles	0...10
	Pause / ms	Stop... 50
	No. of intervals	4
	Decrement ms	0...100
Back-up Pacing	Modes	VOO,VVI, OOO,OVO
	Rate / ppm	30...180
	Amplitude / V	0.1...8.4
	Pulse width / ms	0.1, 0.2, 0.3, 0.4, 0.5, 0.75, 1.0, 1.5
	Pace Polarity	Bipolar, Unipolar

15.3 Programmers

EPR 1000^{PLUS}, TMS 1000^{PLUS}, ICS 3000

15.4 Materials in Contact with Human Tissue

Housing: Titanium

Connector receptacle: Epoxy resin

Sealing Plugs: Silicone Rubber

15.5 Electrical Data/Battery

NOTE:

At 37° C, with pacing impedance of 500 Ohms.

Parameter	Cylos DR	Cylos DR-T	Cylos VR
Pace	Unipolar/bipolar	same	same
Pulse form	Biphasic, asymmetric	same	same
Polarity	Cathodic	same	same
Input impedance	>10 kΩ (A); >10 kΩ (V)	>10 kΩ (A); >10 kΩ (V)	>10 kΩ
Power source	Li/I	same	same
Battery voltage at BOS	2.8 V	same	same
Conducting surface (uncoated)	36.7 cm ²	37.7 cm ²	37.7 cm ²
Conducting surface (coated)	9.2 cm ²	same	same
Conducting Shape (coated) (uncoated)	Ellipsoidal Flattened ellipsoidal	same same	same same

15.6 Mechanical Data

Model	Leads	Size	Mass	Volume
Cylos DR	IS-1	6.4 x 42 x 57 mm	28 g	12 cc
Cylos DR-T	IS-1	6.4 x 45.7 x 57 mm	31 g	14 cc
Cylos VR	IS-1	6.4 x 39 x 57 mm	27 g	11 cc

16. Order Information

Pulse Generator Type	Order Number
Cylos DR	349 799
Cylos DR-T	349 806
Cylos VR	349 811

Appendix A

Mode-Specific Indications and Contraindications

Rate-adaptive Pacing

Cylos DR and

Cylos DR-T: DDDR, DDIR, DVIR, VDDR, VVIR, DDD-CLS, VVI-CLS, AAIR

Cylos VR: VVIR, VOOR, VVI-CLS

NOTE:

For indications specific to the VDDR mode, see Indications for Use on page 1 ([Section 2](#)).

Indications for rate-adaptive pacing may include but are not limited to the following:

- Patients with chronotropic incompetence who have an anticipated moderate or high level of activity and in whom there is a stable atrial rhythm, and for whom DDD, DDI, DVI, VDD, or VVI pacing is also indicated.
- Patients who have persistent VA conduction (dual chamber modes).

These indications include but are not limited to sick sinus syndrome and AV block.

The rate-adaptive modes of the Cylos family of pulse generators are contraindicated for patients who are known to develop angina or ischemia at accelerated pacing rates. In addition, the rate-adaptive modes are contraindicated in circumstances where the applicable non-rate-adaptive mode is noted as contraindicated in the following text.

Dual Chamber

DDD

The DDD mode is **clearly indicated** if

- AV synchrony is needed over a broad range of rates, such as
 - active or young patients with an adequate increase in atrial rate, and/or
 - significant hemodynamic indication, and/or
 - previous occurrence of pacemaker syndrome or of a reduction in systolic blood pressure of more than 20 mm Hg under ventricular pacing with pulse generator implantation (regardless of any evidence of retrograde VA conduction).

The DDD mode is **conditionally indicated** in the case of

- a complete AV block or of sick sinus syndrome and stable atrial rate, and/or
- proof that simultaneously setting the atrial and ventricular rates can inhibit tachyarrhythmia or if the pulse generator can be set to a pacing mode suited for interrupting arrhythmia.

The DDD mode is **contraindicated** in the case of

- frequent or persistent supraventricular tachyarrhythmia, including atrial fibrillation or flutter, and/or
- inadequate intra-atrial complexes that do not permit safe sensing, and/or
- angina pectoris which would be aggravated by increased heart rates.

DDI

The DDI mode is useful in all cases in which dual chamber pacing is necessary, but where intermittent supraventricular arrhythmias frequently occur.

* The ACC/AHA Guidelines cannot replace a study of the relevant specialized literature, especially since the indications and contraindications for using particular pacing modes are subject to constant advances in medical knowledge.

DVI

The DVI mode is **clearly indicated** if

- AV sequential contraction is necessary due to symptomatic bradycardia and slow atrial rate, and/or
- a pacemaker syndrome has already been documented.

The DVI mode is **conditionally indicated** for

- frequent supraventricular arrhythmia in which a combination of pacing and medication has proved therapeutically effective, and/or
- the presence of a bradycardia-tachycardia syndrome, presuming that setting the atrial rate and the AV interval with or without accompanying medication stops or prevents supraventricular arrhythmia.

The DVI mode is **contraindicated** for

- frequent or persistent supraventricular tachyarrhythmia, including atrial fibrillation or flutter.

Dual Chamber Modes

VDD

The VDD mode is **clearly indicated** for

- ventricular pacing when adequate atrial rates and adequate intracavitary complexes are present. The indication includes the presence of complete AV block when
 - the atrial contribution is necessary for hemodynamic optimization, and/or
 - a pacemaker syndrome has already occurred or is expected.

The VDD mode is **conditionally indicated** for

- patients with normal sinus rhythms and normal AV conduction, but who intermittently need ventricular pacing.

The VDD mode is **contraindicated** for

- frequent or persistent supraventricular tachyarrhythmia, including atrial fibrillation or flutter, and/or

- inadequate intra-atrial complexes that do not permit safe sensing, and/or
- intact retrograde conduction.

Single Chamber Modes

VVI

The VVI mode is **clearly indicated** for

- all symptomatic bradyarrhythmias, but particularly if
 - the atrium does not significantly contribute to the hemo-dynamics (persistent or paroxysmal atrial flutter or fibrillation, dilated atria).
 - there are no grounds for development of pacemaker syndrome through loss of the atrial contribution or through negative atrial contribution.

The VVI mode is **conditionally indicated** for

- symptomatic bradycardia when the simplicity of the pacing system is of crucial significance due to
 - senility (for the sole purpose of prolonging life).
 - incurable illness.
 - great distance from the follow-up care center to the patient's home.
 - absence of retrograde VA conduction.

The VVI mode is **contraindicated** if

- a pacemaker syndrome is known to exist or if the patient develops particular symptoms during temporary pacing or pulse generator implantation, and/or
- there is a need to maximize the atrial contribution due to
 - congestive heart failure, and/or
 - a specific need for ventricular rate adaptation.

AAI

The AAI mode is **clearly indicated** for

- symptomatic sino-atrial node dysfunction (sick sinus syndrome), given that adequate AV conduction has been established by an appropriate examination.

The AAI mode is **conditionally indicated** if

- the hemodynamics of patients with bradycardia and symptomatically reduced cardiac output can be improved by raising the heart rate, given that adequate AV conduction has been established by an appropriate diagnostic examination.

The AAI mode is **contraindicated** for

- previously established AV conduction delay or AV block or if diminishing AV conduction has been determined by appropriate tests, and/or
- inadequate intra-atrial complexes that do not permit safe sensing.

Other Modes

In addition to the ACC/AHA guidelines, the modes listed above may have further indications due to medical/technical complications such as electromagnetic interference, sensing defects, fracture of the lead(s), detection of myopotentials, muscle stimulation, etc. The same applies to the asynchronous **D00(R)**, **A00(R)** and **V00(R)** pacing modes derived from the above by restricting the sensing functions [S00(R) mode available with Cylos VR models]. The triggered **DDT**, **DDI/T**, **VDT**, **DVT**, **AAT** and **VVT** pacing modes and the **VDI** and **OFF** modes are indicated for diagnostic purposes to assess intrinsic cardiac activity. Use of the **OFF** mode is contraindicated in pacemaker dependent patients.

Appendix B

Known Software Anomalies

Anomaly	Possible Effect on Patient or Implant Procedure
General Programmer Issues	
Data Export (via .pdf file) cannot be performed if insufficient programmer memory is available. The programmer correctly aborts the data export process but incorrectly displays the message: "Data Export successful"	No effect on patient, inconvenience to clinical personnel. No incorrect data is exported, and the information is available on the printout and the programmer display.
ICS 3000 programmer may not recharge battery when device is in hibernation shut down mode (OFF button quickly pressed).	No effect on patient, If battery has depleted to a low level, system boot may not be possible. The system will need to be connected to a wall electrical outlet. Minor inconvenience to field clinical personnel.
If an Operation Module carrying a new but highly depleted battery (less than 10% capacity) when detached from the docking station an incorrect warning message may be displayed "The battery urgently needs to be replaced,"	No effect on patient, but the ICS 3000 may be returned unnecessarily for battery replacement. The depletion status of the battery is clearly discernible to the user (battery LEDs).
Display and activation of the "Implantation Module" button on the Operation Module (OM) screen may be delayed for 30 sec after the OM has been reattached to the docking station and placed in to hibernation mode. The button will appear light grey until it becomes active.	No effect on patient, but the delay in activating the button may cause user confusion.

Anomaly	Possible Effect on Patient or Implant Procedure
General Programmer Issues (continued)	
Release code entries entered from the Implant List do not respond with a Status Bar message to confirm if it was successful or not.	No effect on patient, but the user may confuse the lack of response with an invalid code entry. Confusion may take more time.
Cylos Software Application	
Abnormal program termination may occur when Cylos RAM Dump function is activated for other implants other than Cylos.	No effect on patient, the confusion may cause the follow-up to take more time (re-boot less than 2 min).
Cylos Pacemakers	
If target pacing mode during Mode Switch is rate adaptive (e.g. DDIR), the activity rate dynamic range may be lower than the programmed parameter range. The absolute maximum sensor rate is limited to 102 ppm. The effective maximum sensor rate may deviate from the programmed value (140 ppm) by a maximum of 27%.	Results in limited dynamic range of activity rate during mode switch. The situation is temporary, and there is no patient risk involved.

Anomaly	Possible Effect on Patient or Implant Procedure
Cylos Pacemakers (continued)	
<p>An ineffective pacing program may continue in the threshold test when the programmer wand is at a border line communications distance. At programming distances close to the loss of communication but still within the magnet range it may occur that the pacemaker does not reliably receive the command to reprogram the amplitude to the selected base value after the test pulses occurred while the wand still receives signals from the device. Lifting the wand corrects the problem.</p>	<p>Results in possibility of more sub-threshold pace pulses delivered than programmed. Physician would be present to immediately recognize non-capture.</p> <p>Lifting the programming wand away from the pacemaker immediately reverts to the previous permanent pacing program and capture condition.</p>

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