Stratos

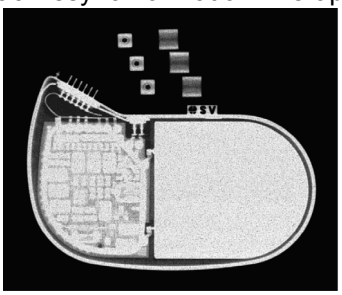
Family of Cardiac Resynchronization Therapy Pacemakers

Technical Manual

BIOTRONIK
excellence for life

Stratos CRT-Ps

Implantable Cardiac Resynchronization Therapy Pacemakers



Stratos
X-Ray identification

Radiopaque Identification

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

Stratos LV/LV-T SV

CAUTION

Lead / CRT-P Compatibility – Because of the numerous available 3.2-mm configurations (e.g., the IS-1 and VS-1 standards), lead/ CRT-P compatibility should be confirmed with the CRT-P and/or lead manufacturer prior to the implantation of the 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)].

Contents

1. General

1.1 Device Description

The Stratos LV and Stratos LV-T CRT-Ps are rate adaptive pacemakers designed to provide Cardiac Resynchronization Therapy (CRT). The Stratos CRT-Ps provide all standard bradycardia pacemaker therapy with the additional capabilities of biventricular pacing for CRT. Biventricular pacing in the Stratos CRT-Ps can be programmed to initially pace in either the right or left ventricular chambers with separately programmable outputs for both left and right channels. Sensing of cardiac signals only occurs in the right ventricular chamber.

The Stratos CRT-Ps can also provide single and dual chamber pacing in a variety of rate-adaptive and non-rate adaptive pacing modes. Pacing capability is supported by an extensive diagnostic set. For motion-based rate-adaptation, the Stratos CRT-Ps are equipped with an internal accelerometer. 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.

The Stratos LV-T additionally also employs BIOTRONIK's Home Monitoring™ technology, which is an automatic, wireless, remote monitoring system for management of patients with implantable devices. With Home Monitoring, physicians can review data about the patient's cardiac status and CRT-P's functionality between regular follow-up visits, allowing the physician to optimize the therapy process. Stratos CRT-Ps are also designed to collect diagnostic data to aid the physician's assessment of a patient's condition and the performance of the implanted device.

The bipolar IS-1 connections are used for pacing and sensing (right atrial and ventricle) and the additional IS-1 connection is used for pacing in the left ventricle in either a bipolar or unipolar configuration depending on the left ventricular lead. The pulse amplitude and pulse width of each of the three channels is separately programmable.

Stratos CRT-Ps are designed to meet all indications for Cardiac Resynchronization Therapy in CHF patients as well as those for bradycardia therapy as exhibited in a wide variety of patients. The Stratos family is comprised of two CRT-Ps that are designed to handle a multitude of situations.

Stratos LV	Triple chamber, rate-adaptive, unipolar/bipolar pacing CRT-P
Stratos LV-T	Triple chamber, rate-adaptive, unipolar/bipolar pacing CRT-P with Home Monitoring

Throughout this manual, specific feature and function descriptions may only be applicable to the Stratos LV-T and those features will be referenced as such. Otherwise, reference to Stratos CRT-Ps refers to both devices.

1.2 Indications

The Stratos LV and Stratos LV-T Cardiac Resynchronization Therapy Pacemakers (CRT-Ps) are indicated for patients who have moderate to severe heart failure (NYHA Class III/IV), including left ventricular dysfunction (EF ≤ 35%) and QRS ≥ 120 ms and remain symptomatic despite stable, optimal heart failure drug therapy.

1.3 Contraindications

Use of Stratos LV and Stratos LV-T CRT-Ps are 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.

1.4 Note to Physician

As with any implantable pulse generator, there are certain infrequent risks associated with Stratos CRT-Ps. Section 1.6 lists the adverse events that have been observed or may potentially occur with these Cardiac Resynchronization Therapy Pacemakers. The warnings and precautions listed in Section 1.5 should be taken under serious consideration in order to aid in avoiding device failures and harm to the patient.

Regular monitoring of the patient and their implanted device should be conducted to identify performance concerns and ensure appropriate therapy is being administered to the patient. Please communicate any performance concerns to BIOTRONIK and to FDA.

All explanted devices should be returned to the manufacturer for testing to help understand device reliability and performance. Refer to Section 10 for recommended procedures for handling explanted devices.

1.5 Warnings and Precautions

Certain therapeutic and diagnostic procedures may cause undetected damage to a Cardiac Resynchronization Therapy Pacemakers, 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 CRT-Ps within the subcutaneous pocket and may cause pain and injury to the patient and damage to the CRT-P. 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.

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

High Output Settings – High output settings combined with extremely low lead impedance may reduce the life expectancy of the Stratos CRT-Ps. 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.

1.5.1 Interactions with Other 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, CRT-P 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 CRT-P and at the implant site. If diathermy therapy must be used, it should not be applied in the immediate vicinity of the CRT-P or leads. The patient's peripheral pulse should be monitored continuously during the treatment.

Transcutaneous Electrical Nerve Stimulation (TENS) – Transcutaneous electrical nerve stimulation may interfere with CRT-P 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 CRT-P/lead system as possible.
- Monitor cardiac activity during TENS use.

Defibrillation – The following precautions are recommended to minimize the inherent risk of CRT-P operation being adversely affected by defibrillation:

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

Radiation – The CRT-P's internal electronics may be damaged by exposure to radiation during radiotherapy. To minimize this risk when using such therapy, the CRT-P should be protected with local radiation shielding.

Lithotripsy – Lithotripsy treatment should be avoided for CRT-P patients since electrical and/or mechanical interference with the CRT-P 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 CRT-P.

Electrocautery – Electrocautery should never be performed within 15 cm (6 inches) of an implanted CRT-P or leads because of the danger of introducing fibrillatory currents into the heart and/or damaging the CRT-P. 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 CRT-P system.

1.5.2 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 CRT-P malfunction (see Section 7.1).

Low Temperatures – Exposure to **low temperatures** (below 0°C) may cause a false elective replacement indication to be present. If this occurs, warm the device to room temperature and reset the ERI with magnet application (see Section 7.1).

Handling – Do not drop. If an unpackaged CRT-P is dropped onto a hard surface, return it to BIOTRONIK (see Section 7.1).

FOR SINGLE USE ONLY - Do not re-sterilize the CRT-P or accessories packaged with the CRT-P, they are intended for one-time use.

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

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

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

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

1.5.3 Lead Connection and Evaluation

Lead Check –

Feature Description: Lead Check is a feature that, when activated, automatically measures the lead impedance with every pace. Based on these measurements, the lead configuration will be set to either unipolar or bipolar. Refer to Section 2.5 for more details regarding this feature.

Caution: Lead check will not lead to disabling of cardiac resynchronization therapy. It limits the use of the resynchronization features.

1. Lead check is possible only when the right ventricle is paced first.
2. Lead check works only when the pacing voltages are programmed between 2.4 and 4.8 V. The lead check feature can be programmed OFF in patients that require cardiac resynchronization therapy.

Care should be taken when programming Stratos CRT-Ps with Lead Check ON as the device may switch from bipolar to unipolar pacing and sensing without warning. This situation may be inappropriate when using a Stratos CRT-P for patients with an Implantable Cardioverter Defibrillator (ICD). The following associated message appears when programming this feature:

> "Lead check may result in a switch to unipolar pacing and sensing, which may be inappropriate for patients with an ICD."

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

Lead / CRT-P Compatibility – Because of the numerous available 3.2-mm configurations (e.g., the IS-1 and VS-1 standards), lead/ CRT-P compatibility should be confirmed with the CRT-P and/or lead manufacturer prior to the implantation of the 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 – The polarity of the implanted lead dictates what lead configuration can be programmed for the CRT-P. Pacing will not occur with a unipolar lead if the lead configuration of the respective channel is programmed to bipolar (see Section 8).

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.

1.5.4 Programming and Operation

IEGM – Due to the compression processes that the signals undergo, the IEGM recordings are not suitable for making some specific cardiac diagnoses, such as ischemia; although, these tracings may be useful in diagnosing arrhythmias, device behavior or programming issues.

Post AES - Before activating post-AES, check whether the selected program can cause Pacemaker Mediated Tachycardia (PMT) and whether post-AES pacing results.

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.

AV Hysteresis – If the AV hysteresis is enabled along with the algorithm for recognizing and terminating PMTs (PMT management), the AV delay for recognizing and terminating a PMT has a higher priority than the AV hysteresis.

Sensing – The Stratos CRT-Ps do not sense in the left ventricle.

AV Conduction – In patients with intact AV conduction, the intrinsic atrial tachycardia is conducted to the ventricle 1:1. With the resynchronization mode activated, spontaneous rate of the right ventricle mode is synchronized for a rate up to 200 ppm in the left ventricle. For this reason, biventricular pacing mode should be turned OFF in such cases.

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

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

Safe Program – Activating the “Safe Program” is a way of quickly programming the device to multiple settings in the event of an emergency. These settings include unipolar pacing with pacing output OFF in the left ventricular channel. Refer to Section 6.3 for further details.

Programmers – Use only BIOTRONIK’s ICS 3000 programmer equipped with appropriate software to program Stratos CRT-Ps. Do not use programmers from other manufacturers.

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

Pacing thresholds – When decreasing programmed output (pulse amplitude and/or pulse width), the pacing threshold must first be accurately assessed to provide a 2:1 safety margin.

EMI – Computerized systems are subject to (Electromagnetic Interference (EMI) or "noise". In the presence of such interference, telemetry communication may be interrupted and prevent programming of the Stratos CRT-P.

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 – The OFF mode can be transmitted as a temporary program only to permit evaluation of the patient's spontaneous rhythm. (see Section 2.1.11)

Myopotential Sensing – The filter characteristics of BIOTRONIK implantable devices have been optimized to sense electrical potentials generated by cardiac activity and to reduce the possibility of sensing skeletal myopotentials. However, the risk of CRT-P's operation being affected by myopotentials cannot be eliminated, particularly in unipolar systems. Myopotentials may resemble cardiac activity, resulting in inhibition of pacing, triggering and/or emission of asynchronous pacing pulses, depending on the pacing mode and the interference pattern. Certain follow-up procedures, such as monitoring CRT-P 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 setting.

Muscle or Nerve Stimulation – Inappropriate muscle or nerve stimulation may occur with unipolar pacing when using a non-coated Stratos CRT-P.

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

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

Triggered Modes – While the triggered modes (DDT, DVT, DDTR/A, DDTR/V, DDI/T, VDT, VVT, and AAT) can be programmed permanently, these modes are intended for use as temporary programming for diagnostic purposes. In triggered pacing modes, pacing pulses are emitted in response to sensed signals, and therefore the pacing pulse can be used as an indicator, or marker of sensed events for evaluating the sensing function of the pulse generator using surface ECG. However, real-time telemetry of marker channels and/or intracardiac electrogram via the programmer and programming wand is recommended over the use of a triggered pacing mode in the clinical setting. A triggered pacing mode may be preferred in situations where positioning the programming head over the pulse generator would be impossible or impractical (i.e., during exercise testing or extended Holter monitoring).

Another possible application of triggered modes is to ensure pacing as a short term solution during a period of inhibition of pacing by extracardiac interference, mechanical noise signals, or other sensing abnormalities. Because triggered modes emit pacing pulses in response to sensed events, this may result in unnecessary pacing during the absolute refractory period of the myocardium, inappropriate pacing in response to oversensing of cardiac or extracardiac signals. The risks associated with triggered pacing include excessive pacing, arrhythmias due to the R-on-T phenomenon, and early battery depletion. Therefore, it is important that the triggered modes are not used for long term therapy, and that the CRT-P is always returned to a non-triggered permanent program.

1.5.5 Home Monitoring

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 Stratos CRT-Ps are provided in Section 1.5.6. 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).

Event Triggered Report - A timely receipt of the event report cannot be guaranteed. The receipt is also dependent on whether the patient was physically situated in the required coverage range of the patient device at the time the event information was sent.

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

Not for Conclusive Diagnosis - Because not all information available in the implant is being transmitted, the data transmitted by Home Monitoring should be evaluated in conjunction with other clinical indicators (i.e., in-office follow-up, patient symptoms, etc.) in order to make a proper diagnosis.

Frequency of Office Follow-Ups When Using Home Monitoring - The use of Home Monitoring does not replace regular follow-up examinations. When using Home Monitoring, the time period between follow-up visits may not be extended.

1.5.6 Electromagnetic Interference (EMI)

The operation of any implanted device may be affected by certain environmental sources generating signals that resemble cardiac activity. This may result in inhibition of pacing 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 device and/or cardiac tissue adjacent to the leads.

BIOTRONIK CRT-Ps 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 CRT-P patients. If the patient may be exposed to one of the following environmental conditions, then the patient should be given the appropriate warnings.

1.5.7 Home and Occupational Environments

The following equipment (and similar devices) may affect normal CRT-P 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 at retail stores 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 pacing or causes a reversion to asynchronous pacing or pacing at magnet rate, moving away from the source or turning it off should allow the CRT-P 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 CRT-P operation if approached too closely.

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

Communication Equipment – Communication equipment such as microwave transmitters, linear power amplifiers, or high-power amateur transmitters may generate enough EMI to interfere with CRT-P 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 CRT-P operation if approached too closely.

Electrical Appliances – Electric hand-tools and electric razors (used over the skin directly above the CRT-P) have been reported to cause pacemaker disturbances. Home appliances that are in good working order and properly grounded do not usually produce enough EMI to interfere with implanted device operation.

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

Radio-Frequency Identification (RFID) – RFID tags may interact with the CRT-Ps. Patients should be advised to avoid leaving a device containing such a tag within close proximity to the CRT-P (i.e., inside a shirt pocket).

1.5.8 Cellular Phones

Recent studies have indicated there may be a potential interaction between cellular phones and pacemaker operation. Potential effects may be due to either the radio frequency signal or the magnet within the phone and could include inhibition or asynchronous pacing when the phone is within close proximity (within 6 inches [15 cm]) to the CRT-P.

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

Patients having an implanted CRT-P who operate a cellular phone should:

- Maintain a minimum separation of 6 inches (15 cm) 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 cm) 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 cm) 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.

1.5.9 Hospital and Medical Environments

Refer to Section 1.5.1 for information regarding CRT-P interaction with the following medical procedures / environments:

- Electrosurgical Cautery
- Lithotripsy
- External Defibrillation
- High Radiation Sources

1.5.10 Device Explant and Disposal

Device Incineration - Never incinerate a CRT-P. Be sure the CRT-P is explanted before a patient who has died is cremated. (see Section 10)

Explanted Devices – Return all explanted devices to BIOTRONIK.

1.6 Potential Effects of the Device on Health

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

Potential Adverse Events

- Air embolism
- Allergic reactions to contrast media
- Arrhythmias
- Bleeding
- Body rejection phenomena
- Cardiac tamponade
- Chronic nerve damage
- Damage to heart valves
- Elevated pacing thresholds
- Extrusion
- Fluid accumulation
- Infection
- Keloid formation
- Lead dislodgment
- Lead fracture / insulation damage
- Lead-related thrombosis
- Local tissue reaction / fibrotic tissue formation
- Muscle or nerve stimulation
- Myocardial damage
- Myopotential sensing
- Pacemaker mediated tachycardia
- Pneumothorax
- Pocket erosion
- Hematoma
- Device migration
- Thromboembolism
- Undersensing of intrinsic signals
- Venous occlusion
- Venous or cardiac perforation

1.7 Clinical Studies

The subsequent sections summarize the following three clinical studies that were used to support the safety and effectiveness of the Stratos LV/LV-T CRT-Ps.

- The AVAIL CLS/CRT clinical study
- The OVID clinical study (OUS)
- The OPTION CRT/ATx clinical study

Two of the studies, AVAIL CLS/CRT and OVID, collected significant safety data supporting use of the Stratos LV/LV-T CRT-P system. The third study, OPTION CRT/ATx, supports the effectiveness of cardiac resynchronization therapy (CRT). The OPTION CRT/ATx study was conducted on a device that delivers CRT but, in addition, also offers defibrillation therapy (CRT-D).

1.7.1 Stratos LV Clinical Study – AVAIL CLS/CRT

Study Design

The AVAIL CLS/CRT was a multi-center, prospective, randomized, blinded clinical study designed to support approval for cardiac resynchronization therapy for a Heart Failure (HF) patient population not requiring back up defibrillation and that are indicated for an ablate and pace procedures. All patients enrolled into the clinical study were randomly assigned to one of three groups using a 2:2:1 ratio for randomization.

- Patients assigned to Group 1 received biventricular pacing with CLS-based rate adaptive pacing using BIOTRONIK's Protos DR/CLS, which is a dual-chamber pulse generator with CLS-based rate adaptive pacing. During this study, the Protos DR/CLS devices were implanted with two ventricular leads: the right ventricular lead was connected to the ventricular port, and the left ventricular lead was connected to the atrial port. Protos DR/CLS was included in this study to evaluate biventricular pacing with a different type of rate adaptive sensor technology.
- Patients assigned to Group 2 received biventricular pacing with accelerometer-based rate adaptive pacing using the Stratos LV.
- Patients assigned to Group 3 (control group) received right ventricular pacing with accelerometer-based rate adaptive pacing using the Stratos LV. Therefore, 60% of the patients received a Stratos LV device.

Primarily, the study evaluated and compared the functional benefits of CRT between the three randomized groups using a composite endpoint consisting of a six-minute walk test (meters walked) and quality of life measurement (assessed using the Minnesota Living with Heart Failure Questionnaire). Relevant measurements were completed twice for each patient: once at the Baseline evaluation (prior to implant and ablation) and again at a six-month follow-up evaluation. The data collected during this clinical study was used to demonstrate superiority of CRT to RV only pacing. This study also evaluated the safety of both the Protos DR/CLS and Stratos LV devices through an analysis of the complication-free rate through six months. Secondarily, the study also evaluated the superiority of CRT with CLS rate adaptation compared to CRT with accelerometer rate adaptation.

Clinical Inclusion Criteria

To support the objectives of this investigation, patients were required to meet the following inclusion criteria prior to enrollment:

- Meet the indications for therapy
- Persistent (documented for more than 7 days), symptomatic AF with poorly controlled rapid ventricular rates or permanent, (documented for more than 30 days with failed cardioversion, or longstanding AF of 6 months or more) symptomatic AF with poorly controlled rapid ventricular rates.
- Eligible for AV nodal ablation and permanent pacemaker implantation
- NYHA Class II or III heart failure
- Age ≥ 18 years
- Understand the nature of the procedure
- Ability to tolerate the surgical procedure required for implantation
- Give informed consent
- Able to complete all testing required by the clinical protocol
- Available for follow-up visits on a regular basis at the investigational site

Clinical Exclusion Criteria

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

- Meet one or more of the contraindications
- Have a life expectancy of less than six months
- Expected to receive heart transplantation within six months
- Enrolled in another cardiovascular or pharmacological clinical investigation
- Patients with an ICD, or being considered for an ICD
- Patients with previously implanted biventricular pacing systems
- Patients with previously implanted single or dual chamber pacing system with > 50% documented ventricular pacing
- Patients with previous AV node ablation
- Six-minute walk test distance greater than 450 meters
- Any condition preventing the patient from being able to perform required testing
- Presence of another life-threatening, underlying illness separate from their cardiac disorder
- Conditions that prohibit placement of any of the lead systems

Follow-Up Schedule

At the enrollment screening, the physician evaluated the patient to verify that all inclusion/exclusion criteria have been met in accordance to the protocol and the patient has signed the informed consent. After successful enrollment, all patients were implanted with either a Stratos LV CRT-P or Protos DR/CLS device. Evaluations at the Four Week, Three and Six Month follow-ups included NYHA classification, medications, and percentage of ventricular pacing.

Clinical Endpoints

Primary Endpoint: Complication-free Rate (Safety)
The safety of the Stratos LV was evaluated based on complications (adverse events that require additional invasive intervention to resolve) related to the implanted CRT system which includes the Stratos LV, the right ventricular, the left ventricular lead, lead ventricular lead adapters (if used) and the implant procedure. The target complication-free rate at six months is 85%.

Primary Endpoint: Six Minute Walk Test & QOL (Effectiveness)
The purpose of Primary Endpoint 1 was to evaluate the effectiveness of the CRT (Groups 1 and 2) compared to RV only (Group 3) pacing as measured by the average composite rate of improvement in six minute walk test and QOL.

Accountability of PMA Cohorts

After randomization and enrollment, 23 patients (8 in Group 1, 8 in Group 2 and 7 in Group 3) did not receive an implant. The reasons for patients not receiving an implant are outlined in **Figure 1**. Two additional patients in Group 1 had an unsuccessful first implant attempt (unable to implant the LV lead), but follow up data was not received.

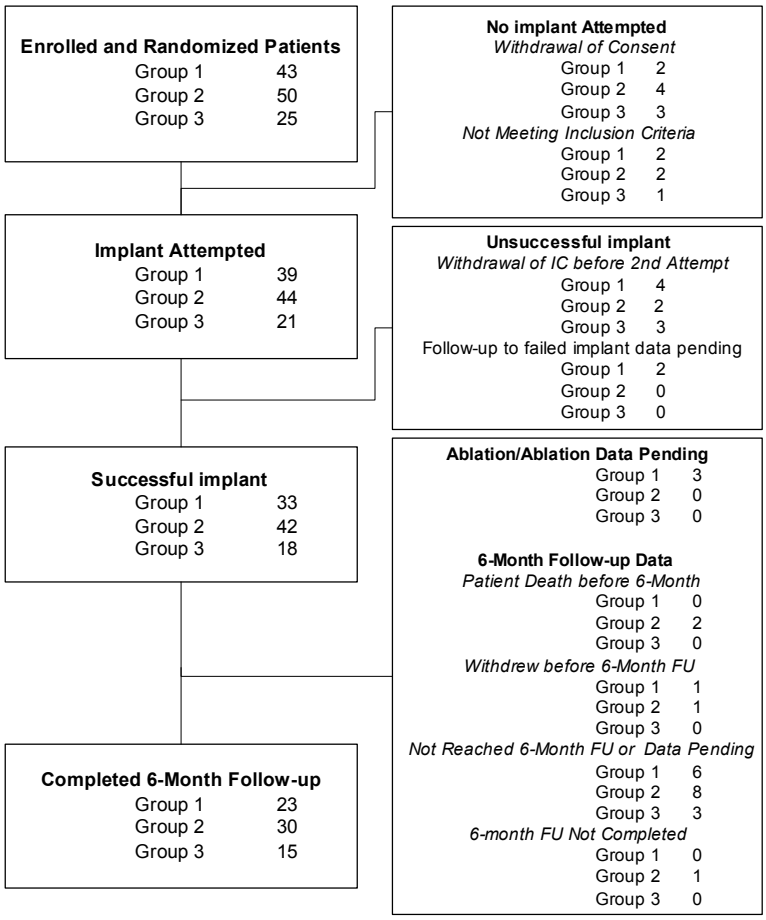


Figure 1: Patient Accountability

Demographics and Baseline Parameters

Table 1 provides a summary of the patient demographics at enrollment. There were no statistical differences in enrollment demographics between the 3 groups.

Table 1: Patient Demographics at Enrollment				
Characteristic	**Group1**	**Group 2**	**Group 3**	**P-value**
Age @ Enrollment (Yrs) Mean ± SE Range	N=42 73.7 ± 1.3 56 to 90	N=50 72.3 ± 1.2 51 to 86	N=25 71.5 ± 1.6 52 to 85	0.534*
Gender Male Female	N=42 18 (42.9%) 24 (57.1%)	N=50 19 (38.0%) 31 (62.0%)	N=25 13 (52.0%) 12 (48.0%)	0.553**
Six-Minute Walk Distance (meters) Mean ± SE Range	N=42 262.7 ± 15.1 78 to 420	N=50 283.6 ± 13.8 37 to 438	N=25 267.8 ± 22.9 23 to 420	0.395*
New York Heart Association Class Class II Class III	N=42 23 (54.8%) 19 (45.2%)	N=50 18 (36.0%) 32 (64.0%)	N=25 10 (40.0%) 15 (60.0%)	0.189**
Underlying Heart Disease Dilated Cardiomyopathy Hypertrophic Cardiomyopathy Valvular Heart Disease Coronary Artery Disease Hypertension No underlying structural heart disease	N=42 8 (19.0%) 4 (9.5%) 12 (28.6%) 19 (45.2%) 37 (88.1%) 3 (7.1%)	N=49 11 (22.4%) 1 (2.0%) 12 (24.5%) 28 (57.7%) 37 (75.5%) 2 (4.1%)	N=25 1 (4.0%) 2 (8.0%) 5 (20.0%) 6 (24.0%) 19 (76.0%) 7 (28.0%)	 0.125** 0.216** 0.792** 0.031** 0.348** 0.007**

Table 1: Patient Demographics at Enrollment				
Characteristic	**Group1**	**Group 2**	**Group 3**	**P-value**
Other Medical History	N=29	N=36	N=17	
Diabetes	13 (44.8%)	9 (25.0%)	4 (23.5%)	0.287**
Chronic Lung Disease	7 (24.1%)	16 (44.4%)	7 (41.2%)	0.211**
Thyroid Disease	12 (41.4%)	12 (33.3%)	5 (29.4%)	0.791**
Chronic Kidney Disease	4 (13.8%)	5 (13.9%)	1 (5.9%)	0.836**
Prior Ischemic Stroke or TIA	7 (24.1%)	10 (27.8%)	6 (35.3%)	0.726**
Prior Embolic Events (non-cerebrovascular)	1 (2.3%)	3 (6.0%)	2 (8.0%)	0.653**

*One-way ANOVA, ** Chi-Square test (2-sided)

Table 2 provides a summary of the AF medical history. Table 3 provides a summary of cardiac medications patients were taking at the time of enrollment. Please note some categories may equal more than 100% as several categories allow more than one response. In some cases, complete demographic data was not provided for all patients. There were no statistical differences in AF medical history and cardiac medication at enrollment between the 3 groups.

Table 2: Atrial Fibrillation Demographics at Enrollment				
Characteristic	**Group 1**	**Group 2**	**Group 3**	**P-value***
Classification of Atrial Fibrillation	N=42	N=50	N=24	0.537
Persistent AF	10 (23.8%)	17 (34%)	6 (25%)	
Permanent AF	32 (76.2%)	33 (66%)	18 (75%)	
Classification of Symptoms Related to AF	N=42	N=49	N=25	
Palpitations	32 (76.2%)	34 (69.4%)	14 (56.0%)	0.236
Chest Pain	6 (14.3%)	7 (14.3%)	3 (12.0%)	1.000
Dyspnea or shortness of breath	36 (85.7%)	40 (81.6%)	19 (76.0%)	0.568
Fatigue	34 (81.0%)	45 (91.8%)	18 (72.0%)	0.149
Lightheadedness or syncope	17 (40.5%)	13 (26.5%)	9 (36.0%)	0.329
Other	9 (21.4%)	11 (22.4%)	10 (40.0%)	0.205
Previous AF Ablation	N=42	N=50	N=25	0.354
No	37 (88.1%)	47 (94.0%)	21 (84.0%)	
Yes	5 (11.9%)	3 (6.0%)	4 (16.0%)	
Past Medications for Rate or Rhythm Control				
Amiodarone	N=41	N=48	N=24	
Digoxin	12 (29.3%)	10 (20.8%)	10 (41.7%)	0.192
Diltiazem	17 (41.5%)	22 (45.8%)	13 (54.2%)	0.683
Disopyramide	17 (41.5%)	23 (47.9%)	12 (50.0%)	0.804
Dofetilide	0 (0.0%)	3 (6.3%)	0 (0.0%)	0.228
Flecanide	4 (9.8%)	3 (6.3%)	2 (8.3%)	0.895
Ibutilide	5 (12.2%)	5 (10.4%)	1 (4.2%)	0.656
Procainamide	0 (0.0%)	0 (0.0%)	1 (4.2%)	0.215
Propafenone	0 (0.0%)	2 (4.2%)	0 (0.0%)	0.506
Sotolol	2 (4.9%)	4 (8.3%)	0 (0.0%)	0.423
Verapamil	9 (22.0%)	10 (20.8%)	2 (8.3%)	0.389
Metoprolol	5 (12.2%)	8 (16.7%)	3 (12.5%)	0.829
Propranolol	19 (46.3%)	28 (58.3%)	10(41.7%)	0.382
Other Beta-Blockers	0 (0.0%)	0 (0.0%)	1 (4.2%)	0.215
Other Medications	7 (17.1%)	15 (31.3%)	4 (16.7%)	0.248
	5 (12.2%)	5 (10.4%)	1 (4.2%)	0.656

Table 2: Atrial Fibrillation Demographics at Enrollment				
Characteristic	**Group 1**	**Group 2**	**Group 3**	**P-value***
Rate Control Medication, Reasons for Discontinuation	N=17	N=20	N=12	
Ineffective	10 (58.8%)	13 (65.0%)	9 (75.0%)	0.558
Not tolerated	8 (47.1%)	7 (35.0%)	3 (25.0%)	0.760
Other	1 (5.9%)	2 (10.0%)	0 (0.0%)	0.800
Rhythm Control Medication, Reasons for Discontinuation	N=22	N=25	N=13	
Ineffective	17 (77.3%)	20 (80.0%)	8 (61.5%)	0.759
Not tolerated	6 (27.3%)	7 (28.0%)	6 (46.2%)	0.530
Other	1 (4.5%)	1 (4.0%)	2 (15.4%)	0.430
Cardioversion History	N=42	N=49	N=25	
Successful prior electrical cardioversion	13 (31.0%)	16 (32.7%)	10 (40.0%)	0.760
Transthoracic	13 (100.0%)	15 (93.8%)	10 (100.0%)	0.808
Transvenous	0 (0.0%)	1 (6.3%)	0 (0.0%)	
Unsuccessful prior electrical cardioversion	15 (35.7%)	14 (28.6%)	7 (28.0%)	0.680
Transthoracic	15 (100.0%)	14 (93.3%)	7 (100.0%)	0.741
Transvenous	0 (0.0%)	2 (13.3%)	0 (0.0%)	
No electrical cardioversion attempted	17 (40.5%)	20 (40.8%)	9 (36.0%)	0.936
Successful prior pharmacological cardioversion	5 (11.9%)	3 (6.1%)	3 (12.0%)	0.547
Unsuccessful prior pharmacological cardioversion	8 (19.0%)	11 (22.4%)	7 (28.0%)	0.678
No pharmacological cardioversion attempted	23 (54.8%)	29 (59.2%)	15 (60.0%)	0.915

*Chi-Square test (2-sided)

Table 3: Current Cardiac Medications at Enrollment				
Drug Category	**Group 1 N=42**	**Group 2 N=50**	**Group 3 N=25**	**P-value***
Anti-Arrhythmics	12 (28.6%)	10 (20.4%)	4 (16.0%)	0.480
Rate Control Medications	32 (76.2%)	43 (87.8%)	20(80.0%)	0.462
Anti-thrombic Agents	17 (40.5%)	19(38.8%)	11 (44.0%)	0.863
Anti-Coagulants	36 (85.7%)	40 (81.6%)	22 (88.0%)	0.686
ACE Inhibitors	16 (38.1%)	16 (32.7%)	8 (32.0%)	0.848
Angiotensin-Receptor Blockers	10 (23.8%)	7 (14.3%)	4 (16.0%)	0.491
Diuretics	30 (71.4%)	34 (69.4%)	13 (52.0%)	0.255
Inotropes	1 (2.4%)	2 (4.1%)	0 (0.0%)	0.803
Nitrates	3 (7.1%)	6 (12.2%)	2 (8.0%)	0.714
Beta-Blockers for CHF	6 (14.3%)	9 (18.4%)	4 (16.0%)	0.947
Other	23 (54.8%)	26 (53.1%)	14 (56.0%)	0.941

*Chi-Square test (2-sided)

Safety and Effectiveness Results

A total of 118 patients were enrolled in the AVAIL CLS/CRT clinical study at 20 sites:

There were 43 Group 1, 50 Group 2, and 25 Group 3 patients in this prospective, multi-center, randomized clinical study. For Group 1, there were 33 successful implants (76.7%) of the Protos DR/CLS system. For Groups 2 and 3, there were 44 and 21 successful implants (88.0% and 84.0%) respectively of the Stratos LV CRT-P system.

- The study was designed to enroll 265 patients. However, the study was terminated early due to slow patient enrollment. There were no safety issues involved in the termination decision. Due to the lack of patient data, the AVAIL CLS/CRT study alone was insufficient to support CRT pacing effectiveness or an ablate and pace indication.
- The cumulative enrollment duration was 416.7 months with a mean duration of 9.7 months for Group 1, 522.4 months with a mean duration of 10.4 months for Group 2, and 261.1 months with a mean duration of 10.4 months for Group 3. 73 (61.9%) of the study patients had enrollment durations greater than 6 months.
- There were 158 adverse events (115 observations in 68 patients and 43 complications in 34 patients). There were no unanticipated adverse device effects reported.
- The overall protocol violation non-compliance rate is 0.4% in Group 1, 0.5% in Group 2, and 0.4% in Group 3. The overall follow-up compliance rate is 99.8% in all groups.
- There were 3 patient deaths reported, two in Group 2 and one in Group 3. The clinical investigators and clinical events committee determined that none of these deaths were related to the study devices.
- Both the CRT pacing and the RV pacing only groups showed improvements in the primary composite endpoint of quality of life and six-minute walk distance between the baseline evaluation and the six-month follow-up. In addition, there was a trend towards improvement between the combined CRT pacing groups compared to the RV pacing only group at six months.

Primary Endpoint—Complication-free Rate (Safety)

The safety of the Stratos LV was evaluated based on complications (adverse events that require additional invasive intervention to resolve) related to the implanted CRT system which includes the Stratos LV, the right ventricular, the left ventricular lead, lead ventricular lead adapters (if used) and the implant procedure. The target complication-free rate at six months is 85%.

13 complications in these categories were seen in 11 patients with cumulative enrollment duration of 783.5 months (64.4 patient-years). 14.7% of the patients had a reported complication in these categories. The rate of complications per patient-year is 0.20. Details of the Stratos LV complications in the AVAIL CLS/CRT study are listed in **Table 4**.

Table 4: AVAIL CLS/CRT Complication-Free Rate at 6 months – Stratos LV				
Category	**Number of Patients**	**% of Patients**	**Number of Complications**	**Complications per patient-year**
Device-Related				
Pocket Infection/Pain	1	1.3%	2	0.03
Total	**1**	**1.3%**	**2**	**0.03**
LV Lead Related				
High Threshold No Capture	1	1.3%	1	0.02
Diaphragmatic Stimulation	1	1.3%	1	0.02
Dislodgement	2	2.7%	2	0.03
Total	**4**	**5.3%**	**4**	**0.06**
RV Lead Related				
High Threshold / No Capture	4	5.3%	4	0.06
Total	**4**	**5.3%**	**4**	**0.06**
Procedure				
Pneumothorax	1	1.3%	1	0.02
User error	1	1.3%	1	0.02
Hematoma	1	1.3%	1	0.02
Total	**3**	**4.0%**	**3**	**0.05**
Total Lead and Procedure Related	**11**	**14.7%**	**13**	**0.20**

Table 4: AVAIL CLS/CRT Complication-Free Rate at 6 months – Stratos LV				
Category	**Number of Patients**	**% of Patients**	**Number of Complications**	**Complications per patient-year**
Other Medical				
Worsening CHF	2	2.7%	2	0.03
Repeat Ablation	3	4.0%	3	0.05
Non-CHF cardiac symptoms	3	4.0%	3	0.05
Other Medical	3	4.0%	3	0.05
Total	**10**	**13.3%**	**11**	**0.17**
Total—All Patients and Categories	**19**	**25.3%**	**24**	**0.37**

Number of Patients = 75 Number of Patient-Years = 64.4

The freedom from Stratos LV system-related and procedure-related complications was 85.33%, with a one sided lower 95% confidence bound of 76.89%. Therefore, the procedure, lead and device related complication-free rate at 6 months met the pre-specified acceptance criterion of equivalence (non-inferiority) within 10% of 85% (p = 0.0196).

Observed Adverse Events

Adverse events are classified as either observations or complications. Observations are defined as clinical events that do not require additional invasive intervention to resolve. Complications are defined as clinical events that require additional invasive intervention to resolve.

Of the 104 adverse events reported in the Stratos LV study groups, there have been 76 observations in 45 patients and 28 complications in 20 patients with a cumulative enrollment duration of 64.4 patient-years. 26.7% of the enrolled Stratos LV patients have experienced a complication. The rate of complications per patient-year is 0.43. 60.0% of the enrolled study patients have a reported observation. The rate of observations per patient-year is 1.18.

Complications and observations for the Stratos LV study groups are summarized in **Table 5** and **Table 6**. The total number of patients may not equal the sum of the number of patients listed in each category, as an individual patient may have experienced more than one complication or observation.

Table 5: Summary of Complications – Stratos LV				
Category	**Number of Patients**	**% of Patients**	**Number of Complications**	**Complications per patient-year**
Device-Related				
Pocket Infection or Pain	2	2.7%	3	0.05
Total	2	**2.7%**	3	0.05
LV Lead-Related				
High Threshold / No Capture	1	1.3%	1	0.02
Diaphragmatic Stimulation	1	1.3%	1	0.02
Dislodgement	2	2.7%	2	0.03
Total	**4**	**5.3%**	**4**	**0.06**
RV Lead Related				
High Threshold / No Capture	4	5.3%	4	0.06
Total	**4**	**5.3%**	**4**	**0.06**
Procedure				
Pneumothorax	1	1.3%	1	0.02
User error	1	1.3%	1	0.02
Hematoma	1	1.3%	1	0.02
Total	**3**	**4.0%**	**3**	**0.05**
Total Lead and Procedure Related	**11**	**14.7%**	**14**	**0.22**
Other Medical				
Worsening CHF	2	2.7%	2	0.03
Non-CHF cardiac symptoms	5	6.7%	5	0.08

Table 5: Summary of Complications – Stratos LV				
Category	**Number of Patients**	**% of Patients**	**Number of Complications**	**Complications per patient-year**
Repeated ablation	3	4.0%	3	0.05
Lead addition	1	1.3%	1	0.02
Other medical	3	4.0%	3	0.05
Total	**12**	**16.0%**	**14**	**0.22**
Total—All Patients and Categories	**20**	**26.7%**	**28**	**0.43**

Number of Patients = 75, Number of Patient-Years = 64.4

Table 6: Summary of Observations – Stratos LV				
Category	**Number of Patients**	**% of Patients**	**Number of Complications**	**Observations per patient-year**
LV Lead-Related				
High Threshold / No Capture	1	1.3%	1	0.02
Diaphragmatic Stimulation	13	17.3%	13	0.20
Total	**14**	**18.7%**	**14**	**0.22**
Device Related				
Pocket Infection or pain	5	6.7%	5	0.08
Total	**5**	**6.7%**	**5**	**0.08**
Procedure				
Pneumothorax	1	1.3%	1	0.02
Atrial edema	1	1.3%	1	0.02
User error	1	1.3%	1	0.02
Total	**3**	**4.0%**	**3**	**0.05**
Total Lead, Device and Procedure Related	**19**	**25.3%**	**22**	**0.34**

Table 6: Summary of Observations – Stratos LV				
Category	**Number of Patients**	**% of Patients**	**Number of Complications**	**Observations per patient-year**
Other Medical				
Dizziness	3	4.0%	3	0.05
Other Medical	24	32.0%	34	0.53
Worsening CHF	8	10.7%	8	0.12
Ventricular arrhythmias	2	2.7%	2	0.03
Shortness of Breath	5	6.7%	5	0.08
Stroke / TIA	1	1.3%	1	0.02
Non-CHF cardiac symptoms	1	1.3%	1	0.02
Total	**35**	**46.7%**	**54**	**0.84**
Total—All Patients and Categories	**45**	**60.0%**	**76**	**1.18**

Number of Patients = 75 Number of Patient-Years = 64.4

There have been 3 patient deaths reported for the Stratos LV groups (out of 75 Stratos LV patients). None of the deaths were related to the implanted CRT-P system. Table 7 provides a summary of reported patient deaths.

Table 7: Summary of Patient Deaths	
	Stratos LV Patients (N = 75)
Sudden Cardiac	1
Non-Cardiac	2
All Causes	**3**

Primary Endpoint: Six Minute Walk Test & QOL (Effectiveness)

The purpose of Primary Endpoint 1 was to evaluate the effectiveness of the CRT (Groups 1 and 2) compared to RV only (Group 3) pacing as measured by the average composite rate of improvement in six minute walk test and QOL.

- Stratos LV Effectiveness (Group 2 compared to Group 3): The average composite rate for Group 2 (N=30) was 48.1% with a standard error of 12.3%. The average composite rate for Group 3 (N=15) was 33.0% with a standard error of 12.3%. The difference in the mean composite rate between Group 2 and Group 3 is 15.1%. The p value for superiority is 0.442.
- Protos DR/CLS Effectiveness (Group 1 compared to Group 3): The average composite rate for the Group 1 (N=23) is 36.8% with a standard error of 7.9%. The average composite rate for Group 3 (N=15) is 33.0% with a standard error of 12.3%. The difference in the mean composite rate between Group 1 and Group 3 is 3.8%. The p value for superiority is 0.788.

Table 8 presents the average composite rate of improvement in six minute walk test distance and QOL score, the average 6-minute walk test distance and the average QOL score at Baseline and at the Six-Month follow-up, as well as the average difference in 6-minute walk test distance and QOL score between Baseline and the Six-Month follow-up for the CRT (Groups 1 and 2) and RV only (Group 3) for those patients with six minute walk test data and complete QOL data at both Baseline and the Six-Month follow-up.

Table 8: Composite of Six Minute Walk Test and QOL (Effectiveness)			
Category	**CRT (Group 1 & 2) (N = 53)** Mean ± SE	**RV only Group 3 (N = 15)** Mean ± SE	**p value (student's t-test, 2-sided)**
Distance Walked at Baseline	262.8 ± 13.7	288.5 ± 22.4	0.369*
Distance Walked at Six-Months	312.8 ± 14.6	345.8 ± 30.0	0.303*
∆ Distance Walked (meters)	50.0 ± 12.2	57.2 ± 26.7	0.790*
∆ Distance Walked (%)	39.0% ± 13.1%	25.7% ± 15.0%	0.610*
QOL Score at Baseline	58.5 ± 2.9	49.3 ± 5.5	0.137*
QOL Score at Six-Months	30.1 ± 3.2	27.7 ± 6.5	0.731*
∆ in QOL Score	28.4 ± 3.4	21.6 ± 7.7	0.367*
∆ in QOL Score (%)	47.4% ± 5.1%	40.4% ± 11.1%	0.537*
Composite Rate	**43.2% ± 7.7%**	**33.0% ± 12.3%**	**0.525***

* p value is provided for informational purposes to show trends only; clinical significance is not indicated by p values for analyses that were not prespecified.

Primary Effectiveness Endpoint Analysis and Conclusions

The primary effectiveness endpoint evaluated CRT effectiveness (Groups 1 and 2) compared to RV only effectiveness (Group 3), as measured by the composite rate of the six minute walk test and QOL improvement from Baseline to the Six-Month follow-up (**Table 8**). For this analysis, both six minute walk test and QOL were equally weighted at 50%. Due to the small number of patients with data available for the analysis of the primary endpoint, the results lack power to demonstrate that biventricular pacing with either the Protos DR/CLS or Stratos LV device is statistically different from RV only pacing with the Stratos LV device in patients undergoing an “ablate and pace” procedure.

Multi-site Poolability and Gender Analysis

The AVAIL CLS/CRT clinical report included data from multiple centers with centralized coordination, data processing, and reporting at BIOTRONIK. All of the clinical centers followed the requirements of an identical clinical protocol, and all of the clinical centers used the same methods to collect and report the clinical data, including New York Heart Association evaluation, six-minute walk test, Minnesota Living with Heart Failure questionnaire, and echocardiographic measurements. In order to justify pooling of the data from multiple centers, several analyses were completed. All of the centers were divided into two groups (Small and Large sites) based on implant volume. Comparisons were then made between the patient populations based on the results of the safety and effectiveness endpoints. Additionally, analyses were performed on the data collected in the AVAIL clinical investigation in order to compare results between males and females. The first type of analysis compared enrollment by patient gender in each of the study groups. The second type of analysis compared effectiveness and safety outcomes in each gender.

The results of these analyses demonstrated poolability of the data between sites. There were no significant differences in the primary safety or effectiveness endpoints between high and low volume implant centers.

The gender distribution in this clinical investigation was consistent within the study groups and included a representative proportion of enrolled female participants (57.2% versus 42.7% male). There were no significant differences in the primary safety or effectiveness endpoints between the male and female population.

1.7.2 Stratos LV Clinical Study – OVID study

The OVID clinical study collected significant safety data supporting the Stratos LV/LV-T CRT-P system.

Study Design

BIOTRONIK conducted the Corox Over-the-Wire Lead Evaluation (OVID) prospective registry outside the United States (OUS) of the Corox OTW Steroid LV lead in a multi-center trial with legally marketed CRT-D and CRT-P pulse generators that provide biventricular pacing therapy. Data from this registry is presented in the following sections to support the safety of the Stratos LV CRT-P.

The multi-center investigation was designed to validate the safety of the Corox OTW Steroid LV lead through a comparison of successfully implanted LV leads against a pre-defined success rate threshold, when no anatomical restrictions prevent access to the coronary sinus. The evaluation of safety is based on the analysis of the incidence of adverse events, defined as any complications or observations judged by the investigator to be in probable relationship with Corox OTW Steroid LV lead system. Additionally, the effectiveness of the leads was evaluated using lead parameter data, including sensing amplitudes, pacing thresholds, and impedance values.

In the OVID study, enrolled patients could be implanted with any legally marketed CRT-P or CRT-D device. There were 121 patients enrolled in the OVID clinical study, and 89 patients were implanted with a Stratos LV device.

Clinical Inclusion Criteria

To support the objectives of this investigation, patients were required to meet the following inclusion criteria prior to enrollment:

- Meet the indications for bi-ventricular pacing
- Age ≥ 18 years
- Receiving optimal drug therapy for Congestive Heart Failure treatment
- Give informed consent

Clinical Exclusion Criteria

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

- Myocardial infarction or unstable angina pectoris
- Acute myocarditis
- Life expectancy ≤ 6 months
- Planned cardiac surgical procedures or interventional measures within the next 6 months
- Pregnancy

Follow-Up Schedule

All patients were implanted with the Corox OTW/Steroid LV lead system and a CRT-P or CRT-D pulse generator capable of providing bi-ventricular pacing for the treatment of CHF. The specific study procedures were performed at:

- Pre-operative Visit
- Implantation
- Pre-discharge follow-up
- One-month follow-up
- Three-month follow-up
- Six-month follow-up
- Twelve-month follow-up

Clinical Endpoints

The safety of the Stratos LV was evaluated based on complications (adverse events that require additional invasive intervention to resolve) related to the implanted CRT system which includes the Stratos LV device, the atrial lead, the right ventricular lead the left ventricular lead and the implant procedure. The target complication-free rate at six months was 85%.

Accountability of PMA Cohorts

During the OVID study, 84 patients were implanted with the Stratos LV CRT-P and Corox OTW/Steroid LV lead system. Additionally, 5 other patients were implanted with a Stratos LV CRT-P device following an unsuccessful Corox OTW/Steroid LV lead implant attempt. Of these 5 patients, three were not implanted with any LV pacing lead, one was implanted with a non-study LV pacing lead and one was implanted with a BIOTRONIK Elox P 60 BP placed in the RV outflow tract for bi-focal ventricular pacing. These 5 patients were excluded from the OVID study at 1 month post-implant, because the primary endpoint of the OVID study was the evaluation of the safety and effectiveness of the Corox OTW/Steroid lead.

Demographics and Baseline Parameters

Table 9 provides a summary of the patient demographics and medical history for the 89 enrolled patients implanted with a Stratos LV. The typical patient implanted with a Stratos LV CRT-P was a 68 year old male with NYHA Class III heart failure, Left Bundle Branch Block (LBBB), a mean QRS duration of 160 ms, and non-ischemic cardiomyopathy.

Table 9: Patient Demographics	
Characteristic	**Results**
Age at Implant (Years)	**n=88**
Mean ± SD	68 ± 10
Range	34 to 84
Gender	**n=89**
Male	66 (74%)
Female	23 (26%)
QRS-width (ms)	**n=70**
Mean ± SD	160 ± 23
Range	110 to 210
Etiology of Heart Failure	**n=87**
Ischemic	32 (37%)
Non-Ischemic	55 (63%)
New York Heart Association (NYHA) Classification	**n=87**
Class III	73 (84%)
Class IV	14 (16%)
Atrial Tachyarrhythmias	**N=87**
None	48 (55%)
Atrial flutter	5 (5.7%)
Paroxysmal atrial fibrillation	19 (22%)
Persistent atrial fibrillation	10 (11.5%)
Other	5 (5.7%)
Ventricular Tachyarrhythmias	**N=87**
None	80 (92%)
Ventricular fibrillation	-
Sustained or non-sustained VT	5 (5.7%)[1)]
Other VT	2 (2.3%)[2)]
Existing/chronic leads prior to Corox OTW/Steroid	**n=88**
None	73 (83%)
Yes, due to previous pacemaker therapy	15 (17%)

[1)] non-sustained VT (n=4); no further information available (n=1); [2)] VES (n=2)

Safety and Effectiveness Results

- The cumulative implant duration was 760 months with a mean duration of 9.2 months. Sixty-five (77%) of the patients had implant durations greater than 6 months.
- The implant success rate for the Stratos LV CRT-P was 100% (89 out of 89). The implant success of the Stratos LV CRT-P in combination with the Corox OTW/Steroid LV lead was 94.4% (84 out of 89).
- The mean LV pacing threshold at implant was 0.9 and at 6-months was 0.9 volts.
- The mean R-wave at implant was 15.7 mV.
- The mean LV lead impedance at implant was 729 ohms and at 6-months was 603 ohms.
- There were 29 adverse events (18 observations in 17 patients and 11 complications in 10 patients). There were no unanticipated adverse device effects reported.
- There were 10 patient deaths reported in the OVID study. The clinical investigators have determined that no deaths were related to the Stratos LV CRT-P system.
- The overall follow-up compliance rate for the OVID study is 93%.

Primary Endpoint—Complication-free Rate (Safety)

The safety of the Stratos LV was evaluated based on complications (adverse events that require additional invasive intervention to resolve) related to the implanted CRT system which includes the Stratos LV device, the atrial lead, the right ventricular lead, the left ventricular lead and the implant procedure. The target complication-free rate at six months was 85%.

Ten (10) complications in these categories were seen in 10 patients with cumulative implant duration of 760 months (63.3 patient-years). 11.2% of the patients had a reported complication in these categories. The rate of complications per patient-year was 0.16. Details of the Stratos LV complications in the OVID study are listed in **Table 10**.

The freedom from Stratos LV system-related and procedure-related complications was 88.76% with a one sided lower 95% confidence bound of 81.69%. Therefore, the null hypothesis was rejected, and it was concluded that the complication-free rate at 6 months is equivalent to 85% within 10% (p = 0.0014).

Observed Adverse Events

Adverse events are classified as either observations or complications. Observations are defined as clinical events that do not require additional invasive intervention to resolve. Complications are defined as clinical events that require additional invasive intervention to resolve.

Of the 29 adverse events reported, there were 18 observations and 11 complications in a total of 89 patients. Table 10 and Table 11 provide a summary by category of each type of adverse event (complications and observations).

Table 10: Summary of Complications at 6 months

Category	Number of Patients	% of Patients	Number of Complications	Complications per patient-year
Corox OTW/Steroid Lead-Related				
Loss of capture	2	2.2%	2	0.03
Phrenic nerve stimulation	1	1.1%	1	0.02
Total	**3**	**3.3%**	**3**	**0.05**
Atrial Lead Related				
Loss of capture	1	1.1%	1	0.02
Total	**1**	**1.1%**	**1**	**0.02**
RV Lead Related				
Loss of capture	3	3.3%	3	0.05
Elevated Pacing thresholds	2	2.2%	2	0.03
Total	**5**	**5.6%**	**5**	**0.08**

Table 10: Summary of Complications at 6 months				
Category	**Number of Patients**	**% of Patients**	**Number of Complications**	**Complications per patient-year**
Device Related				
Pocket infection	1	1.1%	1	0.02
Total	1	1.1%	1	0.02
Total System Related	**10**	**11.2%**	**10**	**0.16**
Other Medical				
Arrhythmias	1	1.1%	1	0.02
Total	1	1.1%	1	0.02
Overall Complication Totals	**10**	**11.2%**	**11**	**0.17**

Number of Patients = 89; Number of Patient-Years = 63.3

Table 11: Summary of Observations at 6 months				
Category	**Number of Patients**	**% of Patients**	**Number of Observations**	**Observations per patient-year**
Corox OTW/Steroid Lead-Related				
Implant failure	5	5.6%	5	0.08
Phrenic nerve stimulation	4	4.5%	4	0.06
Total	**9**	**10.1%**	**9**	**0.14**
Atrial Lead Related				
Loss of capture	1	1.1%	1	0.02
Total	**1**	**1.1%**	**1**	**0.02**
RV Lead Related				
Elevated Pacing thresholds	2	2.2%	2	0.03
Total	**2**	**2.2%**	**2**	**0.03**

Table 11: Summary of Observations at 6 months				
Category	**Number of Patients**	**% of Patients**	**Number of Observations**	**Observations per patient-year**
Device Related				
Pocket infection/ Pericardial Effusion	1	1.1%	1	0.02
Total	**1**	**1.1%**	**1**	**0.02**
Total System Related	**12**	**13.5%**	**13**	**0.21**
Medical				
Arrhythmias	2	2.2%	2	0.03
Shortness of breath, palpitations	1	1.1%	1	0.02
Total	**3**	**3.3%**	**3**	**0.05**
Miscellaneous				
Malfunction of hemostatic valve	1	1.1%	1	0.02
Improper Lead preparation	1	1.1%	1	0.02
Total	**2**	**2.2%**	**2**	**0.04**
Overall Observation Totals	**17**	**19.1%**	**18**	**0.28**

Number of Patients = 89; Number of Patient-Years = 63.3

There were a total of 10 patient deaths reported in the OVID study for patients with the Stratos LV device. The clinical investigators determined that no deaths were related to the Stratos LV device system.

1.7.3 AVAIL and OVID Combined Primary Endpoint-Complication-free Rate (Safety)

The results from for the AVAIL CLS/CRT and OVID studies were pooled to evaluate the safety of the Stratos LV device. The safety of the Stratos LV was evaluated based on complications (adverse events that require additional invasive intervention to resolve) related to the implanted CRT system which includes the Stratos LV, the atrial lead, the right ventricular lead, the left ventricular lead and the implant procedure. The target complication-free rate at six months was 85%.

Twenty-three (23) complications in these categories were seen in 21 patients with cumulative implant duration of 127.7 years. 12.8% of the patients had a reported complication in these categories. The rate of complications per patient-year was 0.18. Details of the Stratos LV complications in the AVAIL CLS/CRT and OVID studies are listed in Table 12.

Table 12: OVID and AVAIL Complication-Free Rate - Stratos LV

Category	Number of Patients	% of Patients	Number of Complications	Complications per patient-year
LV Lead-Related				
High Threshold / No Capture	3	1.8%	3	0.02
Diaphragmatic Stimulation	2	1.2%	2	0.02
Dislodgement	1	1.2%	2	0.01
Total	**7**	**4.3%**	**7**	**0.06**
RV Lead Related				
High Threshold / No Capture	9	5.5%	9	0.07
Total	**9**	**5.5%**	**9**	**0.07**
Atrial Lead Related				
No Capture	1	0.6%	1	0.01
Total	**1**	**0.6%**	**1**	**0.01**

Table 12: OVID and AVAIL Complication-Free Rate - Stratos LV				
Category	**Number of Patients**	**% of Patients**	**Number of Complications**	**Complications per patient-year**
Device Related				
Pocket Infection	2	1.2%	3	0.02
Total	**2**	**1.2%**	**3**	**0.02**
Procedure				
Pneumothorax	1	0.6%	1	0.01
User error	1	0.6%	1	0.01
Hematoma	1	0.6%	1	0.01
Total	**3**	**1.8%**	**3**	**0.02**
Total Lead, Device and Procedure Related	**21**	**12.8%**	**23**	**0.18**
Other Medical				
Arrhythmias	1	0.6%	1	0.01
Repeated ablation	3	1.8%	3	0.02
Worsening CHF	2	1.2%	2	0.02
Other Medical	3	1.8%	3	0.02
Non-CHF cardiac symptoms	3	1.8%	3	0.02
Total	**11**	**6.7%**	**12**	**0.09**
Total—All Patients and Categtories	**29**	**17.7%**	**35**	**0.27**

Number of Patients = 164 Number of Patient-Years = 127.7

The freedom from Stratos LV system-related and procedure-related complications was 87.2% with a one sided lower 95% confidence bound of 82.09%. Therefore, the null hypothesis was rejected, and it was concluded that the complication-free rate at 6 months is equivalent to 85% within 10% and the primary safety endpoint was met (p = 0.0002)*.

1.7.4 Tupos LV/ATx Clinical IDE Study - OPTION CRT/ATx

The CRT functionality of the Stratos CRT-P devices is based on the FDA approved Tupos LV/ATx. Therefore, the data from the OPTION CRT/ATx study supports the effectiveness of CRT. The OPTION CRT/ATx study was conducted on the Tupos LV/ATx, a device that delivers CRT but, in addition, also offers defibrillation therapy (CRT-D).

Study Design

The purpose of the prospective, randomized, multi-center OPTION CRT/ATx study was to demonstrate the safety and effectiveness of the investigational Tupos LV/ATx Cardiac Resynchronization Therapy Defibrillator (CRT-D) in patients with congestive heart failure (CHF) and atrial tachyarrhythmias. Patients in the study group were implanted with a BIOTRONIK Tupos LV/ATx. Patients in the control group were implanted with any legally marketed CRT-D. Patients in both the study and control groups were implanted with a legally marketed left ventricular lead.

* p value is provided for informational purposes to show trends only; clinical significance is not indicated by p values for analyses that were not prespecified.

Primarily, the study evaluates and compares the functional benefits of CRT between the two randomized groups using a composite endpoint consisting of a six-minute walk test (meters walked) and quality of life measurement (assessed using the Minnesota Living with Heart Failure Questionnaire). Relevant measurements were completed twice for each patient: once at the Baseline evaluation (two-week post implant follow-up) and again at a six-month follow-up evaluation. The data collected during this clinical study was used to demonstrate equivalent treatment of CHF in both the study and control groups. This study also evaluated other outcomes including: the percentage of time CRT is delivered, and other measures of CHF status, including NYHA classification, peak oxygen consumption during metabolic exercise testing, and the rate of hospitalization for CHF.

Clinical Inclusion Criteria

To support the objectives of this investigation, patients were required to meet the following inclusion criteria prior to enrollment:

- Stable, symptomatic CHF status
- NYHA Class III or IV congestive heart failure
- Left ventricular ejection fraction $\leq$ 35% (measured within six-months prior to enrollment)
- Intraventricular conduction delay (QRS duration greater than or equal to 130 ms)
- For patients with an existing ICD, optimal and stable CHF drug regimen including ACE-inhibitors and beta-blockers unless contraindicated (stable is defined as changes in dosages less than 50% during the last 30 days)
- Indicated for ICD therapy
- History or significant risk of atrial tachyarrhythmias
- Willing to receive possibly uncomfortable atrial shock therapy for the treatment of atrial tachyarrhythmias
- Able to understand the nature of the study and give informed consent

- Ability to tolerate the surgical procedure required for implantation
- Ability to complete all required testing including the six-minute walk test and cardiopulmonary exercise testing
- Available for follow-up visits on a regular basis at the investigational site
- Age greater than or equal to 18 years

Clinical Exclusion Criteria

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

- Previously implanted CRT device
- ACC/AHA/NASPE indication for bradycardia pacing (sinus node dysfunction)
- Six-minute walk test distance greater than 450 meters
- Chronic atrial tachyarrhythmias refractory to cardioversion shock therapy
- Receiving intermittent, unstable intravenous inotropic drug therapy (patients on stable doses of positive inotropic outpatient therapy for at least one-month are permitted)
- Enrolled in another cardiovascular or pharmacological clinical investigation
- Expected to receive a heart transplant within 6 months
- Life expectancy less than 6 months
- Presence of another life-threatening, underlying illness separate from their cardiac disorder
- Acute myocardial infarction, unstable angina or cardiac revascularization within the last 30 days prior to enrollment
- Conditions that prohibit placement of any of the lead systems

Follow-Up Schedule

After successful enrollment, all patients were randomly assigned to either the study group or the control group. The specific procedures of this study were:

- Pre-enrollment screening
- Randomization
- System implantation
- Pre-discharge follow-up
- Baseline evaluation / CRT activation
- One-Month follow-up
- Three-Month follow-up
- Six-Month follow-up
- Subsequent routine follow-ups (every three months)

Clinical Endpoints

Primary Endpoint 1: Six Minute Walk Test & QOL (Effectiveness)
The purpose of Primary Endpoint 1 is to evaluate the effectiveness of the Tupos LV/ATx system in providing CRT as measured by the average composite rate of improvement in six minute walk test and QOL.

Secondary Endpoint Results

1. The purpose of this secondary endpoint is to evaluate improvement in functional capacity as measured by the six minute walk test. The six minute walk test is a well-accepted measure of functional capacity and exercise tolerance. Also, this test more closely mimics the patient's day-to-day activities than maximal exercise testing.
2. The purpose of this secondary endpoint is to evaluate the improvement in the patient's NYHA classification.

Accountability of PMA Cohorts

After randomization and enrollment, 7 patients (4 in the study group and 3 in the control group) did not receive an implant. The reasons for patients not receiving an implant are outlined in **Figure 2**.

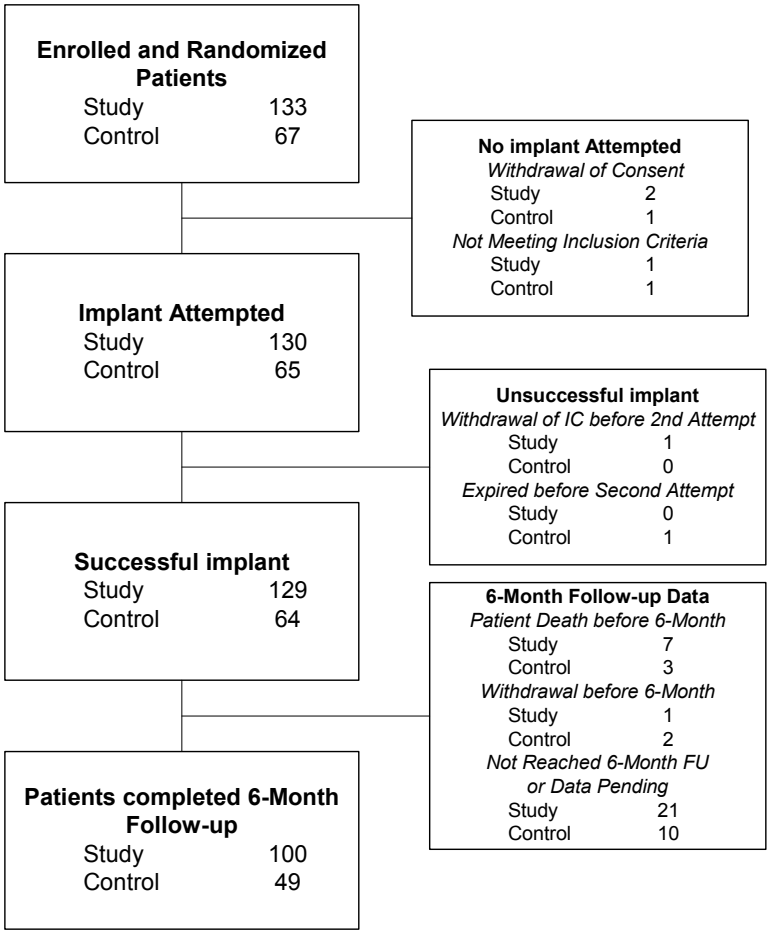


Figure 2: Patient Accountability

Demographics and Baseline Parameters

Table 13 provides a summary of the pre-enrollment demographics of enrolled patients.

Table 13: Patient Demographics at Pre-Enrollment			
Characteristic	**Study N=133**	**Control N=67**	**P-value**
Age at Enrollment (Years)			
Mean ± SE	69.5 ± 0.9	69.1 ± 1.2	0.781*
Range	43 to 88	38 to 84	
Gender			
Male	93 (69.9%)	51 (76.1%)	0.407**
Female	40 (30.1%)	16 (23.9%)	
Underlying Heart Disease			
Ischemic Cardiomyopathy	100 (75.2%)	54 (80.6%)	0.294***
Nonischemic Cardiomyopathy	34 (25.6%)	15 (22.4%)	
Type of Bundle Branch Block			
Left Bundle Branch Block	91 (68.4%)	49 (73.1%)	0.877***
Right Bundle Branch Block	26 (19.5%)	10 (14.9%)	
Other	19 (14.3%)	11 (16.4%)	
New York Heart Association Class			
Class III	121 (91.0%)	60 (89.6%)	0.800**
Class IV	12 (9.0%)	7 (10.4%)	
Intrinsic QRS Duration (ms)			
Mean ± SE	161.9 ± 2.0	156.1 ± 2.3	0.073*
Range	130 to 252	130 to 200	
Left Ventricular Ejection Fraction (%)			
Mean ± SE	22.1 ± 0.6	23.3 ± 0.8	0.255*
Range	5 to 35	10 to 35	
Six Minute Walk Distance (meters)			
Mean ± SE	254.8 ± 8.9	250.5 ± 11.9	0.775*
Range	20 to 451	27 to 447	
Quality of Life Questionnaire Score			
Mean ± SE	54.3 ± 2.1	52.5 ± 3.1	0.638*
Range	0 to 105	0 to 102	

*Student's t-test (2-sided) for means, **Fisher's Exact Test (2-sided) for 2 possible answers, ***Chi-Square test (2-sided) for more than 2 possible answers

Table 14 provides a summary of cardiac medications patients were taking at the time of enrollment. Some categories may be more than 100% as several categories allow more than one response.

Table 14: Cardiac Medications at Pre-Enrollment			
Drug Category	**Study (N=133)**	**Control (N=67)**	**P-value**
Specific CHF Medications			
ACE inhibitors	89 (66.9%)	45 (67.2%)	1.000**
Angiotensin receptor blockers	21 (15.8%)	16 (23.9%)	0.180**
Beta blockers	111 (83.5%)	55 (82.1%)	0.843**
Cardiac glycosides (Digoxin)	60 (45.1%)	35 (52.2%)	0.370**
Diuretic	114 (85.7%)	57 (85.1%)	1.000**
Inotropes	1 (0.8%)	3 (4.5%)	0.110**
Anti-arrhythmics	34 (25.6%)	19 (28.4%)	0.735**
Nitrates	36 (27.1%)	14 (20.9%)	0.390**

*Student's t-test (2-sided) for means, **Fisher's Exact Test (2-sided) for 2 possible answers, ***Chi-Square test (2-sided) for more than 2 possible answers

Safety and Effectiveness Results

A total of 200 patients were enrolled in the OPTION CRT/ATx clinical study at 25 sites:

There were 133 study patients and 67 active control patients in this prospective, multi-center, randomized clinical study. For the study group, there were 129 successful implants (91.4%) of the Tupos LV/ATx CRT-D system. For the active control group, there were 64 successful implants (92.2%) of the legally marketed CRT-D systems.

- There were 192 endocardial and 19 epicardial leads implanted in 193 patients. Investigators were allowed to choose among any legally marketed LV lead according to their familiarity with the lead and patient anatomy. The Tupos LV/ATx CRT-D was implanted with 7 endocardial and 4 epicardial lead models from 6 different manufacturers. There were no adverse events reported attributable to lead-generator incompatibility.
- The cumulative implant duration is 1240.4 months with a mean duration of 9.6 months for the study group. The cumulative implant duration is 596.5 months with a mean duration of 9.3 months for the control group.
- The overall protocol compliance rate is 79.2% in the study group and 85.9% in the control group. The overall follow-up compliance rate is 99.4% in the study group and 98.3% in the control group.
- There have been 10 patient deaths reported in the study group and 4 patient deaths reported in the control group. The clinical investigators have determined that no deaths were related to the study device.

Primary Endpoint 1: Six Minute Walk Test & QOL (Effectiveness)

The purpose of Primary Endpoint 1 is to evaluate the effectiveness of the Tupos LV/ATx system in providing CRT as measured by the average composite rate of improvement in six minute walk test and QOL.

Table 15 presents the average composite rate of improvement in six minute walk test distance and QOL score, the average 6-minute walk test distance and the average QOL score at Baseline and at the Six-Month follow-up, as well as the average difference in 6-minute walk test distance and QOL score between Baseline and the Six-Month follow-up for the Study and Control Groups for those patients with six minute walk test data and complete QOL data at both Baseline and the Six-Month follow-up.

Table 15: Composite of Six Minute Walk Test and QOL (Effectiveness)			
Category	**Study Group (N = 74)** Mean ± SE	**Control Group (N = 38)** Mean ± SE	**P-value***
Distance Walked at Baseline	310.51 ± 10.89	288.76 ± 15.37	0.249
Distance Walked at Six-Months	340.77 ± 12.32	301.84 ± 17.02	0.067
∆ Distance Walked	30.26 ± 10.40 17.27% ± 5.59%	13.08 ± 13.05 8.71% ± 5.26%	0.322 0.326
QOL Score at Baseline	44.39 ± 2.78	45.53 ± 4.13	0.817
QOL Score at Six-Months	28.68 ± 2.66	33.95 ± 4.35	0.279
∆ in QOL Score†	15.72± 2.83 19.08% ± 12.21%	11.58 ± 3.45 -13.42% ± 34.54%	0.376 0.281
Composite Rate‡	**18.18% ± 7.07%**	**-2.36% ± 17.73%**	**0.030**

* The calculated p-values are associated with a Student's t-test (2-sided) of the equality of means in the two groups, except for the p-value of the composite rate, which is associated with a test of equivalence (non-inferiority).

† ∆ in QOL Score is calculated as the average of the individual differences between Baseline and Six-Months for each patient. Negative values for mean ∆ QOL in percent are possible when positive mean values for absolute changes in QOL are recorded. In some cases, small, negative changes in absolute QOL scores resulted in relatively large percentage changes.

‡ The Composite Rate (=(∆ Distance Walked (%) + ∆ QOL Score (%)) / 2) is calculated for each patient and then averaged to obtain the Composite Rates. For all calculations, a positive number represents improvement from Baseline to Six-Months.

Primary Effectiveness Endpoint Analysis and Conclusions

A composite rate of six minute walk test and QOL improvement from Baseline to the Six-Month follow-up is evaluated as a measure of CRT effectiveness. For this analysis both six minute walk test and QOL are equally weighted at 50%.

The mean difference in the composite rate between study and control group was 20.53% with an associated one-sided, 95% confidence bound of (-6.10%). The p-value for non-inferiority within 10% is 0.030. The analysis of the composite rate in six minute walk test distance and QOL score demonstrates that the study group is non-inferior to the control group and that the primary effectiveness endpoint was met (p=0.030).

Secondary Endpoint Results

1. The purpose of this secondary endpoint is to evaluate improvement in functional capacity as measured by the six minute walk test. The six minute walk test is a well-accepted measure of functional capacity and exercise tolerance. Also, this test more closely mimics the patient's day-to-day activities than maximal exercise testing.

   Table 16 summarizes the six minute walk test distance at Baseline and the Six-Month follow-up for patients in the study group and the control group.

Table 16: Six Minute Walk Distance

Distance (meters)	**Study**	**Control**
Baseline		
N	127	61
Mean ± SE	283.14 ± 9.27	269.43 ± 13.77
Range	23 to 511	29 to 507
Median	302.00	244.00
Six-Month		
N	93	44
Mean ± SE	329.73 ± 10.82	310.70 ± 15.49
Range	78 to 596	91 to 489
Median	335.00	313.00

* Student's t-test, 2-sided

There are no clinically relevant differences in the six minute walk test results between the study and the control group.

2. The purpose of this secondary endpoint is to evaluate the improvement in the patient's NYHA classification. Table 17 summarizes the average improvement in NYHA from Baseline to Six-Months for 140 patients that were able to complete both NYHA classification evaluations.

Table 17: Improvement in NYHA Classification at Six-Months from Baseline

Change in NYHA class	Study (N=97)		Control (N=43)	
	Number of Patients	% of Total Patients	Number of Patients	% of Total Patients
Improved 2 classes	10	10.3%	2	4.7%
Improved 1 class	47	48.5%	20	46.5%
Total improved	57	58.8%	23	51.2%
No change	39	40.2%	20	46.5%
Worsened 1 class	1	1.0%	1	2.3%

The study and the control group have similar NYHA classes and similar rates of improvement in NYHA class from Baseline to the Six-Month follow-up.

Multi-site Poolability and Gender Analysis

The OPTION CRT/ATx clinical report includes data from multiple centers with centralized coordination, data processing, and reporting at BIOTRONIK. All of the clinical centers followed the requirements of an identical clinical protocol, and all of the clinical centers used the same methods to collect and report the clinical data. In order to justify pooling of the data from multiple centers, several analyses were completed. All of the centers were divided into two groups based on implant volume. Comparisons were then made between the patient populations based on the results of each of the endpoints. Additionally, analyses were performed on the data collected in the OPTION CRT/ATx clinical investigation in order to compare results between males and females. The first type of analysis compared enrollment by patient gender in each of the study and control groups. The second type of analysis compared effectiveness outcomes in each gender.

The results of these analyses demonstrate poolability of the data between sites. There were no significant differences in the second primary endpoint or any of the secondary endpoints between high and low volume implant centers.

The gender distribution in this clinical investigation is consistent within the study groups and includes a representative proportion of enrolled female participants (28.0% versus 72.0% male). There were no significant differences in any of the primary or secondary endpoints between the male and female population.

1.7.5 Conclusions Drawn from Studies

The clinical study results support the safety and effectiveness of the Stratos LV CRT-P device.

- The OPTION CRT/ATx clinical study completed and reviewed under P050023 provided a reasonable assurance that bi-ventricular pacing is effective in NYHA class III/IV heart failure patients with a prolonged QRS and a left ventricular ejection fraction <35%. The addition of ICD back-up therapy does not affect the biventricular pacing performance of the device.
- The AVAIL CLS/CRT and Corox (OVID) clinical studies demonstrated the safety of the Stratos LV CRT-P in NYHA class III/IV heart failure patients with a prolonged QRS and a left ventricular ejection fraction <35%.(OVID).

2. Programmable Parameters

For a complete list of programmable parameters and the available settings for the Stratos CRT-Ps, see Section 11.

2.1 Pacing Modes

For a complete list of pacing modes available in each Stratos CRT-P configuration, see Section 11.1.

2.1.1 Rate-adaptive Modes

The rate-adaptive modes are designated with an "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 (i.e., DDDR, DDIR, DVIR, VDDR, VVIR, AAIR), it is possible that the atrial and/or ventricular refractory period can comprise a major portion of the basic interval at high sensor-modulated rates. This may limit the detection of spontaneous events or even exclude their recognition altogether.

WARNING

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

2.1.2 DDD

The timing of the Stratos CRT-Ps is based on atrial events.

In the case of an atrial sensed or paced event, the AV delay starts the same time as the basic interval. If a ventricular sensed event does not occur within the AV delay, ventricular pacing is initiated at the end of the AV delay. If ventricular sensing occurs within the AV delay, ventricular pacing is inhibited.

If atrial sensing occurs outside the atrial refractory period, atrial pacing is inhibited and the basic interval is restarted.

In the case of ventricular sensed events outside of the AV delay and the VES discrimination interval after a ventricular extrasystole (VES or PVC), the basic interval starts without simultaneously starting an AV delay. To protect the atrium from retrograde conduction, an extended PMT protection window is started at the same time as the basic interval. If an atrial sensed event does not occur within the basic interval (but outside the refractory period), atrial pacing occurs after the basic interval has elapsed, and the basic interval and AV delay are restarted. Upon an atrial paced event, the AV safety interval starts with a long basic interval. If a ventricular sensed event occurs within the AV delay, ventricular pacing is inhibited.

Table 18 summarizes the intervals initiated by sensing or pacing. The table distinguishes between two kinds of ventricular sensed and ventricular paced events: VP at the end of the AV delay; VP at the end of the safety AV delay, referred to as ventricular safety pace (V_{SP}); V_S within the AV delay; and V_S outside of the AV delay, referred to as “ventricular extrasystole” (VES).

Table 18: Timing Intervals

Timing Interval	Event						
	Ap	As	As (PMT)	Vp	Vsp	VS	VES
Basic interval (DDD)*	X	X					X
Basic interval (DDI)†				X		X	X
Atrial refractory period‡	X	X	X				
Upper basic rate				X	X	X	X
Ventricular Refractory Period				X	X	X	X

* This timing interval is also applicable to the following modes: DDD(R), VDD(R), AAI(R), DDT, VDT, AAT, DOO(R) and AOO(R)

† In DDI(R), DVI(R), VVI(R), DVT(R), DDI/T(R) and V00(R) lower rate timing starts with Vp, and/or Vs, and/or Vs event outside of the AV delay and the VES discrimination window (VES).

‡ In DDI(R), DDI/T, VDD(R), and VDT, the atrial refractory period will also be reset upon time-out of the VA-interval whether or not an atrial pulse is emitted.

Table 18: Timing Intervals							
Timing Interval	**Event**						
	Ap	**As**	**As (PMT)**	**Vp**	**Vsp**	**VS**	**VES**
AV delay	X	X					
Safety AV delay	X						
Interference interval (A)		X	X				
Interference interval (V)						X	X
Blanking time (A) after Ap	X						
Blanking time (V) after RVp				X	X		
Atrial upper rate (AUR)			X				
Far-field Protection (A)				X	X	X	X
PMT Protection (A)				X	X		X
PMT protection extension (A)							X

Trigger Pacing

The triggered pacing modes are identical to the respective demand modes except that the sensing of an atrial/ventricular event outside of the refractory period does not result in inhibition of pacing, but instead a pacing pulse is delivered in the respective chamber.

The corresponding pacing modes are:

Demand Pacing	DDD	VDD	DDI	DVI	AAI	VVI
Triggered pacing	DDT	VDT	DDI/T	DVT	AAT	VVT

However, the following differences exist. There is no AV safety interval in DDT, DDI/T and DVT pacing modes. The safety interval is unnecessary as “cross talk” (ventricular sensing of atrial pulses) can not occur during these modes.

In the DDI/T and DVT pacing modes, the basic interval is not restarted if ventricular sensing occurs within the AV delay.

CAUTION

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

Triggered Modes – While the triggered modes (DDT, DVT, DDTR/A, DDTR/V, DDI/T, VDT, VVT, and AAT) can be programmed permanently, these modes are intended for use as temporary programming for diagnostic purposes. In triggered pacing modes, pacing pulses are emitted in response to sensed signals, and therefore the pacing pulse can be used as an indicator, or marker of sensed events for evaluating the sensing function of the pulse generator using surface ECG. However, real-time telemetry of marker channels and/or intracardiac electrogram via the programmer and programming wand is recommended over the use of a triggered pacing mode in the clinical setting. A triggered pacing mode may be preferred in situations where positioning the programming head over the pulse generator would be impossible or impractical (i.e., during exercise testing or extended Holter monitoring).

Another possible application of triggered modes is to ensure pacing as a short term solution during a period of inhibition of pacing by extracardiac interference, mechanical noise signals, or other sensing abnormalities. Because triggered modes emit pacing pulses in response to sensed events, this may result in unnecessary pacing during the absolute refractory period of the myocardium, inappropriate pacing in response to oversensing of cardiac or extracardiac signals. The risks associated with triggered pacing include excessive pacing, arrhythmias due to the R-on-T phenomenon, and early battery depletion. Therefore, it is important that the triggered modes are not used for long term therapy, and that the CRT-P is always returned to a non-triggered permanent program.

2.1.3 DDI

In contrast to DDD mode, the basic interval in the DDI mode is not restarted by sensed P-waves, but by ventricular sensed or paced events. The VA delay is started together with the basic interval. If atrial or ventricular sensing does not occur during the VA delay, the atrial pacing occurs at the end of the VA delay.

Atrial pacing starts the AV delay. If atrial sensing occurs outside of the atrial refractory period (ARP), a PMT safety interval or the FFP (far-field protection) window, atrial pacing is inhibited. However, the AV delay does not start with a sense event, but at the end of the VA interval. Therefore, P-waves in the DDI mode do not trigger ventricular events.

NOTE:

For additional information on far-field protection window, see Section 2.3 “Timing Functions”.

An atrial sensed event that occurs during the PMT protection window starts the atrial upper basic rate to avoid pacing during the vulnerable phase of the atrium. If the interval of the atrial upper rate is longer than the basic interval, the AV delay is shortened by that same amount after atrial pacing, but only until the end of the safety interval.

2.1.4 DVI

The DVI mode is derived from the DDI mode. In contrast to the latter, atrial sensing does occur. Therefore, atrial pacing is delivered at the end of the AV delay. Ventricular sensing within the AV delay inhibits atrial and ventricular pacing. Ventricular sensing within the AV delay inhibits ventricular pacing.

2.1.5 VDD

The VDD mode corresponds to the DDD mode with the exception that it does not provide atrial pacing. In the absence of a sense event, the basic interval starts with either an atrial sense event, a ventricular extrasystole or after expiration of the preceding basic interval.

2.1.6 AAI and VVI

The pacing modes AAI and VVI provide atrial and ventricular demand pacing. The lower rate timer is started by a sense or pace event. A sense event outside of the refractory period inhibits pacing and resets the lower rate timer; in the absence of a sense event, a pulse generator pulse will be emitted at the end of the lower rate interval.

2.1.7 AAI, VVI

The AAI and VVI single-chamber pacing modes are used in atrial and demand pacing. In each case, pacing and sensing only occur in the atrium (AAI) or the ventricle (VVI).

The basic interval is started by a sense or pace event. If the sense event occurs before the basic interval has expired, pacing is inhibited. Otherwise, pacing occurs at the end of the basic interval.

2.1.8 AOO, VOO

In these modes, atrial, ventricular and AV sequential pulses, respectively, are emitted asynchronously. These modes primarily serve diagnostic purposes during follow-up. When programming to the VOO or VOO mode, the risks associated with asynchronous ventricular pacing should be considered.

2.1.9 DOO

Asynchronous, AV sequential pacing pulses are emitted in this pacing mode. When programming DOO mode, the risks of asynchronous ventricular pacing should be considered.

2.1.10 VDI

The VDI mode corresponds to the VVI mode, with the additional function of providing atrial sensing. However, the timing is the same as the VVI mode. The purpose of the VDI mode is to permit the use of the marker function with the IEGM for the atrial channel, for example, to measure the retrograde conduction time.

The VA conduction time between a ventricular pace or sense event (with marker) and the atrial sense event can be measured directly on the display or printout from the programmer or on an ECG strip chart recorder (IEGM/marker output function).

2.1.11 OFF (ODO)

In this mode, pacing and sensing functions are off. The OFF mode is used to determine and evaluate the morphology of an intrinsic rhythm. With external pulse control, the OFF mode is used for electrophysiological studies. The OFF mode can be programmed temporarily.

CAUTION

OFF Mode – The OFF mode can be transmitted as a temporary program only to permit evaluation of the patient's spontaneous rhythm. (see Section 2.1.11).

2.2 Biventricular Synchronization of the Stratos CRT-Ps

For the Stratos CRT-Ps, there are 2 possible settings for the BiV Sync parameter: OFF and BiV RV RV-T.

OFF - If the BiV sync parameter is set to OFF, the CRT-P ignores the left-ventricular channel and functions like a conventional dual-chamber pacemaker. Consequently, pacing is not delivered into the left ventricle.

BiV RV RV-T - When set to "BiV RV RV-T" the device provides biventricular pacing with sensing in the right ventricle and triggering of a right ventricular sensing event in the left ventricle.

The biventricular synch settings can be activated together with the DDD(R), DDI(R), VDD(R), and VVI(R) pacing modes.

CAUTION

Sensing – The Stratos CRT-Ps do not sense in the left ventricle.

AV Conduction – In patients with intact AV conduction, the intrinsic atrial tachycardia is conducted to the ventricle 1:1. With the resynchronization mode activated, spontaneous rate of the right ventricle mode is synchronized for a rate up to 200 ppm in the left ventricle. For this reason, biventricular pacing mode should be turned OFF in such cases.

During biventricular pacing in the Stratos CRT-Ps, the right ventricle is paced first. Starting from the initially paced chamber (RV), the intraventricular conduction time (VV delay) is permanently set to 5 ms after a right ventricular sensed or paced event.

NOTE:

While ventricular pacing and sensing events are synchronized, synchronization does not occur during ventricular extrasystoles.

The following table presents in detail the effects of the standard pacing modes with the biventricular modes:

Table 19. Biventricular Pacing Modes

	Biventricular Pacing Modes (BiV RV RV/T)								
	DDD	VDD	DDI	VDI	VVI	DDD	VDD	DDI	VDI
RVs inhibits RVp	X	X	X	X	X	X	X	X	X
RVs triggers LVp	X	X	X	X	X	X	X	X	X

2.3 Timing Functions

The availability of parameters and parameter values is determined by the software used for programming / interrogating the CRT-Ps.

2.3.1 Basic Rate

The basic rate is the pacing rate in the absence of an intrinsic rhythm and is programmable up to 180 ppm. The interval for the basic rate is the time between two pacing pulses and is thus called the basic interval.

The basic rate is programmable:

32… (1)…60… (1)…88… (2)…122… (3)…140… (5)…180 ppm.

In atrial-controlled modes, the basic interval is started by an atrial event. In atrial-controlled, dual-chamber modes, the basic interval is also started by a ventricular extrasystole.

In the ventricular-controlled modes, the basic interval is started by a ventricular event.

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.

2.3.2 Rate Hysteresis

Rate Hysteresis can be programmed in DDD(R), DDT(R), DDT(R)/A, DDI(R), VDD(R), VDT(R), VDI(R), VVI(R), VVT(R), AAI(R) and AAT(R) modes. Hysteresis can be programmed OFF or to values as low as -50 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 intrinsic rhythm. The Stratos CRT-Ps operate 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.

In DDD(R), DDT(R)/A, DDT(R), VDD(R), VDT(R), AAT(R) and AAI(R) pacing modes, the hysteresis interval starts with an atrial sense event. In DDI(R), VVI(R), VVT(R) and VDI(R) pacing modes, the hysteresis interval starts with a ventricular sense event. In DDD(R), DDT(R)/A, DDT(R), VDD(R) and VDT(R) pacing modes, the hysteresis interval also starts with ventricular extrasystoles.

NOTE:

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

The rate hysteresis is deactivated in the standard setting, but can be programmed from -5… (-5) … -90.

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

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

2.3.3 Scan Hysteresis

Scan hysteresis is expanded programmability of the Hysteresis feature. Scan hysteresis searches for an underlying intrinsic cardiac rhythm, which exists slightly below the programmed lower rate (or sensor-indicated rate) of the CRT-P. 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 CRT-P inhibits pacing.

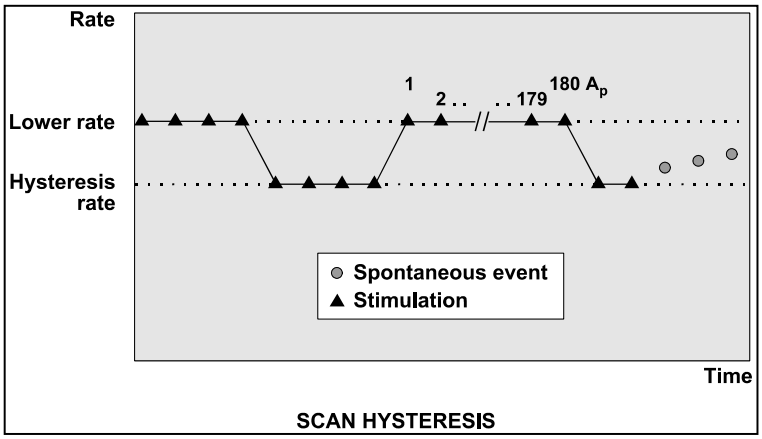


Figure 3. Scan Hysteresis

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

The number of scan interval is programmable, OFF, 1…(1)…15 cycles.

NOTES:

Scan Hysteresis is not active during the programmed Night Mode.

Scan Hysteresis is only available when Hysteresis is selected on.

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

2.3.4 Repetitive Hysteresis

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

If an intrinsic cardiac rhythm is detected within the programmed number of beats between the hysteresis rate and the lower rate, the intrinsic rhythm is allowed and inhibits pacing by the CRT-P.

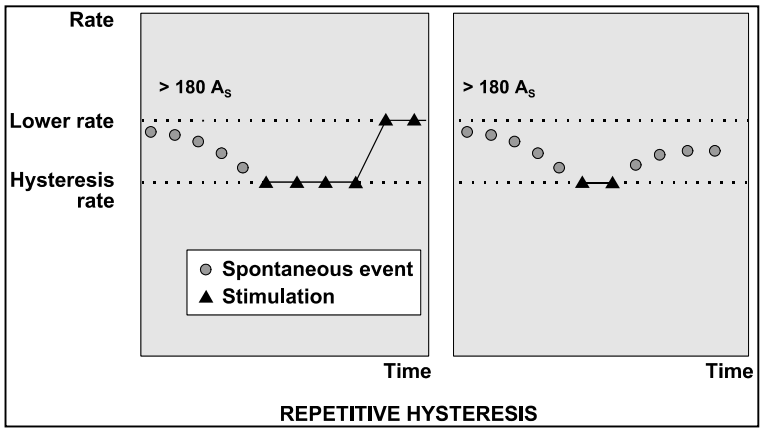


Figure 4. Repetitive Hysteresis

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

NOTES:

Repetitive Hysteresis is not active during the programmed Night Mode.

Repetitive Hysteresis is only available when Hysteresis is selected on.
Magnet application (closing of reed switch) suspends 180 consecutive event counter independent of synchronous or asynchronous magnet effect.
There is one Standard Hysteresis interval which occurs before the programmable number of Repetitive Hysteresis occurs.
The repetitive rate hysteresis is deactivated in the standard setting, but can be programmed to 1… (1) …15 cycles.

2.3.5 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 patients spontaneous night rhythm and may reduce pulse generator energy consumption.

NOTES:

Over time, the Stratos CRT-Ps internal time-of-day clock may exhibit a discrepancy with the actual time (less than 1 hour per year). This may cause a corresponding discrepancy between the programmed sleep and wake times and the actual times that the system changes the rate.
The programmer automatically updates the CRT-P time-of-day clock each time the device 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 device timing.
The rate (ppm/s) at which Night Mode decreases and increases is a function of the Sensor Gain decrease and increase parameters.

2.3.6 Refractory Periods

Sensed events that occur during the refractory period have no effect on pacemaker timing. These atrial or ventricular sensed events are classified as "unused" for normal CRT-P timing.

In the Stratos CRT-Ps, the total atrial refractory period has been subdivided into an atrial refractory period (ARP), atrial far-field protection (FFP) and a PMT protection window (PMT). In terms of priority FFP is first, ARP second and PMT third.

When mode switching is turned ON, the atrial events in the atrial refractory period and the PMT protection window are used as the criteria in order to sense atrial tachyarrhythmias and to ensure high atrial rates are not transmitted to the ventricle.

The behavior of BIOTRONIK CRT-Ps reacts differently depending on the timing interval in which the atrial event occurs. The behavior is summarized in Table 20.

Table 20. Response to Atrial Sense Events in Different Timing Intervals in Stratos CRT-Ps

Timing Interval	Response
A_s occurs during the far-field protection (FFP)	No consequence. A_s is ignored (unused). Neither the AV delay nor the ARP is started. There is no influence on mode switching.
A_s occurs during the Atrial Refractory Period (ARP)	The event influences mode switching.
A_s occurs in the PMT protection window	The AUI (atrial upper interval) starts. The AV delay is not restarted. Post-AES pacing is started if the atrial sense is classified as an AES.

2.3.6.1 Atrial Refractory Period

In all modes in which atrial depolarization can be sensed, the Stratos CRT-Ps will start an atrial refractory period upon each atrial depolarization (programmable: AUTO, 225…(25)…775). In standard "Auto" setting, the atrial refractory period (ARP) is automatically preset to a minimum value of 225 ms and is automatically extended if the AV delay is longer.

In the case an atrial sense event falls within the PMT protection window, the Stratos CRT-Ps start a minimal ARP.

2.3.6.2 Atrial Far-Field Protection

In all dual chamber modes with atrial sensing, the Stratos CRT-Ps start an atrial FFP window upon each ventricular event to prevent sensing of far-field potentials in the ventricle. The atrial far-field protection window is separately programmable for ventricular sensed events at 30…(10)…100…(1)…200 ms and for ventricular paced events at 30…(10)…100 and 100…(10)…220 ms. If an atrial event occurs during the FFP window, the atrial event is classified as an invalid FFP event and has no influence on the timing of the CRT-P.

With ventricular events (right ventricular sensed or paced, left ventricular paced, VES), the Stratos CRT-Ps start an FFP interval.

2.3.7 Atrial PMT Protection

In all atrial-controlled dual-chamber modes, Stratos CRT-Ps start the PMT protection interval after each ventricular stimulus. This prevents retrograde conduction and triggering of pacemaker-mediated tachycardias (PMTs). Right ventricular extrasystoles begin an extended PMT interval.

In all dual-chamber modes controlled by the ventricle, the Stratos CRT-Ps start the PMT protection interval after each initial (right or left) ventricular event.

The PMT protection interval after a Vp is freely programmable, while the PMT interval after VES is automatically set to 225 ms greater than the PMT interval after Vp (Nominal value: 250 ms/ AUTO (175…(5)…600 ms).

If an atrial event occurs within the atrial PMT protection interval, the atrial event is classified such that the AV delay is not restarted.

In the Stratos CRT-Ps, the PMT protection interval is started with a right or left ventricular paced event.

2.3.8 Ventricular Refractory Period

In all modes in which a ventricular depolarization can be sensed, the Stratos CRT-Ps begin a ventricular refractory period after each ventricular event, using a standard value of 250 ms (programmable as 150…(35)…500 ms).

2.3.9 AV Delay

2.3.9.1 Dynamic AV Delay

Programmable values

Lower AV limit:

Nominal value: 60 ppm, (30…(10)…180 ppm)

Upper AV limit:

Nominal value: 130 ppm, (30…(10)…180 ppm)

AV Interval Length for Low Rate:

Standard value: 150 ms (programmable 15… (5) …300 ms)

The AV delay defines the interval between an atrial paced or sensed event and the ventricular pacing pulse. The AV delay can be dynamically programmed in DDD(R), DDT(R)A and VDD(R) modes. In all other mode the AV delay is a fixed value. If the CRT-P 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). When the dynamic AV delays are programmed, the dynamics are calculated from the difference between two atrial sense events (As or Ap).

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.

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

2.3.9.2 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 OFF or a value range of 10…(10)…1000. 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.

CAUTION

AV Hysteresis – If the AV hysteresis is enabled along with the algorithm for recognizing and terminating PMTs (PMT management), the AV delay for recognizing and terminating a PMT has a higher priority than the AV hysteresis.

2.3.9.3 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. (OFF; 1…(1)…10 cycles). 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.

2.3.9.4 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 (OFF; 1…(1)…10 cycles). If an intrinsic rhythm is detected within the extended AV delay and 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.

2.3.10 VES Discrimination after Atrial Sensed Events

Stratos CRT-Ps have a special timing interval (VES/As) – VES discrimination after atrial sense events to identify ventricular extrasystoles.

With each As, a VES discrimination interval is started in the ventricle. If a ventricular sensed event occurs within the discrimination interval, this event is interpreted as a Vs (ventricular sensed event), and no extended PMT protection interval is started.

In the factory setting, the VES discrimination after As is set to 350 ms (programmable: OFF, 250 …(5)… 450 ms). The VES/As terminates with each ventricular event.

If a ventricular event does not fall within the AV delay or the VES discrimination interval, it is classified as a VES. A ventricular event that is sensed within the VES discrimination interval, but outside the AVE delay, starts a VA delay after which an atrial paced is delivered.

2.3.11 Sense Compensation

For hemodynamic reasons, it is desirable to keep constant time between an atrial and a ventricular contraction such that physiological conditions are attained. To this end, the AV delay after atrial sensing can be shortened by sense compensation. For sense compensation, the values are programmable from OFF, -10…(-10)…-120 ms (standard valued -50 ms). The AV delay after an atrial sensing event is shorter by the programmed value after pacing. The AV delay after atrial pacing then corresponds to the programmed AV delay.

2.3.12 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.

Values between 30 ms and 70ms (30… (10) …70 ms) can be set for the ventricular blanking period. The value should be set as low as possible and yet high enough to ensure ventricular sensing.

However, it must be programmed to ensure atrial pacing is not sensed in the ventricle.

2.3.13 Safety AV Delay

The safety AV delay (set at 100 ms) applies to all dual chamber pacing modes

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 5**). 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).

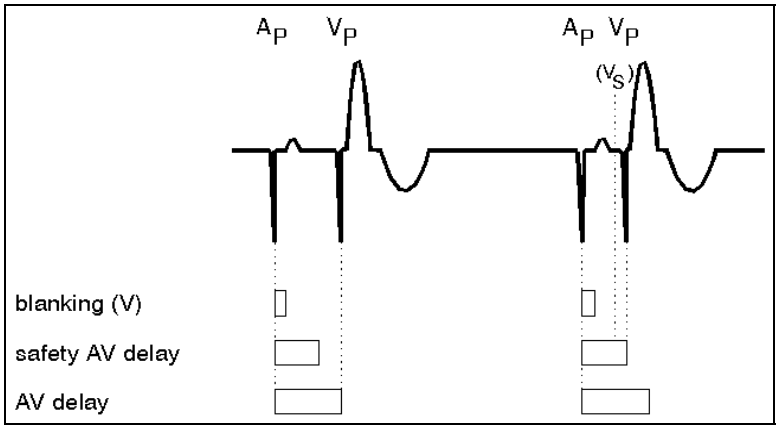


Figure 5. Ventricular blanking time and safety AV

2.4 Pacing and Sensing Functions

2.4.1 Pulse Amplitude and Pulse Width

The pulse amplitude and pulse width can be independently programmed for all three channels of the Stratos CRT-Ps.

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 7.2 volts. The pulse amplitude remains consistent throughout the service life of the CRT-Ps. The pacing safety margin is therefore not reduced by a decrease in the CRT-P's battery voltage.

CAUTION

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

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

2.4.2 Sensitivity

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

If intracardiac signals are of low amplitude, a change to a higher sensitivity (lower value) may be indicated. Conversely, if the sensing amplifier is responding to extraneous signals, such as artifacts or interference, a change to a lower sensitivity (higher value) may resolve the difficulty. In dual chamber sensing modes, the sensitivity values for the atrial and ventricular channels are independently programmable. With Unipolar programming, the highest possible sensitivity setting is 1.0 mV.

2.4.3 Lead Polarity

The programmed lead polarity determines whether the CRT-P senses or paces in a unipolar or bipolar configuration. Lead polarity can be programmed separately for sensing and pacing in all three chambers.

CAUTION

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

The Stratos CRT-Ps have a specially designed header that allows the CRT-Ps to simultaneously sense and pace in both the right and left ventricles. Biventricular pacing therapy requires programming of a bipolar pacing configuration in the ventricle. Refer to Section 8.1 for a summary of the sensing and pacing configurations in the ventricle.

If a bipolar lead is connected to the CRT-P, 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 device pocket or diaphragm.

2.5 Automatic Lead Check

When Lead Check is activated, the lead impedance is automatically measured with every pace. If the impedance values are consecutively greater or less than the limits (<200 Ω and >3000 Ω) for repeated measurements, the system automatically switches from bipolar to a unipolar lead configuration. A bipolar lead failure is verified if the lead impedance measurement falls outside of the acceptable range for three consecutive readings. When a lead failure has been detected, a message is displayed on the programmer screen at the next follow-up visit in order to notify the physician of the change.

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

CAUTION

Lead Check – Lead check will not lead to disabling of cardiac resynchronization therapy. It limits the use of the resynchronization features.

1. Lead check is possible only when the right ventricle is paced first.
2. Lead check works only when the pacing voltages are programmed between 2.4 and 4.8 V. The lead check feature can be programmed OFF in patients that require cardiac resynchronization therapy.

Care should be taken when programming Stratos CRT-Ps with Lead Check ON as the device may switch from bipolar to unipolar pacing and sensing without warning. This situation may be inappropriate when using a Stratos CRT-P for patients with an Implantable Cardioverter Defibrillator (ICD). The following associated message appears when programming this feature:

> "Lead check may result in a switch to unipolar pacing and sensing, which may be inappropriate for patients with an ICD."

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

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

NOTE:

In the Stratos CRT-Ps, an automatic lead check cannot be programmed ON if left ventricular paces are programmed to occur before right ventricular paces.

2.6 Antitachycardia Functions:

The antitachycardia functions include:

- Upper basic rate
- Tachycardia mode
- Tachycardia behavior
- Mode Switching
- PMT Management
- Preventive Overdrive Pacing
- Post-AES Pacing

2.6.1 Upper Rate and UTR Response

In atrial-controlled dual chamber modes, the upper tracking interval (UTI), along with the atrial refractory period or PMT protection window limits the ventricular pacing rate such that it will never exceed the programmed upper rate regardless of the patient's atrial rate.

In all triggered modes, the upper tracking interval limits the pacing rate that is triggered by sensing.

NOTE:

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

2.7 Wenckebach 2:1

Wenckebach behavior or 2:1 behavior is available depending on the programming of the atrial refractory period, the PMT protection window and the upper tracking interval in the modes DDD, DDT/A, VDD, DDT and VDT.

Wenckebach Behavior

If the end of the AV delay falls within the upper threshold rate interval, ventricular pacing occurs at the end of the upper tracking interval.

2:1 Behavior

If the high-rate atrial event occurs in the ARP, the FFP or PMT protection window, an AV delay is not started.

In Wenckebach mode, the CRT-P switches to ventricular timing. This means that a VA delay is started after a ventricular event to avoid the atrial basic interval extend the duration of the Wenckebach mode. The VA delay is calculated from the basic (hysteresis) interval minus the AV delay (or the AV safety interval).

The timing of the Stratos CRT-Ps ensures that the ventricular paced event (Vp) following the VA delay allows atrial pacing at the end of the AV delay; thus, terminating the Wenckebach cycle.

The CRT-P counts the number of Wenckebach cycles. In more than four Wenckebach cycles are detected, a shortened VA delay is started after a right or left ventricular paced event to guarantee constancy of the ventricular rate. The short VA delay is in this instance calculated from the ventricular interval of the upper tacking interval minus the AV delay (or the AV safety interval). If the Wenckebach mode has been terminated, the counter of the CRT-P is reset.

2.8 Mode Switching

Mode switching prevents the conduction of paroxysmal atrial tachycardias to the ventricle. Therefore, after sensing an atrial tachycardia while in activated mode switching, the CRT-P automatically switches to an atrial-controlled R-mode. Like the programmed atrial-controlled P-mode, the corresponding R-modes can be programmed:

Table 21. Mode Switching

Programmed P mode	Programmed R mode in case of sensed atrial tachycardias
DDD	DDI
DDD	DDIR
DDDR	DDIR
VDD	VDI
VDD	VDIR
VDDR	VDIR
DDTA	DDI
DDTA	DDIR
DDTAR	DDIR

The Mode Switching algorithm causes the CRT-P 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…(10)…250 bpm.

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 2 atrial-paced events occur or if no atrial paced or sensed events have occurred for at least 2 seconds. Each occurrence of mode switching resets the corresponding counter (X or Z) to a value of zero.

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

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

Mode Switching is temporarily suspended during magnet application and are inactive during ERI.

2.9 PMT Management

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

2.9.1 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, Stratos CRT-Ps start an atrial PMT protection interval after each ventricular paced event (right or left). If an atrial even 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 175 ms after a Vp, and 400 ms after VES.

2.9.2 PMT Detection

It is the objective of PMT detection to identify ongoing PMTs, to distinguish them from the sinus rhythm and to terminate them. The detection of a PMT starts by measuring the Vp-As intervals. If these lie below the programmable PMT VA criterion (programming depends on the retrograde conduction time of the patient), the measurement of the stability of the Vp-As interval is started.

The Stratos CRT-P's 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 (Vp-As) 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 Vp-As intervals is less than the Stability criterion parameter, defined with respect to upper and lower values is ±25 ms.

Confirmation

When the suspicion criterion has been met, the Stratos CRT-Ps slightly modify the AV delay interval (+ or - 50 ms) for one cardiac cycle. If the Vp-As interval remains stable, a PMT is confirmed. Otherwise, a PMT is not confirmed and the algorithm restarts. Once the PMT algorithm has confirmed a PMT, the cycle is terminated.

The upper interval limit range must be shorter than the limit of the VA delay (350 ms, for example). The test method is based on the length of the pacing interval or the AV delay (refer to Table 22).

Table 22. PMT Test Method

Interval Length	AV Delay	Test Method
> UTI (upper tracking interval)	≤ 200 ms	Increasing the AV delay by 50 ms
> UTI + 50 ms	> 200 ms	Reducing the AV delay by 50 ms
≤ UTI	≤ 200 ms	Increasing the UTI by 50 ms
≤ UTI	> 200 ms	Increasing the UTI by 50 ms
> UTI and ≤ UTI + 50 ms	> 200 ms	Length of UTI = TA + 50 ms

Termination

Stratos CRT-Ps extend TARP (Total Atrial Refractory Period) for one cycle to equal the V-V interval + 50 ms.

2.10 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 two days, the length of the PMT protection interval is reduced by another 50 ms. If additional PMTs occur, the PMT protection interval is increased by another 50 ms. This occurs until no more PMTs are detected. In the absence of PMTs, the PMT protection interval is successively reduced. The initial values of the PMT protection interval in the automatic setting at 175 ms after Vp and 400 ms after VES.

2.11 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 200 ppm (atrial upper interval (AUI), 300 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. To guarantee stability of the ventricular rate, the AV delay is shortened to no less than the safety interval when the basic interval is lengthened.

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.

2.12 Preventive 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 modes DDD(R), DDT/A(R), AAI(R) and AAT(R).

The features of Atrial Overdrive pacing include:

After every atrial sensed event (non-AES), the pacing rate is increased by a programmable rate increase above the last P-P interval (2… (2)…10 ppm). 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 the programmed number of cycles has been completed. Values between 1 and 32 cycles can be assigned to the overdrive pacing plateau.

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

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

- When the programmed maximum overdrive rate (MOR, 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 MOR, 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.

2.13 AES Detection and Pacing

Post atrial extrasystoles (AES) pacing is intended to prevent the occurrence of pro-arrhythmic long-short-long sequences due to an atrial extrasystole, which can lead to atrial tachycardias. This is achieved through a shortened post AES basic interval, which is incrementally lengthened again during subsequent cycles until the basic interval is attained.

The algorithm "Post AES Stimulation" is comprised of two parts. First, an AES must be recognized (AES detection), and secondly, the respective stimulation, Post AES Stimulation, must then occur.

2.13.1 AES Detection

To detect atrial extrasystoles (AES), an "AES (timing) window" is defined, the length of which is calculated from the averaging of the rates of the four paced or intrinsic cardiac events prior to an AES. The AES window is shortened by a programmable percentage (5... (5) ...50%) from the averaged interval (nominal setting is 25%). If an intrinsic atrial event falls within this AES window and the coupling interval <750 ms, the cardiac event is classified as an AES.

2.13.2 Post AES Stimulation

The post AES stimulation (pacing) can be programmed for all atrial-controlled modes (i.e., DDD(R), DDT/A(R), AAI(R) and AAT(R). If an AES is detected, the pacemaker starts a "Post AES Interval". The duration of the post-AES interval is equal to the coupling interval of the Post-AES plus the "decrement step size" (programmable 5 ... (5) ... 40 ppm). After the post AES interval has expired, pacing occurs in the atrium. In each subsequent cycle, the pacing rate is reduced by the value of the "decrement step size" per stimulus until the basic rate (or sensor rate) is again reached, or until the intrinsic cardiac rhythm takes precedence again. The post AES stimulation is then concluded, and it is repeated after each AES. The post-AES interval is never shorter than the Upper Tracking Rate Interval (UTR). Additionally, if the post-AES coupling interval is longer than the current sensor rate, pacing occurs at the sensor rate.

NOTE:

When “preventative overdrive pacing” is activated, post-AES pacing is not automatically activated. Both parameters can be programmed independently of one another.

CAUTION

Post AES - Before activating post-AES, check whether the selected program can cause Pacemaker Mediated Tachycardia (PMT) and whether post-AES pacing results.

2.14 Parameters for Rate-Adaptive Pacing

2.14.1 Rate-Adaptation

The Stratos CRT-Ps are equipped with accelerometers that located within the CRT-P. 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 remain 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.

The following diagnostic functions are available to tailor rate adaptive pacing for the individual patient.

2.14.2 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 (see **Figure 6**).

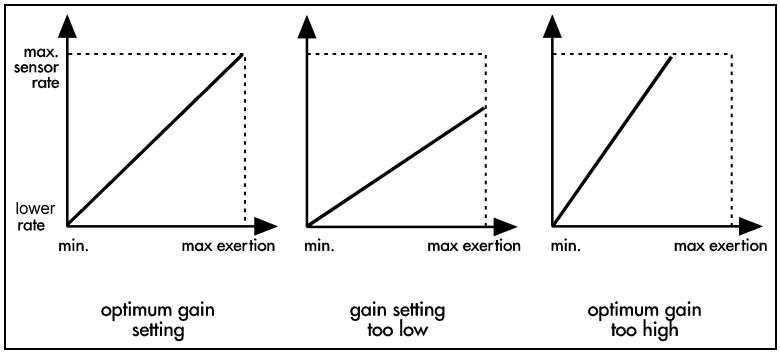


Figure 6 Influence of sensor gain on the rate response.

2.14.3 Automatic Sensor Gain

Stratos CRT-Ps 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 CRT-P samples the sensor-indicated rate. If, during the 24 hour period beginning at midnight, the total time recorded at maximum sensor rate exceeds 90 seconds, the sensor gain setting is reduced by one step. The sensor gain will be increased by one step if for 7 consecutive days; the time recorded at maximum sensor rate is less than 90 seconds each day.

2.14.4 Sensor Threshold

The effects of rate adaptive pacing are limited to sensor signals exceeding the programmable sensor threshold. Sensor signals below this threshold do not affect rate response (**Figure 7**). 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.

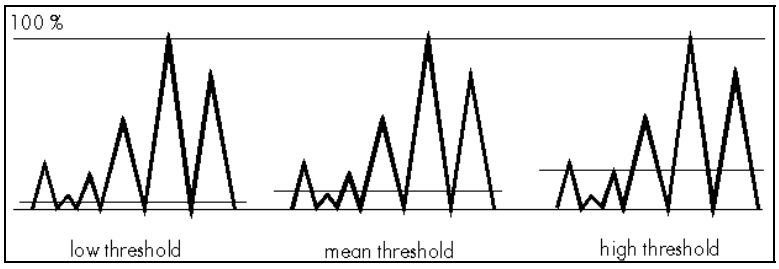


Figure 7 Effect of sensor threshold

2.14.5 Rate Increase

The rate increase parameter determines the maximum rate of change in the pacing rate if the sensor signal indicates increasing exertion.

The “rate attack” is set to standard value of 2 ppm/cycle and is programmable (0.5; 1… (1)…6 ppm/cycle).

The programmed rate increase applies only to the sensor-controlled operation and does not affect the rate changes during atrial-controlled ventricular pacing.

2.14.6 Maximum Activity Rate

Regardless of the sensor signal amplitude, the pacing rate during sensor-driven operation will never exceed the programmed maximum activity rate (MAR). The maximum activity rate only limits the pacing rate during sensor-driven operation and is independent of the rate limit. The rate increase and rate decrease parameters are upper rate limited by the MAR and lower rate limited by the basic rate (night rate) (MAR, standard setting 120 ppm, programmable: 90 ppm… (5) …180 ppm).

The pacing rate is determined by the highest rate from the parameters of rate adaptation, the overdrive rate and the post-AES rate.

2.14.7 Rate Decay

The “rate decay” is set to a standard value of 0.5 ppm/cycle and is programmable (0.25… (0.25)…1.25 ppm/cycle).

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

2.15 Sensor Stimulation

Even when a non-rate adaptive mode is programmed, the behavior of the sensor is recorded if a rate-adaptive mode has been selected in the Mode Switching mode. The rate-adaptive mode is only effective in Mode Switching. The sensor stimulation indicates how a sensor would have reacted with the displayed sensor setting if a rate-adaptive mode had been programmed.

This function is helpful to find the optimum sensor settings and to compare the sensor rate with the intrinsic rate. When rate adaptation is activated, sensor data are available that can be used to evaluate the sensor behavior.

NOTE:

In the sensor stimulation, only values for the sensor threshold that are greater than those used for the permanent program maybe selected.

2.16 Rate Fading

Rate Fading is intended to prevent a sudden drop in heart rate when the Stratos CRT-Ps transition from tracking an intrinsic rhythm to pacing due to an abrupt decrease in the intrinsic rate or due to Mode Switching. This smooth drop in pacing rate is designed to prevent symptoms such as dizziness, light headedness, lack of energy and fainting spells. With Rate Fading enabled, the Stratos CRT-Ps calculate a "Backup Rate" that is always active in the background. As soon as the rate decreases, the CRT-P begins pacing at the Backup Rate. The Backup Rate corresponds to a delay of the intrinsic rate corresponding to a programmable rate increase and programmable rate decrease; these parameters determine the sensitivity of the controlled rate smoothing. After four consecutive intrinsic events (A_s – A_s), the CRT-P calculates the Target Rate for the "Backup Rate", which is a four beat average of the intrinsic rate reduced by 10 ppm. The Target Rate cannot exceed the Maximum Fading Rate (programmed as Max Activity Rate) and cannot increase faster than the RF Rate Increase (programmable in ppm/cycle).

When the intrinsic rate drops considerably (below the Target Rate), the pacing rate drops to the Backup Rate and is then decreased gradually by the programmable Decay Rate to the Sensor Indicated Rate or Basic Rate. The Backup and Target Rates are defined in **Table 23**.

If an atrial tachycardia occurs suddenly, triggering a mode switch, the target rate is set to the sensor rate or basic rate. The current pacing rate in the ventricle results from the current value of the Target rate before the mode switching event.

If the pacing rate reaches the intrinsic rate during rate decay, at least four consecutive intrinsic cycles above the pacing rate are required before the pacing rate is once again adapted to the last intrinsic event. Controlled rate smoothing is thereby continued during intermittent sensed events.

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

Table 23. Backup and Target Rates	
Feature	**Description**
Backup Rate	Rate that the CRT-P uses to pace when there is a sudden rate decrease. This can be a maximum of 10 ppm less than the intrinsic rate and follows the Target Rate with a 1 to 6 ppm per cycle increase or 0.25…1.25 ppm per cycle If the Target Rate is less than the current Back Up Rate.
Target Rate	The Target Rate is either the current detection rate minus 10 ppm, or the sensor or basic rate. The Backup Rate follows the Target Rate with the programmed rate increase or decrease.

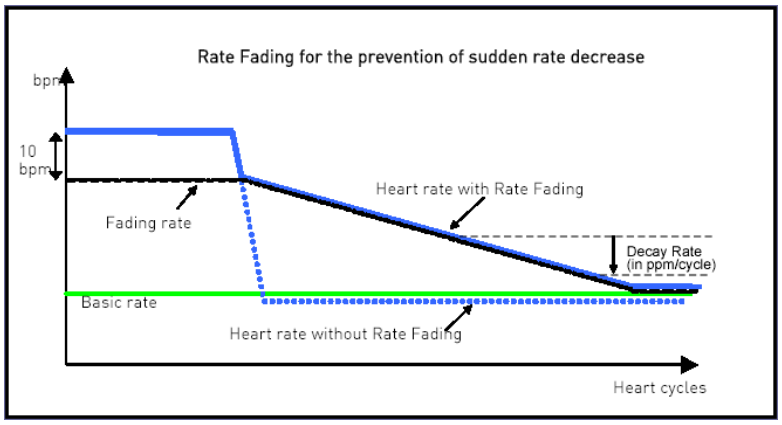


Figure 8: Rate Fading

2.17 Home Monitoring (Stratos LV-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.

CAUTION

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 Stratos CRT-Ps are provided in Section 1.5.6. 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).

Event Triggered Report - A timely receipt of the event report cannot be guaranteed. The receipt is also dependent on whether the patient was physically situated in the required coverage range of the patient device at the time the event information was sent.

CAUTION

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

Not for Conclusive Diagnosis - Because not all information available in the implant is being transmitted, the data transmitted by Home Monitoring should be evaluated in conjunction with other clinical indicators (i.e., in-office follow-up, patient symptoms, etc.) in order to make a proper diagnosis.

Frequency of Office Follow-Ups When Using Home Monitoring - The use of Home Monitoring does not replace regular follow-up examinations. When using Home Monitoring, the time period between follow-up visits may not be extended.

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

NOTE:

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

2.17.1 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 transmissions may also be activated by the patient with the application of a magnet over the implant and by certain cardiac events, as programmed. The types of transmissions are discussed in Section 2.17.4.

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

2.17.2 Patient Device

The patient device (**Figure 9**) 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.

2.17.3 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 24**. Additionally, **Table 24** provides system specifications that are recommended for optimizing usage of the Internet.

Table 24: System Requirements / Recommendations		
	System Requirements	**System Recommendations (for Optimal Usage)**
Screen Resolution	800 x 600	≥ 1024 x 768
Internet Bandwidth	56 kB/sec	≥ 128 kB/sec (DSL, cable modem)
PC	600 MHz, 128 MB RAM	N/A
Internet Browser	MS Internet Explorer 5.0 - or - Netscape Navigator 4.72	≥ MS Internet Explorer 5.5 - or - ≥ Netscape 7/Mozilla
Acrobat Reader	Version 4	Version 5 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 9: Example of Patient Device with Charging Stand

2.17.4 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
- Patient report – the patient initiates the report

2.17.4.1 Trend Report

The time of the report transmission is programmable. For periodic messages, the time can be set anywhere between 0:00 and 23:50 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.

2.17.4.2 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".

The following cardiac and technical events initiate a message transmission:

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

CAUTION

Event Triggered Report - A timely receipt of the event report cannot be guaranteed. The receipt is also dependent on whether the patient was physically situated in the required coverage range of the patient device at the time the event information was sent.

*) Examples: The programmed sensitivity is 1.0 mV.
A) Average of the measured P/R-Wave amplitudes is 2.6 mV. Therefore, measured value is greater than 100% of the safety margin. Event report is not triggered.
B) Average of the measured P/R-Wave amplitudes is 1.9 mV. Therefore, measured value is less than 100%, but greater than 50% of the safety margin. Event report is not triggered.
C) Average of the measured P/R-Wave amplitudes is 1.4 mV. Therefore, measured value is smaller than 50% of the safety margin. As a result, an event report is triggered.

NOTE:

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

2.17.4.3 Patient Report

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

CAUTION

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

2.17.5 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

Type of Last Home Monitoring Message and Time of the Transmission of the last Home Monitoring Message provide information regarding the interval of Home Monitoring data.

Resynchronization Therapy

- % Pacing in the Atrium / 24 hours [%]
- Atrial intrinsic rhythm [%]
- CRT - %ventricular pacing [%]
- Ventricular paces (AV Delay expired) [%]
- Ventricular paces (triggered by RV Sense) [%]

Heart Failure Diagnostics

- Mean Ventricular Heart Rate [ppm]
- Mean Ventricular Heart Rate at Rest [ppm]
- VES / 24 Hour
- Daily Activity (hours)
- Number of Mode Switches / 24 hours
- Duration of Mode Switching / 24 hours [%]

Ventricular Rhythm

- Mean Ventricular Rate at Mode Switching [ppm]
- Number of Ventricular Episodes (>8 consecutive VES)
- Number of Ventricular Runs (4…8 consecutive VES)
- PMTs Detected

AV Conduction

- With Intrinsic Rhythm (As-Vs) [%]
- With Atrial Stimulation (Ap-Vs) [%]
- With Ventricular Stimulation (As-Vp) [%]
- With Atrial and Ventricular Stimulation (Ap-Vp) [%]

Leads

- Mean P-Wave amplitude [mV]
- Mean R-Wave amplitude [mV]
- Atrial Pacing Impedance [ohms]
- Right Ventricular Pacing Impedance [ohms]
- Left Ventricular Pacing Impedance [ohms]

System Status

- Battery Voltage [V]
- Battery Impedance [ohms]
- Battery Status

2.18 Statistics

Stratos CRT-Ps 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.

2.18.1 Timing

- Event Counters
- Event Episodes
- A / V Rate Histogram
- A / V Rate Trend

2.18.2 Arrhythmia

- Tachy Episode Trend
- AF Classification
- AES Classification
- AES vs. Atrial Rate
- VES Classification
- VES versus ventricular rate
- VES Coupling Intervals

2.18.3 Sensor

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

2.18.4 Sensing

- P-wave Trends
- R-wave Trends

2.18.5 Pacing

- A / V Impedance Trends

2.18.6 General Statistical Information

- The Stratos CRT-P's 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 CRT-Ps
- The counters within the statistic features are reset each time the Stratos CRT-Ps are permanently programmed.
- Event counters are displayed as bar charts showing the event totals expressed as a percentage.
- Histograms count how often events occur in different time or rate intervals (for example, how many events occurred in a 160 to 169 ppm range).
- Trends represent a certain number of events at a fixed point in time (e.g., rates). The trends are plotted as points that are joined together by a curve. In the Stratos CRT-Ps, the trends of the three different channels are identified with different colors.

NOTE:

When a magnet is applied, Stratos CRT-Ps can only continue recording diagnostic data when in the "synchronous magnet mode or during the first 10 cycles of the "auto" magnet mode.

2.19 Interrogating and/or Starting Statistics

The recorded diagnostic data (saved data contents of the pacemaker) are always read (transmitted through interrogation) at the beginning of the follow-up and saved to the programmer. This allows relevant data to be displayed on the programmer at anytime.

All statistics can be reset with the "Clear Statistics" function and the "Transmit" function in the "Parameter" selection menu. The start time and duration are automatically saved for all statistics.

2.20 Timing Statistics

2.20.1 Event Counter

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

- Atrial: detection (As), detection during ARP (ARS), FFP (As_FFP), and the PMT window (As_PMT), pacing (Ap)
- Ventricular: RV sensing, RV pacing and LV pacing
- Ventricular extrasystoles are counted both as VES and as ventricular sense 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.

Additionally, the Stratos CRT-Ps have a PMT counter and a counter for safety power-down overdrive.

2.20.2 Event Episodes

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

- As followed by Vs
- As followed by Vp
- Ap followed by Vs
- Ap followed by Vp
- Vx followed by Vx

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

NOTE:

The VV value can deviate from the number of VES' since the Stratos CRT-Ps can also classify ventricular sensed events that were preceded by an atrial event such as extrasystoles via the AVES discrimination function after As.

In Stratos CRT-Ps:

- RVs followed by LVp.
- RVp followed by LVp
- LVp followed by RVp

A total counter that records grand total of all conductions is located below the conduction counters.

2.20.3 Rate Trend

The rate trend is displayed as a line chart and consists of the heart rate trend and the pacing rate trend. The atrial event, the ventricular events and the events in the remaining third channel are 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. In the Stratos CRT-Ps, the trends of the three different channels are identified by three different colors.

Please note that a gap in the trend will be displayed for the duration of an asynchronous magnet program or temporary program.

2.20.4 Atrial and Ventricular Rate Histogram

The Stratos CRT-Ps 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 390 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.

2.21 Arrhythmia Statistics

2.21.1 Tachy Episode Trend

The Tachy Episode trend can only be selected when Mode Switching has been programmed ON and for events that occur at less than 1 minute intervals are combined in the tachy episode and stored.

In the tachy episode trend, each tachycardic mode switching episode is recorded in the statistics table with its initial date and time as well as its duration. This documents both the frequency and length of the tachycardic periods which can be evaluated in the follow-up.

Mode Switch Counter – A counter reports the number of mode switches that occurred since the last follow-up visit.

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

NOTE:

When the elective replacement indication (ERI) has been attained, the contents of the tachy episode trends as well as all memory contents are “frozen” and further recording is stopped.

2.21.2 AF Classification

To adequately record atrial fibrillation (AF) and reduce the number of times the recording is turned ON and OFF, a lower and upper AF detection rate can be set. Both the lower sensing rate as well as well as the upper resolution rate is programmable: (100… (10)…300…… (2)…400 ppm).

In addition to the detection rate, an AF is classified using X-out-of-8 algorithm of mode switching. If mode switching is not programmed, the standard setting of 5-out-of-8 is used.

In the statistics, the AF duration (1 min, 10 min, 60 min 4 h, 12 h, 24 h, 48 h, > 48 h) as well as the AF start time (0-3 hours, 3-6 hours, 6-9 hours, 9-12 hours, 12-15 hours, 15-18 hours, 18-21 hours, 21-24 hours) are shown in the histograms.

2.21.3 AES Statistics

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

AT/AES Classification

The Stratos CRT-Ps classify AES events that occur according to their complexity. The following information is available when AES statistics are enabled.

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

Additionally, the following accelerations between zones are reported.

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

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

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

The average number of AES per hour and the shortest AES-AES interval are also reported.

AES vs. Atrial Rate

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

For Stratos CRT-Ps, single AES bar chart displays the percentage of specific AES in 17 different rate ranges (< 40 ppm to > 180 ppm). The atrial rate of the last interval before the AES serves to classify the AES.

Two sequential AES are saved as a couplet, and three sequential AES are saved as a triplet.

AES Coupling Interval

The AES coupling interval shows in which millisecond range the prematurity (distance As/Ap to AES) has occurred. The intervals of the AES-AES Sequences are displayed from < 200 to 1040 ms in 24 histograms classes. The graphic display shows the percentage values if the individual classes in the form of a bar chart and the total number of events.

2.21.4 VES Statistics

The detected VES are ventricular events outside of the AV delay and the VER discrimination interval after As.

Therefore, it is recommended that the atrial sensing be stable before activating the VES analysis. If the atrial lead is bipolar, bipolar sensing should be considered.

The VER prematurity histogram is subdivided into three percentage classes:

- 0-25% (premature VES-VES from 750 to 1000 ms at 60 ppm in the preceding interval).
- 25-50% (premature for VES-VES from 500 to 750 ms at 60 ppm in the preceding interval).
- >50%(premature for VES-VES from < 500 ms at 60 ppm in the preceding interval)

The VES sequence histogram also displays single VES', couplets, triplets, runs and VT episodes.

VES Classification

VES vs. Ventricular rate

The VES versus the ventricular rate is likewise displayed in a histogram with 16 equidistant classes of < 40 to 180 ppm. The graphic display shows the percentage values of the individual classes in the form of a bar chart and the total number of events.

Subsequent VES' (couplets, triplets) are recorded as one event.

VES Coupling Interval

The VES coupling interval shows in which millisecond range the prematurity has occurred. The intervals of the VES-VES sequences are displayed from < 200 to 1040 ms in 24 histogram classes. The graphic display shows the percentage values of the individual classes in the form of a bar chart and the total number of events.

In the case of subsequent VES' (couplets, triplets), these are no longer included. Only the first VES is classified.

2.22 Sensor Statistics

2.22.1 Sensor Rate Histogram

This function records how often the sensor rate is within in 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.

2.22.2 Activity Report

This feature operates by recording characteristic pulse generator data related to patient activity and pacing the system. It is divided into three ranges:

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

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

2.22.3 Sensor Optimization

The sensor optimization is displayed in the form of a line graph containing the length of the time intervals and the trend data. The sensor parameters are simulated and displayed as a trend.

The thicker line represents the recorded (intrinsic) trend) and the thinner line the simulated (sensor) trend. A movable cursor simplifies the reading of the intrinsic and the sensor trends.

2.23 Sensing Statistics

P-Wave Trend

This is the display of the sensitivity course in the atrium. The P-wave trend is displayed in the form of a line chart. This P-wave trend is a rolling, long-term trend with the programmed resolution of 45 s – 36 h. Therefore, the 240 time windows with the 36 h recording periods result in actual recordings for approximately one year. The P-wave trend can record amplitudes from 0.0 to 20 mV.

The trend is only displayed when sensed events are present. During paced events, in the temporary program, or in the magnet “asynchronous” mode, recordings are not made in the trend (there are gaps).

R-Wave Trend

This is the sensitivity of the ventricles displayed over time. The R-wave trend is displayed in the form of a line chart. The R-wave trend is a rolling, long-term trend with a fixed resolution of 36 hours. Therefore, the 240 time windows with 36 hour recording periods result in actual recordings of approximately one year. The R-wave trend can record amplitudes from 0.0 to 20 mV. In the Stratos LV, the specific RV and LV amplitudes are shown in trends of different colors. The R-wave trend is available in all modes that sense in the ventricle, except triggered modes DDI(R)/T, DVT(R), VDT(R) and VVT(R).

2.24 Pacing Statistics

Impedance Trend

The atrial and ventricular impedances are measured in the Stratos CRT-Ps and both values are displayed in the impedance trend in the form of a line chart. The impedance trend is a long-term trend with a fixed resolution of 36 hours per window. Therefore, the 240 possible windows, each with 36 hour recording periods, result in an actual recording time of approximately one year. This recording only occurs in paced events.

After approximately one year of recording, the impedance trend begins to roll. The impedance can also be recorded in the left atrial and left ventricular channel. The values of the impedance trend lie between 0 to 10k Ω. The atrial and both ventricular channels are shown as different colored trends.

3. Follow-up Procedures

3.1 General Considerations

The CRT-P 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 CRT-Ps. 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.

A detailed description of the follow-up functions and the programming procedures are provided in the corresponding software manual.

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.

4. Real-Time IEGM

Stratos CRT-Ps offer the option of real-time transmission of the unfiltered intracardiac electrogram (IEGM). In the Stratos devices, it is possible to simultaneously transmit the IEGM from all three channels as well as the IEGM marker channel. The IEGM simultaneously recorded in the four channels at a scan rate of 256 Hz. All the markers from the three channels are also transmitted together with the IEGM. The IEGM and markers together with the surface ECG can be displayed directly on the screen of the programmer, on a connected ECG recorded or they can be printed by the programmer printer.

NOTE:

When interpreting IEGM, any limitations that result from applying the programmer head (which contains the magnet) must always be considered.

4.1 IEGM Recordings

The recording of the intracardiac information over a short period of time before the tachycardic phase provides valuable details about the arrhthmogenesis of the tachycardia. An IEGM recoding can be triggered by the following events:

- High atrial rates (AF recording)
- Mode switching recording
- High ventricular rate recording
- Patient-triggered recording

Every instantaneous recording provides information from the recording period about:

- The type of triggering event
- Time and date of the recording
- Sensed and paced events in the atrium and the ventricle including the IEGM, markers and events during the refractory period an in the PMT protection window.
- Duration of the triggering events

A total of 64 recordings can be stored. Each of the four triggering types of recording can be assigned a specific number (i.e., X out of 64). When a newly saved recording exceeds the programmed number of recordings per event, the oldest recording is deleted. An exception is the first recording and those with the longest duration for each event. These are not over-written.

NOTE:

The total length of each recording can be up to 10 seconds. While the associated marker chain is always 10 seconds long, the associated IEGM can be shorter depending on the amplitude and rate since the rate and amplitude influence the amount of data to be saved.

In Snap-Shot Pretrigger, it is possible to define the percentage of the recordings before the trigger event.

In addition, it is possible to make a recording at the end of the tachycardia (criterion for deactivation) of the respective event (exception: patient-triggered recordings that do not last).

At the next follow-up examination, the programmer automatically notes the recordings that have been made. When interrogated, the recording appears on the screen.

Note: If the recording has been triggered by the patient (by placing a magnet over the pacemaker), make sure that the synchronous magnet effect is selected.

CAUTION

IEGM – Due to the compression processes that the signals undergo, the IEGM recordings are not suitable for making some specific cardiac diagnoses, such as ischemia; although, these tracings may be useful in diagnosing arrhythmias, device behavior or programming issues.

If the “patient-triggered recording function has been activated, please instruct the patient on how to use the magnet to trigger an IEGM recording.

5. Battery, Pulse and Lead Data

The following pulse, battery and lead data can be measured noninvasively by means of analog telemetry:

Table 25. Measurable Parameters of Analog Telemetry	
Parameters	**Measuring Unit**
Battery voltage	V
Battery impedance	kΩ
Battery current	µA
Pulse voltage	V
Pulse current	mA
Pulse energy	µJ
Pulse charge	µC
Lead impedance	Ω

5.1 Threshold Test - Testing the Pacing Function

Stratos CRT-Ps are equipped with a high-precision threshold test with a resolution of 0.1 V ranging from 0.1 V to 7.2 V. The threshold test is activated as a temporary program whose specific operation is defined by the applicable software version. The threshold is determined by observing the ECG. Likewise, all determinations of threshold or threshold margin, by any means, should only be performed by use of temporary programming to permit immediate reactivation of the permanent program in case of loss of capture. Removal of the programmer head immediately stops the test and reactivates the permanent program. Please refer to the appropriate software technical manual for a description of the threshold test operation.

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

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

NOTE:

With successful biventricular pacing of patients with congestive heart failure, the QRS complex should be visibly shortened.

5.2 P/R Measurement - Testing the Sensing Function

Stratos CRT-Ps 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 CRT-P 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.

5.3 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 Stratos CRT-Ps feature 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.

5.4 Non-Invasive Programmed Stimulation (NIPS)

WARNING

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

5.4.1 Description

The implanted CRT-P/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.

5.4.2 Burst Stimulation

Burst Stimulation offers a burst of pacing pulses to either atrium or ventricle when the programming wand is placed directly over the CRT-P. 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 touch screen. When the **Step Up** or **Step Down** key is touched, NIPS is invoked starting at the nominal burst rate and then steps up or down respectively in 25 ppm steps. As soon as the step up or step down key is released, NIPS terminates. Subsequent inductions resume at the initially programmed burst rate.

5.4.3 Programmed Stimulation

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

5.4.4 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** touch key 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.

5.4.5 NIPS Safety Features

The BIOTRONIK offers the following safety features during NIPS sessions.

- Before the NIPS feature can be used, NIPS must be specifically selected and then is released through user acknowledgment. In addition, before NIPS is performed in the Ventricle, the user must acknowledge that delivering NIPS into the Ventricle may induce dangerous arrhythmias.
- When the battery voltage has reached the Elective Replacement Indicator point (ERI), the NIPS feature is no longer available.
- Ventricular pacing support is available to CRT-P 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 CRT-P. Removing the programmer wand or placement to distance greater than 15 cm from the implanted device returns the CRT-P 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 CRT-P to enable continuous telemetry.

6. Other Functions/Features

Stratos CRT-Ps offer many additional functions and features to assist with the physician in the care of the pacemaker patient.

6.1 Temporary Programming

CAUTION

OFF Mode – The OFF mode can be transmitted as a temporary program only to permit evaluation of the patient's spontaneous rhythm. (see Section 2.1.11).

A temporary program is a pacing program which remains activated while the programming head is positioned over the CRT-P. Upon removal of the programming head (at least 10 cm away from the CRT-P), 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 Stratos CRT-Ps, 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.

6.2 Patient Data Memory

Individual patient data can be stored in the Stratos CRT-Ps. For example, the following are stored:

- Patient name
- Patient index (how the patient name is coded)
- Implantation date
- Symptoms
- Etiology
- ECG indication
- QRS width
- LV ejection fraction
- Lead polarity

6.3 Safe Program Settings

Activating the preset values for the Safe Program is a quick and convenient way to provide VVI / SSI pacing at a high output setting in urgent situations. Listed in Table 26 are the Safe Program settings for Stratos CRT-Ps.

Table 26: Safe Program Settings

Parameter	Safe Program Settings
Mode	VVI
Pacing Rate	70 ppm
Amplitude	4.8 V (ventricle)
Pulse Width	1.0 ms
Sensitivity	2.5 mV
Ventricular Refractory Period	300 ms
Pacing Polarity	Unipolar
Sensing Polarity	Unipolar
Single Chamber Hysteresis	OFF
Magnet Effect	AUTO

6.4 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. Stratos CRT-Ps pace asynchronously at 90 ppm as long as the magnet is over the CRT-P. Upon magnet removal, the current basic interval is completed before the CRT-P 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 CRT-P. 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 magnet application with either ‘Asynchronous’ or ‘Synchronous’ magnet effect.

6.5 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 CRT-P.

6.6 Pacing When Exposed to Interference

CAUTION

EMI – Computerized systems are subject to (Electromagnetic Interference (EMI) or "noise". In the presence of such interference, telemetry communication may be interrupted and prevent programming of the Stratos CRT-P.

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

Depending on the programmed pacing mode and the channel in which electromagnetic interference (EMI) occurs, **Table 27** details the resulting pacing modes for the duration of exposure to EMI.

Table 27: Response to EMI			
MODE	**EMI* (A)**	**EMI* (V)**	**EMI* (A+V)**
DDD(R)	DVD(R)	DAD(R)	DOO(R)
DDI(R)	DVI(R)	DAI(R)	DOO(R)
DVI(R)	---	DOO(R)	---
VDD(R)	VVI(R)	VAT(R)	VOO(R)
VVI(R)	---	VOO(R)	---
AAI(R)	AOO(R)	---	---
DDT	DVT	DAT	DOO
DDI/T	DVT	DAT	DOO
DVT	---	DOO	---
VDT	VVT	VAT	VOO
VDI	VVT	VOO	VOO
VVT	---	VOO	---
AAT	AOO	---	---

* EMI = Electromagnetic Interference

7. Product Storage and Handling

7.1 Sterilization and Storage

Stratos CRT-Ps are 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 for the particular CRT-P. The box contains a double blister container with the CRT-P and product documentation.

The Stratos CRT-P 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 CRT-P 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 CRT-P malfunction (see Section 7.1).

Low Temperatures – Exposure to **low temperatures** (below 0°C) may cause a false elective replacement indication to be present. If this occurs, warm the device to room temperature and reset the ERI with magnet application (see Section 7.1).

Handling – Do not drop. If an unpackaged CRT-P is dropped onto a hard surface, return it to BIOTRONIK (see Section 7.1).

CAUTION

FOR SINGLE USE ONLY - Do not re-sterilize the CRT-P or accessories packaged with the CRT-P, 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.

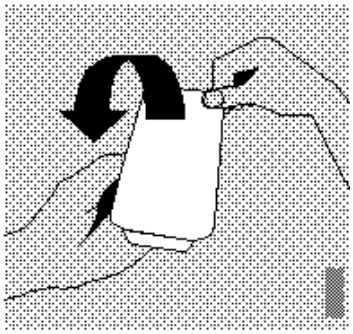
Storage (magnets) – Store the device in a clean area, away from magnets, kits containing magnets, and sources of electromagnetic interference (EMI) to avoid damage to the device.

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

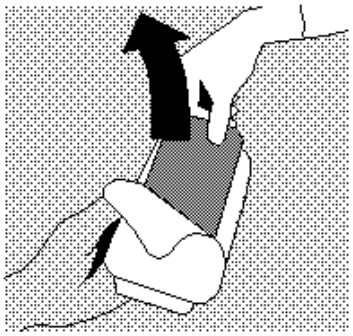
If a replacement CRT-P is needed, contact your local BIOTRONIK representative.

7.2 Opening the Sterile Container

Stratos CRT-Ps are 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.

CAUTION

Muscle or Nerve Stimulation – Inappropriate muscle or nerve stimulation may occur with unipolar pacing when using a non-coated Stratos CRT-P.

Myopotential Sensing – The filter characteristics of BIOTRONIK implantable devices 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 inhibition of pacing, 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 setting.

7.3 Pulse Generator Orientation

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

8. Lead Connection

8.1 Lead Configuration

The Stratos CRT-Ps allows programming of separate lead polarities for pacing and sensing. Lead polarity can also be programmed separately in both the atrial and ventricular channels.

CAUTION

Lead Configuration – The polarity of the implanted lead dictates what lead configuration can be programmed for the CRT-P. Pacing will not occur with a unipolar lead if the lead configuration of the respective channel is programmed to bipolar (see Section 8).

Atrial Channel

In a unipolar lead configuration, the CRT-P pace and sense between the tip electrode of the atrial lead (cathode) and the housing (anode). In a bipolar lead configuration, the CRT-Ps pace and sense between the tip and ring electrodes of the atrial lead. Therefore, bipolar lead polarity should only be programmed when a bipolar atrial lead is implanted.

Ventricular Channel

The Stratos CRT-Ps have a specially designed header that allows sensing with only the RV channel while pacing in both the right and left ventricles. Biventricular Therapy requires programming of a bipolar or unipolar pacing configuration in the ventricle as desired. Table 28 summarizes the sensing and pacing configuration in the ventricle.

Table 28: Lead Configuration			
Configuration			**Description**
Sensing[*]	RV	bipolar	RV tip → RV ring
		unipolar	RV tip → Case
Pacing[†]	RV	bipolar	RV tip → RV ring
		unipolar	RV tip → Case
	LV	bipolar	LV tip → LV ring
		unipolar	LV tip → Case

8.2 Lead Connection

Stratos CRT-Ps have been designed and are recommended for use with bipolar or unipolar leads having an IS-1 connector.

CAUTION

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

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

Overview of the Lead Polarities

If a bipolar lead is connected to the CRT-P, unipolar or bipolar configurations 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 device pocket or diaphragm.

[*] RV only
[†] RV only and BiV, BiV = RV + LV with programmed VV-Delay

Lead Compatibility

The Stratos CRT-Ps have been designed for connection with a bipolar lead in the atrium and two bipolar leads in the ventricle. All connections are IS-1 compatible. Appropriate adapters (e.g., A1-A) should be fitted when using leads with a different connection.

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-device compatibility, consult your BIOTRONIK representative.
In case of device replacement, ensure that the existing lead connector and leads are not damaged.

CAUTION

Lead / CRT-P Compatibility – Because of the numerous available 3.2-mm configurations (e.g., the IS-1 and VS-1 standards), lead/ CRT-P compatibility should be confirmed with the CRT-P and/or lead manufacturer prior to the implantation of the 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)].

Connecting the Stratos LV with the IS-1 Connector

In order to avoid programming errors with the Stratos LV, always connect the leads to the following ports:

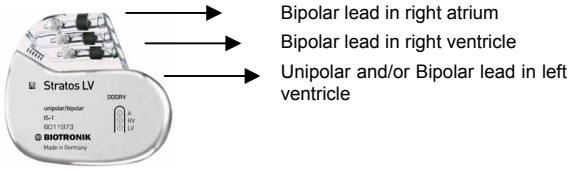


Figure 10. Connecting the Leads

Stratos CRT-Ps have a self-sealing header. Refer to the following steps when connecting a lead(s) to the CRT-P.

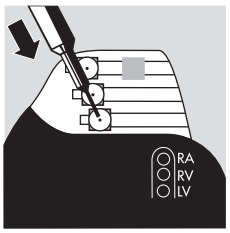
First, confirm that the setscrew(s) is not protruding into the connector receptacle. To retract a setscrew, insert the enclosed torque wrench through the perforation in the self-sealing plug at an angle perpendicular to the lead connector until it is firmly placed in the setscrew.

CAUTION

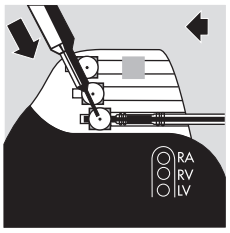
Setscrew Adjustment – Back-off the setscrew(s) prior to insertion of lead connector(s) as failure to do so may result in damage to the lead(s), and/or difficulty connecting lead(s).

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.

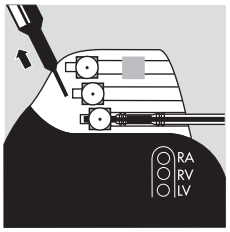


1. Insert the enclosed torque wrench through the perforation in the self-sealing plug at an angle perpendicular to the lead connector until it is firmly placed in the setscrew.

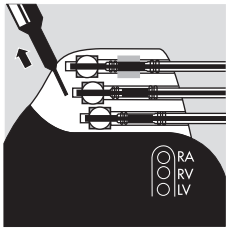


2. Insert the lead connector pin into the connector receptacle of the CRT-P without bending the lead until the connector pin becomes visible behind the setscrew. Hold the connector in this position.

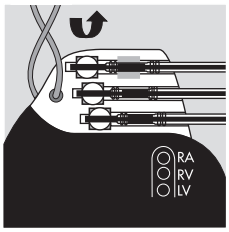
3. Securely tighten the setscrew of the connector clockwise with the torque wrench until torque transmission is limited by the wrench.



4. 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.



5. Attach the other ventricular lead to the right ventricular port (RV) and the atrial lead to the right atrial port (RA) in the same manner.



6. Pass non-absorbable ligature through the hole in the connector receptacle to secure the CRT-P in the pocket.

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.

NOTE:

Do not lubricate the grommets.

9. Elective Replacement Indication (ERI)

Service times for the Stratos CRT-Ps 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 29: 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 Stratos CRT-Ps indicate the need for replacement by a defined decrease in the programmed pacing rate without a magnet applied. The rate change is dependent on the programmed pacing mode.

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

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

The Stratos CRT-Ps indicate the need for replacement by a defined decrease of its rate after magnet application and the programmer displays it upon interrogation of the programmed parameters. The magnet rate in all modes decreases as shown in **Table 30**.

Table 30: Stratos CRT-Ps 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 CRT-P 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. Upon reaching the replacement indication, the following functions are automatically deactivated:

- Post-AES pacing
- Preventive overdrive pacing
- Rate adaptation
- Rate fading
- Statistics
- Snap-shots (Holter)
- Automatic lead check

The following functions remain active when the replacement indication is reached:

- Mode switching
- PMT detection and termination
- Biventricular synchronization

NOTE:

The statistics are frozen when ERI is reached.

WARNING

High Output Settings – High output settings combined with extremely low lead impedance may reduce the life expectancy of the Stratos CRT-Ps. 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.

Table 31 shows the expected longevity (in months) from BOS to ERI at standard program for Stratos CRT-Ps. The Stratos programmer software 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. The data is based on the referenced lead impedance for each chamber, 100% biventricular pacing and the data supplied by the battery manufacturer.

Table 31: Nominal pulse generator longevity

Pulse Generator	Standard* (BOS - ERI) in Months
Stratos LV / LV-T (500 ohms)	51
Stratos LV / LV-T (1000 ohms)	60

* Standard: 60 ppm, 3.6 V, 0.4 ms

Table 32 shows the mean* expected time intervals (in months) from ERI to EOS at standard program for Stratos CRT-Ps. All service intervals, including the above-cited nominal longevity, are based on the battery discharge behavior and the hybrid circuit properties including current consumption and replacement indicator. The statistical calculations are based on 500 ohm lead impedances, 100% pacing, and data supplied by the battery manufacturer.

Table 32: Remaining Expected Service time (ERI to EOS)

Pacing Program	Stratos LV, (months)
Standard†, Mean	8
Program with high pulse energy‡	8

* 50% of all pacemakers reach or exceed the given value
† Standard: DDDR, 60 ppm, 3.6 V, 0.4 ms
‡ High: DDDR, 90 ppm, 4.8 V, 1.0 ms

10. Explantation

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

All implantable electronic devices should be explanted before cremation of a deceased patient.

CAUTION

Device Incineration - Never incinerate a CRT-P. Be sure the CRT-P is explanted before a patient who has died is cremated. (see Section 10)

Explanted Devices – Return all explanted devices to BIOTRONIK.

11. Technical Data

11.1 Available Pacing Modes

DDDR, DDTRA, DDTR, DDIR, DDITR, DVIR, DVTR, DOOR, VDDR, VDTR, VDIR, VVIR, VVTR, VOOR, AAIR, AATR, AOOR

DDD DDTA, DDT, DDI, DDIT, DVI, DVT, DOO, VDD, VDT, VDI, VVI, VVT, VOO, AAI, AAT, AOO, OFF

VV synchronization for the Stratos CRT-Ps: BiV RV RV-T, OFF

11.2 Pulse- and Control Parameters

Basic Rate

32... (1)...**60**... (1)...88... (2)...122... (3)...140... (5)...180 ppm

Night Rate

Off, 32... (1)...88... (2)...122... (3)...140... (5)...180 ppm

Night Rate Start Time

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

Rate Hysteresis

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

Repetitive Rate Hysteresis

Off; 1… (1)…15

Scan Rate Hysteresis

Off: 1… (1)…15

Upper Rate

90… (10)…180 ppm

UTR Response

2:1; Wenckebach (WKB)

Upper Tracking Rate, Atrium

Off, 200 ppm

Dynamic AV Delay (Dual chamber only)

low; medium; high; individual; fixed

AV Delay Values (Dual chamber modes only)

15… (5)…300

AV Hysteresis

Off; 10… (10)…100 ms

Repetitive AV Hysteresis

Off; 1… (1)…10

Scan AV Hysteresis

Off; 1… (1)…10

Sense Compensation

Off; -10… (-10)…-120 ms

Safety AV Delay

100 ms

Ventricular Blanking Time

30… (5)…70 ms

Magnet effect

Automatic; Auto; 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

High Rate Protection

205…215 ppm

Pulse Amplitude

0.2... (0.1)...**3.6**... (0.1)...6.2; 7.2 V

(3 channels separately programmable)

Pulse Width

0.1; 0.2; 0.3; **0.4**; 0.5…(0.25)…1.5 ms

(3 channels separately programmable)

Sensitivity

A 0.1... (0.1)...**1.0**… (0.1)…1.5… (0.5)...7.5 mV

RV 0.5... (0.5)...**2.5**... (0.5)...7.5 mV

First Chamber Paced

RV

VV Delay after Pace/Sense

5 ms

Ventricular Refractory Period

150… (25)…500 ms

Atrial Refractory Period

Auto; 225… (25)…775 ms

Atrial Far-field Protection

After Vp: 30… (10)…220 ms

After Vs: 30… (10)…200 ms

PMT Detection/Termination

Off; On

PMT VA Criterion

250… (10)…500

PMT Protection

Auto; 175… (25)…600 ms

PMT Protection after VES

400… (25)…600 ms

Mode Switching

Off; On

Intervention Rate

100… (10)…250 ppm

X-out-of-8 Activation Criterion

3… (1)…8

Z-out-of-8 Termination Criterion

3… (1)…8

DDI(R) Basic Rate

32… (1)…88… (2)…122… (3)…140… (5)…180 ppm

Overdrive Modes:

Off; On

Available in the modes DDD, DDTA, AAI, AAT with and without rate adaptation

Maximum Overdrive Pacing Rate

90… (5)…160 ppm

Overdrive Pacing Increment (Rate Increase)

2… (2)…10 ppm

Overpacing Level (Rate Drop After)

1… (1) …32 cycles

Post-AES Pacing

Off; On

AES Increment

5… (5)…40 ppm

AES Prematurity

5…50%

VES discrimination after As

OFF; 250… (50)…450 ms

Rate Fading

Off; On

Rate Fading Rate Increase

0.5; 1; 2… (1)…6 ppm/cycle

Rate Fading Rate Decrease

0.25; 0.5… (0.25)…1.25 ppm/cycle

Lead Configuration

Pacing for the Stratos LV / LV-T:

UNIP; BIPL (3 separate channels)

Sensing for the Stratos LV / LV-T:

UNIP; BIPL (2 separate channels; 3 IEGM channels)

Lead check

Off; On (3 separate channels)

Rate Adaptation

Off; On

Sensor

Accelerometer

Sensor Gain

Auto; 1…40 (in 32 steps)

Automatic Sensor Gain

Off; On

Sensor Threshold

Very low; low; medium, high; very high

Rate Increase

0.5; 1… (1)…6 ppm/cycle

Rate Decrease

0.25… (0.25)…1.25 ppm/cycle

Maximum Sensor Rate

90… (5)…120… (5)…180 ppm

11.3 Diagnostic Memory Functions

IEGM Recoding AF

OFF; 3… (1)…31 count

AF Detection Rate

100… (10)…300… (20)…400 ppm

AF End Rate

100… (10)…300… (20)…400 ppm

Mode Switching Recording

Off; 3… (1)…31 count

High Ventricular Rate Recording

OFF; 3… (1)…31 count

Ventricular Sense Rate

100… (10)…250 ppm

Patient Activated Recording

OFF; 1… (1)…31 count

Pre-trigger Recording

0… (10)…80%

Recording when Switching off

Off; On

11.4 Home Monitoring (Stratos LV-T)

Mean Ventricular Heart Rate at Rest – Start Time

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

Event Messages

ON, OFF

Home Monitoring

ON, OFF

Patient-Triggered Messages

ON, OFF

Time of Trend Message

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

11.5 Additional Functions

NOTE:

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

- Permanent IEGM transmission with comprehensive marker annotation
- Storing of comprehensive patient data
- Comprehensive statistics with AES and VES classification, Histogram and event counters and Tachy episode trend
- Guided follow-up
- Retrograde conduction test
- NIPS

NIPS Specifications

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

11.6 Programmers

ICS 3000 Implant Control System

11.7 Default Programs

Stratos LV / LV-T

Parameter/ Function	Factory settings/ Standard Program	Safe Program
Mode	DDD	VVI
VV Synchronization	BiV RV RV-T	-
AV delay	150 ms at 60 ppm	120ms at 130 ppm
First Chamber Paced	RV	-
VV delay after pace	5 ms	-
VV delay after sense	5 ms	-
Pulse Amplitude	3.6 V (A); 3.6 V (RV); 3.6 V (LV)	4.8 V
Sensing A/RV	UNIP	UNIP (RV)
Refractory Period	Auto (A); 250 ms (V)	A: N/A V: 300 ms

11.8 Materials in Contact with Human Tissue

- Housing: Titanium
- Connector receptacle: Epoxy resin
- Sealing Plugs: Silicone Rubber

11.9 Electrical Data/Battery

NOTE:

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

Parameter	Stratos LV
Pace	Unipolar/bipolar
Pulse form	Biphasic, asymmetric
Polarity	Cathodic
Input impedance	> 10kΩ (RV/LV)
Power source	Li/I_2
Battery voltage at BOS	2.8 V
Conducting surface	37.4^2
Conducting Shape	Flattened ellipsoidal

11.10 Mechanical Data

Model	Leads	Size	Mass	Volume
Stratos	IS-1	6.4 x 50.3 x 57 mm	30.85	14.0

12. Order Information

Pulse Generator Type	Order Number
Stratos LV	338 200
Stratos LV-T	338 202

Appendix A

Known Software Anomalies

Anomaly	Possible Effect on Patient or Implant Procedure
General Programmer Issues	
If a long patient name is entered without blank spaces, it may be cut off in the printout under the section 'Patient Data'	The last letters of the patient name may be missing from the printout. However, the patient name is not a therapy-relevant parameter.
Pacemaker detection disturbed after interrogation under EMI conditions	If this occurs, the programmer must be re-started, so that the Stratos cannot be communicated with for about 1 minute. The follow-up process is delayed by this time.
Display test results on programmer screen and printout is inconsistent	Limited clarity and consistency in the display of measurement values from follow-up testing.
During transfer of follow-up information from Stratos CRT-Ps to the GE/CARDDAS system, the following data are not displayed: • the programmed data and follow-up data of the left ventricular channel • lead data of all channels in Stratos	Missing programing information in the exported data may cause user confusion
Interrogation data after Auto Implant Detect (1.5 h after lead attach) may show an incorrect, superfluous entry: "AF episodes detected >48h" in the Event List. AF statistics are always correctly displayed.	Display/printout of incorrect diagnostic information may cause user confusion or incorrect diagnosis

Distributed by:
BIOTRONIK, Inc.
6024 Jean Road
Lake Oswego, OR 97035-5369
(800) 547-0394 (24-hour)
(503) 635-9936 (FAX)

Manufactured by:
BIOTRONIK GmbH & Co. KG
Woermannkehre 1
12359 Berlin Germany

M4122-A 5/08