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BIOTRONIK

Evia Pulse Generators

Technical Manual

# Evia Family of Implantable Pulse Generators


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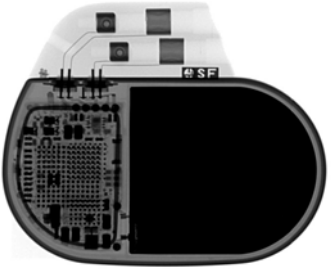
excellence for life

**Evia**

Implantable Pulse Generators



Evia DR

X-Ray identification

Evia DR-T

X-Ray identification

**Radiopaque Identification**

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

Evia DR, DR-T, SR, and SR-T SF

**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).

# Contents

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# 1. Device Description

Evia is a multi-programmable, dual chamber pulse generator with rate-adaptive pacing. The Evia 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 Evia 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.

Evia 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.

Evia 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]).

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

| | |
|---|---|
| **Evia DR** | Dual chamber, rate-adaptive, unipolar/bipolar |
| **Evia DR-T** | Dual chamber, rate-adaptive, unipolar/bipolar, with Home Monitoring |
| **Evia SR** | Single chamber, rate-adaptive, unipolar/bipolar |
| **Evia SR-T** | Single 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 Evia family. If specified as dual chamber configurations, the descriptions are specifically referring to Evia DR and Evia DR-T. If specified as single chamber configurations, the descriptions are specifically referring to Evia SR and Evia SR-T.

## 2. Indications

Rate-adaptive pacing with Evia 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 Evia 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**).

**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 sterility and longevity may be compromised.

## 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 Ventricular Capture Control.

**Lead Check—**The Evia pulse generators have an automatic lead check feature which may switch from bipolar to unipolar pacing and sensing without warning. This situation may be inappropriate for patients with an Implantable Cardioverter Defibrillator (ICD).

**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 VCC—**If the SA/CV sequence is not successful, program another pulse width or test start amplitude. If still unsuccessful, program the pacing pulse amplitude manually.

**NIPS—**Life threatening ventricular arrhythmias can be induced by stimulation in the atrium. 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 Evia 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.

**Programmers—**Use only appropriate BIOTRONIK programmers equipped with appropriate software to program Evia 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.

**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 Ventricular 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.

**CLS Rate-Adaptation—**Under certain circumstances (e.g., EMI, lead dislodgment), the Evia 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, 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 Evia 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).

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

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

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

| Category | # pts (n-273) | % of pts | # of AEs | AE/ pt-mo (n-1418) | Pt-mos between AEs |
|---|---|---|---|---|---|
| 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.

**NOTE:**

The Dromos family of pulse generators is an earlier generation of BIOTRONIK devices. The Evia 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.

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

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 Inos$^{2+}$ CLS Clinical Study

The adverse events reported below are from the Inos$^{2+}$ 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 Evia 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
- Cardiac perforation
- Air embolism
- Pocket erosion
- Infection
- Lead fracture/insulation damage
- Lead dislodgment
- Lead-related thrombosis
- Body rejection phenomena
- Muscle or nerve stimulation
- Elevated pacing thresholds
- Pocket hematoma
- Myopotential sensing
- Local tissue reaction/fibrotic tissue formation
- Pulse generator migration
- 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 symptomology 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 VO2 (mL/kg/minute) | 20.4 ± 8.0 | 17.8 ± 6.2 | 2.67* ± 2.77 [1.5, 3.8] |
| VO2 @ 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

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

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 Ventricular Capture Control

All references to Active Capture Control feature are now synonymous with Ventricular Capture Control (VCC) in the Evia devices. 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 sino-atrial node (85%) and an abnormal conduction system (57%) at implant.

### 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)<br>[Lower CI = 97.2%] |
| Efficacy: pauses observed during 24 hour Holter | 0% (0/3189 non captures)<br>[Upper CI = 0.1%] |
| Efficacy: ACC threshold comparison to manual threshold | N=140<br>Mean difference ±<br>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.

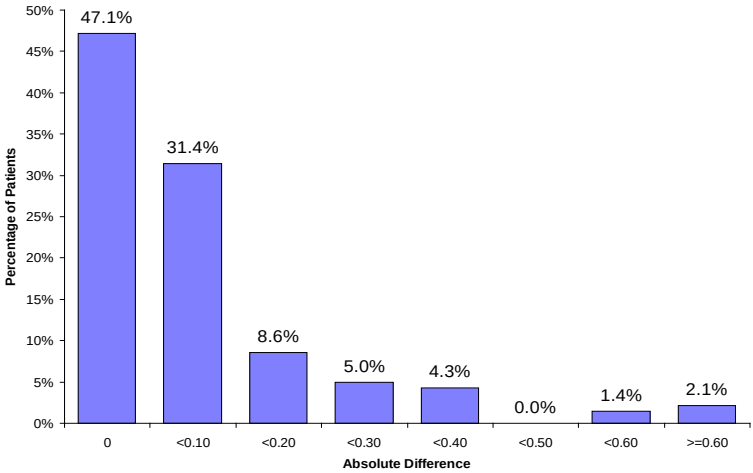
A total of 87.1% (122/140) of the patients enrolled in the PACC study had individual average absolute differences between manual and ACC thresholds of 0.2 volts or less. There were 18 of the 140 patients (13%) that had an average difference higher than 0.2 volts. Of these 18 patients, 16 patients had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

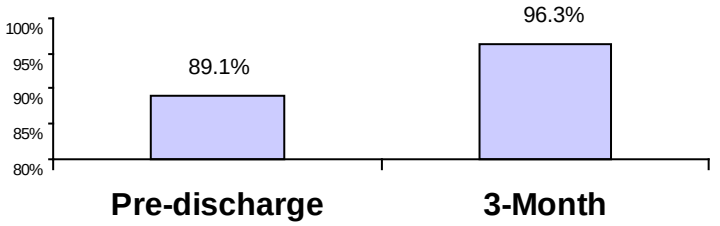
It is concluded that the automatic ventricular pacing threshold is equivalent within 0.2 volts to the manual determination. The threshold measurement analysis clearly demonstrates the ACC algorithm is able to accurately perform threshold measurements in both acute and chronic conditions.

**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 $AxV_p$ 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

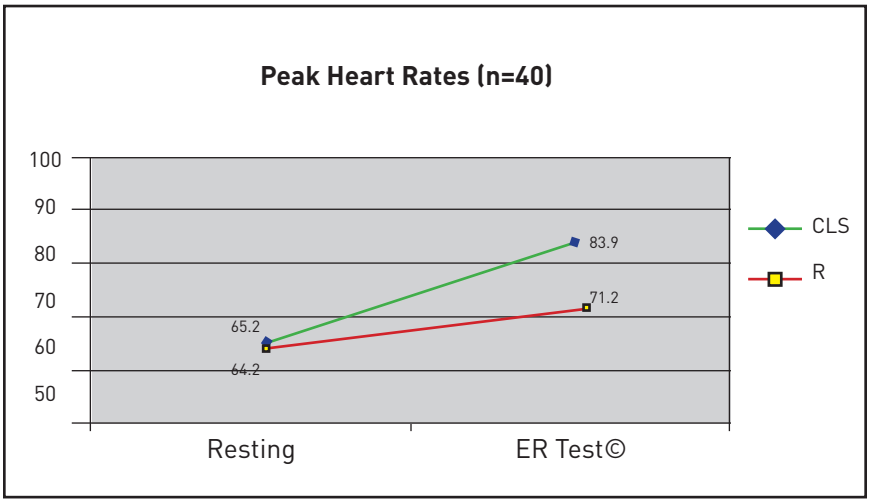
**Primary Endpoint:** Effectiveness of the CLS Algorithm during Emotional Stressors

$H_o$: 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 more

**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 $AxV_p$ 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.

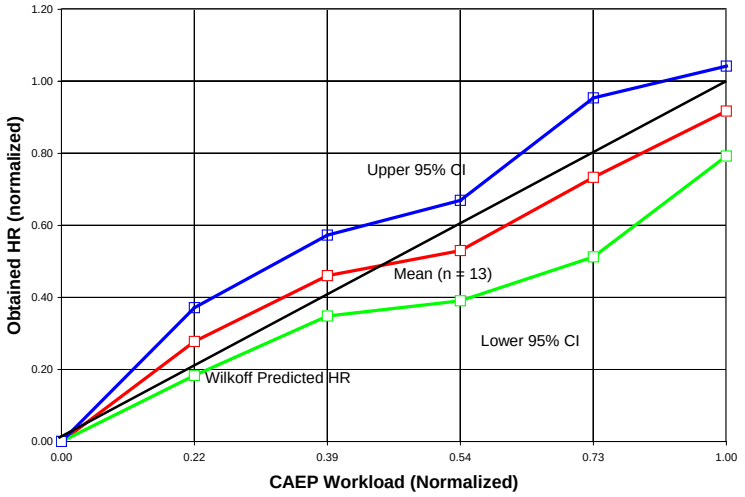
**Table 7: Percentages of Patients Meeting Success Criteria**

| 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 Inos$^{2+}$ 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% |

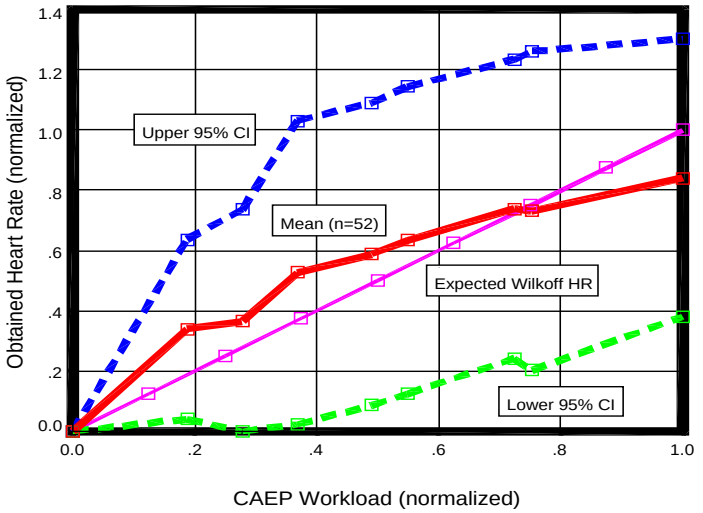
The number and percentages of patients who met certain performance criteria are presented in Table 9.

**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<br>1.3 ± 1.0 per pt yr<br>13.1% actionable | n = 401<br>0.6 ± 1.7 per pt yr<br>29.7% actionable | **1.9 ± 1.9 per pt yr** |
| **Group 2 (Control)** | 414 | n = 1110<br>3.0 ± 1.1 per pt yr<br>10.7% actionable | n = 117<br>0.4 ± 1.4 per pt yr<br>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 (HØ) can be rejected, indicating that the average number of office visits per year is statistical 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.

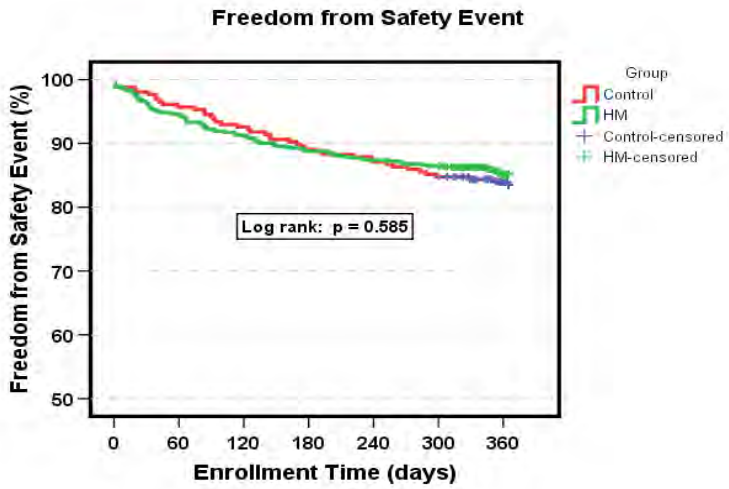
* Up to and including 12 month follow-up data

† 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%.

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).

* Only includes events occurring within 12 months of enrollment

† 2-sided Fisher Exact test

### 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.

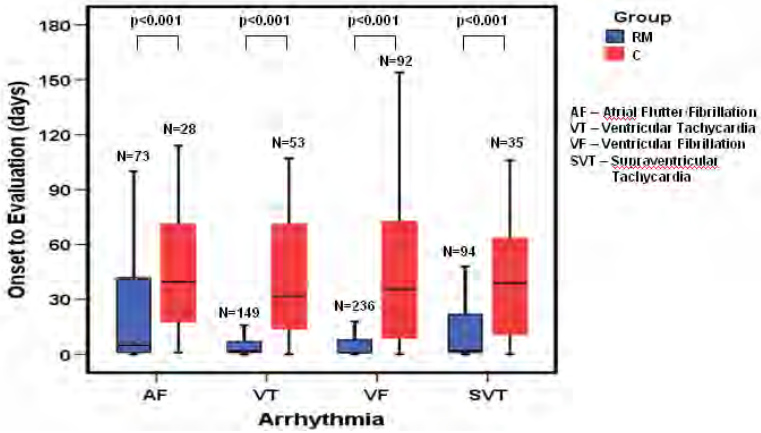
Table 12 compares the time from onset to evaluation of the first AF, VT and VF events for each patient that have occurred in each group, as well as the first of any type of event for each patient in each group. Figure 7 illustrates the time from onset to evaluation of arrhythmic events in a boxplot graph.

**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<br>Mean ± SD (days)<br>Min<br>Max<br># of patients with events | 5.0<br>25.2 +/- 34.2<br>0<br>171<br>73 (7.5%) | 39.5<br>46.8 +/- 33.7<br>1<br>114<br>28 (5.9%) | p < 0.001<br>p = 0.005 |
| **VT1 & VT2** | | | |
| Median<br>Mean ± SD (days)<br>Min<br>Max<br># of patients with events | 2.0<br>12.9 +/- 33.8<br>0<br>256<br>149 (15.3%) | 32.0<br>46.6 +/- 46.9<br>0<br>245<br>53 (11.2%) | p < 0.001<br>p < 0.001 |
| **VF** | | | |
| Median<br>Mean ± SD (days)<br>Min<br>Max<br># of patients with events | 1.0<br>10.5 +/- 22.2<br>0<br>145<br>236 (24.3%) | 35.5<br>45.0 +/- 47.0<br>0<br>287<br>92 (19.5%) | p < 0.001<br>p < 0.001 |

| Time from Event Onset to Evaluation of First Event/ Patient | Group 1 N=972 | Group 2 N=471 | p value |
|---|---|---|---|
| **SVT** | | | |
| Median | 2.0 | 39.0 | |
| Mean ± SD (days) | 16.6 ± 27.4 | 42.1 ± 35.6 | p < 0.001 |
| Min | 0 | 0 | p < 0.001 |
| 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 $p < 0.001$).

## 6.5 Atrial Capture Control (ACC) and Ventricular Pacing Suppression ($V_pS$)

The Evia Master Study was used to support the safety and effectiveness determination of the ACC and $V_p$ Suppression features for the Evia family of pulse generators

### 6.5.1 Primary Objectives

The clinical study included evaluation of the safety and effectiveness of the ACC feature to demonstrate that the feature functions appropriately.

### 6.5.2 Methods

A total of 175 patients were implanted with Evia pulse generators and were enrolled in a controlled, prospective study. The investigation was conducted at 34 centers. The average patient was a 74 year-old (52.6% male, 47.4% female), having an intermittent or complete AV block (48.6%) and/or symptomatic bradycardia (41.7%).

**Primary Endpoint**

The purpose of primary endpoint 1 (ACC efficacy) was to compare the automatic atrial pacing threshold measurements of the ACC algorithm to the manual right atrial pacing threshold measurement at one-month follow-up. The associated hypothesis is evaluated based on the difference in the ACC and manual thresholds as smaller than 0.2 V and greater than -0.2 V.

**Secondary Endpoints**

The purpose of secondary endpoint 1 was to evaluate the safety of the Evia devices by requiring the investigator to record any complication possibly related to the implanted pacemaker during the entire course of the study.

The purpose of secondary endpoint 2 was to evaluate the ACC feature through an analysis of the rate of loss of capture caused by inappropriate functioning of the ACC feature in patients with Evia DR/DR-T pacemakers. This evaluation was based on the occurrence of inappropriate loss of capture observed at one and three month follow-up right after interrogation of the pacemaker.

**Additional Data of Interest**

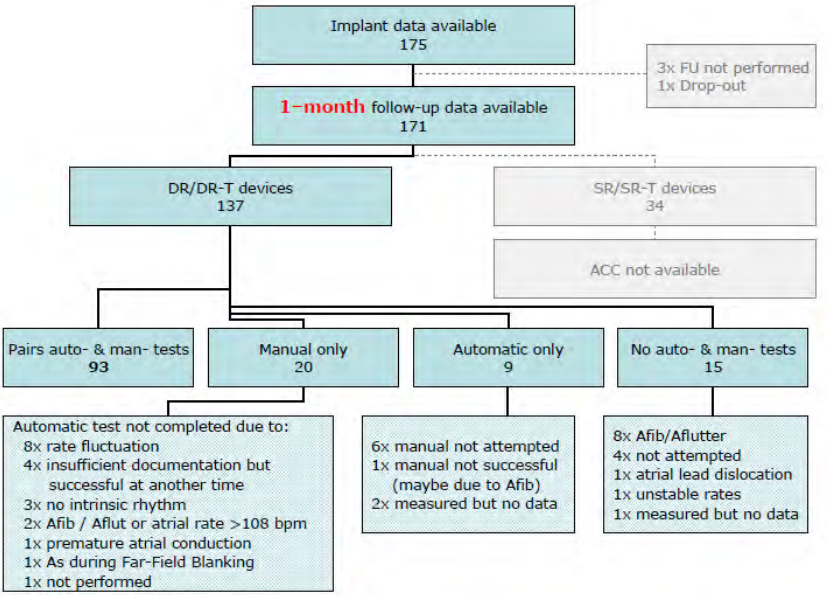
In addition to the data collected in order to support the predefined endpoints, BIOTRONIK also collected information about other measurements associated with Evia devices. The additional information collected included:

- The Home Monitoring function of the Evia DR-T/SR-T devices was investigated using the information provided by the HMSC 3.0. The investigator was asked to evaluate if the Cardio Report with the periodic IEGM provides them with sufficient information about the technical functionality for the pacemaker.
- The ACC and $V_p$ Suppression features were investigated through an analysis of 24 hour Holter recordings in a subgroup of patients with Evia DR/DR T devices between the discharge and the three-month follow-up.
- Adverse events and adverse device effects that may occur during the course of the study were analyzed.

## 6.5.3 Summary of Clinical Results

The study involved 175 patients (92 males and 83 females), which were implanted with the following: 121 Evia DR-T, 20 Evia DR, 27 Evia SR-T, and 7 Evia SR devices. The mean follow-up time was 5.7 ± 1.2 months with a median of 6.0 months. To address the difference in the number of enrolled patients versus the number of paired measurements for ACC, a flowchart is provided in Figure 8. The flowchart specifies the number of patients at pre-discharge, number of patients with paired measurements and the reasons why patients were excluded from the measurements.

**Figure 8: ACC Flowchart of Paired Measurements**

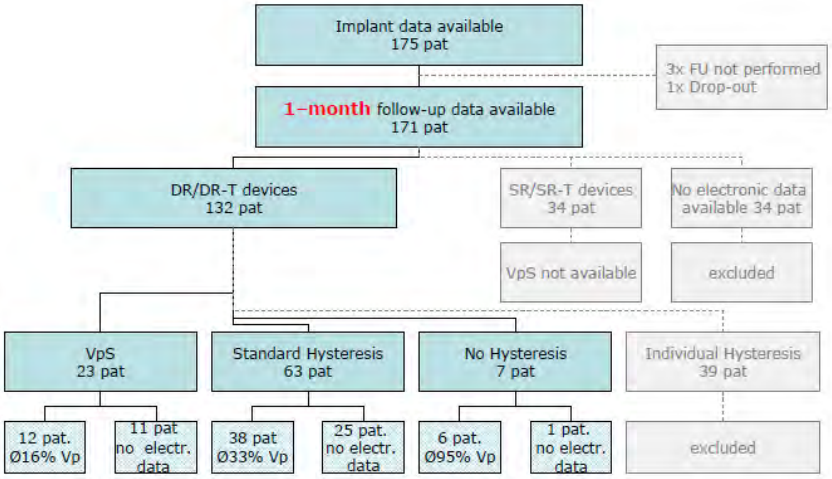



The review of the reasons for missing data showed the following most common reasons:

- 8 subjects had rate fluctuations (as defined by the algorithm)
- 8 subjects had atrial fibrillation or atrial flutter
- 6 subjects did not have the manual test performed

To address the difference in the number of enrolled patients versus the number of patients with $V_p$ Suppression activated, a flowchart is provided in Figure 9.

**Figure 9: $V_p$ Suppression Flowchart of Ventricular Pacing Percentage Data**




The review of the reasons for missing data showed the following most common reasons as being:

- 23 patients were programmed with $V_pS$, but 11 of these subjects did not have electronic data available.
- 63 subjects were programmed with AV-delay with Hysteresis, but 25 of these subjects did not have electronic data available.
- 7 subjects were programmed with no Hysteresis, but 1 subject did not have electronic data available.

Review of the missing data revealed that this data would not have altered the main study results and did not raise additional concerns about the effectiveness of the ACC feature.

#### 6.5.3.1 Primary Endpoint 1: Comparison of Automatic Atrial Threshold Testing vs. Manual Measurement

In total 93 pairs of measurements at the one month follow-up were available with a mean ± standard deviation = 0.01 V ± 0.14 V, minimum = -0.7 V, maximum = 0.6 V. The two sided 95% confidence interval for the mean calculates to [-0.03 V, 0.02 V]. Since this interval is entirely included in the equivalence-defining interval [-0.2 V, 0.2 V] it can be concluded that the two measurements can be regarded as equivalent, so the alternative hypothesis can be accepted.

In 19 out of a total of 384 threshold tests (4.9%) the difference between the automatic and manual atrial threshold was greater than ± 0.2 V. Detailed primary endpoint 1 results are presented in Table 13.

**Table 13: Mean Difference Between Triggered Automatic and Manual Threshold Test**

| Item | Visit Type | N | Mean | Std Dev | Min | Median | Max |
|---|---|---|---|---|---|---|---|
| Difference in Atrium [V] Automatic-manual | Pre-discharge | 95 | -0.01 | 0.11 | -0.4 | 0.0 | 0.3 |
| | One Month | 93 | -0.01 | 0.14 | -0.7 | 0.0 | 0.6 |
| | Three Month | 103 | -0.01 | 0.13 | -0.5 | 0.0 | 0.7 |
| | Six Month | 93 | -0.02 | 0.09 | -0.4 | 0.0 | 0.3 |
| | Total | 384 | -0.01 | 0.12 | -0.7 | 0.0 | 0.7 |

The low number of pacing threshold measurements that differed significantly between ACC and manual methods was consistent with acceptable ACC performance.

### 6.5.3.2 Secondary Endpoint 1: Complication Free Rate

The purpose of the secondary endpoint 1 was to evaluate the safety of the Evia (SR, SR-T, DR, DR-T) pacemaker by asking the investigator to record any complication possibly related to the implanted pacemaker during the entire course of the study.

Complications related to the implanted pacemaker have been reported in two patients. Hence a complication free rate of 173/175 = 98.9% results. The exact two-sided 95% confidence interval is [95.9%, 99.9%], p = 0.007. Therefore the null-hypothesis can be rejected and it can be concluded that the complication free rate is statistically significant greater than 95%.

One of the two complications was caused by a damage of the sealing plugs, very likely caused by strong forces during the introduction of the torque wrench at implantation, but there were no signs of a material or manufacturing problem. The second complication was a repositioning of the pacemaker due to pain in the circumference of the device, but there were no signs of infection, and the examinations of the blood samples were normal. The low rate of complications was consistent with acceptable, high overall device performance.

#### 6.5.3.3 Secondary Endpoint 2: Appropriate Atrial Capture Control Performance Based on Follow-Up Measurements

The purpose of secondary endpoint 2 was to evaluate the ACC feature through an analysis of the rate of loss of capture caused by inappropriate functioning of the ACC feature in patients with Evia DR and DR-T pacemakers. This evaluation was based on the occurrence of inappropriate loss of capture observed at one and three month follow-ups after interrogation of the device.

In total, atrial capture control performance was evaluated in 156 cases in 92 patients at one and three month follow-up. In 155 cases the atrial stimulation was successful and classified as capture. Once, intermittent atrial fibrillation was the reason for non-capture.

The proportion of successful atrial capture control performance was 155/156 = 99.4%, two-sided 95% confidence interval: [96.5%, 100.0%], p = 0.006 (one-tailed). Since the events are correlated within patients, a GEE-correction was carried out, yielding a two-sided (GEE-corrected) 95% confidence interval of [99.4%, 100.0%]. Therefore the null-hypothesis can be rejected and it can be concluded that the rate of successful atrial capture is statistically significant greater than 95%.

Table 14 lists the distribution as to whether the pacemaker delivers stimuli to the atrium at device interrogation. If the device delivered stimuli, the atrial pacing performance was retrieved (capture/non-capture) as summarized in Table 15.

**Table 14: At Device Interrogation the Pacemaker Delivers Stimuli to the Atrium, N(%)**

| Visit Type | No | Yes | Total |
|---|---|---|---|
| One Month | 61 (44.5) | 76 (55.5) | 137 (100.0) |
| Three Month | 49 (37.1) | 83 (62.9) | 132 (100.0) |
| Six Month* | 55 (41.4) | 78 (58.6) | 133 (100.0) |
| Total | 165 (41.0) | 237 (59.0) | 402 (100.0) |

* not endpoint related

**Table 15: Atrial Pacing Performance at Device Interrogation, N (%)**

| Visit Type | Capture | Non-Capture | Not Assessable | Total |
|---|---|---|---|---|
| One Month | 75 (98.7) | 0 (0.0) | 1 (1.3) | 76 (100.0) |
| Three Month | 80 (96.4) | 1 (1.2) | 2 (2.4) | 83 (100.0) |
| Six Month* | 77 (100.0) | 0 (0.0) | 0 (0.0) | 77 (100.0) |
| Total | 232 (98.3) | 1 (0.4) | 3 (1.3) | 236 (100.0) |

The rate of successful atrial capture was calculated by (1-(number of follow-ups where inappropriate loss of capture is observed divided by the number of analyzable assessments)). However, the atrial capture control feature cannot prevent loss of capture under certain circumstances. For example, lead dislodgement could results in an elevated pacing threshold beyond the programmed maximum pacing output. Therefore, events where the true measured pacing output is above the maximum programmed ACC output are not counted against the ACC feature. Patients who had the ACC feature disabled at the previous follow-up due to insufficient signal quality were not included in the analysis of the endpoint. The high rate of pacing capture with the ACC feature activated was consistent with acceptable, high overall performance of the algorithm.

### 6.5.3.4 Additional Study Results

- For ACC, the core laboratory analyzed 21 Holter ECG recordings with a duration of 24 hours, and revealed short episodes of atrial non-capture in 3 Holter ECGs. In one patient 3 consecutive beats, in another 9 beats within 1 minute, and in a third patient atrial non-capture was recorded, but not linked to the ACC feature.
- In total, 98 adverse events were reported, where two were classified as pacemaker-related complications. The per-patient complication-free rate is 173/175 = 98.9%, 95% confidence interval [95.9%, 99.9%].

* not endpoint related

### 6.5.3.5 $V_p$ Suppression Results

- For $V_pS$, the corelab and in-house group analyzed 17 Holter ECG recordings for patients who had completed the 1 and 3 month follow-ups and had the feature enabled. The purpose of the analysis was to identify sequences that were indicative of pauses (≥2 seconds) related to the feature. In all of the patients, the analysis did not find a persistent problem with respect to the $V_pS$ behavior.
- For $V_pS$, an analysis of 1 month follow-up data for 132 patients in the Master Study was conducted to demonstrate how the percentage of ventricular pacing varied between the following patient groups:
  - Patients with their device programmed to $V_p$ Suppression (Group 1)
  - Patients with their device programmed to AV-delay with Hysteresis (Group 2)
  - Patients with their device programmed to normal AV-delay (Group 3)
- The overall percentage of ventricular pacing between patients programmed with $V_pS$ versus the patients programmed with AV-delay with Hysteresis or the patients programmed with normal AV-delay demonstrated that $V_pS$ resulted in the lowest percentage of ventricular pacing as shown in Table 16 and Table 17.

**Table 16: Percentage of Ventricular Pacing**

| FU Interval | $V_pS$ (Group 1) Mean [95% CI](N) | Hysteresis (Group 2) Mean [95% CI](N) | No Hysteresis (Group 3) Mean [95% CI](N) | %-pacing $V_pS$ versus %-pacing Hysteresis, % pacing $V_pS$ versus %-pacing No Hysteresis |
|---|---|---|---|---|
| 1 Month | 16% [-5, 36] (12) | 33% [23, 44] (38) | 95% [85, 106] (6) | S, S |
| 3 Months | 17% [2, 31] (13) | 37% [27, 47] (42) | 91% [75, 107] (7) | S, S |
| | | | S = Significant<br>NS = Not Significant | |

**Table 17: Mean Percentage of Ventricular Pacing for Patients without AV-Block**

| Indication | % Ventricular Pacing @ 1 month | % Ventricular Pacing @ 3 months |
|---|---|---|
| SSS, Brady-Tachy | 0 | N/A |
| SSS, SA exit block | 0 | 0 |
| Syncope unknown origin | N/A | 0 |
| SSS unspecified | N/A | 0 |
| SSS, Brady-Tachy | 1 | 3 |
| SSS, Bradycardia | N/A | 12 |
| SSS, Brady-Tachy | 0 | N/A |
| SSS, Brady-Tachy | 56 | 27 |
| SSS, Brady-Tachy | 3 | 3 |
| SSS, Brady-Tachy | 6 | N/A |
| SSS, Brady-Tachy | 2 | N/A |
| **Total Number patients** | **11** | |
| **Total Mean % VentricularPacing** | **11.3 %** | |

- Overall, the $V_pS$ group (Group 1) had a much lower percentage of ventricular pacing compared to the patient group with Hysteresis enabled (Group 2) as well as compared to the patient group with normal AV delays (Group 3).

### 6.5.3.6 Conclusion

All study endpoints were achieved successfully. The final analysis showed that the ACC feature worked as expected. The mean difference and standard deviation for automatic versus manual threshold test was 0.01 V ± 0.14 V. A similar result of -0.1 V ± 0.12 V was achieved when including all 384 available paired measurements of all the follow-ups. The triggered automatic atrial threshold test was successfully completed in 80.4%, and accordingly 19.6% were correctly aborted by the pacemaker due to high atrial rates > 108 bpm (37.0%), rate fluctuation (26.0%) or other reasons.

- Atrial capture performance was evaluated at the beginning of each follow-up. Only one out of 236 evaluations atrial stimulation was not successful due to atrial fibrillation. Other than this exception, the automatically adjusted pacing output always led to successful atrial stimulation.
- Over the course of the study, 21 Holter ECGs were recorded and analyzed with respect to the atrial pacing performance with ACC activated. In 3 Holter ECGs the core laboratory revealed atrial non-capture events (only 3 beats and 9 beats within 24 hours). These atrial non-capture events might have been avoided with higher programmed safety margin.
- The pacemaker related complication free rate showed the expected appropriate behavior of Evia. In total 98 adverse events were reported, where two were classified as endpoint related. One complication was caused by damage to the sealing plugs, very likely due to strong forces during the introduction of the torque wrench during implantation, but there were no signs of a material or manufacturing problem. The second was a repositioning of the pacemaker due to pain in the circumference, but there were no signs of infection.
- The $V_p$ Suppression feature was safe as there were no issues caused by the $V_p$S feature reported over the course of the Evia Master Study or during analysis of seventeen 24 hour Holter recordings; the feature was effective in demonstrating a significant reduction in the percentage of ventricular pacing compared to patients programmed to AV-delay with Hysteresis or patients programmed to normal AV-delay. Analysis of the reduction in percentage of ventricular pacing in patients without AV block and the $V_p$ Suppression feature activated showed that most had meaningful reductions as intended for this feature.

# 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 Evia configuration, see **Section 15.1**.

**NOTE:**

Ventricular Capture Control is only available with the following pacing modes: DDD-CLS, VVI-CLS, DDDR, VDDR, VVIR, DDD, VDD, VVI, DDD-ADI, and DDDR-ADIR.

### 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, AATR, VVTR, VDIR, 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, Evia also can be programmed to use a unique rate-adaptive principle called Closed Loop Stimulation (CLS) to adapt the patient's pacing rate.

The Evia 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 Evia 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 Evia pacemaker perform similarly to earlier generations of BIOTRONIK pulse generators (i.e., Philos II DR and Dromos DR).

### 7.1.4 Mode Switching

Evia provides Mode Switching to change pacing modes as a result of atrial tachycardias. Mode Switching is designed to avoid tracking of non-physiologic atrial rates due to paroxysmal atrial tachycardias (PATs). Mode Switching is only available in atrial tracking modes DDD(R), VDD(R), DDD-CLS, and DDDR-ADIR.

#### 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 18.

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.

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 Found in the Holter Tab
- Mode Switch Counter
- Total Mode Switch Duration

Mode Switching is available during magnet application after 10 cycles of ASYNC pacing and during ERI. Mode Switching occurs as described in Table 18.

**Table 18: Programmable Mode Switches**

| Programmed Pacing Mode | Programmable Mode Switch Pacing Modes | |
|---|---|---|
| | Rate-Adaptive | Non-Rate-Adaptive |
| DDDR, DDD-CLS and DDDR-ADIR | DDIR | N/A |
| VDDR | VDIR | N/A |
| DDD and DDD-ADI | DDIR | DDI |
| VDD | VDIR | VDI |

### 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 | VVI | AAI |
| Triggered: | DDT | VVT | AAT |

The triggered pacing mode fixes the AV delay to 150 ms and does not provide a safety AV delay.

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, 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 200 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 -5 bpm and as high as -90 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, and DVIR 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.

During night mode the rate will not fall below the programmed night rate even if Hysteresis can take it to a lower rate. 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.

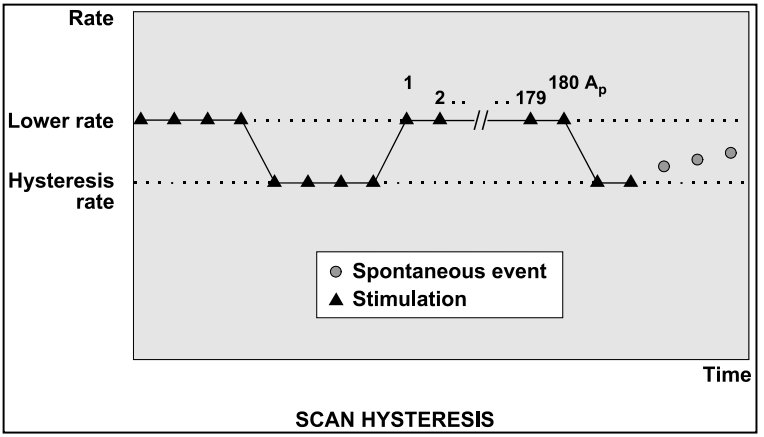
### 7.2.3 Scan Hysteresis

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 10: Scan Hysteresis**




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

**NOTE:**

Scan Hysteresis can be used during night mode, but it will not take the rate below the programmed night rate.

Scan Hysteresis is only available when Hysteresis is selected on.

After the ASYNC effect following magnet application, hysteresis is available.

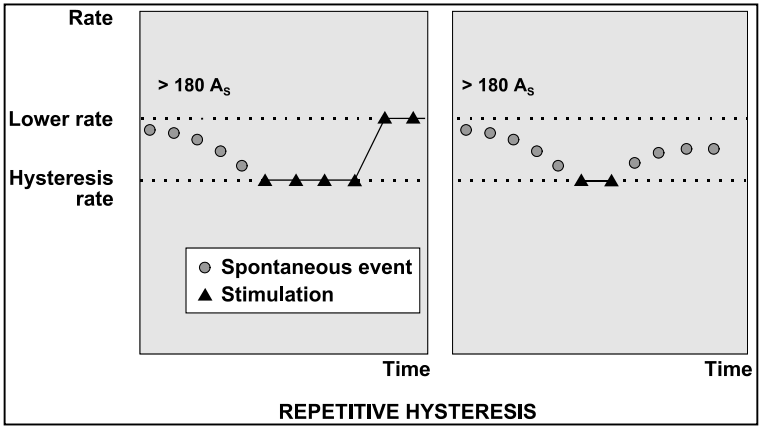
## 7.2.4 Repetitive Hysteresis

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 15). 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 11: Repetitive Hysteresis**




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

**NOTE:**

Repetitive Hysteresis can be used during night mode but it will not take the rate below the programmed night rate

Repetitive Hysteresis is only available when Hysteresis is selected on.

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 Ventricular Capture Control are programmed ON simultaneously in VVI(R), VCC will not take the rate below the programmed night 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

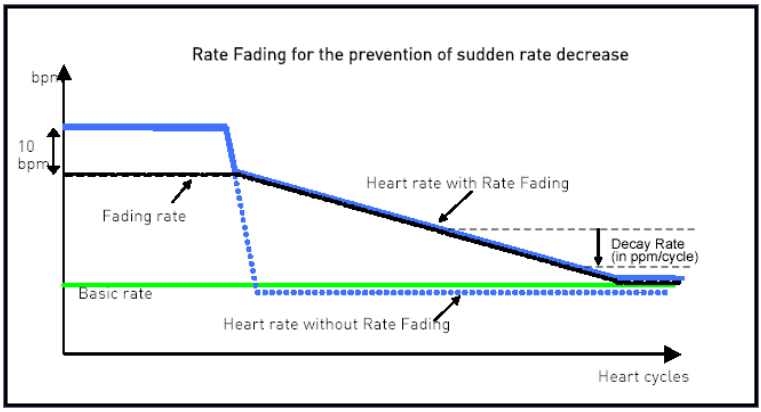
Rate Fading is intended to prevent a sudden drop in heart rate when the pulse generator transitions from tracking an intrinsic rhythm to pacing due to an abrupt decrease in the intrinsic rate, in order to prevent potential reactions such as dizziness, light headedness, lack of energy and fainting.

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 12.

**NOTE:**

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

**Figure 12: Rate Fading**




The Rate Fading feature is available after 10 ASYNC 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 7.5 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 VCC is programmed to ON or ATM, the pulse amplitude cannot be programmed by the user to a value higher than the programmed Maximum VCC Amplitude (Max. Ampl.). When VCC 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 VCC Amplitude (fixed at 0.7V.)

**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 7.0 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 VCC is programmed to ON or ATM, the pulse width cannot be programmed to a value higher than 0.4 ms.

## 7.4 Automatic Sensitivity Control (ASC)

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. The sensitivity values for the atrial and ventricular channels are independently programmable or automatic sensing control can be utilized. With Unipolar programming, the highest possible sensitivity setting is 0.5 mV.

The Automatic Sensitivity Control (ASC) feature allows the pulse generator to automatically measure the peak amplitude of a sensed event and adapts the sensing threshold accordingly. After each sensed detection (electrogram is above actual threshold for 2 consecutive samples) the ASC is starting the detection hold-off period of 121 ms in the ventricle (atrium 101 ms) and detects within the first 80 ms of this interval the highest amplitude of the peak. After this initial period, the

sensing threshold is first set to 50% of the measured peak amplitude. After the step duration of 125 ms the threshold is set to 25% of the peak amplitude (atrium 82 ms) but never below the minimum threshold of 2.0 mV in the ventricle (atrium 0.2 mV bipolar and 0.5 mV unipolar).

## 7.5 Timing Features

Features related to pulse generator timing cycles.

### 7.5.1 Refractory Periods

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. There are two refractory periods in the atrium:

- Regular atrial refractory period, which is automatically adjusted by the Auto Aref functionality
- PVARP is started with each ventricular pace outside of the AV delay. In DDI mode, PVARP is also started with a regular ventricular sense
- PVARP after PVC is started after a premature ventricular sensed event (PVC)

Far-field protection is activated in the atrium for ventricular sensed and paced events. The pulse generator's ventricular refractory period is always initiated by a sensed or paced ventricular event.

**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 PVARP

The Post Ventricular Atrial Refractory Period (PVARP) is a function in the pacemaker to help prevent Pacemaker Mediated Tachycardia (PMT), by preventing false classification of a retrograde conduction as an atrial event.

There are 2 different behavior modes of PVARP based on programmed mode, which is described below.

- In P-synchronous modes(e.g. DDD), the PVARP timer is started after : $V_p$, $V_p$(WKB), $V_p$(SW), $V_p$(BU)
- In R-synchronous modes(e.g. DDI), the PVARP timer is started after : $V_p$, $V_p$(SW), $V_p$(BU), VES, $V_s$ and $V_s$(AVC).
- After a VES, the parameter PVARP after PVC is automatically extended to PVARP + 150ms, up to a maximum of the user programmable "PMT VA Criterion limit" + 50 ms. This parameter was formerly known as PMT protection after PVC.

This behavior is demonstrated in Figure 13.

**Figure 13: PVARP Timing**

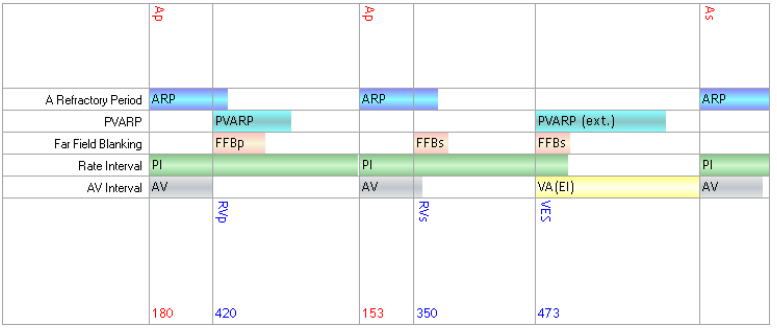



Table 19 shows the PVARP parameter values and ranges.

**Table 19: PVARP Parameter Values and Ranges**

| Parameter Name | Range | Standard Value | Units |
|---|---|---|---|
| PVARP | AUTO, 175..(5)..600 | AUTO | ms |
| PVARP after PVC | PVARP + 150ms | 400ms | ms |

### 7.5.2.1 AUTO PVARP

If the PVARP feature is set to AUTO, the algorithm optimizes the PVARP to reduce the incidence of PMT. The nominal values of PVARP value is set to 250ms, and PVARP after PVC is set to 400ms. Once a PMT is detected, the algorithm automatically extends the PVARP and PVARP after PVC by 50ms, up to the maximum value of 600ms.

If there is no PMT detected by the algorithm, both the PVARP and PVARP after PVC is reduced by 50ms every 7 days, but no less than the minimum value of 175ms.

## 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 20.

**Table 20: Dynamic AV delay settings**

| Rate Ranges | LOW |
|---|---|
| **Non-CLS Modes** | |
| below 70 bpm | 180 ms |
| 70—90 bpm | 170 ms |
| 91—110 bpm | 160 ms |
| 111—130 bpm | 150 ms |
| above 130 bpm | 140 ms |
| **CLS Modes** | |
| below 70 bpm | 150 ms |
| 70—90 bpm | 140 ms |
| 91—110 bpm | 130 ms |
| 111—130 bpm | 120 ms |
| above 130 bpm | 120 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 OFF and –10 ... (-5) ... -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.

### 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 21 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 21: AV Hysteresis Settings**

| AV Setting | Low | Medium | High |
|---|---|---|---|
| 15ms | 85ms | 125ms | 165ms |
| 50ms | 120ms | 160ms | 50ms |
| 75ms | 145ms | 135ms | 100ms |
| 100ms | 170ms | 210ms | 150ms |
| 120ms | 190ms | 230ms | 170ms |
| 130ms | 200ms | 240ms | 180ms |
| 140ms | 210ms | 250ms | 190ms |
| 150ms | 220ms | 260ms | 200ms |
| 160ms | 230ms | 270ms | 225ms |
| 170ms | 240ms | 280ms | 225ms |
| 180ms | 250ms | 290ms | 250ms |
| 190ms | 260ms | 300ms | 250ms |
| 200ms | 270ms | 310ms | 350ms |
| 225ms | 295ms | 330ms | 370ms |
| 250ms | 320ms | 360ms | 400ms |
| 300ms | 370ms | 410ms | 450ms |
| 350ms | 420ms | 450ms | 450ms |

### 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 ... 10). 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 ... 10). 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, multiplied by approximately 2/3, limited to a minimum of 15 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 22: I-Opt Parameters**

| Function | I-Opt | Standard Program |
|---|---|---|
| AV Hysteresis | 400 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.

### 7.5.6 Far-Field Protection

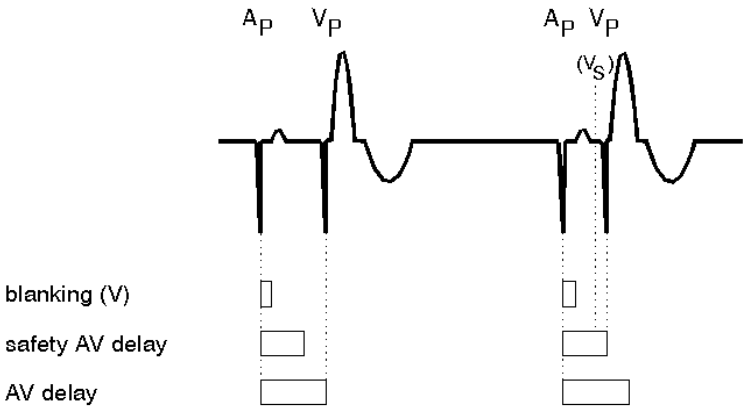
Far-field protection affects the atrial channel for both sensed and paced events to prevent inappropriate mode switching. The blanking interval begins with a ventricular paced / sensed event. The device recognizes the paced / sensed far-field event on the atrial channel but does not use the event in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

## 7.5.7 Safety AV Delay

The safety AV delay (set at 100 ms) applies to the pacing modes DDD-CLS, DDD(R), DVI(R), DDI(R), and DDD(R)-ADI(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 14). 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 14: Ventricular blanking time and safety AV delay (Dual chamber)**




## 7.5.8 Upper Rate and UTR Response

The upper rate is programmable (up to 200 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.

## 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.

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 **Evia** models can be used with either unipolar or bipolar IS-1 leads.

## 7.7 Parameters for Rate-Adaptive Pacing

The Evia 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 Evia, 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.

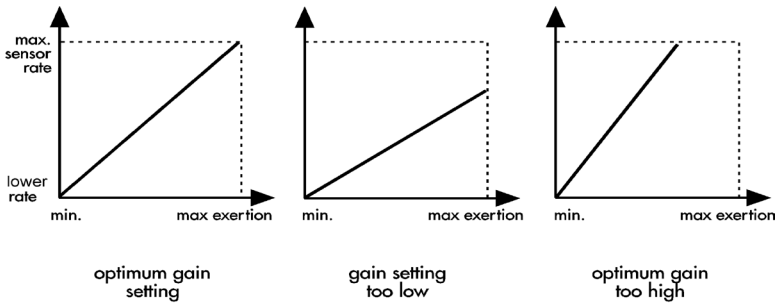
### 7.7.1 Sensor Gain

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 15: Influence of sensor gain on the rate response.**




## 7.7.2 Automatic Sensor Gain

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

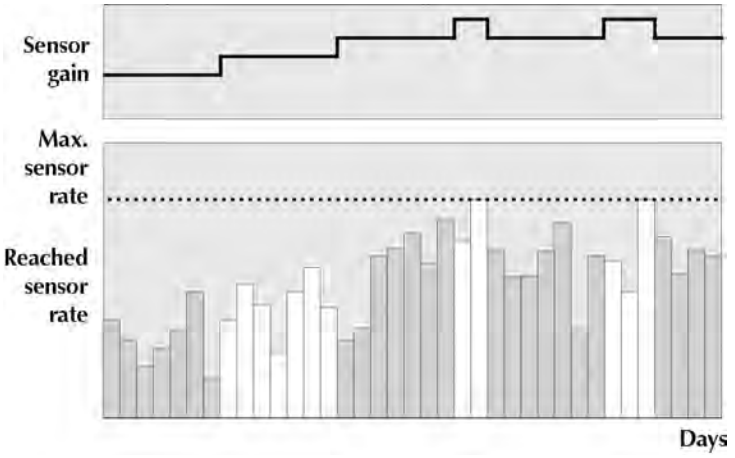
When the Automatic Sensor Gain is activated, the pulse generator samples the sensor-indicated rate. The sensor gain will be increased by 10%, if the activity rate does not reach or exceed the programmed activity rate (fixed to 90% of maximum sensor rate) for 30 minutes each day over 7 consecutive days. 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 16: Automatic Sensor Gain**

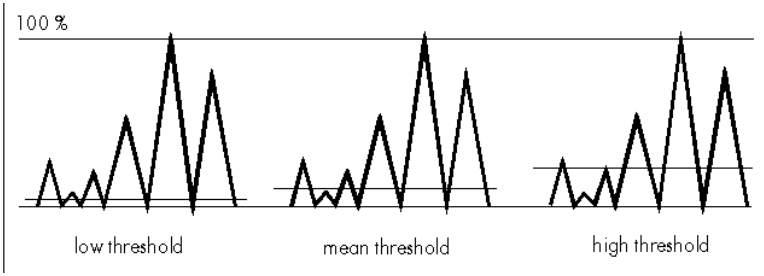



## 7.7.3 Sensor Threshold

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 17). 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 17: 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 (Table 23). 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 23: Rate Increase**

| Increase in Rate (ppm/s) | Time to Increase Rate (seconds) |
|---|---|
| 1 | 90 |
| 2 | 45 |
| 4 | 23 |
| 10 | 9 |

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.

### 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 160 ppm) must be less than or equal to the programmed UTR.

**NOTE:**

In the DDIR and DVIR modes, the sensor rates control the ventricular pacing rates independent of the AV Delay.

### 7.7.6 Maximum Closed Loop Rate

With the Evia 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. In DDDR, VDDR, DOOR, VVIR, VOOR, AAIR, and AOOR, the rate decrease setting of 0.5 ppm per second decrease in pacing rate would take 180 seconds to change from 150 ppm to 60 ppm.

**Table 24: Rate Decrease**

| Decrease in Rate (ppm/s) | Time to Decrease Rate (seconds) |
|---|---|
| 0.1 | 900 |
| 0.2 | 450 |
| 0.5 | 180 |
| 1.0 | 90 |

The programmed rate decrease setting applies only to the decrease in pacing rate during sensor-driven operation in the primary chamber being paced.

## 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 protection intervals 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 ($V_pA_s$) 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 ($A_sV_p$) and far-field protection intervals (FFB).
- The mean deviation of these 8 $V_pA_s$ intervals is less than the 2:1 Lock-In Stability Criterion, defined as 50ms.

### Confirmation

When the suspicion criteria have been met, the AV delay is increased by the programmed far-field protection interval (up to a maximum of 300 ms. 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 far field protection period is programmable to allow the physician to ensure that the protection period is sufficient to recognize cases where a 2:1 lock-in is likely to occur. Refer to **Section 7.5.6** for recommendations for programming the far field protection period in conjunction with the 2:1 Lock-In Management feature.

## 7.9 Atrial Upper Rate

The atrial upper rate (AUR) prevents atrial pacing from occurring in the vulnerable phase after an atrial sensed event during the PMT protection interval, and ensures that the next atrial paced event occurs after the heart's natural atrial refractory period.

To avoid this, an atrial upper rate of 240 ppm (atrial upper interval (AUI), 250 ms) is started after a PMT-As.

The next Ap can only be emitted after the expiration of the AUI. When there are high sensor rates, the atrial pacing is shifted.

**NOTE:**

Right atrial pacing does not occur when mode switching is activated, and when the atrial upper rate is activated in DDI mode at the end of the sensor or basic interval.

## 7.10 Atrial Overdrive Pacing (Overdrive Mode)

The atrial pacing rate increases after each atrial sensed event that is not classified as an atrial extrasystole, in an attempt to suppress atrial tachyarrhythmias. The overdrive algorithm triggers atrial overdrive pacing and guarantees that pacing occurs at a rate slightly above the intrinsic sinus rate. Atrial overdrive pacing thereby minimizes the number of atrial sensed events. The overdrive mode is available in DDD(R).

The features of Atrial Overdrive pacing include:

After every atrial sensed event (non-AES), the pacing rate is increased by a fixed rate increase (8 ppm) above the last P-P interval. If the intrinsic rate does not continue to rise after the programmable number of cycles (overdrive pacing plateau), the overdrive pacing rate is reduced in steps of 1 ppm. In each instance, the rate drop occurs after a fixed 20 cycles has been completed.

The pacing rate is reduced until an atrial event is again sensed. Afterwards, the overdrive pacing cycle begins again at an increased rate.

**Protection Function of the Algorithm**

Atrial overdrive pacing (Overdrive Mode) consists of different functions that become effective at high atrial rates:

- When the maximum activity rate (MAR, standard setting 120 ppm, (90... (5)...160 ppm) is exceeded as with atrial tachycardias, the algorithm is automatically deactivated. If the rate falls below the MAR, the overdrive algorithm is reactivated.

- The function is deactivated when the mean of the atrial rate over a period of twelve hours exceeds the average safety rate ("overdrive average rate limit = OAR"). The average safety rate is determined indirectly from the maximum overdrive pacing rate (MOR minus 10ppm). If the average safety rate is exceeded, the pacing rate is incrementally reduced to the basic rate. If the average atrial heart rate falls below the average safety rate, the preventive overdrive pacing is reactivated (activation/deactivation only in a 12 hour rhythm).
- If the function is deactivated for a third time because the average safety rate has been exceeded, overdrive pacing remains OFF permanently. The overdrive mode can not be reactivated until after the pacemaker has been programmed.

**CAUTION**

**Overdrive Pacing Mode—**When programming the overdrive pacing mode, check whether the selected program can cause PMT, and whether atrial over drive pacing would result. Corresponding to the measured retrograde conduction time, the PMT protection interval must be programmed to a correct value.

## 7.11 Management of Specific Scenarios

### 7.11.1 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.

### 7.11.2 PMT Protection

Pacemaker-mediated tachycardia (PMT) is normally triggered by ventricular depolarizations that are not synchronized with atrial depolarizations (e.g., VES). The tachycardia is maintained in a retrograde direction by intrinsic VA conduction of the stimulated ventricular depolarization and in an antegrade direction by ventricular pacing of the pacemaker that is triggered by P-waves. It is the objective of the atrial PMT protection interval to not use retrogradely conducted atrial sensed events for pacemaker timing, but only to statistically evaluate them for detection of atrial tachycardia incidents.

To prevent occurrence of a PMT, Evia pacemakers start an atrial PMT protection interval after each ventricular paced event. If an atrial event is sensed within this PMT protection interval, this will neither start an AV delay nor a basic interval.

The length of the PMT protection can be set to automatic (Auto). In this case, the PMT protection window can be automatically extended after the PMT is detected and terminated.

**NOTE:**

The initial values of the PMT protection interval in the automatic setting at 250 ms after a $V_p$, and 400 ms after PVC.

### 7.11.2.1 PMT Detection and Termination

In addition to PMT prevention, Evia 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 Evia 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 pace-A sense ($V_p$-$A_s$) 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 Evia slightly modifies the AV delay interval (+ or—50 ms) or the upper tracking rate (+50ms) for one cardiac cycle. If the $V_p$-$A_s$ 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

Evia extends PVARP (Post Ventricular Atrial Refractory Period) to the VA interval + 50 ms.

## 7.12 Adjustment of the PMT Protection Window

The PMT protection window can be automatically adjusted. This automatic adjustment functions in the following manner:

When the PMT is detected and terminated, the PMT protection interval is extended by 50 ms. If no additional PMTs arise within seven days, the length of the PMT protection interval is reduced by 50 ms. The initial values of the PMT protection interval in the automatic setting at 250 ms after $V_p$ and 400 ms after a PVC.

## 7.13 Ventricular Capture Control (VCC)

### 7.13.1 Feature Description

The VCC 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 Ventricular Capture Control algorithm, it was demonstrated that use of Ventricular 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 18 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 18: Example of a Capture and a Non-Capture beat**

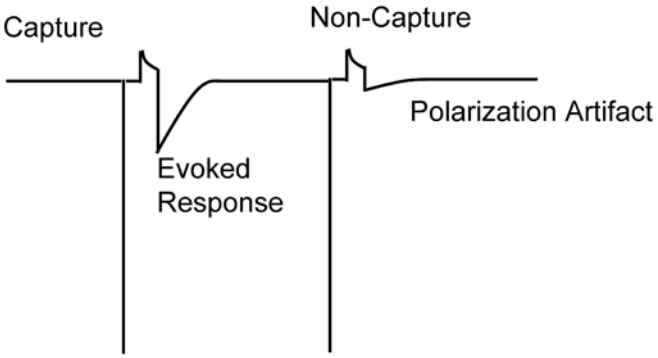


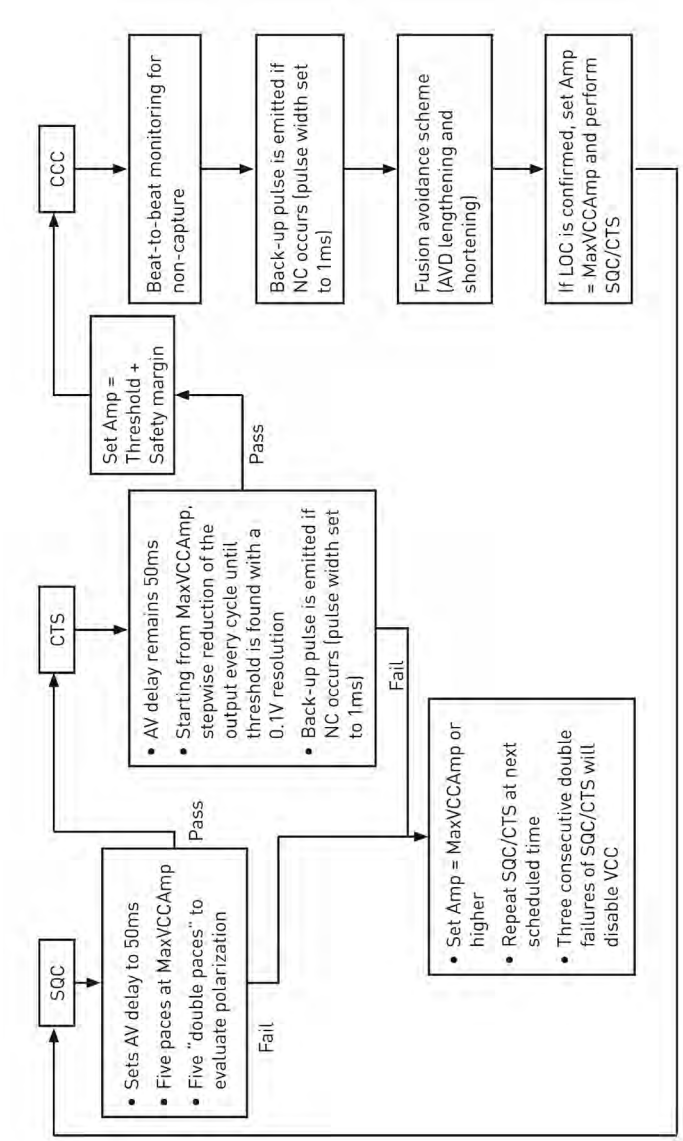

Table 25 contains a list and description of the acronyms and terms pertaining to the VCC feature used in this manual.

**Table 25: Acronyms and Terms**

| Term | Definition |
|---|---|
| CV | Capture Verification—A component of the VCC feature that provides beat-to-beat classification of capture and non-capture. |
| ATM | Automatic Threshold Measurement—A component of the VCC feature that periodically measures the ventricular pacing threshold. ATM can only occur after a successful CV. |
| Evoked Response | The intracardiac signal measured during electrical activation of the cardiac tissue. |
| LOC | Loss-of-Capture—The VCC 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). |
| MaxVCCAmp | Threshold test start—This programmable parameter is the maximum voltage setting that VCC will set after a successful CV. |
| NC | Non-Capture—The VCC 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. |

| Term | Definition |
|---|---|
| Safety Margin | The safety margin is the difference between the pacing threshold and the programmed pacing amplitude. |
| SA | Signal Analysis—A component of the VCC feature that periodically determines whether evoked responses are appropriately detected and that pacing artifact is sufficiently small in amplitude. If the SA determines that the signal is not acceptable, then the other portions of the VCC feature cannot be activated. |

**Figure 19: VCC flow chart**




The feature includes three primary components: Signal Analysis, Capture Threshold Search, and Capture Verification. The following paragraphs describe the operation of these three components (SA, ATM, and CV) of VCC while active in DDD(R) pacing mode. In the other modes (VDD(R) and VVI(R)), there are slight variations in the operation of VCC.

Figure 19 provides a flow chart of the VCC operation.

**Signal Analysis (SA)**

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 SA analyzes the evoked response and the amplitude of the polarization artifact. A successful SA must always be completed before the Capture Threshold Search or the activation of Capture Verification.

- SA 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 MaxVCCAmp, which is the programmable maximum voltage setting (2.4, 3.0, 3.6, 4.2, 4.8V). If non-capture is detected at the maximum voltage setting, the second phase of the SA 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 SA is classified as unsuccessful. If necessary, this test can be repeated at a lower maximum voltage setting.
- If the first SA after activating VCC is not completed successfully, VCC is immediately disabled, and the pacing amplitude is programmed to MaxVCCAmp. VCC then requires manual reactivation of the feature with the programmer.
- If the first SA after activating VCC is completed successfully, but subsequent SA's are not completed successfully, then VCC is suspended, and the pacing amplitude is programmed to the last measured threshold plus the safety margin. The SA will be attempted up to three times. After the 3rd failure, VCC is disabled, and the pacing amplitude is programmed to the MaxVCCAmp plus the Safety Margin of 1.2V. VCC then requires manual reactivation of the feature with the programmer.

**Automatic Threshold Measurement**

- The Automatic Threshold Measurement is the component of the VCC feature that measures the ventricular pacing threshold by stepping down the output until non-capture occurs.
- The Automatic Threshold Measurement occurs over a series of cardiac cycles and begins at the threshold test start 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 4event to ensure ventricular pacing.
- The pacing amplitude decrements with every paced beat by 0.6V, until the first non-captured beat. The algorithm then decrements by smaller increments of 0.1V until the first failed capture, at which point it determines that the capture threshold is preceding value. .
- If two out of three non-capture events are detected, the pacing amplitude is set to the sum of the pacing threshold voltage and the programmed safety margin. If two non-captures are detected when the voltage decrements are greater than 0.1 V, the pacing amplitude is set to the previous amplitude and then the amplitude decrements by 0.1 V until the pacing threshold is determined. When another two non-capture are detected, the previous voltage setting is the pacing threshold.
- The pacing amplitude is then set to the pacing threshold plus a programmable safety margin (0.5 V through 1.2 V in steps of 0.1 V).
- In addition to performing the threshold search after a loss of capture, the search is also conducted at a programmable interval or a specific time during the day to provide an accurate safety margin even with gradual changes in the pacing threshold. Note that a CV initiated by spontaneous loss of capture will reset the timer that triggers the next periodic measurement if the search is programmed to interval.

**Capture Verification (CV)**

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

- If VCC determines that capture has been maintained, then the pulse amplitude remains at that current setting and no action is required.
- If VCC 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.

- If a series of ventricular pacing pulses at varying AV delays result in loss-of-capture, a Signal Analysis (SA) and Automatic Threshold Search are initiated to determine the current pacing threshold.
- 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 Analysis and Automatic 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 VCC 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.

#### 7.13.1.1 Algorithm Suspension, Abort and Disabling

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

The SA/CV sequence will fail when the following events occur:

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

An ongoing SA/CV sequence will abort when the following events occur:

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

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

A SA/CV sequence will be postponed when the following events occur:

- Mode switch is ongoing: If Mode switch is ongoing when an SA/CV is scheduled, the SA/CV will be postponed until reversion back to the programmed mode.
- The presence of a magnet is detected: A scheduled SA/CV is postponed when a magnet (programmer wand) is detected. After removal of the magnet, the SA/CV is started.
- The ventricular rate is higher than 110 bpm: A scheduled SA/CV is postponed when the ventricular rate is higher than 100 bpm. When the ventricular rate drops below 10 bpm, the SA/CV is started.

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

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

- The initial SA/CV sequence after activating VCC failed
- Three subsequent and consecutive failed SA attempts
- The occurrence of 25 Losses of Capture between two consecutive days
- ERI: the device will be set to ERI mode with VCC OFF
- Unipolar lead failure is detected

The occurrence of these unsuccessful, aborted or postponed SA/CV sequences and disabling of the VCC feature are reported in the Status log in the VCC statistics.

## 7.13.2 Ventricular Capture Control Programming

VCC is programmable to ON, Active Threshold Monitoring (ATM) modes, and OFF. Table 26 provides details about the VCC programmability.

**Table 26: VCC Programmability**

| | Programmable Modes for VCC | |
|---|---|---|
| **VCC Components** | **ON** | **ATM** |
| Pulse width programmability | less than or equal to 0.4 ms | |
| SA and Capture Threshold searches | Yes | Yes |
| Set output to threshold + safety margin | Yes | No |
| Capture Verification (CV) | 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 1ms) within 130 ms. If loss-of-capture (LOC) occurs, the device will initiate an SA/CV. Additionally, the device will perform regular threshold searches at the programmed time each 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 fixed minimum VCC Amplitude (Min Ampl.) of 0.7V.

**NOTE:**

After programming the Ventricular Capture Control feature to ON or ATM, the device will perform a Signal Analysis and a capture threshold search. This sequence can take up to 2 minutes.

## 7.14 Atrial Capture Control (ACC)

## 7.14.1 Feature Description

Automatic atrial threshold measurement can be performed during follow-up using the programmer. The ACC feature periodically measures the pacing threshold and amplitude adjustment in the atrium. The standard setting is one threshold measurement per day, but the user may choose another frequency of measurement. The threshold search is based on the presence or absence of atrial sensing markers generated by the device. The atrium is stimulated at a pacing rate higher

then the intrinsic rate to suppress atrial intrinsic events. As soon as the pacing output is lower then the atrial threshold, sensed atrial event will be detected either due to the emerging intrinsic rhythm or due to retrograde conducted events caused by ventricular paces. The detection of sensed atrial activity is used to discriminate between atrial capture and non-capture. The atrial capture control is performed in four steps:

1. Setup-Phase: The device monitors the rate and rhythm condition and determines the actual rate in the atrium immediately before it starts the threshold search. Automatic measurements are allowed if the atrial and ventricular rate is below 110 ppm and no mode switching is active. If these conditions are met, the activation of the capture control algorithm causes a mode switch to DDI with an atrial overdrive pacing of +20 % of the actual determined rate. The $A_p$-$V_p$ interval will be programmed to 50 ms, to avoid retrograde conduction from the ventricle.
2. Threshold search: The threshold is determined by decreasing the amplitude stepwise at a programmed pulse duration until loss of capture occurs. Loss of capture for one test amplitude is declared if in a test window of five cardiac cycles (5 $A_p$-$V_p$ intervals) two or more intrinsic atrial events are sensed which indicates unsuccessful pacing.
3. Confirmation phase: The pacing threshold is considered to be confirmed if capture is determined with the first step and loss of capture is confirmed with the second step.
4. Amplitude adjustment: The pacing amplitude is defined by adding the programmed safety margin to the determined threshold.

## 7.15 Ventricular Pace Suppression ($V_p$-Suppression)

### 7.15.1 Feature Description

$V_p$-Suppression is a feature that is available in DDD(R)-ADI(R) mode. This feature promotes the intrinsic AV conduction by only pacing the ventricle when intrinsic conduction becomes unstable or disappears. Depending on the presence or absence of AV conduction, the feature is implemented either in the ventricular pacing suppression state ADI(R), which promotes the intrinsic conduction, or in the DDD(R) ventricular pacing state $V_p$ DDD(R), which provides ventricular pacing. Automatic switching capabilities between those two states promote the intrinsic conduction as much as possible without harming the patient. Scheduled $V_s$ searching tests look for intrinsic conduction using an extended AV delay of 450ms. In order to protect the patient from high ventricular rates, the feature provides Mode Switching independent of the present state of the algorithm. The feature itself becomes suspended for the

time of Mode Switching. When $V_p$-Suppression becomes enabled, the device starts in the $V_p$-DDD(R) state and looks for intrinsic conduction by starting a $V_s$-searching. Following any suspension (e.g. Mode Switch), the $V_p$ Suppression feature will resume in $V_p$-DDD(R) state. The feature provides user programmability with respect to the switching criteria in order to support intrinsic conduction.

### 7.15.2 Programmability

The $V_p$-Suppression feature will provide the following programmability:

| Parameter | Range | Default |
|---|---|---|
| $V_p$-Suppression feature | On, Off | Off |
| $V_pS$ to DDD(R) x/8 cycles without VS | 1,2,3,4,5,6,7,8 | 3 |
| DDD(R) to $V_pS$ x consecutive $V_s$ | 1,2,3,4,5,6,7,8 | 6 |

$V_p$ Suppression works only if DDD(R)-ADI(R) mode is selected.

## 7.16 Program Consult®

ProgramConsult® provides clinicians with the option to increase programming efficiency by providing programming suggestions for frequent pacemaker patient conditions and having the capability to store individual programming for future usage (can store up to three individual parameter sets for future programming).

Program Consult is not an algorithm but uses preset settings based on the recommendations of the ACC/AHA/HRS guidelines for device based therapy*. Program Consult only shows recommendations for specific parameter settings to the user and clearly highlights them as modifications to the active permanent program prior to making any changes to device programming.

This feature is part of the ICS parameter section and is located on the main Evia programmer screen under the selection Program Sets. Upon selection of Program Consult, a subwindow opens with multiple selections depending on the underlying disease. Upon selection of a

* ACC/AHA/HRS 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities: Executive Summary: A Report of the American College of Cardiology/ American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the ACC/AHA/NASPE 2002 Guideline Update for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices) Developed in Collaboration With the American Association for Thoracic Surgery and Society of Thoracic Surgeons

Andrew E. Epstein, John P. DiMarco, Kenneth A. Ellenbogen, N.A. Mark Estes, III, Roger A. Freedman, Leonard S. Gettes, A. Marc Gillinov, Gabriel Gregoratos, Stephen C. Hammill, David L. Hayes, Mark A. Hlatky, L. Kristin Newby, Richard L. Page, Mark H. Schoenfeld, Michael J. Silka, Lynne Warner Stevenson, and Michael O. Sweeney

particular option, the parameter page displays the suggested parameter values in blue color. This indicates the recommended setting changes to the user (from the current settings) so that they can confirm them prior to activation. If desired, modifications can be made prior to transmitting the new program to the pulse generator as an updated permanent program. The following tables compare the suggested Program Consult and standard parameters for different patient conditions:

**Table 27: SSS including Brady-Tachy Syndrome and SSS with Chronotropic Competence**

| | Standard Program | SSS including Brady-Tachy Syndrome | SSS with Chronotropic Competence |
|---|---|---|---|
| Valid for: | DR(-T) | DR(-T) | DR(-T) |
| **Parameters** | | | |
| Mode | DDD-R | DDD-CLS | DDD-ADI |
| Rate Hysteresis (ppm) | OFF | --- | OFF |
| CLS $V_p$ required | --- | No | --- |
| CLS Resting Rate Control | --- | +20 | --- |
| AV Hysteresis | OFF | IOPT | --- |
| **Holter settings** | | | |
| High atrial rate | AT | ModeSw | ModeSw |
| HVR limit (bpm) | 180 | 160 | 160 |

**Table 28: Permanent High-Degree AV Block and Paroxysmal High-Degree AV Block**

| | Standard Program | Permanent High-Degree AV Block | Paroxysmal High-Degree AV Block |
|---|---|---|---|
| Valid for: | DR(-T) | DR(-T) | DR(-T) |
| **Parameters** | | | |
| Mode | DDD-R | DDD | DDD |
| Rate Hysteresis (ppm) | OFF | -10 | -10 |
| Rate Hysteresis Rep. Cycles | --- | 5 | 5 |

| | Standard Program | Permanent High-Degree AV Block | Paroxysmal High-Degree AV Block |
|---|---|---|---|
| Rate Hysteresis Scan Cycles | --- | 5 | 5 |
| AV Hysteresis | OFF | OFF | --- |
| **Holter settings** | | | |
| High atrial rate | AT | OFF | OFF |
| High ven. Rate | ON | OFF | OFF |
| Pre-trigger recording (%) | 75 | --- | --- |
| IEGM signal | Filtered | --- | --- |
| HAR limit (bpm) | 200 | --- | --- |
| HVR limit (bpm) | 180 | --- | --- |
| HVR counter | 8 | --- | --- |

**Table 29: Bradycardia with Permanent Atrial Fibrillation and Dual Node Disease + Permanent AV Block**

| | Standard Program | Bradycardia with Permanent Atrial Fibrillation | Dual node Disease + Permanent AV Block |
|---|---|---|---|
| Valid for: | DR(-T) | DR(-T), SR(-T) | DR(-T) |
| **Parameters** | | | |
| Mode | DDD-R | VVI-CLS | DDD-CLS |
| Rate Hysteresis (ppm) | OFF | --- | --- |
| CLS $V_p$ required | --- | No | Yes |
| CLS Resting Rate Control | --- | +20 | +20 |
| AV Hysteresis | OFF | --- | OFF |
| 2:1 Lock-in Protection | ON | --- | ON |
| Mode switch | ON | --- | ON |
| PMT | ON | --- | ON |

| | Standard Program | Bradycardia with Permanent Atrial Fibrillation | Dual node Disease + Permanent AV Block |
|---|---|---|---|
| **Holter settings** | | | |
| High atrial rate | AT | OFF | ModeSw |
| High ven. Rate | ON | ON | ON |
| HAR limit (bpm) | 200 | --- | 200 |
| HVR limit (bpm) | 180 | 160 | 160 |
| HVR counter | 8 | 8 | 8 |

**Table 30: Dual Node Disease + Paroxysmal AV Block and Vasovagal Syncope**

| | Standard Program | Dual Node Disease + Paroxysmal AV Block | Vasovagal Syncope |
|---|---|---|---|
| Valid for: | DR(-T) | DR(-T) | DR(-T) |
| **Parameters** | | | |
| Mode | DDD-R | DDD-CLS | DDD-CLS |
| Rate Hysteresis (ppm) | OFF | --- | --- |
| CLS $V_p$ required | --- | No | No |
| CLS Resting Rate Control | --- | +20 | OFF |
| AV Hysteresis | OFF | IOPT | IOPT |
| **Holter settings** | | | |
| High atrial rate | AT | ModeSw | OFF |
| High ven. Rate | ON | ON | OFF |
| Pre-trigger recording (%) | 75 | 75 | --- |
| IEGM signal | Filtered | Filtered | --- |
| HAR limit (bpm) | 200 | 200 | --- |
| HVR limit (bpm) | 180 | 160 | --- |
| HVR counter | 8 | 8 | --- |

**Table 31: Symptomatic First-Degree AV Block and Infrequent Paroxysmal Pauses (< 5%)**

| | Standard Program | Symptomatic First-Degree AV Block | Infrequent Paroxysmal Pauses (< 5%) |
|---|---|---|---|
| Valid for: | DR(-T) | DR(-T) | SR(-T) |
| **Parameters** | | | |
| Mode | DDD-R | DDD | VVI |
| Rate Hysteresis (ppm) | OFF | OFF | -10 |
| Rate Hysteresis Rep. Cycles | --- | --- | 5 |
| Rate Hysteresis Scan Cycles | --- | --- | 5 |
| AV Hysteresis | OFF | OFF | --- |
| 2:1 Lock-in Protection | ON | ON | --- |
| Mode switch | ON | ON | --- |
| PMT | ON | ON | --- |
| **Holter settings** | | | |
| High atrial rate | AT | OFF | OFF |
| High ven. Rate | ON | OFF | OFF |
| Pre-trigger recording (%) | 75 | --- | --- |
| IEGM signal | Filtered | --- | --- |
| HAR limit (bpm) | 200 | --- | --- |
| HVR limit (bpm) | 180 | --- | --- |
| HVR counter | 8 | --- | --- |

## 7.17 Home Monitoring (Evia 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.

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.

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

### 7.17.2 Patient Device

The patient device (Figure 20) 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.

### 7.17.3 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 32.

**Table 32: 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 | ⩾ 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 20: Example of Patient Device with Charging Stand**


## 7.17.4 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

### 7.17.4.1 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.

### 7.17.4.2 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" as part of the daily transmission.

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

- Atrial Lead Check < 100+/-50 Ohm and > 2500+/-500 Ohm
- Ventricular Lead Check < 100+/-50 Ohm and > 2500+/-500
- VCC Disabled
- ERI detected
- Atrial Capture Control
- High Ventricular rate
- Atrial tachyarrhythmia persisting beyond a programmable time limit or
- Mode Switch episode persisting beyond a programmable time limit

**NOTE:**

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

## 7.17.5 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.

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

**Device Status & Home Monitoring Settings**

Containing device and message identifying values that pertain to the implant and Home Monitoring:

- Implantation Date
- Device Status
- Remaining capacity for ERI calculation (done by the Service Center)
- Last Follow-up
- Message Creation Date/Time
- Device Serial Number

**Leads**

- Automatic Threshold Monitoring
  - Measured RV pacing threshold
  - RV enabled/disabled
  - RA enabled/disabled
  - Date/time of ATM measurement
  - RA Threshold
- Pacing Impedance (RA, RV)
- Sensing Amplitude (RA, RV)

**Pacing Counters (Brady)**

- AV-Sequences
  - Intrinsic Rhythm ($A_sV_s$)
  - Conducted Rhythm ($A_sV_p$)
  - Atrial Paced Rhythm ($A_pV_s$)
  - Complete Paced Rhythm ($A_pV_p$)

**Atrial Arrhythmia**

- Atrial Tachy Episodes (36 out of 48 criteria)
  - Counter on AT/AF detections per day
  - Atrial Burden per day
  - Ongoing Atrial Episode Time (programmable for 6, 12 or 18 hrs)
- Mode Switching
  - Number of Mode Switches
  - Duration of Mode Switches

**Ventricular Arrhythmia**

- High Ventricular Rate Counters

**Transmitted Device Settings**

The primary programmed parameters for the following are sent in the data package:

- Leads—(e.g., Pacing Output, Configuration)
- Brady—(e.g., Basic Rate, UTR, AV-Delays, RV Sensitivity)
- IOPT—(ON/OFF)
- HM Settings—(e.g., ON/OFF, transmission time (daily), IEGM transmissions ON/OFF, periodic IEGM, ongoing atrial episode, statistics, holter)
- Miscellaneous other information

### 7.17.5.1 IEGM Online HDs

The Evia provides the ability to transmit periodic IEGM Online HD (IEGM and marker data) from the periodic follow-ups as an addition to the current messages.

An IEGM with up to 2 channels (RV and/or RA) are sent in one message, depending on the number of IEGM channels programmed in the Holter configuration.

The following markers are also transmitted: $A_S$ (including $A_{rs}$), $A_S$ (PMT), $A_P$, $V_S$ (including $V_{rs}$), $V_P$ (atrial and refractory sensed events included with sensed events).

The Evia includes a programmable parameter to disable or enable the IEGM transmission.

# 8. Statistics

## 8.1 Statistics Overview

Evia 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
- Event Episodes
- Rate Trend 24 hours
- Rate Trend 240 days
- Rate Histograms

### 8.1.2 Atrial Arrhythmia

- Atrial Burden
- Time of Occurrence
- Mode Switching

### 8.1.3 Sensor

- Sensor Histogram
- Activity Report

### 8.1.4 Sensing

- P/R -wave Trends
- Far Field Histogram
- $A_s$-$V_s$ Interval Distribution Curve
- $A_p$-$V_s$ Interval Distribution Curve

### 8.1.5 Ventricular Arrhythmia

- PVC
- Couplets
- Triplets
- Runs 4...8
- Runs > 8
- High Ventricular Rate Episode Count

### 8.1.6 Pacing

- Lead Impedance Trends
- Pulse amplitude / Threshold Trend
- Pulse Amplitude Histogram
- Capture Control Status

### 8.1.7 General Statistical Information

- The Evia 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:

$$\text{Bar Length} = \frac{\text{percentage of total events occurring represented by the events counted in this class x 10}}{\text{rate width of this class}}$$

## 8.2 Timing Statistics

### 8.2.1 Event Counter

The event counter totals all of the sensed and paced events. With the event counter, the following events and event sequences can be registered over several years:

- Atrial:
  - $A_s$, atrial sensed events
  - $A_s$ (PVARP), atrial events sensed in the PVARP window
  - $A_{rs}$, atrial events sensed in the ARP
  - $A_s$ (FFP), atrial events sensed in the far field protection period
  - $A_p$, atrial paced events
- Ventricular:
  - $V_s$, ventricular sensed events
  - PVC, ventricular sensed event not preceded by an atrial sensed event.
  - $V_{rs}$, ventricular sensed events that occur within the ventricular refractory period.
  - $V_p$, ventricular paced events

**NOTE:**

All event counter data are transmitted to the programmer and evaluated there, but not all events are displayed in detail on the programmer.

### 8.2.2 Event Episodes

In contrast to the event counter, it is not the individual events, but rather the event sequences that are counted:

- $A_s$ followed by $V_s$
- $A_s$ followed by $V_p$
- $A_p$ followed by $V_s$
- $A_p$ followed by $V_p$
- $V_x$ followed by $V_x$

The event sequence V-V means two consecutive ventricular events (sensing or pacing) without a previous atrial event.

### 8.2.3 Rate Trend 24 Hours

The rate trend is displayed as a trend chart and consists of the heart rate trend and the pacing rate trend. The atrial and ventricular events recorded at a set time. In the rate trend, the heart rate in pulses per minute (ppm) is recorded in the upper rate chart, and the percentage of pacing is shown in the lower chart. Please note that a gap in the trend will be displayed for the duration of an asynchronous magnet program or temporary program.

### 8.2.4 Rate Trend 240 Days

The rate trend is displayed as a trend chart and consists of the heart rate trend and the pacing rate trend recorded over 240 days. The atrial and ventricular events recorded at a set time. In the rate trend, the heart rate in pulses per minute (ppm) is recorded in the upper rate chart, and the percentage of pacing is shown in the lower chart.

### 8.2.5 Atrial and Ventricular Rate Histogram

The Evia pacemakers are provided with separate atrial and ventricular histograms. A bar chart displays the heart rate as a percentage and corresponding absolute value. The number of times in which the heart rate occurs in specific ranges is recorded separately according to sensing and pacing. The rate range between <40 and >380 ppm is divided

into 10 ppm increments along a rate measuring axis. The distribution of 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.

## 8.3 Arrhythmia Statistics

### 8.3.1 Atrial Burden

Atrial Burden is the time that the patient is in an atrial tachycardia during the day. The graphs are divided into the number of episodes which occur during the day and the duration the atrial tachycardia is present during a 240 day period.

### 8.3.2 Time of occurrence

Time of occurrence is the time of day the atrial tachycardia begins. The total number of events are displayed at the bottom of the graph. Each event is counted in the time bins and the percentage of events in each time bin (24h) is calculated and displayed.

### 8.3.3 Mode Switching

Mode Switching shows the total number Modes switches that have occurred along with the total time of Mode switching since the last follow-up. The intervention rate is also displayed.

### 8.3.4 Ventricular Arrhythmia

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

**PVC Classification**

PVC Sequence

- Single PVC V- PVC
- Couplets V-PVC-PVC
- Triplets V-PVC-PVC-PVC
- Runs (4...8) V-PVC-PVC-...
- #VT Episodes More than 8 consecutive PVC

The High Ventricular Rate count is also displayed.

**NOTE:**

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

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

## 8.4 Sensor Statistics

### 8.4.1 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).

### 8.4.2 Activity Report

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

- No Activity
- Activity
- Maximum Sensor 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.

## 8.5 Pacing Statistics

**Lead Impedance Trends with Lead Check**

Evia 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 30 seconds, the lead impedance measurements are taken and are available for diagnostic trend display. The programmer will display a long-term trend of 240 days.

Impedance trends are always recorded. The lead impedance measurements are used to determine if a lead failure has occurred. The range for normal lead impedance is from 100 to 2500 ohms.

If the Evia pulse generator detects a bipolar lead failure, 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 is temporarily suspended during magnet application and is inactive during ERI.

### 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 categories ranging from 0.1 V to >6.0 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 VCC 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 V Pacing Threshold Trend

This trend records the ventricular pacing threshold measured during SA/CV sequences. A threshold sample is measured every 24 hours. The maximum trend duration is approximately 240 days with a sampling interval of approximately 24 hours.

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

### 8.5.3 Capture Control Status

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

## 8.6 Sensing Statistics

**P- and R-wave Trends**

Evia pulse generators periodically perform P- and R-wave amplitude measurements to be displayed later as trend data. A P- and R-wave long-term trend of up to 240 days is available. After the initial timeframe has elapsed, the first data stored is overwritten with new data; therefore, the most recent data are available for review.

**Far-field Histogram**

The Far-field Histogram provides information related to cross-talk following $V_p$ and $V_s$ events. The range is <30 ms to >220 ms for each type of event. The display provides the percentage of far-field events at each value.

**Ap-$V_s$ interval distribution curve**

This graph provides information related to the amount of $V_s$ response to atrial paced events. The information is divided into 5 rate bins and provides the minimum, mean and maximum $A_p$-$V_s$ intervals for each rate bin. The programmed AV Delay is also shown.

The data is also displayed on a graph with the Y axis showing the range of programmable AV Delay options and the X axis graph showing heart rate.

The number of successful AV hysteresis scans is provided on this graph.

**$A_v$-$V_s$ interval distribution curve**

This graph provides information related to the amount of $V_s$ response to atrial sensed events. The information is divided into 5 rate bins and provides the minimum, mean and maximum $A_p$-$V_s$ intervals for each rate bin.

The data is also displayed on a graph with the Y axis showing the range of programmable AV Delay options and the X axis graph showing heart rate.

The number of successful AV hysteresis scans is provided on this graph.

$V_p$ Suppression

This section provides information related to the number and amount of $V_p$ suppression that has occurred. Data in this section includes the number of $V_p$ suppression switches and the number of $V_s$ searches for $V_p$ suppression. The graph shows the percentage of $V_p$ suppression for each day.

## 8.7 IEGM Recordings

Evia pulse generators can provide IEGM Recordings, 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
- High ventricular rates
- Patient activation (by applying a magnet)
- Mode Switches

Evia 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, Evia 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

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

Upon interrogation of the Evia pulse generator containing stored IEGMs, a list of the stored IEGMs (with date and time stamp) is displayed under the Holter tab. If the number of events triggering a snapshot is greater than the available memory, the IEGMs 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

Evia 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 33 are the Safe Program settings for Evia pulse generators.

**Table 33: 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
- Gender
- Symptom
- Etiology
- ECG Indication
- Physician
- Implantation Date
- Lead Polarity (A / V)
- Lead Type
- Lead Manufacturer
- Lead Position
- NYHA Class
- LVEF
- Hospital
- City

**WARNING**

**Unipolar/Bipolar**—All Evia 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 51 ms.

Depending on the programmed pacing mode and the channel in which electromagnetic interference (EMI) occurs, Table 34 details the resulting pacing modes for the duration of exposure to EMI.

**Table 34: 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 | VVT | VAT | VOO |
| VDI | VVT | VOO | VOO |
| VVT | --- | VOO | --- |
| AAT | AOO | --- | --- |

* 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.

**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 Evia 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

Evia 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 Evia 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.

**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 Evia pulse generators are available for use. Evia 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 is 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 Evia pulse generator continuously delivers sub-threshold paces in both the ventricular and the atrial channel to measure the lead impedance. The Evia pulse generator considers a lead "detected" when the measured impedance is within 100 and 2500 Ohms.

2. **Detection and Configuration of the Lead Polarity**

   The Evia pulse generator switches the lead polarity to bipolar immediately after a bipolar lead is detected. When the lead impedance is between 100 and 2500 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. **10-Minute Confirmation Phase**

   A 10-minute confirmation phase is initiated after detection of the lead. The lead impedance measurement is performed alternating between the atrial and ventricular channel. Additional impedance measurements at the end of this phase confirm the lead detection and lead polarity. The impedance measurements need to fall within the range of 100 to 2500 Ohms.

   A lead impedance measurement outside this range restarts the confirmation process.

   Interrogation of the pulse generator during the confirmation phase results in a message that implant detection is activated. The confirmation phase is terminated and the pulse generator features are activated if it is reprogrammed during this time.

**4. Activation of Pulse Generator Features**

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

- Auto Lead Check
- Capture Control
- Statistics
- Rate response
- 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)
- PMT Management
- Auto PVARP
- 2:1 Lock-In protection

# 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 Real-time IEGM Transmission

The pulse generators provide real time transmission of the intracardiac electrogram (IEGM) to the programmer. During dual chamber operation, IEGMs from the atrium and ventricle can be simultaneously recorded. 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.

## 12.3 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 7.5 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 or IEGM. 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 or IEGM 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 VCC function to determine the threshold. Once the threshold is determined, VCC 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 Non-Invasive Programmed Stimulation (NIPS)

**WARNING**

**NIPS—**Life threatening ventricular arrhythmias can be induced by stimulation in the atrium. 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).

### 12.6.1 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.

### 12.6.2 Burst Stimulation

Burst Stimulation offers a burst of pacing pulses to the atrium 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 10 ms steps. As soon as the step up or step down key is released, NIPS terminates. Subsequent inductions resume at the initially programmed burst rate.

### 12.6.3 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 10 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.

### 12.6.4 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.

### 12.6.5 NIPS Safety Features

The BIOTRONIK offers the following safety features during NIPS sessions.

- When the battery voltage has reached the Elective Replacement Indicator point (ERI), the NIPS feature is no longer available.

- Atrial 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.

## 12.7 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.

### 12.7.1 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.

### 12.7.2 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.

### 12.7.3 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.

## 13. Elective Replacement Indication (ERI)

The service time of Evia 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 35 shows the service cycle definitions.

**Table 35: 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) and DVI(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 36.

**Table 36: 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 37 shows the expected longevity (in years) from BOS to ERI for Evia pulse generators. The programmer software for the Evia 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 37: Nominal Pulse Generator Longevity**

| Amplitude | Impedance (Ohms) | Pacing | | | | | |
|---|---|---|---|---|---|---|---|
| | | 10% | | 50% | | 100% | |
| **2.5 V** | 500 | DR(-T) | SR(-T) | DR(-T) | SR(-T) | DR(-T) | SR(-T) |
| | | 12.1 | 15.0 | 10.7 | 14.1 | 8.2 | 11.9 |

The mean* expected time intervals from ERI to EOS at standard program for Evia 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 basic rate of 60 ppm, pulse width of 0.4 ms, shelf life of 1.5 years, and data supplied by the battery manufacturer.

* 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 38 summarizes some of the more common reasons for pulse generator explant.

**Table 38: 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. |

| Source | Cause | Possible Effect |
|---|---|---|
| Circuitry | Electrical parameter changes due to shorts, opens, or component parametric drift<br>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<br>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. |
| 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. |

| Source | Cause | Possible Effect |
|---|---|---|
| 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 pneumo-thorax. |

# 15. Technical Data

## 15.1 Modes

| Modes | DR | DR-T* | SR | SR-T | Modes | DR | DR-T* | SR | SR-T |
|---|---|---|---|---|---|---|---|---|---|
| DDD-CLS | X | X | | | DVI | X | X | | |
| VVI-CLS | X | X | X | X | VDD | X | X | | |
| DDD(R)-ADI(R) | X | X | | | | | | | |
| DDDR | X | X | | | VVI | X | X | X | X |
| DDIR | X | X | | | VDI | X | X | | |
| DVIR | X | X | | | AAI | X | X | X | X |
| VDDR | X | X | | | DOO | X | X | | |
| VVIR | X | X | X | X | VOO | X | X | X | X |
| AAIR | X | X | X | X | AOO | X | X | X | X |
| VDIR | X | X | | | DDT | X | X | | |
| | | | | | VVT | X | X | X | X |
| VVTR | X | X | X | X | AAT | X | X | X | X |
| | | | | | OFF | X | X | X | X |
| AATR | X | X | X | X | DDD | X | X | | |
| DOOR | X | X | | | | | | | |
| VOOR | X | X | X | X | | | | | |
| AOOR | X | X | X | X | | | | | |

**NOTE:**

Programmability dependent on programmer software utilized.

Bold parameters indicate factory settings.

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

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

## 15.2 Pulse- and Control Parameters

**Basic Rate**

30...(1)...**60**...(1)...88...(2)...122...(3)...140...(5)...200 ppm

**Night Rate**

**Off**, 30...(1)...60...(1)...88...(2)...122...(3)...140...(5)...200 ppm

**Rate Hysteresis**

**Off**; -5...(5)...-90 bpm

**Repetitive Hysteresis**

**Off**; 1...(1)...15

**Scan Hysteresis**

**Off**: 1...(1)...15

**Upper Rate**

90...(10)...**130**...(10)...200 ppm

**$V_p$ Suppression**

Off; On

**UTR Response**

WRL (automatic selection)

**Rate Limitation*,†,‡**

190...220 ppm

**Dynamic AV Delay (Dual chamber only)**

Off; **low**; medium; high, (individual, or fixed), I-Opt

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* 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...(5)...**180**...(5)...350 ms

(Programmable in 5 ranges)

**AV Delay Hysteresis (Dual chamber only)**

**Off**; low; medium; high; negative, IOPT

**AV Repetitive Hysteresis (Dual chamber only)**

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

**AV Scan Hysteresis (Dual chamber only)**

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

**Repetitive AV Delay Hysteresis (Negative AV Hysteresis)**

**Off**, 1...(1)...10...(5)...100...(10)...180

**AV Safety Delay (Dual chamber only)**

100 ms

**Sense Compensation**

Off; -10...(5)...**45**...(5)...-120 ms

**Far Field after $V_s$**

**100**...(10)...220 ms

**Far Field after $V_p$**

**100**...(10)...**150**...(10)...220 ms

**Ventricular Blanking after $A_p$**

**30**...(5)...70 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 0.2...(0.1)...**3.0**...(0.1)...6.0...(0.5)...7.5 V

**V** 0.2...(0.1)...**3.0**...(0.1)...6.0...(0.5)...7.5 V

**Pulse Width**

**A** 0.1; 0.2; 0.3; **0.4**; 0.5; 0.75; 1.0; 1.25; 1.5 ms

**V** 0.1; 0.2; 0.3; **0.4**; 0.5; 0.75; 1.0; 1.25; 1.5 ms

**Sensitivity**

**A** **AUTO**, 0.1...(0.1)...1.5...(0.5)...7.5 mV

**V** **AUTO**, 0.5...(0.5)...2.5...(0.5)...7.5 mV

**Refractory Period**

**A** AUTO

**V** 200...(25)...250...(25)...500 ms

**PVARP**

**AUTO**, 175...(5)...250...(5)...600 ms

**Automatic Lead Check**

Off; **On**

**Mode Switch (X out of Y)**

**Off**; On

**X** = 3...(1)...8

**Z**= 3...(1)...8

**Intervention Rate**

100, 110...(10)...**160**...(10)...250 ppm

**Mode Switch Basic Rate**

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

**2:1 Lock-In Protection**

Off; **On**

**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, 2.3, 2.6, 3.0, 3.3, 3.7, **4.0**, 4.5, 5.0, 6.0, 7.0, 8.0, 8.5, 10, 11,13, 14, 16, 18, 20, 23

**Sensor Threshold**

very low; low; **medium**; high; very high

**Rate Increase**

1...(1)...**4**...(1)...10 ppm/cycle

**Maximum Sensor Rate**

80...(5)...**120**...(5)...160 ppm

**Rate Decrease**

0.1, 0.2, **0.5**, 1.0 ppm/cycle

**Automatic Sensor Gain**

**Off**; On

## 15.2.2 Atrial Capture Control (ACC)

**Atrial Capture Control**

OFF;**ON**; ATM (monitoring only)

**Minimum Amplitude**

0.5...(0.1)...**1.0**...4.8V

**Safety Margin**

0.3...(0.1)...**1.0**...1.2V

**Search Scheduling**

Interval, **Time of Day**

**Interval**

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

**Time of Day**

00:00...23:50 in 10 minute increments, nominal **02:00**

### 15.2.3 Ventricular Capture Control (VCC)

**Ventricular Capture Control**

Off, **On**, ATM

**Maximum VCC Amplitude**

2.4, **3.0**, 3.6, 4.2 4.8 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

**Time of Day**

00:00 ... 23:50 in 10 minute increments, nominal **02:00**

### 15.2.4 Home Monitoring Parameters

**Home Monitoring**

**Off**, On

**Monitoring Interval**

1 day

**Time of the Trend Report Transmission**

**Auto**, 00:00...(30)...23:30 hours

**Periodic Transmission**

Off, 30, 60, 90, 120, 180 days

**Ongoing Atrial Episode**

6, 12, 18 hours

**Event Report**

Off, **On**

**Patient Report**

**Off**, On

### 15.2.5 Additional Functions

**NOTE:**

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

- Temporary Program Activation
- High Precision Threshold test in the range up to 7.5 V with 0.1 V resolution
- PAC (pulse amplitude control) system produces consistent pulses
- 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
- Retrograde Conduction Test
- 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
- Automatic Lead Check
- Rate Fading

### 15.2.6 NIPS Specifications

| Burst Mode | Burst Chamber | Atrium |
|---|---|---|
| Burst stimulation A. Only | Coupling Interval / ms | None... 2000 |
| | Burst Type | Pushbutton, Ramp |
| | Burst Range / ppm | 125...800 |
| Programmed Stimulation A. Only | 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 |
| | Rate / ppm | 30...200 |
| | Amplitude / V | 0.2...7.5 |
| | Pulse width / ms | 0.1, 0.2, 0.3, 0.4, 0.5, 0.75, 1.0, 1.25, 1.5 |
| | Pace Polarity | Bipolar, Unipolar |

## 15.3 Programmer

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 37º C, with pacing impedance of 500 Ohms.

| Parameter | Evia DR | Evia DR-T | Evia SR | Evia SR-T |
|---|---|---|---|---|
| Pace | Unipolar/ bipolar | same | same | same |
| Pulse form | Biphasic, asymmetric | same | same | same |
| Polarity | Cathodic | same | same | same |
| Input impedance | >10 kΩ (A); >10 kΩ (V) | >10 kΩ (A); >10 kΩ (V) | >10 kΩ | >10 kΩ |
| Power source | LiJ | Ag/SVO/CFx (QMR), MDX | Same as Evia DR | Same as Evia DR-T |
| Battery voltage at BOS | 2.8 V | 3.0 V | 2.8 V | 3.0 V |
| Conducting surface (uncoated) | 33 $cm^2$ | same | same | same |
| Conducting surface (coated) | 7 $cm^2$ | same | same | same |
| Conducting Shape (coated) (uncoated) | Ellipsoidal Flattened ellipsoidal | same same | same same | same same |

## 15.6 Mechanical Data

| Model | Leads | Size | Mass | Volume |
|---|---|---|---|---|
| Evia DR | IS-1 | 6.5 x 43 x 53 mm | 26 g | 11 cc |
| Evia DR-T | IS-1 | 6.5 x 44.5 x 53 mm | 25 g | 12 cc |

| | | | | |
|---|---|---|---|---|
| Evia SR | IS-1 | 6.5 x 39 x 53 mm | 25 g | 10 cc |
| Evia SR-T | IS-1 | 6.5 x 39 x 53 mm | 24 g | 11 cc |

## 16. Order Information

| Pulse Generator Model | Order Number |
|---|---|
| Evia DR | 359 524 |
| Evia DR-T | 359 529 |
| Evia SR | 359 531 |
| Evia SR-T | 359 533 |

FCC Statement: (FCC ID: QRIPRIMUS): This transmitter is authorized by rule under the Medical Device Radiocommunication Service (in part 95 of the FCC Rules) and must not cause harmful interference to stations operating in the 400.150-406.000 MHz band in the Meteorological Aids (i.e., transmitters and receivers used to communicate weather data), the Meteorological Satellite, or the Earth Exploration Satellite Services and must accept interference that may be caused by such stations, including interference that may cause undesired operation. This transmitter shall be used only in accordance with the FCC Rules governing the Medical Device Radiocommunication Service. Analog and digital voice communications are prohibited. Although this transmitter has been approved by the Federal Communications Commission, there is no guarantee that it will not receive interference or that any particular transmission from this transmitter will be free from interference.

This device complies with part 15 of the FCC Rules. Operation is subject to the following two conditions:

1. This device may not cause harmful interference, and
2. This device must accept any interference received, including interference that may cause undesired operation.

# Appendix A

## Mode-Specific Indications and Contraindications

**Rate-adaptive Pacing**

| | |
|---|---|
| Evia DR and Evia DR-T: | DDDR, DDDR-ADIR, DDIR, DVIR, VDDR, VVIR, DDD-CLS, VVI-CLS, AAIR, VVTR, DOOR, VOOR, AOOR, AATR, VDIR |
| Evia SR and Evia SR-T: | VVIR, VOOR, VVI-CLS, VVTR, AATR, AOOR, AAIR |

**NOTE:**

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

Indications for 2ate-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 Evia 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.

**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 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.

- 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 **DOO(R)**, **AOO(R)** and **VOO(R)** pacing modes derived from the above by restricting the sensing functions [SOO(R) mode available with Evia SR models]. The triggered **DDT**, **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 |
|---|---|
| **Evia Software Application** | |
| If the sensing test fails during automatic follow-up test sequence, the error messages are displayed too quickly to read (less than 1 second). | No effect on patient, the test will need to be re-run as no result will be displayed. |
| **Evia Pacemakers** | |
| Application of the programming wand in a narrow time window may result in a missing data point on the trend graph. In very rare instances, this error can lead to statistics not being displayed until statistics are restarted. | Diagnostic data may not be available for a short amount of time. The situation is temporary, and there is no patient risk involved. |

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