IMPULSE DYNAMICS

OPTIMIZER® INTEGRA™ CCM-D®
Implantable Pulse Generator

INSTRUCTIONS FOR USE

Limited by United States (Federal) law to investigational use

Part No.: 12-290-005-US Rev. 03

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Please read the documentation provided completely before you use the device.

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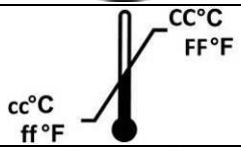
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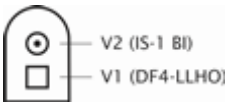
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EXPLANATION OF SYMBOLS ON LABELS

Symbol	Description
	Catalogue number
	Serial number
	Date of manufacture
	Use-by date
	Lot number
	Do not use if package is damaged
	Do not re-use
	Single sterile barrier system with protective packaging inside
	Storage and transport temperature limits
	Medical device
	Caution, consult instructions for use
	Caution: Federal (USA) law restricts this device to sale by or on the order of a physician.
	Sterilized with ethylene oxide
	Dangerous voltage
	State of device when shipped
	Manufacturer
	Consult instructions for use

Symbol	Description
	Available pacing therapies (anti-tachycardia – bradycardia)
	Device header connector cavity types and locations
	Torque wrench
	Open here

LIST OF ACRONYMS

Acronym	Description
AC	Alternating Current
AE	Adverse Event
AF	Atrial Fibrillation
ATP	Antitachycardia Pacing
BI	Bipolar
BOS	Beginning of Service
CCM®	Cardiac Contractility Modulation
CHF	Congestive Heart Failure
CRT	Cardiac Resynchronization Therapy
ECG	Electrocardiogram
EGM	Electrogram
EOS	End of Service
EHR	Extended High Rate
ERI	Elective Replacement Indicator
FVT	Fast Ventricular Tachycardia
HR	Heart Rate
HRV	Heart Rate Variability
HV	High Voltage
ICD	Implantable Cardioverter Defibrillator
IEGM	Intracardiac Electrogram
IPG	Implantable Pulse Generator
LS	Local Sense
LLHO	Low, Low, High, Open
MRI	Magnetic Resonance Imaging
NMR	Nuclear Magnetic Resonance
PETG	Polyethylene Terephthalate Glycol
PSA	Pacing System Analyzer
RF	Radio Frequency
RRT	Recommended Replacement Time (synonymous with ERI)
RV	Right Ventricle
SR	Slow Rhythm
SAE	Serious Adverse Event
SVC	Superior Vena Cava
TENS	Transcutaneous Electrical Nerve Stimulation
VT	Ventricular Tachycardia
VF	Ventricular Fibrillation
VVE	Ventricle Defibrillation, Ventricle Antitachycardia Pacing, Detection by Electrogram
VVI	Ventricle Paced, Ventricle Sensed, Inhibited by Sensed Signal

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1.0 THE OPTIMIZER® INTEGRA™ CCM-D® SYSTEM

The OPTIMIZER INTEGRA CCM-D system is comprised of the following components:

- OPTIMIZER INTEGRA CCM-D Implantable Pulse Generator (IPG)
- Intelio Programmer
- Guardio Charger

Note: In certain circumstances, the Vesta Charger may be substituted for the Guardio Charger.

1.1 Description of the OPTIMIZER INTEGRA CCM-D System

The OPTIMIZER INTEGRA CCM-D Implantable Pulse Generator (IPG) is a Class III medical device used for the treatment of moderate to severe heart failure; a condition wherein the heart muscle does not pump blood as well as it should, resulting in reduced cardiac output. The OPTIMIZER INTEGRA CCM-D IPG monitors the heart's intrinsic activity and delivers Cardiac Contractility Modulation (CCM®) therapy to cardiac tissue during the ventricular absolute refractory period, when the cardiac tissue is not capable of activation, thus rendering the CCM therapy as non-excitatory. CCM therapy delivery is synchronized with the detected local electrical activity and is designed to treat heart failure by increasing the cardiac output or increasing cardiac muscle contractility.

The OPTIMIZER INTEGRA CCM-D IPG also functions as an implantable cardioverter defibrillator (ICD) and can provide shock therapy, antitachycardia pacing (ATP), and emergency short-term bradycardia pacing (VVE-VVI) when it detects an abnormal heart rhythm.

The Intelio Programmer uses telemetry to interrogate and program the OPTIMIZER INTEGRA CCM-D IPG. With the Intelio Programmer, the physician can obtain diagnostic data from the OPTIMIZER INTEGRA CCM-D IPG as well as tailor the operating parameters of the OPTIMIZER INTEGRA CCM-D IPG to meet the specific requirements of each patient.

The Guardio/Vesta Charger is powered by a rechargeable battery and is used by the patient to charge their implanted OPTIMIZER INTEGRA CCM-D IPG transcutaneously using inductive energy transfer. It incorporates a graphical display that shows a different screen for each operational state as well as alerts and other information it receives through daily communications with the OPTIMIZER INTEGRA CCM-D IPG.

1.2 OPTIMIZER INTEGRA CCM-D IPG Implantable Leads Requirements

The OPTIMIZER INTEGRA CCM-D IPG is designed to be used with two (2) commercially available implantable leads, which are implanted in the right ventricle.

The V1 port of the OPTIMIZER INTEGRA CCM-D IPG is compatible with a standard defibrillator lead equipped with a DF4-LLHO connector. The implanting physician may select any standard defibrillator lead with the following characteristics:

- Dedicated bipolar lead (has a ring electrode separate from the coil)

  Caution: Do not use DF4 leads with integrated bipolar sensing.
- DF4 Connector (LLHO configuration)
- Single coil
- Active fixation with an electrically-active helix and distal electrode with an electrically-active surface area of ≥ 3.6 mm^2
- Distal (tip) electrode coated with low-polarization coating (e.g., titanium nitride or iridium oxide)
- Proximal (Ring) electrode electrically-active surface of at least 15 mm^2, and Tip-Ring spacing between 8 and 30 mm
- Maximum total wire resistance of 200 Ω

Defibrillator leads that currently meet these criteria are the following:

- Abbott (SJM) Durata 7122Q
- Abbott (SJM) LDA210Q
- Biotronik Plexa ProMRI S
- Biotronik Protego S

The V2 port of the OPTIMIZER INTEGRA CCM-D IPG is compatible with a standard pacemaker lead equipped with an IS-1 connector. The implanting physician may select any standard ventricular pacing lead with the following characteristics:

- Bipolar lead approved for transvenous intracardiac ventricular pacing
- Standard IS-1 BI (bipolar) connector
- Active fixation with an electrically-active helix and distal electrode with an electrically-active surface area of ≥ 3.6 mm^2
- Distal (tip) electrode coated with a low-polarization coating (e.g., titanium nitride or iridium oxide)
- Proximal (Ring) electrode electrically-active surface of at least 15 mm^2, and Tip-Ring spacing between 8 and 30 mm
- Maximum total wire resistance of 200 Ω

Note: The leads qualified for delivering CCM therapy from OPTIMIZER IPGs must be commercial models that are FDA approved.

Pacing Leads Suitable for use with the OPTIMIZER IPG for CCM Signal Delivery
Current Offerings as of August 2021

Requirement for CCM	**Medtronic CapSureFix Novus MRI™ SureScan™ 4076, 5076, 5086 Leads**	**Medtronic SelectSecure ™ MRI SureScan™ 3830 Lead**	**Abbott (St Jude) 2088TC Tendril STS lead**	**Abbott (St Jude) LPA1200M Tendril MRI Lead**	**Boston Scientific Ingevity + 7840, 7841, 7842 Leads**	**Biotronik Solia-S Leads**
Bipolar lead approved for transvenous intracardiac ventricular pacing	YES	YES	YES	YES	YES	YES
Standard IS-1 bipolar connector	YES	YES	YES	YES	YES	YES
Active fixation with an electrically-active helix distal electrode with a minimal electrically-active surface area of 3.6 mm^2	YES, 4.2 mm^2	YES, 3.6 mm^2	YES, 6.9 mm^2	YES, 6.0 mm^2	YES, 4.5 mm^2	YES, 4.5 mm^2

Requirement for CCM	Medtronic CapSureFix Novus MRI™ SureScan™ 4076, 5076, 5086 Leads	Medtronic SelectSecure ™ MRI SureScan™ 3830 Lead	Abbott (St Jude) 2088TC Tendril STS lead	Abbott (St Jude) LPA1200M Tendril MRI Lead	Boston Scientific Ingevity + 7840, 7841, 7842 Leads	Biotronik Solia-S Leads
Distal electrode coated with a low-polarization coating (e.g., titanium nitride or iridium oxide)	YES, titanium nitride coating	YES, titanium nitride coating	YES, titanium nitride coating	YES, titanium nitride coating	YES, IROX™ (iridium oxide) coating	YES, "Fractal Iridium" (iridium oxide) coating

1.3 OPTIMIZER INTEGRA CCM-D IPG Lead Connectors

The connector block accepts one (1) DF4-LLHO connector and one (1) bipolar IS-1 BI connector. The terminals are marked as follows:

- "V1 (DF4-LLHO)": Ventricle 1 – for CCM and ICD sensing, CCM therapy delivery, antitachycardia pacing (ATP), emergency short-term bradycardia pacing, and shock therapy delivery
- "V2 (IS-1 BI)": Ventricle 2 – for CCM sensing and CCM therapy delivery

1.4 OPTIMIZER INTEGRA CCM-D IPG Physical Dimensions

The OPTIMIZER INTEGRA CCM-D IPG has the following nominal dimensions:

- Height: 95.4 mm
- Width: 53 mm
- Thickness:13.8 mm
- Volume: 49.5 cm^3
- Mass: 85 g

The nominal exposed metallic surface area of the OPTIMIZER INTEGRA CCM-D IPG is 99.8 cm^2 and serves as an indifferent electrode for unipolar CCM sensing and stored unipolar EGMs.



Figure 1: OPTIMIZER INTEGRA CCM-D IPG

1.5 OPTIMIZER INTEGRA CCM-D IPG Batteries

The OPTIMIZER INTEGRA CCM-D IPG is powered by two medical-grade batteries:

- One lithium-ion (Li-ion) rechargeable battery
- One lithium hybrid high-rate non-rechargeable battery

The rechargeable battery is used to power the CCM and ICD functions performed by the OPTIMIZER INTEGRA CCM-D IPG while the non-rechargeable battery supplies power for the delivery of antitachycardia pacing (ATP), shocks, rescue and post shock brady pacing, and arrhythmia induction.

1.5.1 OPTIMIZER INTEGRA CCM-D IPG Rechargeable Battery

1.5.1.1 Rechargeable Battery Specifications

The rechargeable battery used by the OPTIMIZER INTEGRA CCM-D IPG is a medical-grade, rechargeable, lithium-ion (Li-ion) battery, Model 2993, manufactured by Greatbatch Medical. It has a nominal voltage of 4.1 V and a nominal charge capacity of 215 mAh.

1.5.1.2 Rechargeable Battery Behavior

When fully charged, the voltage of the rechargeable battery in the OPTIMIZER INTEGRA CCM-D IPG is approximately 4.1 V.

When the voltage of the rechargeable battery in the OPTIMIZER INTEGRA CCM-D IPG drops to 3.5 V, the IPG places itself in OOO mode (Standby mode) and stops performing any CCM therapy related functions except for telemetric communication with the Intelio Programmer and Guardio/Vesta Charger. The OPTIMIZER INTEGRA CCM-D IPG will resume its CCM therapy related functionality whenever its rechargeable battery voltage rises above 3.6 V during the battery recharging process.

If the voltage of the rechargeable battery in the OPTIMIZER INTEGRA CCM-D IPG drops below 3.2 V, the IPG disconnects its circuitry from the rechargeable battery and stops performing any CCM therapy related functions, including telemetric communication with the Intelio Programmer and Guardio/Vesta Charger (charging of the device can still be performed). The OPTIMIZER INTEGRA CCM-D IPG will resume its normal operation whenever the rechargeable battery is recharged.

Note: If the rechargeable battery voltage of the OPTIMIZER INTEGRA CCM-D IPG drops below 3.2 V, ICD functions remain active and are powered by the non-rechargeable battery until the rechargeable battery is recharged or the non-rechargeable battery is depleted.

It is therefore recommended that the patient be instructed to charge the OPTIMIZER INTEGRA CCM-D IPG at least once a week. Immediate recharging is also recommended if the voltage of the rechargeable battery in the OPTIMIZER INTEGRA CCM-D IPG, after interrogation with the Intelio Programmer, is noted to be at or below 3.6 V.

Note: The OPTIMIZER INTEGRA CCM-D IPG consumes energy from the rechargeable battery when recording information during arrhythmic episodes. Instruct the patient to charge their implanted OPTIMIZER INTEGRA CCM-D IPG soon after experiencing an arrhythmia episode, even if they had recently recharged their device, in order to avoid interrupting the delivery of CCM therapy or consuming energy from the non-rechargeable battery.

1.5.1.3 Rechargeable Battery Longevity

The rechargeable battery inside the OPTIMIZER INTEGRA CCM-D IPG should provide at least 20 years of service under the following conditions:

- Combined (parallel) lead impedance of enabled CCM channel(s): 250 Ω (either singular impedance if one CCM channel is enabled or parallel impedance if both CCM channels are enabled – e.g., 500 Ω lead impedance for both the V1 and V2 leads, with both channels enabled, would result in a parallel CCM impedance of 250 Ω)
- CCM therapy delivery: 5 hours per day
- Heart rate and CCM delivery percentage equating to a CCM therapy delivery rate of 60 CCM trains per minute
- ICD mode programmed ON (monitoring state), pre-trigger EGM recording programmed OFF
- Weekly recharging of the OPTIMIZER INTEGRA CCM-D IPG's rechargeable battery

Note: Deviations from the conditions listed above may decrease the service life of the rechargeable battery in the OPTIMIZER INTEGRA CCM-D IPG.

Over time the rechargeable battery in the OPTIMIZER INTEGRA CCM-D IPG, being subjected to repeated charge and discharge cycles, will lose its ability to maintain its charge capacity. The OPTIMIZER INTEGRA CCM-D IPG will need to be replaced when its rechargeable battery, after being fully recharged, can no longer maintain enough charge to deliver CCM therapy for a full week without becoming severely depleted.

1.5.2 OPTIMIZER INTEGRA CCM-D IPG Non-Rechargeable Battery

1.5.2.1 Non-Rechargeable Battery Specifications

The non-rechargeable battery used by the OPTIMIZER INTEGRA CCM-D IPG is a medical-grade, non-rechargeable Lithium Carbon Monofluoride/Silver Vanadium Oxide (Li/CFx-SVO) Hybrid high-rate battery, 2nd-generation Q_{HR} Model 3340, manufactured by Greatbatch Medical. It has a nominal voltage of 3.2 V and a nominal charge capacity of 1.784 Ah.

1.5.2.2 Non-Rechargeable Battery Beginning of Life (BOL)

The beginning of life (BOL) voltage of the non-rechargeable battery voltage in the OPTIMIZER INTEGRA CCM-D IPG is approximately 3.2 V.

1.5.2.3 Non-Rechargeable Battery Recommended Replacement Time (RRT)

The Recommended Replacement Time (RRT) (also known as Elective Replacement Indicator or ERI) condition is declared when the non-rechargeable battery reaches 2.65 Volts (± 5 mV). Upon reaching RRT, the battery has sufficient energy remaining to continue supporting antitachycardia therapies for at least three months and to support at least six full-energy charges (once every 15 days).

1.5.2.4 Non-Rechargeable Battery RRT to EOS (Prolonged Service Period or PSP)

The Prolonged Service Period (PSP) is the time between the RRT and End of Service (EOS). The PSP is defined as three months, assuming six full-energy charges and Rescue Brady Pacing is programmed OFF. The EOS may be indicated before the end of 3 months if the device exceeds these conditions. The OPTIMIZER INTEGRA CCM-D IPG will continue to operate according to specifications in the PSP with no change in specifications.

Warning: Replace the OPTIMIZER INTEGRA CCM-D IPG within three months of reaching the RRT indication. Replace the OPTIMIZER INTEGRA CCM-D IPG **immediately** after it reaches RRT if there is frequent high-voltage charging or if Rescue Brady Pacing is programmed ON.

1.5.2.5 Non-Rechargeable Battery End of Service (EOS)

The EOS condition is declared when the non-rechargeable battery reaches 2.52 Volts (± 5 mV). Below the EOS value, the OPTIMIZER INTEGRA CCM-D IPG will continue to function until the battery voltage drops below 2.0 Volts, but may do so out of specification. High-voltage charge times will be extended. If the capacitors take longer than 45 s to reach the programmed voltage, charging stops and the pulse generator delivers whatever voltage is present on the capacitors. There is no guarantee that the pulse generator will deliver a high-voltage shock after the EOS condition has been declared by the non-rechargeable battery.

1.5.2.6 Non-Rechargeable Battery Usage

The non-rechargeable battery's primary purpose is to provide the energy needed for the OPTIMIZER INTEGRA CCM-D IPG to deliver ICD therapy. However, if the rechargeable battery is allowed to become depleted, then the OPTIMIZER INTEGRA CCM-D IPG will begin to use its non-rechargeable battery to provide the power necessary to continue the operation of its ICD functions.

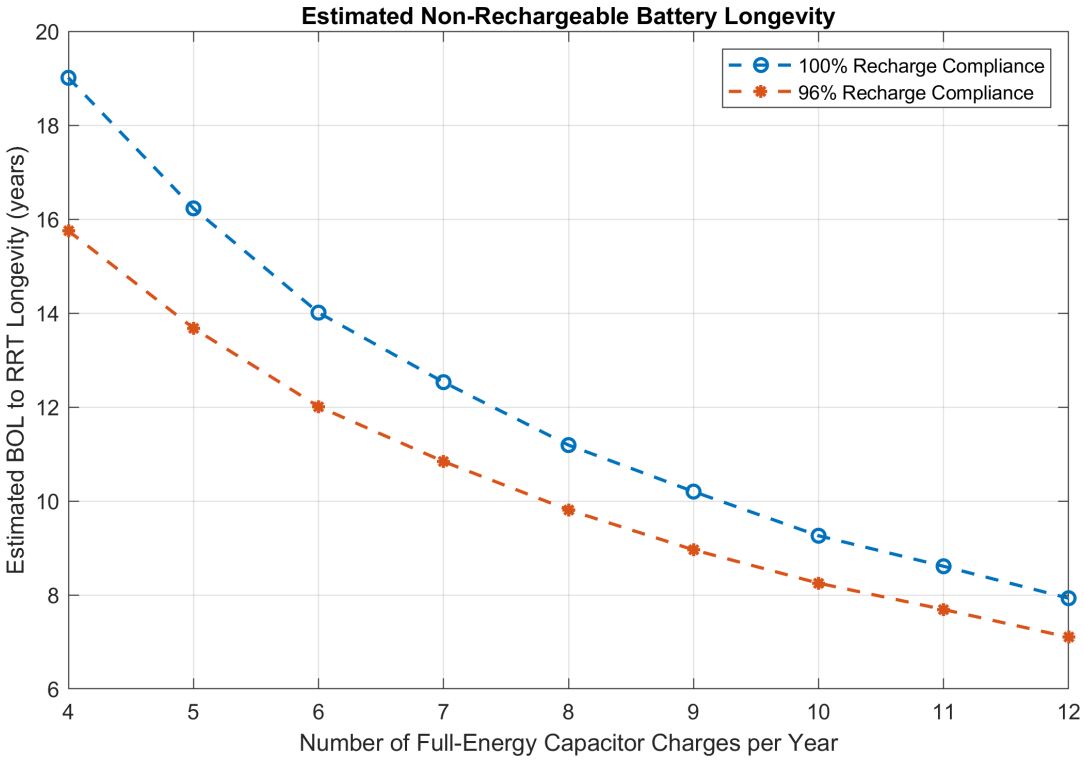
Therefore, it is recommended that the patient be instructed to charge the OPTIMIZER INTEGRA CCM-D IPG at least once a week. Immediate recharging is also recommended if the rechargeable battery level of the OPTIMIZER INTEGRA CCM-D IPG, after interrogation with the Intelio Programmer, is noted to be at or below 3.6 V.

1.5.2.7 Non-Rechargeable Battery Longevity

The non-rechargeable battery in the OPTIMIZER INTEGRA CCM-D IPG is expected to last at least 20 years from its Beginning of Life (BOL) to Recommended Replacement Time (RRT) under the following conditions:

- The IPG has been on the shelf for no more than 1 year after manufacture.
- At most 44 full-energy charges have been conducted between Beginning of Life (BOL) and Recommended Replacement Time (RRT). These include: 2 shocks at implant, and 2 full-energy capacitor charges per year for 20 years (defibrillation shocks or capacitor reform every 6 months).
- The patient has been fully compliant throughout the life of the device with charging the IPG.
- Rescue Brady Pacing has not been delivered to the patient.
- The IPG has been operating normally throughout its service life.

The following graph shows the estimated longevity of the device as a function of the total number of maximum energy capacitor charges (cardioversion/ defibrillation pulses delivered or capacitor reforms) when these occur more often than the conditions above:



Estimates are provided for 96% and 100% patient compliance with weekly recharge of the IPG. The graph assumes that the total number of maximum energy charges is spaced uniformly over the estimated life of the implantable pulse generator. A full-energy capacitor reform charge is performed every 6 months after any previous full-energy charge (delivered cardioversion/defibrillation pulse or reform).

Note: Projected longevity estimates are based on accelerated battery discharge data and device modeling as specified. Do not interpret these values as precise numbers.

1.6 OPTIMIZER INTEGRA CCM-D IPG Packaging

The OPTIMIZER INTEGRA CCM-D IPG is packaged in a sterile TYVEK/PETG blister package and placed inside a shelf box that also contains the following items:

- Peel-off labels for use with implantation documents
- Literature pack (includes a printed copy of this document or a card referring the User to the Impulse Dynamics website where this IFU can be obtained electronically, an Implanted Medical Device Identification Card, and other important information)

The TYVEK/PETG blister package has been sterilized with ethylene oxide gas and is comprised of an inner TYVEK/PETG blister pack within an outer TYVEK/PETG blister package.

The inner blister pack contains the following items:

- One (1) OPTIMIZER INTEGRA CCM-D IPG
- One (1) Allen #2 torque wrench (77.68 mNm = 11 oz-in)

1.7 OPTIMIZER INTEGRA CCM-D IPG Storage

The recommended storage conditions for the OPTIMIZER INTEGRA CCM-D IPG are as follows:

- Ambient temperature: 0°C to 40°C (32°F to 104°F)
- Atmospheric pressure: 50 kPa to 304 kPa (14.81 inHg to 90.02 inHg)

Relative humidity has no impact on the OPTIMIZER INTEGRA CCM-D IPG.

2.0 USER PROFILE AND TRAINING

The operators of the OPTIMIZER INTEGRA CCM-D system include patients, physicians (and the trained medical personnel who assist them). Physicians and medical personnel who operate the OPTIMIZER INTEGRA CCM-D system should be qualified and familiar with the operation of electronic medical equipment, particularly the operation of implanted medical devices and programmers.

Physicians and medical personnel can participate in a Company-sponsored training program that will provide theoretical and hands-on training regarding the technology, device features, and detailed operating instructions for the OPTIMIZER INTEGRA CCM-D IPG, the Intelio Programmer, and the Guardio/Vesta Charger.

Patient training will be limited to the use of the Guardio/Vesta Charger and will be offered by post-implant.

3.0 INDICATIONS OF USE

The OPTIMIZER INTEGRA CCM-D System is indicated for the prevention of sudden cardiac death, improvement of quality of life, and 6-minute walk in Stage C or D heart failure patients who remain symptomatic despite being on guideline-directed medical therapy (GDMT), are not indicated for Cardiac Resynchronization Therapy (CRT), and have heart failure with reduced left ventricular ejection fraction (LVEF ≤ 40%).

The OPTIMIZER INTEGRA CCM-D system delivers non-excitatory CCM signals to the heart and performs ICD and short-term pacemaker functions.

4.0 CONTRAINDICATIONS AND PRECAUTIONS

Use of the OPTIMIZER INTEGRA CCM-D system is **contraindicated** in:

1. Patients with a mechanical tricuspid valve
2. Patients in whom vascular access for implantation of the leads cannot be obtained
3. Patients implanted with a concomitant device (e.g., Pacemaker, CRT; ICD; OPTIMIZER IVs, Smart, or Smart Mini IPG)

5.0 WARNINGS

5.1 Potential Complications of Device Implantation

Just like any surgical procedure, implantation of an OPTIMIZER INTEGRA CCM-D IPG is associated with certain risks. Complications of device implantation reported in the literature include, but are not limited to:

- Infection
- Skin necrosis
- Device migration
- Hematoma formation
- Seroma formation
- Histotoxic reactions (also see: Potential Adverse Effects, Section 7)

Acute and chronic complications reported in the literature include, but are not limited to:

- Lead fracture
- Lead displacement
- Atrial or ventricular perforation
- Rare cases of pericardial tamponade

Perforation of the ventricular wall can induce direct stimulation of the phrenic nerve or the diaphragm. A significant impedance change noted during a routine check-up can indicate a lead fracture, lead displacement, lead insulation damage, or perforation (also see: Potential Adverse Effects, Section 7).

In very rare cases (<1%), transvenous lead placement can lead to venous thrombosis and subsequent superior vena cava (SVC) syndrome.

Loss of sensing shortly after implant can be the result of lead displacement. Loss of CCM, cardioversion, defibrillation, or pacing therapy delivery could be due to a lead fracture. In addition, fractures in the defibrillation lead may cause noise that may be identified by the OPTIMIZER INTEGRA CCM-D IPG as a ventricular tachyarrhythmia, leading to unnecessary shocks.

5.2 Potential Arrhythmias

5.2.1 Atrial and Ventricular Arrhythmias Potentially Caused by Lead Implantation

The use of transvenous leads may lead to arrhythmias, some of which may be life-threatening, such as ventricular fibrillation and ventricular tachycardia. The use of screw-in leads, such as those used for CCM therapy delivery, has the potential of causing conduction disturbances such as bundle branch block. These can be minimized by performing the implant under fluoroscopic guidance, ensuring that the leads are placed in the appropriate position prior to fixation, as well as limiting the number of lead manipulations.

Please read and follow all directions in the Instruction for Use document provided with the leads that you intend to use in order to minimize adverse events associated with lead implantation.

5.2.2 Ventricular Arrhythmias Potentially Caused by CCM Therapy Pulses

CCM therapy pulses possess more energy than typical pacing pulses. Thus, they are capable of eliciting activation of cardiac tissue when delivered outside of the absolute refractory period. CCM therapy pulses delivered outside of the ventricular absolute refractory period have the potential of causing pulse-induced arrhythmias (some of which may be life-threatening, such as ventricular fibrillation and tachycardia). For this reason, CCM therapy delivery parameters must be chosen carefully. Most importantly, the various settings related to conditions that inhibit CCM therapy delivery (e.g., LS Alert Window, refractory periods, and IEGM sensitivities) must be selected to allow delivery of CCM therapy only on normally conducted (e.g., non-arrhythmic) beats, but inhibit them on beats of suspected ectopic or premature origin.

In addition, CCM therapy pulses may cause changes in the electrical conduction of tissue. For this reason, the delivery of CCM therapy pulses to the ventricular septum has the potential of causing bundle branch block that could lead to bradycardia. Through similar mechanisms, CCM-induced changes in the electrical conduction of the myocardium have the potential of inducing tissue refractoriness that may facilitate the induction of reentrant tachyarrhythmias. It is recommended that the patient be monitored carefully for changes in heart rhythm when CCM therapy is temporarily activated during lead implantation, as well as during the first permanent activation of CCM therapy after implant and subsequent follow-up visits. Changes in ventricular rhythm caused by the delivery of CCM therapy pulses may require repositioning the leads and/or changing the CCM train delay and CCM amplitude parameters to values that do not adversely affect the patient’s ventricular rhythm.

5.2.3 Atrial Arrhythmias Potentially Caused by CCM Therapy Pulses

Atrial and supraventricular arrhythmias could theoretically be initiated when CCM-induced ventricular activity is conducted retrograde to the atria, resulting in premature atrial depolarization. The OPTIMIZER INTEGRA CCM-D IPG may sense the ventricular activation resulting from the retrograde-induced atrial event and deliver CCM therapy as programmed. In addition, strong CCM therapy pulses delivered through leads implanted in a basal position close to the atria can directly stimulate the atria. If CCM therapy causes atrial activation through either of these mechanisms, and the atrial signal is then conducted to the ventricles, it may look like couplet PACs (AVAV) but the second complex would be identified as “VT” by the OPTIMIZER INTEGRA CCM-D IPG.

The main variables that may cause CCM therapy pulses to lead to atrial activation are ventricular lead placement location on the right ventricular septum, CCM pulse amplitude, and CCM train delay. To prevent atrial arrhythmias due to CCM therapy pulses, it is recommended that basal lead implant locations be avoided.

The potential for direct atrial activation by CCM therapy pulses can be tested during implant by setting the CCM pulse amplitude to the highest possible value and extending the CCM train delay by 40 to 50 ms beyond its recommended setting while ensuring that the CCM therapy pulse train, including its balancing phase, remains entirely within the bounds of the ventricular absolute refractory period, then delivering CCM therapy while monitoring the patient's heart rhythm for episodes of atrial activation. The testing should confirm the absence of atrial activation with the increased CCM amplitude and extended CCM train delay.

5.3 Electrocautery

Warning: The use of surgical electrocautery devices, especially of the monopolar kind, can induce CCM therapy inhibition or trigger the OPTIMIZER INTEGRA CCM-D IPG to deliver inappropriate antitachycardia therapy. It may also cause the OPTIMIZER INTEGRA CCM-D IPG to revert to its Safe mode (OOO mode, with no CCM or ICD therapy delivery). If the device is found to have reverted to its Safe mode, it will need to be reset, which will clear the statistical data stored in the device. The device can be damaged if high energies are coupled into the system.

Use of electrocautery in close proximity to an implanted OPTIMIZER INTEGRA CCM-D IPG can also couple radiofrequency (RF) energy directly through the leads and lead tips into the cardiac muscle tissue, producing burns or possibly cardiac arrhythmias. If electrocautery is used, brief signal bursts should be considered, with the neutral electrode positioned such that its affects on the OPTIMIZER INTEGRA CCM-D IPG and its attached leads are minimized. The risk of adverse effects can be mitigated by placing the OPTIMIZER INTEGRA CCM-D IPG into Medical Procedure mode (see Section 12). The patient's peripheral pulse should be monitored throughout the procedure and the correct operation of the OPTIMIZER INTEGRA CCM-D IPG should be verified immediately after the procedure.

5.4 RF Ablation

Warning: RF ablation can cause the OPTIMIZER INTEGRA CCM-D IPG to inhibit CCM therapy delivery, deliver inappropriate antitachycardia therapy, or revert to its Safe mode (equivalent to OOO mode, with no CCM or ICD therapy delivery) with the possible loss of statistical data. Depending on the amount of energy coupled into the system, the device could also be damaged. If an RF ablation procedure is performed in close proximity to the leads, the leads can couple radio frequency (RF) energy via the lead tips into the myocardium, producing burns or possibly cardiac arrhythmias.

If an RF ablation procedure has to be performed, the neutral electrode should be positioned such that the current flowing through the OPTIMIZER INTEGRA CCM-D IPG and the leads is minimized. Avoid direct contact between the ablation catheter and the OPTIMIZER INTEGRA CCM-D IPG or its leads. The risk of adverse effects can be mitigated by placing the OPTIMIZER INTEGRA CCM-D IPG into Medical Procedure mode (see Section 12). The patient's peripheral pulse should be monitored throughout the procedure and the correct operation of the OPTIMIZER INTEGRA CCM-D IPG should be verified immediately after the procedure. If the device has gone into its Safe mode, it will need to be reset by qualified personnel. A consequence of a device reset is that all statistical data stored in the IPG is cleared.

5.5 Diathermy (Medical "Short Wave" Induction Heating)

Warning: Medical diathermy is generally contraindicated in patients with implanted devices. The effects of such intense energies on the OPTIMIZER INTEGRA CCM-D IPG cannot be predicted. Although damage to the circuitry of the IPG and/or the myocardium appears unlikely, it nevertheless could occur.

If diathermy is to be used notwithstanding the contraindication, it should not be applied in close proximity to the OPTIMIZER INTEGRA CCM-D IPG and its associated leads. The risk of adverse effects can be mitigated by placing the OPTIMIZER INTEGRA CCM-D IPG into Medical Procedure mode (see Section 12). The patient's peripheral pulse should be monitored throughout the procedure and the correct operation of the OPTIMIZER INTEGRA CCM-D IPG should be verified immediately after the procedure. If the device has gone into its Safe mode, it will need to be reset by qualified personnel. A consequence of a device reset is that all statistical data stored in the IPG is cleared.

5.6 Defibrillation and Cardioversion

Warning: Any implanted device can be damaged by external cardioversion or defibrillation. In addition, the myocardium adjacent to the lead tips and/or the tissue in the area of the device may be damaged. Altered signal thresholds could also be one of the consequences. The defibrillation current can also make the OPTIMIZER INTEGRA CCM-D IPG to revert to its Safe mode (equivalent to OOO mode, with no CCM or ICD therapy delivery). In addition, the OPTIMIZER INTEGRA CCM-D IPG and its leads may be damaged by exposure to the high energies discharged by external defibrillators.

There are no particular paddle placement positions that can guarantee damage to the implanted OPTIMIZER INTEGRA CCM-D system will not occur. However, to decrease the risk of damage, it is recommended to position the paddles anterior and posterior, as far away from the OPTIMIZER INTEGRA CCM-D IPG as possible. In addition, paddle positions that would bring the OPTIMIZER INTEGRA CCM-D IPG into the direct path of the defibrillation current should be avoided.

After defibrillation, the function of the OPTIMIZER INTEGRA CCM-D IPG should be closely monitored. In the unlikely event of abnormal function, lead repositioning (or replacement) and IPG reprogramming (or replacement) may be required. If the device is found to have reverted to its Safe mode, it will need to be reset by qualified personnel. A consequence of a device reset is that all statistical data stored in the IPG is cleared.

5.7 Hand-Held Transmitters

Warning: A minimum separation distance of 15 cm (6 in) must be maintained between hand-held transmitters and an implanted OPTIMIZER INTEGRA CCM-D IPG.

5.8 Therapeutic Ultrasound

Warning: Direct exposure of the OPTIMIZER INTEGRA CCM-D IPG to therapeutic ultrasound can damage the device. In addition, the OPTIMIZER INTEGRA CCM-D IPG can inadvertently concentrate the ultrasound field and cause harm to the patient.

Therapeutic ultrasound can be used, provided the implant is located far away from the ultrasound field. The risk of adverse effects can be mitigated by placing the OPTIMIZER INTEGRA CCM-D IPG into Medical Procedure mode (see Section 12). The patient's peripheral pulse should be monitored during the procedure. Immediately after the treatment, the OPTIMIZER INTEGRA CCM-D IPG should be checked for proper function. If the device is found to have reverted to its Safe mode, it needs to be reset. A consequence of a device reset is that all statistical data stored in the IPG is cleared.

5.9 Nuclear Magnetic Resonance (NMR), Magnetic Resonance Imaging (MRI)

Warning: Patients with an implanted OPTIMIZER INTEGRA CCM-D IPG should not be exposed to NMR or MRI.

Exposure of the OPTIMIZER INTEGRA CCM-D system to strong magnetic and electromagnetic fields encountered within MRI systems has not been investigated. Even though placing the OPTIMIZER INTEGRA CCM-D IPG into Medical Procedure mode (see Section 12) reduces the risk of adverse events, exposure of the patient to an MRI scan could result in the following:

- Unintended cardiac stimulation (induced tachycardia)
- Tissue damage near the IPG and lead electrodes, resulting in the inability of the implanted device to sense electrical signals from the heart or deliver CCM and ICD therapy
- Device malfunction (discharge of the device batteries, damage to device electronics, reversion to its Safe mode, inappropriate delivery of antitachycardia therapy)

If the device is found to have reverted to its Safe mode, it will need to be reset, which will clear the statistical data stored in the device.

5.10 Radiation Therapy

Warning: Therapeutic equipment generating ionizing radiation, such as linear accelerators and cobalt machines employed for treating malignant diseases, can damage the circuits used in most active implantable devices. Because the effect is cumulative, both dose rate and total dose determine if damage will occur and its possible extent. Be aware that certain types of damage might not be immediately detectable. In addition, the electromagnetic fields generated by some types of radiation equipment for beam "steering" purposes can affect the function of the OPTIMIZER INTEGRA CCM-D IPG.

Radiation therapy can lead to a broad spectrum of effects, reaching from transient interference to permanent damage. Therefore, it is advisable to locally shield the OPTIMIZER INTEGRA CCM-D IPG against radiation if radiation therapy is to be used. During radiation treatment and thereafter, the function of the IPG needs to be monitored. If the tissue in the vicinity of the implant has to be irradiated, it may be advisable to relocate the OPTIMIZER INTEGRA CCM-D IPG.

5.11 Lithotripsy

Warning: Direct exposure of the OPTIMIZER INTEGRA CCM-D IPG to shock waves can damage the device. A device implanted outside the shock wave path presents no clear-cut contraindication to lithotripsy. The risk of adverse effects can be mitigated by placing the OPTIMIZER INTEGRA CCM-D IPG into Medical Procedure mode (see Section 12). The patient's peripheral pulse should be monitored during the procedure. Immediately after the treatment, the OPTIMIZER INTEGRA CCM-D IPG should be checked for proper function. If the device is found to have reverted to its Safe mode, it will need to be reset by qualified personnel. A consequence of a device reset is that all statistical data stored in the IPG is cleared.

5.12 Transcutaneous Electrical Nerve Stimulation (TENS)

Warning: TENS is generally contraindicated in patients with implanted electrical devices. The high-voltage impulse delivered into the body by the TENS unit can impair the operation of the OPTIMIZER INTEGRA CCM-D IPG or cause it to deliver inappropriate antitachycardia therapy.

If a TENS unit is used, the TENS electrodes should be attached as far as possible from the OPTIMIZER INTEGRA CCM-D IPG and its leads. In addition, aiming for a limited current path, consider placing the TENS electrodes as close to each other as possible. The patient's peripheral pulse should be closely monitored while TENS is applied. The risk of adverse effects can be mitigated by placing the OPTIMIZER INTEGRA CCM-D IPG into Medical Procedure mode (see Section 12).

5.13 Handling

Warning: Do not implant the OPTIMIZER INTEGRA CCM-D IPG if the package is damaged or if the device has been dropped onto a hard surface from a height of 12 in or more while still in the shipping box. Do not implant the device if it has been dropped onto a hard surface after unpacking. Damaged packages or dropped devices should be returned to Impulse Dynamics for evaluation.

5.14 Resterilization and Reuse

Warning: An OPTIMIZER INTEGRA CCM-D IPG that has been explanted for any reason must not be reused in another patient.

Do not resterilize and/or reuse the OPTIMIZER INTEGRA CCM-D IPG or the torque wrench provided with the device.

5.15 Cremation

Warning: Never incinerate an OPTIMIZER INTEGRA CCM-D IPG. The IPG must be explanted before the deceased patient is cremated.

The OPTIMIZER INTEGRA CCM-D IPG contains two sealed chemical batteries. Make absolutely certain that an implanted OPTIMIZER INTEGRA CCM-D IPG is removed before a deceased patient is cremated.

6.0 CAUTIONS

6.1 Environmental Conditions

The following discussion on potential hazards from the environment focuses on maintaining the utmost patient safety. Although the OPTIMIZER INTEGRA CCM-D IPG was designed to provide the highest possible protection against such hazards, complete immunity against these risks cannot be guaranteed.

The OPTIMIZER INTEGRA CCM-D IPG should not be used in the vicinity of other electrical equipment capable of producing signals that could interfere with its operation. If proper separation is not feasible, the OPTIMIZER INTEGRA CCM-D IPG must be monitored to ensure normal function.

Similar to other cardiac rhythm management IPGs, the OPTIMIZER INTEGRA CCM-D IPG can be affected by interference from magnetic, electrical, and electromagnetic signals, provided these are sufficiently strong or have characteristics resembling cardiac activity. Most interference will lead to inhibition of CCM therapy delivery. In rare cases, an interfering signal could trigger inappropriate CCM or antitachycardia therapy delivery. In addition, interfering signals exceeding a certain threshold may couple enough energy into the IPG to damage the IPG circuits and/or the myocardial tissue in the vicinity of the leads. The Patient's Manual addresses these risks, which should be discussed during consultations with the patient.

The susceptibility of a particular device is dependent on the location of the IPG pocket, the type of interfering signal, and the programmed operating parameters.

Because of the diversity of the potential causes of electromagnetic interference, Impulse Dynamics cannot characterize and describe all sources of interference and their effects in this manual.

Caution: Patients should be instructed to be cautious in the vicinity of equipment that generates strong electrical or electromagnetic fields and seek medical advice before entering an area with posted warnings advising pacemaker patients (or patients with other types of implantable devices) not to approach.

6.2 Home Appliances

Home and commercial microwave ovens do not affect the operation of the OPTIMIZER INTEGRA CCM-D IPG, provided they are in good condition and used as intended. Even microwave energy from a severely defective microwave oven directly radiating onto the IPG does not damage the device. However, such exposure may impair the sensing function of the device, which could eventually impact CCM therapy delivery and ICD functionality.

Patients with an implanted OPTIMIZER INTEGRA CCM-D IPG should be advised not to use or come in close proximity to induction stoves as they could interfere with the normal operation of the OPTIMIZER INTEGRA CCM-D IPG.

Patients with an implanted OPTIMIZER INTEGRA CCM-D IPG should be advised that some electric razors, electric power tools, and electric ignition systems, including those of gasoline-powered engines, could cause interference. Generally, patients implanted with an OPTIMIZER INTEGRA CCM-D IPG may use gasoline-powered engines, provided that protective hoods, shrouds, and other shielding devices have not been removed.

6.3 Store Anti-Theft Systems/Airport Security Screening Systems

Certain types of anti-theft systems, such as those installed at entrances/exits of stores, libraries, and other facilities, as well as airport security systems, can interfere with the OPTIMIZER INTEGRA CCM-D IPG. Such interference would most often inhibit CCM therapy delivery but may also impact ICD functionality. Patients should be advised to walk through such systems at a normal pace, i.e., not to slow down while passing through. Prior to passing through airport security systems, patients should notify the attendant security personnel that they carry an implant and should present their implant ID card.

6.4 Industrial Machinery

High voltage power lines, electric and arc welders, electric smelters, and power-generating equipment can interfere with the operation of the OPTIMIZER INTEGRA CCM-D IPG. For that reason, one needs to consider the field strengths and modulation characteristics of all electromagnetic fields patients are exposed to in their workplaces or due to their lifestyle. Patients need to be specifically warned about these risks, or the OPTIMIZER INTEGRA CCM-D IPG should be programmed to minimize its susceptibility.

6.5 Magnet Fields

Exposure to a strong magnetic field can adversely affect the operation of the OPTIMIZER INTEGRA CCM-D IPG. Such exposure may temporarily disable the delivery of ICD therapy. Patients should be advised to avoid equipment or entering areas that may expose them to a strong magnetic field.

6.6 Transmitting Devices

Communication equipment such as radio and TV transmitters (including amateur [“ham radio”] transmitters, microwave radio, and CB radio transmitters with power amplifiers) as well as radar transmitters can interfere with the operation of the OPTIMIZER INTEGRA CCM-D IPG. For that reason, one needs to consider the field strengths and modulation characteristics of all electromagnetic fields patients are exposed to in their workplaces or due to their lifestyle. Patients need to be specifically warned about these risks, or the OPTIMIZER INTEGRA CCM-D IPG should be programmed to minimize its susceptibility.

6.7 Cellular and Mobile Phones

Cell phones and other mobile phones can adversely affect the operation of the OPTIMIZER INTEGRA CCM-D IPG. They can be caused by the radio frequencies emitted by the phones or by the phones’ speaker and charging magnets (e.g., iPhone 12). The potential consequences of exposure include inhibition of or inappropriate CCM therapy delivery and ICD functionality if the phone is in very close proximity < 10 in of an OPTIMIZER INTEGRA CCM-D IPG and the corresponding leads.

Because of the incredible variety of mobile phones as well as the significant physiologic differences between patients, it is impossible to make specific recommendations. However, as a general guideline, patients implanted with an OPTIMIZER INTEGRA CCM-D IPG who would like to use a mobile phone are advised to hold the phone to the ear that is contralateral to the implant site. Patients should not carry the phone in a breast pocket or on a belt closer than 10 in from the implanted IPG because some phones emit signals even when they are turned on but not in use.

Compared to smaller cell phones, portable (handbag) and mobile (permanent car or boat installation) phones will generally transmit at higher power levels. For phones with higher transmission power levels, it is recommended to maintain a minimum separation of 20 in between the antenna and the implanted IPG.

7.0 POTENTIAL ADVERSE EFFECTS

Examples of adverse effects that may occur as the result of the surgical procedure are listed below in the order of their clinical severity:

1. Death
2. Arrhythmias (brady or tachyarrhythmias including fibrillation)
3. Stroke or TIA (“transient ischemic attack”)
4. Formation of blood clots
5. Respiratory/ventilatory failure
6. Cardiac perforation
7. Hemorrhage
8. Infection

9. Pleura or pericardial effusion
10. Pneumothorax
11. Injury to the heart or blood vessels
12. Damage to the heart muscle
13. Damage to the tricuspid valve, potentially resulting in tricuspid valve regurgitation
14. Damage to specialized tissue in the heart responsible for initiating each heartbeat (i.e., the heart's conduction system)
15. Pain at the incision site
16. Superior vena cava syndrome (SVCS)

Examples of additional adverse effects potentially occurring secondary to CCM therapy delivery are listed below in the order of their clinical severity:

1. Abnormal cardiac function
2. Atrial and ventricular tachyarrhythmias
3. Atrial and ventricular bradyarrhythmias
4. Worsening heart failure
5. Myocardial tissue damage
6. Lead dislodgement
7. Chest pain
8. Chest wall sensations

8.0 DEVICE IMPLANTATION

Warning: The use of general anesthesia for the implant procedure will result in the inability to assess patient comfort during CCM therapy delivery and may cause adverse events associated with CCM therapy.

Warning: Heating of the IPG due to short-circuit fault in one of the internal batteries can cause a temperature in excess of 41°C at distance of up to 5 mm from the surface of the IPG. Therefore, during implantation of the IPG, ensure that all surfaces of the IPG's enclosure are not placed within 5 mm of any critical structure in the patient.

Preferably, the OPTIMIZER INTEGRA CCM-D IPG should be implanted in the left pectoral region of the chest. The two leads implanted with the OPTIMIZER INTEGRA CCM-D IPG are to be placed in the right ventricle. Preferably, the DF4 (defibrillator) lead should be placed in a lower septal location and the IS-1 (pacing) lead should be placed in a posterior mid-septal location, making sure that the distance between the lead placement locations is at least 2 cm.

8.1 Opening the Lead Package(s)

Visually inspect the lead packages before opening them for implantation. Damaged packages should be returned to the lead manufacturer. To prepare the lead for vascular implantation, follow the instructions provided by the lead manufacturer. Unless otherwise indicated by the lead manufacturer, proceed as follows with each sterile package:

- Open the shelf box outside the sterile field and remove the TYVEK/PETG molded tray.
- Using the provided tab, peel back the TYVEK from the outer PETG molded tray, taking strict care not to touch the inner sterile package.
- Maintaining strict sterile technique, make the inner sterile package accessible to the scrub nurse. At the recess adjacent to the molded tab, the inner TYVEK/PETG container can be removed from the outer tray with a pair of forceps.
- Peel back the inner cover starting at the provided peel tab.
- Remove the lead from the inner package and place it on a sterile and lint-free surface.

8.2 Implanting the Leads

Implant the leads in accordance with the instructions in the lead manufacturer's literature provided with the leads.

Please follow all indications listed in the lead manufacturer's literature.

Warning: Pinching the lead can damage the lead conductor or insulation, which may cause unwanted high-voltage therapies or result in the loss of sensing or pacing therapy.

Warning: Avoid Subclavian crush by proper lead access and placement. Patients need to be monitored closely after the implantation procedure.

Warning: Exercise care while placing the leads to avoid swelling of the steroid plug or formation of a blood clot, which could prevent extension and/or retraction of the helix.

Warning: It is important to avoid prolonged manipulation of the leads and catheters in the venous system, which could lead to venous thrombosis.

Warning: During implantation, leads and catheters need to be manipulated with extra caution to avoid right ventricular wall perforation. Obtain X-rays, perform echocardiography, and device interrogation after implantation to detect perforations even in the absence of related symptoms. Throughout the procedure and post-operative care, cardiac hemodynamic and respiratory status should be continuously monitored by subjective assessment, pulse oximetry, and blood pressure monitoring via automatic cuff or intra-arterial cannula.

Warning: In order to prevent vascular injury and hemorrhage, be extremely cautious when introducing catheters and leads into veins

8.3 Opening the OPTIMIZER INTEGRA CCM-D Sterile Package

Caution: Visually inspect the package before opening it for the implantation procedure. Check the package for any signs of damage suggesting that the sterility of the package or its contents has been compromised. Damaged packages should be returned to Impulse Dynamics for evaluation. Do not attempt to resterilize any of the contents of the sterile inner blister pack that has been damaged or compromised.

Open the shelf box outside the sterile field and remove the TYVEK/PETG molded insert. Establish a link between the IPG and the Programmer by performing the following steps:

1. Place the Intelio Programming Wand over the OPTIMIZER INTEGRA CCM-D IPG
2. Open the Optimizer INTEGRA application on the Intelio Programmer
3. Click on the **Start OPTIlink** button shown on the **OPTIlink Session Pane**
4. If the link is successful, the **OPTIlink Session Pane** will display the device model and serial number along with the **Close OPTIlink** button. In addition, the **CCM Status Pane** will display the current CCM therapy status and the **ICD Status Pane** will display the current ICD therapy status.

Once the programmer is linked to the IPG, proceed to the opening of the sterile OPTIMIZER INTEGRA CCM-D IPG package.

To open the sterile package, proceed as follows:

1. Starting at the provided tab, peel back the TYVEK from the outer PETG molded insert, taking care not to touch the sterile inner package.
2. Maintaining strict sterile technique, make the inner sterile blister pack accessible to the scrub nurse. The inner TYVEK/PETG container can be removed from the outer tray with a pair of forceps inserted at the recess next to the molded tab.
3. Peel back the inner cover starting at the provided peel tab.
4. Remove the OPTIMIZER INTEGRA CCM-D IPG and the accessories from the inner pack and place them on a sterile, lint-free surface.

8.4 Connecting the Implanted Leads to the OPTIMIZER INTEGRA CCM-D IPG

Before connecting the implanted leads to the OPTIMIZER INTEGRA CCM-D IPG, it is recommended that each ventricular lead be tested with a Pacing System Analyzer (PSA).

Using a PSA, measure the impedance and sensing amplitude for each implanted ventricular lead. When measuring the sensing and pacing thresholds, measure between the tip (cathode) and ring or coil (anode) of each bipolar pacing/sensing lead.

It is also recommended that the pacing capture threshold, which is a traditional indicator of proper electrode anchoring into the myocardium, be measured for each ventricular lead. Lastly, test each ventricular lead for stimulation and discomfort.

Acceptable values for ventricular lead assessment are as follows:

- Lead impedance: between 250 Ω and 1500 Ω with no more than 20% fluctuation in readings
- Sensing amplitude: ≥ 5 mV
- Pacing Capture Threshold: ≤ 1 V at 0.5 ms pulse width
- No palpable diaphragmatic stimulation or chest discomfort with the delivery of an 8 V pacing pulse at 1.0 ms pulse width

Important points to consider when connecting the implanted leads to the OPTIMIZER INTEGRA CCM-D IPG include:

- When tightening or loosening the set screws, always insert the tip of the torque wrench fully and in line with the set screw. Do not insert the wrench into the set screw at an angle.
- Before inserting the DF4 and IS-1 lead connectors, visually verify that none of the set screws protrude into any of the IPG header cavities (please refer to the diagram on the IPG). Back off any set screw found protruding beyond the wall into the header cavity by turning it back with the Allen wrench in a counterclockwise direction. Turn the set screw just enough so that its tip is no longer inside the header cavity.

  Caution: Do not back the set screw completely out of the terminal block.
- Under no circumstances should items other than the implantable lead connectors be introduced into the port of the IPG connector terminal.

Note: Provided the connectors are correctly installed, the connector retention force in the terminals is at least 10 N (2.24 lbf).

Clean the DF4 lead connector pin with sterile distilled water (if using saline, wipe the connector dry with a surgical sponge afterwards) and then fully insert the lead connector into the V1 connector terminal in the header of the OPTIMIZER INTEGRA CCM-D IPG.

Warning: Fluid in the DF4 connector terminal may lead to poor sensing, high impedance readings, and inability of IPG to deliver CCM and ICD therapy.

Clean the IS-1 lead connector pin with sterile distilled water (if using saline, wipe the connector dry with a surgical sponge afterwards) and then fully insert the lead connector into the V2 connector terminal in the header of the OPTIMIZER INTEGRA CCM-D IPG.

Warning: Fluid in the IS-1 connector terminal may lead to poor sensing, high impedance readings, and inability of IPG to deliver CCM therapy.

Note: Before tightening the set screws, visually inspect each connector terminal in the header of the IPG and verify that the tip of each lead connector is fully inserted into its respective lead tip terminal.

Tighten the tip set screw for the DF4 lead using the sterile #2 Allen torque wrench included in the IPG package. Turn the torque wrench clockwise until you hear and feel clicking. This feature limits the amount of torque placed on the set screw and prevents it from being over-tightened.

Carefully apply traction on the strain relief of the DF4 lead to make sure that it is securely anchored in its terminal.

Tighten the tip set screw for the IS-1 lead using the sterile #2 Allen torque wrench included in the IPG package. Turn the torque wrench clockwise until you hear and feel clicking. Carefully apply traction on the strain relief of the IS-1 lead to make sure that it is securely anchored in its terminal.

Tighten the ring set screw for the IS-1 lead using the torque wrench. Turn the torque wrench clockwise until you hear and feel clicking.

8.5 Verifying Lead Placement

Note: If the Optimizer INTEGRA Programmer application is still linked to the OPTIMIZER INTEGRA CCM-D IPG, then the Intelio Programming Wand does not need to be introduced into the sterile field. However, if the OPTIlink between the Optimizer INTEGRA Programmer application and the OPTIMIZER INTEGRA CCM-D IPG has closed, the Intelio Programming Wand will need to be introduced into the sterile field and placed directly over the OPTIMIZER INTEGRA CCM-D IPG before the OPTIlink can be reestablished.

Note: The Intelio Programming Wand is not sterile and cannot be sterilized. If the Intelio Programming Wand needs to be introduced into the sterile field, it must first be placed in a sterile probe cover or sleeve.

Ask the person operating the Intelio Programmer (outside the sterile field) to perform the following using the Optimizer INTEGRA Programmer application:

1. Program the OPTIMIZER INTEGRA CCM-D IPG to deliver CCM therapy
    a. Tap the **Parameters** button on the Menu Bar
    b. Select the **CCM Therapy** tab
    c. On the **CCM Therapy** panel, tap the **Mode** parameter
    d. Set the **Mode** to **OVO-LS-CCM** mode
    e. On the **CCM Therapy** panel, tap the **CCM Therapy Mode** parameter
    f. Set the **CCM Therapy Mode** to **ON**
    g. Select the **CCM Sensing** tab
    h. On the **CCM Setting** panel, tap the **OPTIset IEGM Sensitivities** button
    i. The **Acquisition Time** window will appear. Tap the **Accept** button.
    j. When OPTIset has completed its proposal of sensitivities, tap the **Propose** button
    k. If the analysis was successful, tap the **Accept & Continue to Optiset Timing** button
    l. When OPTIset has completed its proposal of CCM algorithm timing, tap the **Propose** button
    m. If the analysis was successful, tap the **Accept & Continue to Optiset Amplitude** button
    n. When OPTIset has completed its proposal of CCM algorithm amplitude, set the **CCM Amplitude** to **7.5 V** and then tap the **Accept & Continue** button
    o. Tap the blinking **Program** button on the Programming Buttons Pane to load modified parameters into the OPTIMIZER INTEGRA CCM-D IPG with the new parameter settings
2. Measure the CCM lead impedances
    a. Tap the **Diagnostics** button on the Menu Bar
    b. Select the **Leads** tab
    c. On the **Leads** panel, tap the **Measure CCM Leads Impedance** button
    d. Verify that the CCM lead impedance measurements are within expected values.

Under local anesthesia or conscious sedation, ask the patient if they feel any sensation while the OPTIMIZER INTEGRA CCM-D IPG is delivering CCM therapy. If the patient reports having sensation at 7.5 V, step decrease the CCM amplitude in 0.5 V increments until the sensation is no longer felt by the patient.

If the patient expresses discomfort or any other kind of sensation at 6.0V or lower, identify the lead causing it by disabling the CCM delivery to the RV channel. If the patient continues to experience sensations, re-enable the RV channel and disable the LS channel. Once the lead that is causing the sensation has been identified, its placement should be relocated to allow cardiac contractility modulation therapy to be delivered at the maximum amplitude through both CCM channels.

It is good practice to check fluoroscopy in a steep LAO (left anterior oblique) 45 degree or greater angle to visually identify any placement issues with the offending lead prior to repositioning.

Once placement of the leads has been completed, use the lead suture sleeve of each lead to secure the leads in place. Clean the lead body with sterile saline before securing the suture sleeve of each lead. Secure the suture sleeve with two non-absorbable ligatures and tighten gently -- Do Not Over-Tighten.

Note: Any significant lead impedance deviation at a subsequent check-up may be a sign of lead displacement or indicative of another problem requiring further investigation.

8.6 Dissection of the IPG Pocket

Surgical dissection directly on top of the fascia is the preferred method for creating the pocket, which should be large enough to accommodate the OPTIMIZER INTEGRA CCM-D IPG and any loops of excess lead.

Note: When dissecting the pocket, please bear in mind that for charging to be possible, the distance between the charging wand and the OPTIMIZER INTEGRA CCM-D IPG must not exceed 4 cm (1.5 in).

8.7 Inserting the OPTIMIZER INTEGRA CCM-D IPG and Defibrillation Testing

Insert the OPTIMIZER INTEGRA CCM-D IPG into the subcutaneous pocket. Although the OPTIMIZER INTEGRA CCM-D IPG can theoretically be interrogated and charged in any position, the preferred placement is such that the engraved side of the device is facing superior towards the skin, which provides the best link between the charging coil inside the header and the Guardio/Vesta Charger.

While the OPTIMIZER INTEGRA CCM-D IPG may be implanted at a depth of up to 4 cm (1.5 in), the maximum recommended depth of implant for proper device interrogation and charging is 2.5 cm (1 in).

When placing the IPG into the subcutaneous pocket, take special care to allow a smooth curvature of redundant lead segments within the pocket and place them around the IPG or in the pocket inferior to the device.

If Defibrillation Testing is to be conducted, proceed to the steps below then refer to the OPTIMIZER INTEGRA CCM-D protocol for the specific ICD settings to be programmed into the device before continuing.

Warning: Make sure that cardiac resuscitation equipment is available and in working order before conducting Defibrillation Testing!

Ask the person operating the Intelio Programmer (outside the sterile field) to perform the following using the Optimizer INTEGRA Programmer application:

1. Program the ICD parameters for the OPTIMIZER INTEGRA CCM-D IPG
    a. Click the **Parameters** button on the Menu Bar
    b. Select the **ICD General** tab
    c. On the **ICD General** panel, set the **ICD Mode** to **ON**, then enable and/or set the ICD General parameters as specified in Section 13

d. Select the **ICD Detection** tab

e. On the **ICD Detection** panel, modify the ICD Detection parameters as specified in Section 13

f. Select the **ICD Therapy** tab

g. On the **ICD Therapy** panel, modify the ICD Therapy parameters as specified in Section 13

h. Tap the blinking **Program** button on the Programming Buttons Pane to load modified parameters into the OPTIMIZER INTEGRA CCM-D IPG

WARNING: Do not handle the OPTIMIZER INTEGRA CCM-D IPG once ICD Mode has been programmed ON. Doing so may cause you to be subjected to Dangerous High-Voltage Shocks!

2. Measure ICD lead impedances

   a. Tap the **Diagnostics** button on the Menu Bar

   b. Tap the **Measure Coil Lead Impedance** button

   c. Tap the **Measure HV Lead Impedance** button

   d. Verify that the ICD lead impedance measurements are within expected values.

Note: Perform Coil Lead Impedance and HV Lead Impedance before performing any Defibrillation Testing.

If required, proceed with Defibrillation Testing as specified in the OPTIMIZER INTEGRA CCM-D protocol.

8.8 Closing the Pocket

Once the Defibrillation Testing has been successfully completed, proceed to secure the IPG to the fascia with a non-absorbable suture and close the pocket.

Radiographs should be obtained after device implantation to verify device and lead placement, as well as rule out pneumothorax and other surgical complications, even if there are no symptoms. Thereafter, patients should receive the facility's standard post-operative care for similar procedures such as implantable cardiac defibrillator (ICD) implantation.

Prior to discharge, check the lead sensitivity threshold for each implanted lead, measure the lead impedance, and then compare these results to the values obtained during implant. Any significant changes may indicate lead dislodgement.

Note: As the depth of the implant increases, the charger's efficiency in charging the implanted device decreases. This may impact the time it takes to charge the implanted device.

9.0 DEVICE EXPLANTATION / REPLACEMENT

9.1 Device Removal

WARNING: Before starting explantation procedure, make sure that the ICD Mode in the OPTIMIZER INTEGRA CCM-D IPG has been programmed OFF. Failure to do so may result in Dangerous High-Voltage Shocks!

Important points to consider when explanting the OPTIMIZER INTEGRA CCM-D IPG include:

- Special care should be exercised when opening the IPG pocket so as not to damage the leads implanted with the OPTIMIZER INTEGRA CCM-D IPG.
- When loosening a set screw, always insert the tip of the torque wrench fully into and in line with the set screw. Do not insert the torque wrench into the set screw at an angle.
- If the OPTIMIZER INTEGRA CCM-D IPG is being explanted and not replaced, abandoned leads need to be capped after they are disconnected from the IPG.

Carefully open the IPG pocket and gently remove the IPG from the pocket. Once the IPG is out of the pocket, loosen the set screws with a sterile #2 Allen wrench. When all the set screws have been loosened, grasp the connector of a lead between the thumb and forefinger of one hand while holding the IPG in the other hand, and pull the lead connector from the terminal by cautious application of constant traction.

Note: Grasping the lead connector with a sterile pad can help improve traction.

Caution: Never apply traction to the actual lead body; it could damage the lead and result in lead failure.

9.2 Device Replacement

Important points to consider when replacing the OPTIMIZER INTEGRA CCM-D IPG include:

- When tightening a set screw, always insert the tip of the torque wrench fully into and in line with the set screw. Do not insert the torque wrench into the set screw at an angle.
- Make sure to visually verify that the lead insulation is intact when replacing an OPTIMIZER INTEGRA CCM-D IPG. Prior to connecting the leads to the replacement IPG, the impedances, sensing thresholds, and pacing thresholds should be assessed with a Pacer System Analyzer (PSA).
- Before inserting the DF4 and IS-1 lead connectors, visually verify that none of the set screws protrude into any of the IPG header cavities (please refer to the diagram on the IPG). Back off any set screw found protruding beyond the wall into the header cavity by turning it back with the Allen wrench in a counterclockwise direction. Turn the set screw just enough so that its tip is no longer inside the header cavity.

  Caution: Do not back the set screw completely out of the terminal block. Doing so may render the IPG unusable.
- Under no circumstances should items other than the implantable lead connectors be introduced into the port of the IPG connector terminal.

Clean the DF4 lead connector pin with sterile distilled water (if using saline, wipe the connector dry with a surgical sponge afterwards) and then fully insert the lead connector into the V1 connector terminal in the header of the OPTIMIZER INTEGRA CCM-D IPG.

Clean the IS-1 lead connector pin with sterile distilled water (if using saline, wipe the connector dry with a surgical sponge afterwards) and then fully insert the lead connector into the V2 connector terminal in the header of the OPTIMIZER INTEGRA CCM-D IPG.

Note: Before tightening the set screws, visually inspect each connector terminal in the header of the IPG and verify that the tip of each lead connector is fully inserted into its respective lead tip terminal.

Tighten the tip set screw for the DF4 lead using the sterile #2 Allen torque wrench included in the IPG package. Turn the torque wrench clockwise until you hear and feel clicking. This feature limits the amount of torque placed on the set screw and prevents it from being over-tightened. Carefully apply traction on the strain relief of the DF4 lead to make sure that it is securely anchored in its terminal.

Tighten the tip set screw for the IS-1 lead using the sterile #2 Allen torque wrench included in the IPG package. Turn the torque wrench clockwise until you hear and feel clicking. Carefully apply traction on the strain relief of the IS-1 lead to make sure that it is securely anchored in its terminal.

Tighten the ring set screw for the IS-1 lead using the torque wrench. Turn the torque wrench clockwise until you hear and feel clicking.

9.3 Disposition of Explanted OPTIMIZER INTEGRA CCM-D IPGs

All explanted OPTIMIZER INTEGRA CCM-D IPGs should be returned to Impulse Dynamics for testing and analysis, which can provide valuable information on how to further improve device quality and reliability.

Warning: An OPTIMIZER INTEGRA CCM-D IPG that has been explanted for any reason must not be reused in another patient.

10.0 OPTIMIZER INTEGRA CCM-D IPG CCM FUNCTIONS AND PROGRAMMING OPTIONS

10.1 CCM Therapy

10.1.1 Device Modes

The implantable OPTIMIZER INTEGRA CCM-D IPG features two device modes:

- **OOO**: The device is in standby; no events are sensed, and no CCM therapy is delivered.
- **OVO-LS-CCM**: The device senses RV and LS events while ignoring any atrial events and is capable of CCM therapy delivery without the need for the detection of atrial sense events.

10.1.2 CCM Therapy Mode

The OPTIMIZER INTEGRA CCM-D IPG features two CCM therapy modes:

- **OFF**: Turns OFF the delivery of CCM therapy
- **ON**: Enables the OPTIMIZER INTEGRA CCM-D IPG to deliver CCM therapy a set number of hours per day within the timeframe set by the Start Time and End Time parameters. The delivery of CCM therapy occurs in one-hour intervals with pauses in between each interval for a calculated amount of time-based on the hours per day, Start Time, and End Time parameter settings.

10.1.3 CCM Therapy Hours/Day

The **CCM hs/days** parameter sets the total number of hours per day the OPTIMIZER INTEGRA CCM-D IPG is scheduled to deliver CCM therapy. By default, the **CCM hs/days** parameter is set to 5 hs/day.

10.1.4 Start Time and End Time

The **Start Time** and **End Time** parameters set the general start and end time of CCM therapy delivery during each day. By default, the CCM therapy schedule is set to be distributed over a 24-hour period each day.

10.1.5 Extend on Low CCM%

If the percentage of CCM therapy a patient receives during scheduled CCM therapy delivery periods is lower than 90%, the OPTIMIZER INTEGRA CCM-D IPG offers the option of extending this CCM therapy delivery time period. When the **Extend on Low CCM%** feature is enabled, the OPTIMIZER INTEGRA CCM-D IPG extends the On Time period for CCM therapy delivery based on the percentage of CCM therapy delivered during the original 1 hour On Time period. The amount in which the On Time is extended is as follows:

- If the CCM% is 80% to 90%, the On Time is extended 11%
- If the CCM% is 70% to 79%, the On Time is extended 26%
- If the CCM% is 60% to 69%, the On Time is extended 46%
- If the CCM% is less than 60%, the On Time is extended 72%

In all cases, the Off Time is correspondingly reduced by the same amount.

10.2 Suspension of CCM Delivery

The delivery of CCM therapy by the OPTIMIZER INTEGRA CCM-D IPG will be suspended if one of the following conditions occurs:

10.2.1 Disable CCM Command

The Optimizer INTEGRA Programmer application includes a button on the CCM Status Pane that allows the user to permanently suspend CCM therapy. If the button in its default “DISABLE CCM” state is tapped, this action permanently suspends CCM therapy and toggles the button to say “ENABLE CCM”. When the button in its “ENABLE CCM” state is tapped, this action unsuspends CCM therapy and toggles the button back to display “DISABLE CCM”.

10.2.2 CCM Magnet Mode

Note: To find out how the placement of a magnet over the implant site of the OPTIMIZER INTEGRA CCM-D IPG affects ICD Therapy delivery, see Section 11.4.2.

In CCM Magnet Mode, CCM therapy delivery is suspended but the OPTIMIZER INTEGRA CCM-D IPG still senses and classifies cardiac events. A health care provider (or patient) can force the OPTIMIZER INTEGRA CCM-D IPG into the CCM Magnet Mode state by placing a cardiac device magnet [minimum field strength of 90 Gauss @ 4.0 cm (1.5 in)] over the implant site of the OPTIMIZER INTEGRA CCM-D IPG, keeping it over the implant site for at least two cardiac cycles (3 seconds), and then removing it from the implant site. This CCM Magnet Mode state is maintained even after the magnet is removed from the implant site.

The CCM Magnet Mode has two setting options:

Note: The CCM Magnet Mode setting does not affect the ICD functionality of the OPTIMIZER INTEGRA CCM-D IPG.

- **Off 1 day**: At this setting, the OPTIMIZER INTEGRA CCM-D IPG shall remain in a CCM Off state for 24 hours. This 24-hour period starts the moment the magnet is moved away from the implanted device. When this 24-hour period has been completed, the device will resume delivering CCM therapy using the previously programmed parameters.

  Note: If at any time during this 24-hour period, a cardiac device magnet is reapplied over the implant site of the OPTIMIZER INTEGRA CCM-D IPG for at least two cardiac cycles (3 seconds) and then removed again from the implant site, the 24-hour period is restarted.

- **Off**: At this setting, the OPTIMIZER INTEGRA CCM-D IPG shall remain in a CCM Permanent Off state until the Program command is sent to the device. This status can only be changed by using the Optimizer INTEGRA Programmer application to reprogram the OPTIMIZER INTEGRA CCM-D IPG under the direction or supervision of a physician.

10.2.3 Safe Mode

When the CCM module of the OPTIMIZER INTEGRA CCM-D IPG is in Safe Mode, CCM therapy delivery is suspended and may not sense cardiac events. The reversal of this state can only be accomplished by resetting the OPTIMIZER INTEGRA CCM-D IPG with the Optimizer INTEGRA Programmer application under the direction or supervision of a physician. In the unlikely event of inconsistent operation of the system’s logic circuits, the OPTIMIZER INTEGRA CCM-D IPG will automatically assume the Safe state until it is reset.

Note: The CCM module’s Safe Mode state may be the result of the OPTIMIZER INTEGRA CCM-D IPG’s ICD module entering Safe Mode. When the ICD module is in a Safe Mode state, the OPTIMIZER CCM-D IPG will not deliver ICD or CCM therapy.

10.3 CCM Sensing

Through leads implanted in the heart, the OPTIMIZER INTEGRA CCM-D IPG can sense, detect, and analyze electrical signals from the heart. The signal input and controller circuitry of the OPTIMIZER INTEGRA CCM-D IPG are designed to receive these electrical signals, analyze the characteristics of each signal (for example, magnitude and timing), and to determine whether or not to deliver CCM therapy, if CCM therapy is to be delivered, and when to deliver it.

10.3.1 Sensing Leads

Right heart events are detected through two sensing leads:

- Ventricular 1: lead placed on the septum of the right ventricle (V)
- Ventricular 2: lead placed on the septum of the right ventricle (V)

10.3.2 CCM Sensing Parameters

Sensitivity and polarity are the parameters that determine how right heart events are sensed by the CCM module of the OPTIMIZER INTEGRA CCM-D IPG.

- **Sensitivity**: To configure lead sensitivity, the Optimizer INTEGRA Programmer application provides the following settings:
    1. **Ventricle 1 and 2**: Ventricle sensitivity to set to any one of 16 values between 1.0 mV and 10 mV.
- **Polarity**: The Optimizer INTEGRA Programmer application allows the polarity of the ventricular leads to only be set to the following option:
    2. **Bipolar**: The CCM signal is sensed between the lead “tip” (distal electrode) and “ring” (proximal electrode) of a bipolar lead.

10.4 CCM Timing

10.4.1 Post-V Ventricular (RV) Refractory Period

The Post-V Ventricular (RV) Refractory Period is the time interval after a ventricular (RV) event when signals sensed on the RV channel are not acknowledged as ventricular (RV) events. With the Optimizer INTEGRA Programmer application, the Post-V Ventricular (RV) Refractory Period can be set to values between 148 ms and 452 ms, in 8 ms increments.

10.4.2 CCM Inhibit Parameters

By analyzing the train of sensed cardiac events based on their succession and their temporal order, the OPTIMIZER INTEGRA CCM-D IPG “decides” for each heartbeat whether to deliver CCM therapy or not.

10.4.2.1 CCM Inhibit Cycles

One can program the number of cycles for which CCM therapy delivery will continue to be inhibited after the initial inhibiting event. With the Optimizer INTEGRA Programmer application, the number of CCM inhibit cycles can be set to values between 1 and 16. This means that CCM therapy delivery can be inhibited from zero to 15 additional cycles beyond the initial inhibiting event.

Note: The number of inhibited cycles applies to the most recent detected event that caused CCM therapy inhibition. If a new inhibiting event is detected during a period of CCM therapy inhibition, this will trigger a new inhibition period.

10.4.2.2 Conditions Causing Inhibition

When the OPTIMIZER INTEGRA CCM-D IPG is in its **Active** state, certain conditions may cause CCM therapy delivery to be inhibited. A record of each condition that caused the inhibition of CCM therapy delivery is stored by the IPG and can be viewed as statistical data whenever the device is interrogated by the Optimizer INTEGRA Programmer application. The conditions that cause inhibition of CCM therapy delivery are the following:

- **LS out of Window**: A local sense event detected before or after the Local Sense Alert Window triggers an LS out of Window condition. The Local Sense Alert Window is the time interval during which the leading edge of valid LS events triggers CCM therapy delivery. How this is programmed is detailed in section 10.4.3.3.
- **Tracking**: Whenever the ventricular tracking rate limit is exceeded, CCM therapy delivery is automatically inhibited. Using the Optimizer INTEGRA Programmer application, the tracking rate limit can be set to one of 25 possible values between 62 bpm and 110 bpm. CCM therapy delivery is *always inhibited* when the tracking rate limit is exceeded.
- **After ATP**: Whenever antitachycardia pacing (ATP) has been delivered, CCM therapy delivery is automatically suspended. Using the Optimizer INTEGRA Programmer application, the suspension after ATP can be set to values between 1 h and 24 h, in 1 h increments. CCM therapy delivery is *always suspended* after ATP has been delivered.
- **After HV Shock**: Whenever a high voltage (HV) shock has been delivered, CCM therapy delivery is automatically suspended. Using the Optimizer INTEGRA Programmer application, the suspension after HV shock can be set to values between 1 h and 24 h, in 1 h increments. CCM therapy delivery is *always suspended* after HV shock has been delivered.
- **Ventricular noise**: Despite various methods for detecting and filtering noisy signals implemented in the OPTIMIZER INTEGRA CCM-D IPG, noise from powerful electromagnetic sources (e.g., from portable telephones, radio transmitters, etc.) as well as noise from physiological events (e.g., myopotentials, etc.) can interfere with the detection of cardiac events.

  Any time higher rate signals (greater than 11.6 Hz) are detected on the ventricular channel, the control logic of the OPTIMIZER INTEGRA CCM-D IPG assumes the presence of noise and declares a ventricular noise condition. CCM therapy delivery is *always inhibited* if ventricular noise is detected.

10.4.3 Local Sense Parameters

The detected local electrical activity of the ventricular myocardium with respect to right ventricle (RV) electrical activity is known as Local Sense (LS) events.

10.4.3.1 Assignment of Local Sense Channel

The OPTIMIZER INTEGRA CCM-D IPG features the option of allowing the Local Sense (LS) channel to be assigned to either ventricular port. Using the Optimizer INTEGRA Programmer application, the physical port V1 or V2 can be electrically designated as the LS channel. Accordingly, when one physical port is designated as the LS channel, the other physical port is automatically designated as the RV channel.

10.4.3.2 CCM Triggering Based on Local Sense Events

Delivery of CCM therapy is dependent on the intrinsic myocardial electrical activity in the vicinity of the designated Local Sense (LS) channel. The LS channel is configured to sense the electrical activity of a small, localized area of the heart (near the fixation site of the designated ventricular electrode). In response to this sensed activity, the OPTIMIZER INTEGRA CCM-D IPG evaluates the myocardial electrical signal to determine whether it meets the criteria defined by the set of LS parameter values programmed into the device. If the criteria are met, then the IPG delivers CCM therapy. Within a cardiac cycle, the timing of the signal detected by the ventricular lead designated as the LS channel, especially with regards to the R wave, is the main criterion for the

OPTIMIZER INTEGRA CCM-D IPG to classify the cycle as normal or abnormal. CCM therapy is *not delivered* during cycles classified as abnormal.

10.4.3.3 Local Sense Alert Window

When the internal logic of the device detects ventricular events corresponding to cardiac cycles not classified as abnormal because of noise or tachycardia, it will open a Local Sense Alert Window.

The first event detected within the window serves as a trigger for CCM therapy delivery.

Valid Local Sense events detected outside the Alert Window are considered invalid and inhibit CCM therapy delivery for a programmable number of cycles. Inhibiting Local Sense events can be detected even between a triggering Local Sense event and the start of the corresponding CCM therapy, which in this case will not be delivered.

The Local Sense Alert Window is the time interval during which the leading-edge of a valid LS event is used to trigger CCM therapy delivery.

The temporal characteristics of this window are determined by two programmable parameters:

- **LS Alert Start**: The start of the time interval during which a valid LS event must be sensed in order to trigger the delivery of CCM therapy. Using the Optimizer INTEGRA Programmer application, Alert Start can be set to values between - 40 ms and 80 ms, in 2 ms increments.
- **LS Alert Width**: The time interval duration in which a valid LS event must be sensed in order to trigger the delivery of CCM therapy. Equivalent to the duration of the Alert Window. Using the Optimizer INTEGRA Programmer application, the Alert Width can be set to values between 1 ms and 40 ms, in 1 ms increments.

The leading edge of the first event detected within this window is used to trigger CCM therapy delivery. When an event is detected, the Local Sense Alert Window is immediately closed. Any Local Sense events detected after the window closes are considered to lie outside the Alert Window and lead to the **LS out of Window Status**.

If a Local Sense event is detected outside the Alert Window, CCM therapy delivery is *always inhibited.*

10.4.3.4 Local Sense Blanking Refractory Periods

Local Sense (LS) Blanking Refractory Periods allows for the masking of signals (e.g., noise) that may be detected before or after an RV or LS event.

The LS Blanking Refractory parameters are the following:

- **Pre RV Refractory Period**: The time interval before the RV event where all signals are masked from detection. With the Optimizer INTEGRA Programmer application, the duration can be set to values between 0 ms and 55 ms, in 5 ms increments.
- **Post RV Refractory Period**: The time interval after the RV event where all signals are masked from detection. With the Optimizer INTEGRA Programmer application, the duration can be set to values between 0 ms and 39 ms, in 1 ms increments.
- **Post LS Refractory Period**: The time interval after the LS event where all signals are masked from detection. With the Optimizer INTEGRA Programmer application, the duration can be set to values between 15 ms and 250 ms in 5 ms increments.

10.5 CCM Therapy Delivery

CCM therapy is a pulse train comprising a programmable number of consecutive pulses, each with two phases of opposite polarity and programmable duration.

10.5.1 CCM Train Parameters

The following are the CCM Train Parameters that can be programmed using the Optimizer INTEGRA Programmer application:

- **CCM Train Delay**: CCM therapy delivery is triggered by the Local Sense event. The CCM Train Delay is the time interval between the leading edge of the Local Sense triggering event and the start of CCM pulse train delivery. With the Optimizer INTEGRA Programmer application, the delay parameter can be set to values between 3 ms and 45 ms, in 1 ms increments.
- **CCM Amplitude**: This parameter sets the voltage of the CCM therapy pulse. With the Optimizer INTEGRA Programmer application, the amplitude can be set to values between 4.5 V and 7.5 V, in 0.5 V increments.
- **Number of Biphasic Pulses**: With the Optimizer INTEGRA Programmer application, the number of biphasic CCM therapy pulses can be set to 1, 2, or 3.
- **Balancing**: Delivery of each CCM pulse train is completed by a Balancing phase, which discharges any residual polarization at the electrode/tissue interface. Balancing is accomplished by short-circuiting the channels used to deliver the CCM therapy. With the Optimizer INTEGRA Programmer application, the Balancing phase can be set to values between 40 ms and 100 ms, in 10 ms increments.
- **First Phase Polarity**: The first phase polarity of the CCM therapy pulse can be set with the Optimizer INTEGRA Programmer application to “Positive” or “Negative”. When the polarity of the first phase is set to one value, the polarity of the second phase is automatically set to the opposite value.

  Note: If a patient expresses discomfort when the OPTIMIZER INTEGRA CCM-D IPG is delivering CCM therapy, setting the first phase polarity to “Negative” may help alleviate this discomfort.
- **Phase Duration**: The width of each CCM therapy pulse phase can be set with the Optimizer INTEGRA Programmer application to one of 4 possible values between 5.13 ms and 6.60 ms. The duration of both phases is automatically set to identical values.

  Note: Do not change the Phase Duration from the default setting of 5.13 ms unless directed by a physician.
- **Interval**: The interval is the time delay between each CCM therapy pulse phase. With the Optimizer INTEGRA Programmer application, the interval can be set to values between 0 ms and 7 ms, in 1 ms increments.

  Note: If a patient expresses discomfort when the OPTIMIZER INTEGRA CCM-D IPG is delivering CCM therapy, setting the Interval to a value > 1 ms may help alleviate this discomfort.
- **CCM Channels**: CCM therapy can either be delivered through one or both of the following channels:
  - **RV**
  - **LS**

10.5.2 Parameter Restrictions and Warnings

Whenever a parameter value is modified, the Optimizer INTEGRA Programmer application performs a check of the modified value against all the other parameter values currently programmed into the OPTIMIZER INTEGRA CCM-D IPG. If the modified parameter value violates one of the following restrictions, an error message is generated and displayed in the error message window.

1. *Total CCM event period (Alert Start + Alert Width +CCM Train Delay + CCM Train Duration + Balancing Phase Duration) must be shorter than the refractory period minus 86 ms (noise window)*

   Rationale: To avoid false event detections, the CCM therapy must be delivered entirely within the refractory period. Before the end of these refractory periods, an 86 ms long noise window is activated to detect external interference. Therefore, CCM therapy delivery has to be completed before the noise window is opened.

2. *Alert Start + CCM Train Delay must be equal to or greater than 3 ms*

   Rationale: The Alert Start time relates to the right ventricular event. Thus, if the Alert Start value is negative and a local sense event is detected during the AV interval, a right ventricular event will have to occur and be detected before the device can determine if the event fell inside the alert window. This implies that CCM therapy delivery will not occur before the detection of a right ventricular event. Thus, this constraint allows for the detection of a right ventricular event before CCM therapy delivery.

3. *Post LS Refractory Period cannot be greater than the CCM Train Delay*

   Rationale: Since the Post LS Refractory Period masks any event (e.g., CCM event) that may occur after the detection of the LS event, the delivery of CCM therapy cannot begin during the Post LS Refractory Period.

4. *LS Alert Window Start shall not be in the Pre or Post Ventricular Local Sense Refractory period*

   Rationale: If the LS Alert Window starts inside the Pre or Post RV Refractory period, only LS events falling inside the Alert Window and outside the RV Refractory Periods will be detected and trigger CCM therapy delivery. This effectively shortens the LS Alert window and may prevent the detection of an LS event.

5. *LS Alert Window End shall not be in the Pre or Post Ventricular Local Sense Refractory period*

   Rationale: If the LS Alert Window ends inside the Pre or Post RV Refractory period, only LS events falling inside the Alert Window and outside the RV Refractory Periods will be detected and trigger CCM therapy delivery. This effectively shortens the LS Alert window and may prevent the detection of an LS event.

6. *Post LS Refractory period should not be greater than the CCM Train Delay*

   Rationale: If the CCM Train Delay is shorter than the Post LS Refractory period, then the CCM therapy will be delivered within the Post LS Refractory period while the LS event is not sensed.

11.0 OPTIMIZER INTEGRA CCM-D IPG ICD FUNCTIONS AND PROGRAMMING OPTIONS

11.1 ICD General

11.1.1 ICD Mode

The OPTIMIZER INTEGRA CCM-D IPG features two ICD modes:

- **Off**: Disables the ICD module of the OPTIMIZER INTEGRA CCM-D IPG but permits CCM sensing and CCM therapy delivery by the CCM module
- **On**: Enables the ICD module of the OPTIMIZER INTEGRA CCM-D IPG and permits ICD sensing, detection, and therapy as well as CCM sensing and CCM therapy delivery by the CCM module

11.1.2 ICD General Parameters

The following are the ICD General Parameters that can be programmed using the Optimizer INTEGRA Programmer application:

- **Sense Slope Filter**: When this parameter is set to ON, it enables the filtering of the sensed signal by the ICD to reject waves with lower slopes (e.g., T-waves). This filter is beneficial for T-wave rejection in cases where large T-waves are misidentified as R-waves.
- **Long/Short Filter**: When this parameter is set to ON, it enables the filtering of waves that occur too close to a previous R-wave. This filter is used to reject T-waves and slow R-waves.
- **Onset**: When this parameter is set to ON, it enables the ICD to discriminate between slow acceleration due to exercise and sudden acceleration that is typically associated with tachyarrhythmias.
- **Onset (∆ rate)**: This parameter sets the rhythm onset discrimination threshold. When the Onset parameter is set to ON, the Onset (∆ rate) can be set to values between 30% and 85%, in 5% increments.
- **Morphology Threshold Percentage**: This parameter sets the threshold the ICD will use when classifying each R-wave for template matching. With the Optimizer INTEGRA Programmer application, the Morphology Threshold Percentage can be set to values between 60% and 95%, in 5% increments.
- **ICD Highest Sensitivity**: This sets the maximum sensitivity the ICD will use to recognize and classify ventricular events. With the Optimizer INTEGRA Programmer application, the ICD sensitivity can be set to one of 9 possible values between 0.3 mV and 3.5 mV.
- **Conduction Velocity History**: This parameter sets the number of intervals to be surveyed by the ICD when using conduction delay for arrhythmia discrimination. With the Optimizer INTEGRA Programmer application, the Conduction Velocity History can be set to values between 3 cycles and 6 cycles, in 1 cycle increments.
- **EHR (Timeout)**: When this parameter is set to ON, it enables the extended high rate (EHR) timer. The timer continues to run until slow rhythm (SR) is reestablished or it expires. EHR time expiration sets the prevailing rhythm to VF and the appropriate therapy sequence is started. When this parameter is set to ON, the Extended High Rate Timeout duration can be set to values between 10 s and 300 s, in 10 s increments.
- **Pre-trigger EGM Recording**: When this parameter is set to ON, it enables the OPTIMIZER INTEGRA CCM-D IPG to record 15 seconds of the EGM waveform that precedes a tachyarrhythmia episode.
- **Stored EGM Waveform Source**: This sets the source of the EGM waveform used by the OPTIMIZER INTEGRA CCM-D IPG when recording a tachyarrhythmia episode.

11.2 ICD Detection

ICD detection is initiated whenever the R-R intervals in a series of sensed R-waves are less than the interval threshold set for an enabled ICD detection zone interval. Whenever ICD detection is active, the OPTIMIZER INTEGRA CCM-D IPG undertakes the following actions:

- switches to the 3 - 40Hz bandpass filter
- disables CCM therapy

If the number of sensed R-wave within an enabled ICD detection zone exceeds the Binning parameter value set for the zone (e.g., 18 of 24), OPTIMIZER INTEGRA CCM-D IPG declares the ICD detection zone as the prevailing rhythm and begins recording the EGM of the episode at a sampling rate of 250 samples per second.

11.2.1 Episode EGM Storage

The INTEGRA CCM-D IPG has a maximum of eight buffers available to store recorded episode EGMs. Each buffer is divided into two sections that collectively store a 2 minute recording of each episode EGM. The first section stores the EGM that occurs about 15 seconds before the start of the episode and about 45 seconds after the start of the episode (if the “Pre-trigger EGM Recording” is enabled) or about 60 seconds after the start of the episode (if the “Pre-trigger EGM Recording” is disabled). The second section stores the EGM that occurs about 45 seconds before the end of the episode end and about 15 seconds after the end of the episode.

Note: If the length of the entire episode is less than 90 seconds (with “Pre-trigger EGM Recording” enabled) or 105 seconds (with “Pre-trigger EGM Recording” disabled), the EGM will continue to be recorded at the conclusion of the episode until the episode recording is 2 minutes in length.

If all the buffers are full and an EGM needs to be stored for a new episode that has priority over any of the already stored EGMs, a stored EGM that has a lower priority will be deleted from one of the buffers to allow for the storage of the new episode EGM. The order of priority used for the storage of episode EGMs is the following:

1. Stored EGMs corresponding to episodes where ICD therapy was delivered, in chronological order (the more recent the episode, higher the priority)
2. Other stored EGMs in chronological order (the more recent the episode, higher the priority)

11.2.2 ICD Detection Episode Termination

An ICD detection episode is terminated when any of the following criteria are met:

- Eight consecutive R-R intervals of sensed R-waves are greater than the interval threshold set for all the enabled ICD detection zone intervals
- Prevailing rhythm is classified as “Not Determined” when one of the following events occur:
    - Eight consecutive R-R intervals are a mix of SR, Monitor, or unsensed intervals
    - Sensing noise detection triggered during VT or FVT detections zones episodes
- The Optimizer INTEGRA Programmer application is used to send the Program command to the OPTIMIZER INTEGRA CCM-D IPG during an ICD Detection episode

11.2.3 ICD Detection Zone

The OPTIMIZER INTEGRA CCM-D IPG features four ICD detection zones:

- **Monitor**: When this parameter is set to ON, the parameter settings for the Monitor zone become visible.
- **VT**: When this parameter is set to ON, the parameter settings for the VT zone become visible.
- **FVT**: When this parameter is set to ON, the parameter settings for the FVT zone become visible.
- **VF**: When this parameter is set to ON, the parameter settings for the VF zone become visible.

11.2.4 Rate [Interval]

The Rate [Interval] parameter sets the interval threshold used by the ICD to classify each R-wave. The ICD measures the R-R interval of each sensed R-wave and then classifies it as belonging to a particular zone (e.g., VT) if its R-R interval is less than the interval threshold set for that zone.

With the Optimizer INTEGRA Programmer application, each of the following detection zones, when enabled, can be set to their own unique rate:

- **Monitor**: When the Monitor detection zone is set to ON, the rate threshold can be set to values between 110 bpm and 240 bpm, in 5 bpm increments.
- **VT**: When the VT detection zone is set to ON, the rate threshold can be set to values between 110 bpm and 240 bpm, in 5 bpm increments.
- **FVT**: When the FVT detection zone is set to ON, the rate threshold can be set to values between 110 bpm and 240 bpm, in 5 bpm increments.
- **VF**: When the VF detection zone is set to ON, the rate threshold can be set to values between 150 bpm and 300 bpm, in 5 bpm increments.

Note: The Rate [Interval] setting for each enabled zone cannot overlap and must be set to a higher rate for each subsequent enabled zone. The setting for this parameter has the following restriction: Monitor rate < VT rate < FVT rate < VF rate.

11.2.5 Binning

Successive heartbeat intervals are often not uniform in length, especially during an episode, so the OPTIMIZER INTEGRA CCM-D IPG uses an X-of-Y heuristic to identify the prevailing arrhythmia at any given time. Each interval is classified by length into a set of “bins”, of which there is one for each of the four zones. If X of the most recent series of Y intervals is of a single type, then the OPTIMIZER INTEGRA CCM-D IPG identifies that as the prevailing arrhythmia type. If no single type meets the X-of-Y threshold, then the prevailing type is Unknown. This X-of-Y binning is referred to as “majority”. If the programmed Binning count for an ICD detection zone has been met, then the arrhythmia for that zone is declared as the prevailing arrhythmia.

The Binning parameter sets the majority criteria used by the ICD to declare a prevailing arrhythmia.

With the Optimizer INTEGRA Programmer application, each enabled detection zone can be set to its own unique Binning count:

- **Monitor**: When the Monitor detection zone is set to ON, the Binning count can be set to Short (6 of 8), Regular (18 of 24), or Extended (30 of 40).
- **VT**: When the VT detection zone is set to ON, the Binning count can be set to Short (6 of 8), Regular (18 of 24), or Extended (30 of 40).
- **FVT**: When the FVT detection zone is set to ON, the Binning count can be set to Short (6 of 8), Regular (18 of 24), or Extended (30 of 40).
- **VF**: When the VF detection zone is set to ON, the Binning count can be set to Short (6 of 8), Regular (18 of 24), or Extended (30 of 40).

11.2.6 Stability (Δ variability)

Rate Stability assesses the consistency of R-R intervals to discriminate atrial fibrillation (AF), which is generally associated with inconsistent interval lengths, from ventricular tachycardia (VT), which produces a high-rate ventricular rhythm with more consistent interval lengths. A rhythm is deemed to be stable when 6/8 of the prior intervals fall within a programmed window defining the maximum allowable difference between the longest and shortest interval in the group of 8. Variation in the R-R interval outside of the window implies that the rhythm is AF rather than VT. The Rate Stability gate opens whenever the stability criteria are met and closes whenever it is not.

The Stability parameter enables rate stability criteria to be used for AF discrimination when it occurs within the VT or FVT detection zones. The Stability Window setting defines the maximum allowable difference between the longest and shortest interval in the group of 8 within these two zones.

With the Optimizer INTEGRA Programmer application, the VT and FVT detection zones can be set to unique Stability Window settings:

- **VT**: When the VT detection zone and the Stability parameter are both set to ON, the Stability Window can be set to values between 30 ms and 80 ms, in 10 ms increments.
- **FVT**: When the FVT detection zone and the Stability parameter are both set to ON, the Stability Window can be set to values between 30 ms and 80 ms, in 10 ms increments.

11.2.7 AF Gap (gap)

An AF Gap is identified whenever an R-R interval is greater than the average of the prior four R-R intervals plus a programmed gap duration. The AF Gap gate remains closed for 24 cardiac cycles following the identification of an AF Gap and opens thereafter. The 24-cycle count is reset every time an AF Gap is observed. **See Figure 2**.

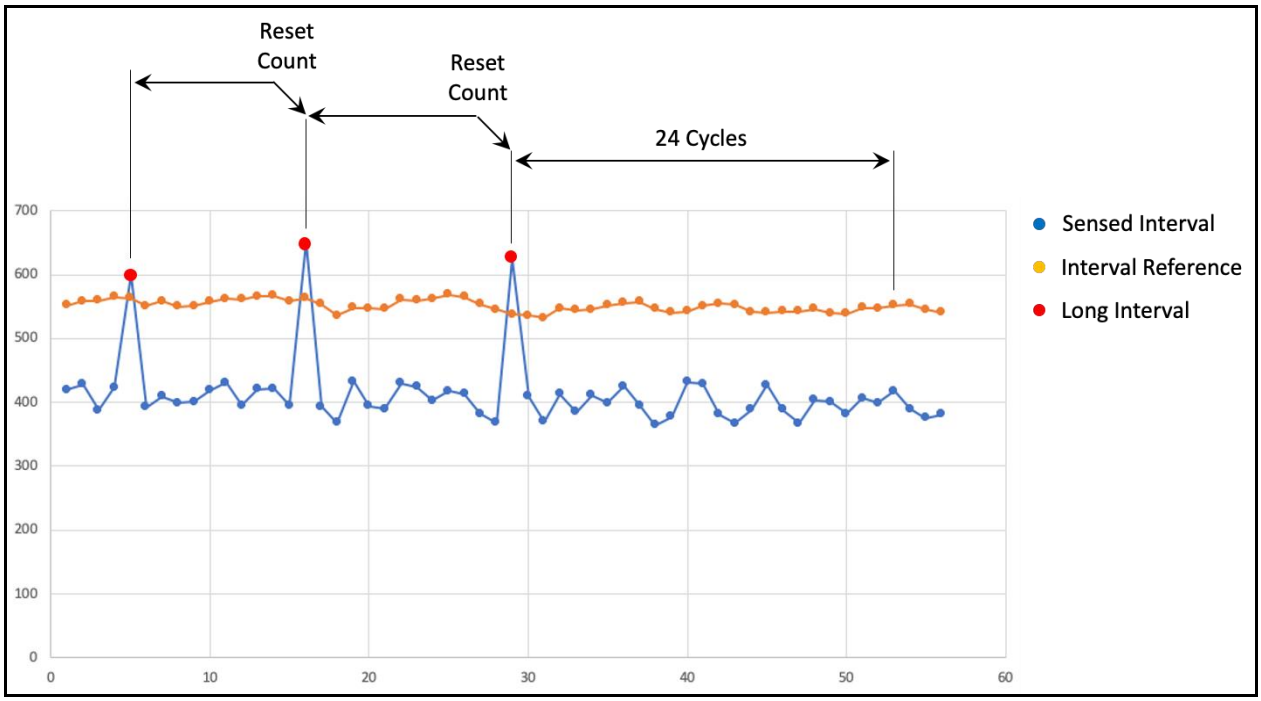


Figure 2: Example of AF Gap

The AF Gap parameter enables the AF gap to be used for AF discrimination when it occurs within the VT or FVT detection zones. The AF Gap threshold setting specifies the gap duration to be used when identifying an AF Gap in these two detection zones.

With the Optimizer INTEGRA Programmer application, the VT and FVT detection zones can be set with their own unique AF gap threshold settings:

- **VT**: When the VT detection zone and the AF Gap parameter are both set to ON, the AF Gap threshold can be set to values between 50 ms and 200 ms, in 10 ms increments.
- **FVT**: When the FVT detection zone and the AF Gap parameter are both set to ON, the AF Gap threshold can be set to values between 50 ms and 200 ms, in 10 ms increments.

11.2.8 AF Gap Persistence Interval

The AF Gap persistence interval specifies the number of cardiac cycles the AF Gap remains closed when an AF Gap is detected within the VT or FVT detection zones.

With the Optimizer INTEGRA Programmer application, the VT and FVT detection zones can each be set with their own unique AF gap persistence interval:

- **VT**: When the VT detection zone is set to ON, the AF Gap persistence interval can be set to OFF or values between 10 cycles and 30 cycles, in 2 cycle increments.
- **FVT**: When the FVT detection zone is set to ON, the AF Gap persistence interval can be set to OFF or values between 10 cycles and 30 cycles, in 2 cycle increments.

Note: If a new gap is detected during the AF Gap persistence interval, then the interval cycle is restarted.

11.2.9 Conduction Velocity

The Conduction Velocity setting uses LS Alert Window timing to prevent the inappropriate delivery of ICD therapy. Timing measurements are provided by CCM module and compared against programmed limits by the ICD module in order to determine whether the gate should be opened or closed.

With the Optimizer INTEGRA Programmer application, the Conduction Velocity can be individually enabled for the VT and FVT detection zones:

- **VT**: When the VT detection zone is set to ON, the Conduction Velocity can be set to OFF or ON for this zone.
- **FVT**: When the FVT detection zone is set to ON, the Conduction Velocity can be set to OFF or ON for this zone.

11.2.10 Morphology Binning

The Morphology Binning setting enables morphology binning for the VT or FVT detection zones. Once enabled, the Morphology Binning count parameter sets the majority criteria used by morphology to discriminate SVTs when they occur within these two detection zones.

With the Optimizer INTEGRA Programmer application, the VT and FVT detection zones can each be set with their own unique Morphology Binning settings:

- **VT**: When the VT detection zone and the Morphology Binning parameter are both set to ON, the VT Morphology Binning count can be set to Short (6 of 8), Regular (18 of 24), or Extended (30 of 40).
- **FVT**: When the FVT detection zone and the Morphology Binning parameter are both set to ON, the FVT Morphology Binning count can be set to Short (6 of 8), Regular (18 of 24), or Extended (30 of 40).

11.3 ICD Therapy

The following are the ICD Parameters that can be programmed using the Optimizer INTEGRA Programmer application:

- **Shock Waveform**: This parameter specifies the waveform used for all high voltage (HV) therapy pulses. With the Optimizer INTEGRA Programmer application, the Shock Waveform can be set to Biphasic (50/50 tilt) or Monophasic (75% tilt). **See Figure 3**.
- **Shock Waveform Polarity**: This parameter specifies the polarity of the high voltage (HV) therapy pulse for the first shock of an episode. With the Optimizer INTEGRA Programmer application, the Shock Waveform Polarity can be set to Positive (Anode is RV coil) or Negative (Cathode is RV coil). **See Figure 3**.

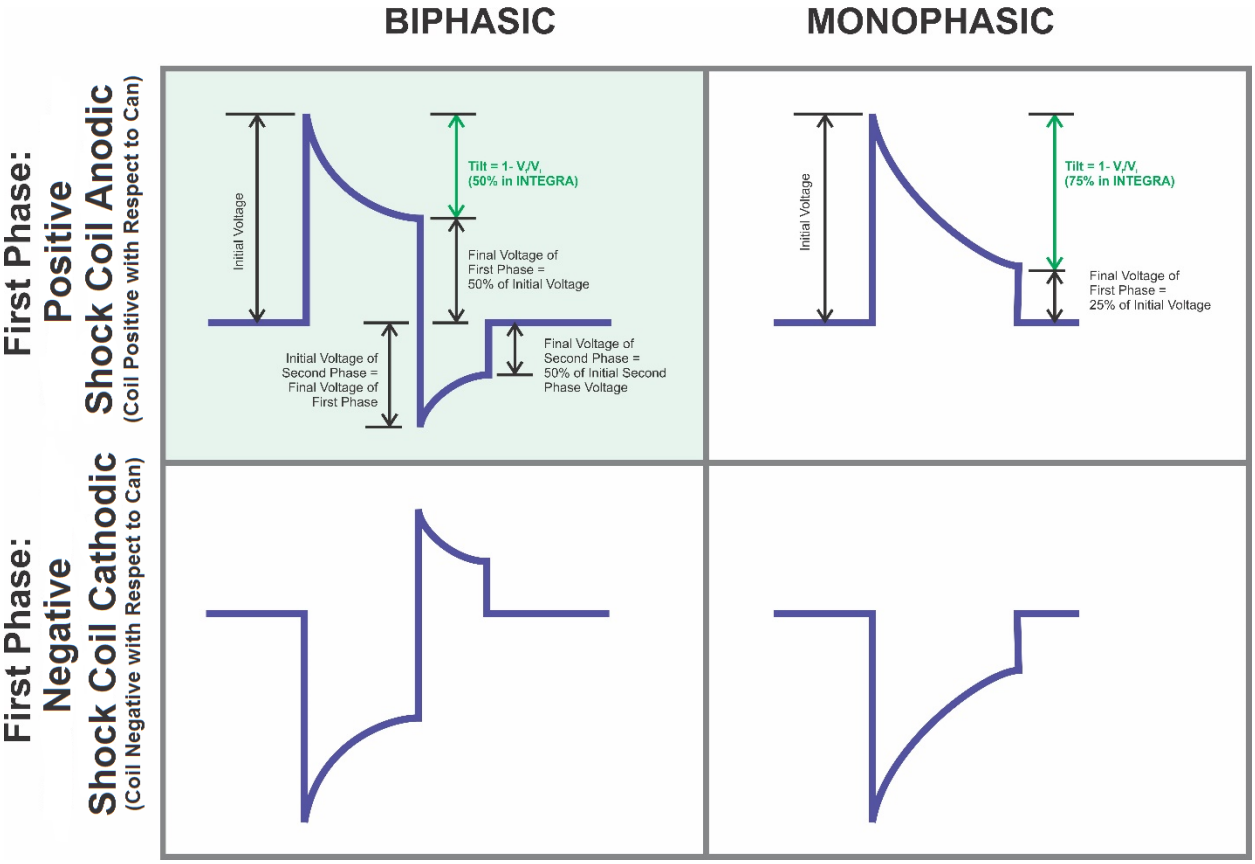


Figure 3: Illustration of the Shock Waveforms Options in the OPTIMIZER INTEGRA CCM-D IPG

- **Inverting Shock Polarity**: When this parameter is set to ON, it enables the ICD to alternate the polarity of each subsequent shock after the first failed shock in an episode.
- **Rescue Brady Pacing**: When this parameter is set to ON, it enables the ICD to deliver monophasic VVI bradycardia pacing at a fixed rate of 40 bpm when the detected R-R interval exceeds 1500 ms (40 bpm).

  WARNING: The OPTIMIZER INTEGRA CCM-D IPG is not indicated for the treatment of sustained bradyarrhythmias. The delivery of pacing stimulation by the OPTIMIZER INTEGRA CCM-D IPG quickly drains the non-rechargeable battery. Hence, the Rescue Brady Pacing feature is to be used only as an emergency measure when a patient develops profound bradycardia until a device indicated for the treatment of bradyarrhythmia is implanted.

  Note: Rescue Brady Pacing is not available while in an episode or during a post-shock bradycardia pacing period.

- **Post-Shock Brady**: When this parameter is set to ON, the ICD delivers monophasic VVI bradycardia pacing at 60 bpm for a programmable duration of time after any shock delivery if the detected R-R interval after a shock is below 1000 ms (60 bpm). When the Post-Shock Brady parameter is set to ON, the Pacing Duration can be set to one of 15 possible values between 10 s and 600 s.

  Note: Post-Shock Brady Pacing will be terminated if patient's heart rate exceeds 60 bpm at any time during the post-shock period and will no longer be available until after the delivery of another shock.

11.3.1 ICD Therapy Zone

The OPTIMIZER INTEGRA CCM-D IPG features three ICD therapy zones:

- **VT**: When this parameter is set to ON, the parameter settings for the VT zone become visible.
- **FVT**: When this parameter is set to ON, the parameter settings for the FVT zone become visible.
- **VF**: When this parameter is set to ON, the parameter settings for the VF zone become visible.

Note: An ICD therapy zone cannot be enabled unless its corresponding ICD Detection zone is enabled.

Note: The VT or FVT therapy zone cannot be enabled unless the VF therapy zone is also enabled.

11.3.2 HV Shock

With the Optimizer INTEGRA Programmer application, one can set the shock counts and energies for each ICD therapy zone:

- **VT**: When the VT therapy zone is set to ON, one shock is enabled and can be set to values between 6 J and 36 J, in 5 J increments. Up to three additional shocks can be also enabled and each additional shock can be set to OFF or values between 6 J and 36 J, in 5 J increments.
- **FVT**: When the FVT therapy zone is set to ON, one shock is enabled and can be set to values between 6 J and 36 J, in 5 J increments. Up to three additional shocks can be also enabled and each additional shock can be set to OFF or values between 6 J and 36 J, in 5 J increments.
- **VF**: When the VF therapy zone is set to ON, the Shocks parameter can be set to values between 1 and 6, and shock #1 and #2 can each be set to values between 6 J and 36 J, in 5 J increments.

Note: If the VT or FVT therapy zone is set to ON, at least one shock or ATP Burst Sequence must be enabled for that zone.

Note: If the number of shocks selected for the VF therapy zone is 1 or 2, the last shock value must be set to 36 J. If the number of shocks for the VF therapy zone is set to 3, 4, 5, or 6, then all subsequent shocks after the second shock will be delivered at 36 J.

11.3.3 Therapy Delay

The Therapy Delay setting specifies the amount of time ICD therapy is delayed for the VT and FVT therapy zones before the delivery sequence for the therapy zone is initiated.

With the Optimizer INTEGRA Programmer application, the VT and FVT therapy zones can each be set with their own unique Therapy Delay period:

- **VT**: When the VT therapy zone is set to ON, the Therapy Delay period can be set to one of 26 possible values between 0 s and 1200 s.
- **FVT**: When the FVT therapy zone is set to ON, the Therapy Delay period can be set to one of 26 possible values between 0 s and 1200 s.

11.3.4 ATP Bursts

The ATP Bursts setting specifies the number of biphasic antitachycardia pacing (ATP) bursts to be delivered for the VT and FVT therapy zones.

With the Optimizer INTEGRA Programmer application, the VT and FVT therapy zones can each be set with their own unique ATP Burst sequences:

- **VT**: When the VT therapy zone is set to ON, the number of ATP Burst sequences can be set to values between 0 (OFF) and 6 bursts, in 1 burst increments.
- **FVT**: When the FVT therapy zone is set to ON, the number of ATP Burst sequences can be set to values between 0 (OFF) and 6 bursts, in 1 burst increments.

11.3.4.1 ATP Initial Train

Setting the ATP Bursts to a non-zero value for either the VT or FVT therapy zone enables the Initial Trains parameter, which sets the number of antitachycardia pacing (ATP) train pulses to be delivered during the initial burst.

With the Optimizer INTEGRA Programmer application, the number of initial ATP pulses can be set for the VT and FVT zones:

- **VT**: When the VT therapy zone is set to ON and the ATP Bursts setting is set to a non-zero value, the ATP Train (pulses) can be set to values between 5 and 10 pulses, in 1 pulse increments.
- **FVT**: When the FVT therapy zone is set to ON and the ATP Bursts setting is set to a non-zero value, the ATP Train (pulses) can be set to values between 5 and 10 pulses, in 1 pulse increments.

Note: When the number of ATP bursts is set to a value greater than 1 and the number of ATP Initial Train pulses is set to less than 10, the number of ATP Train pulses in each successive ATP Burst is increments by 1.

11.3.4.2 Start from Last Successful

Setting the ATP Bursts to a non-zero value for either the VT or FVT therapy zone allows this parameter to become visible. When set to ON, the OPTIMIZER INTEGRA CCM-D IPG uses the number of ATP train pulses delivered in the last successful ATP Burst as the number of ATP train pulses it delivers in subsequent initial ATP Bursts.

11.3.4.3 ATP R-S1 (%RR)

Setting the ATP Bursts to a non-zero value for either the VT or FVT therapy zone enables the R-S1 (%RR) parameter, which specifies the interval of the ATP therapy pulses as a percentage of the detected R-R interval.

- **VT**: When the VT therapy zone is set to ON and the ATP Bursts setting is set to a non-zero value, the R-S1 (%RR) can be set to values between 70% and 90%, in 1% increments.
- **FVT**: When the FVT therapy zone is set to ON and the ATP Bursts setting is set to a non-zero value, the R-S1 (%RR) can be set to values between 70% and 90%, in 1% increments.

11.4 Suspension of ICD Therapy

The suspension of ICD therapy delivery by the OPTIMIZER INTEGRA CCM-D IPG can be accomplished by utilizing ICD Magnet Mode.

11.4.1 Disable ICD Command

The Optimizer INTEGRA Programmer application includes a button on the ICD Status Pane that allows the user to permanently suspend ICD therapy. If the button in its default “DISABLE ICD” state is tapped, this action permanently suspends ICD therapy and toggles the button to say “ENABLE ICD”. When the button in its “ENABLE ICD” state is tapped, this action unsuspends ICD therapy and toggles the button back to display “DISABLE ICD”.

11.4.2 ICD Magnet Mode

Note: To find out how the placement of a magnet over the implant site of the OPTIMIZER INTEGRA CCM-D IPG affects CCM Therapy delivery, see Section 10.2.2.

A health care provider (or patient) can force the OPTIMIZER INTEGRA CCM-D IPG to suspend ICD therapy delivery (all antiarrhythmic therapies) whenever a cardiac device magnet [minimum field strength of 90 Gauss @ 4.0 cm (1.5 in)] is applied over the implant site of the device. The delivery of ICD therapy will remain suspended as long as the magnet is maintained over the implant site. When the magnet is removed from the implant site, the OPTIMIZER INTEGRA CCM-D IPG will resume ICD therapy delivery using the previously programmed parameters. The ICD Magnet Mode has two setting options:

- **Therapy OFF when applied**: ICD therapy delivery is suspended whenever a pacemaker magnet is applied and maintained over the implant site of the OPTIMIZER INTEGRA CCM-D IPG.
- **Disabled**: ICD therapy delivery is not suspended whenever a pacemaker magnet is applied over the implant site of the OPTIMIZER INTEGRA CCM-D IPG.

12.0 MEDICAL PROCEDURE MODE

The OPTIMIZER INTEGRA CCM-D IPG features a Medical Procedure mode that allows the user to turn OFF the CCM and ICD therapy functions for patients scheduled to undergo a medical procedure that will subject them to an environment that may adversely affect the functionality of their implanted device.

Activation of the Medical Procedure mode requires the use of the Intelio Programmer. For further instructions on the use of the Medical Procedure mode, please refer to Section 3.19.2 of the Intelio Programmer for OPTIMIZER INTEGRA CCM-D System Instructions for Use.

13.0 DEVICE SETTINGS FOR INTEGRA-D STUDY

The following device parameter settings are to be used for the INTEGRA-D study:

Note: The parameter values listed below assume the presence of normal operating conditions.

CCM THERAPY

Parameter Name	Value
Mode	OVO-LS-CCM
CCM Therapy Mode	ON
Timed	5 hs/day
CCM Magnet Mode	Off 1 day
Extend on low CCM%	ON

CCM SCHEDULE

Parameter Name	Value
Start Time	00:00
End Time	23:59

CCM SENSING

Parameter Name	Value
Ventricle 1 Sensitivity	(set using OPTIset or adjust setting as needed)
Ventricle 1 Polarity (CCM only)	Bipolar
Ventricle 2 Sensitivity	(set using OPTIset or adjust setting as needed)
Ventricle 2 Polarity (CCM only)	Bipolar

V REFRACTORY

Parameter Name	Value
Post-V RV Refractory Period	(adjust setting as needed)

CCM INHIBIT

Parameter Name	Value
CCM Inhibit Cycles	1 beat
Tracking	110 bpm
After ATP	24 hours
After HV Shock	24 hours

TIMING ALGORITHM

Parameter Name	Value
LS Assignment	(set using OPTIset or adjust setting as needed)
LS Alert Start	(set using OPTIset or adjust setting as needed)
LS Alert Width	(set using OPTIset or adjust setting as needed)

LS BLANKING REFRACTORIES

Parameter Name	Value
Pre RV LS Refractory Period	(adjust setting as needed)
Post RV LS Refractory Period	(adjust setting as needed)
Post LS Refractory Period	(adjust setting as needed)

CCM TRAIN

Parameters Name	Value
CCM Train Delay	(set using OPTIset or adjust setting as needed)
CCM Amplitude	7.5 V (adjust as needed to prevent sensation)
Number of Biphasic Pulses	2
Balancing	40 ms
First Phase Polarity	(adjust setting as needed)
Phase Duration	5.13 ms
Interval	(adjust setting as needed)
CCM Channels	(adjust setting as needed)

ICD GENERAL

Parameters Name	Value
ICD Mode	ON
Sense Slope Filter	ON or physician discretion
Long/Short Filter	OFF or physician discretion
Onset	ON or physician discretion
Onset (Δ rate)	80% or physician discretion
Morphology Threshold Percentage	N/A
ICD Highest Sensitivity	0.3 mV or physician discretion
Conduction Velocity History	N/A
EHR (Timeout)	OFF or physician discretion
Pre-trigger EGM Recording	ON
Stored EGM Waveform Source	Bipolar or physician discretion

ICD DETECTION

Note: ICD Detection parameter values must be programmed in accordance with the INTEGRA-D Clinical Trial Protocol.

Parameters Name	Category	Value
Zone	Monitor	ON
	VT	OFF unless secondary indication present
	FVT	ON
	VF	ON
Rate [Interval]	Monitor	175 bpm [343 ms] – unless VT zone enabled, then physician discretion
	VT	180 bpm [333 ms] – unless VT zone enabled, then physician discretion
	FVT	190 bpm [316 ms]
	VF	250 bpm [240 ms]
Binning	Monitor	Extended (30 of 40)
	VT	OFF – unless VT zone enabled, then Extended (30 of 40)
	FVT	Extended (30 of 40)
	VF	Regular (18 of 24)
Stability (Δ variability)	VT	OFF – unless VT zone enabled, then ON
	FVT	ON
Stability Window	VT	OFF – unless VT zone enabled, then 70 ms or physician discretion
	FVT	70 ms or physician discretion
AF gap	VT	OFF – unless VT zone enabled, then ON or physician discretion
	FVT	ON or physician discretion
AF Gap threshold	VT	OFF – unless VT zone enabled, then 150 ms or physician discretion
	FVT	150 ms or physician discretion
AF-Gap persistence intervals	VT	OFF – unless VT zone enabled, then 20 cycles or physician discretion
	FVT	20 cycles or physician discretion
Conduction Velocity	VT	OFF
	FVT	OFF
Morphology Binning	VT	OFF
	FVT	OFF
Morphology Binning Count	VT	OFF
	FVT	OFF

ICD THERAPY (General)
Note: ICD Therapy parameter values must be programmed in accordance with the INTEGRA-D Clinical Trial Protocol.

Parameters Name	Value
Magnet Mode	Therapy OFF when applied
Shock Waveform	Biphasic
Shock Waveform Polarity	Positive or physician discretion
Inverting Shock Polarity	ON or physician discretion
Rescue Brady Pacing	OFF or physician discretion
Post-Shock Brady	ON
Pacing Duration	60 s or physician discretion
ATP Initial Train	8 pulses or physician discretion
ATP Start from last successful	ON or physician discretion
ATP R-S1 (%RR)	90% or physician discretion

ICD THERAPY (Zone-Specific)
Note: ICD Therapy parameter values must be programmed in accordance with the INTEGRA-D Clinical Trial Protocol.

Parameters Name	Category	Value
Zone	VT	OFF unless secondary indication present
	FVT	ON
	VF	ON
HV Shocks	VT	OFF – unless VT zone enabled, then 1 shock at 26 J and 3 shocks at 36 J (total of 4 shocks)
	FVT	4 shocks at 36 J
	VF	6 shocks at 36 J
Therapy Delay	VT	OFF – unless VT zone enabled, then 30 s or physician discretion
	FVT	10 s or physician discretion
ATP Bursts	VT	OFF – unless VT zone enabled, then 2 ATP bursts
	FVT	1 ATP burst

LOW-PRIORITY ALERTS

Parameters Name	Value
Alert Delivery Mode	Scheduled
Alert Delivery Mode Start Time, End Time	09:00, 21:00
Charger Battery Low	ON
Charger Failure	ON
Rechargeable Battery Low	ON
Battery Recharge Reminder	ON
Battery Recharge Reminder days	10 days
Long time without communicating with the IPG	ON
Long time without communicating with the IPG days	3 days
Long time without transmitting data to the remote monitor	OFF
Long time without transmitting data to the remote monitor days	N/A
Minimum CCM%	ON
Minimum CCM% Percentage	70%
Maximum lead impedance change	ON
Maximum lead impedance change Percentage	50%
CCM Not Sensing/Noise	ON
CCM therapy suspended	ON
CCM Safe Mode	ON
ICD battery RRT	ON
ICD Not sensing	ON
ICD battery EOS	ON
HV lead impedance not OK	ON
ICD Safe Mode	ON
ICD Anomaly	ON

HIGH-PRIORITY ALERTS

Parameters Name	Value
Detected VF Event	ON
Detected FVT Event	ON
Detected VT Event	ON
Detected Monitor Event	ON
Delivered HV Shock	ON
Delivered ATP	ON
Delivered Rescue Brady Pacing	ON

14.0 SERVICE AND WARRANTY

14.1 Limited Warranty Information

Impulse Dynamics warrants that all IPGs will be free from defects in materials and workmanship and conform, in all material respects, with their specifications.

EXCEPT AS EXPRESSLY SET FORTH HEREIN, IMPULSE DYNAMICS MAKES NO REPRESENTATION OR WARRANTY, EXPRESS OR IMPLIED, INCLUDING WITHOUT LIMITATION ANY WARRANTY THAT A PRODUCT OR SERVICE IS MERCHANTABLE OR FIT FOR ANY PARTICULAR PURPOSE.

14.2 Mandatory Battery Charging

The rechargeable battery in the OPTIMIZER INTEGRA CCM-D IPG is designed to provide optimal performance if it is completely recharged on a weekly basis. Regular weekly recharging sessions are required to prevent deterioration of the rechargeable battery and depletion of the non-rechargeable battery, which will lead to decreased device longevity.

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APPENDIX I

As a convenience to the user, the following overview provides a brief and succinct summary of the characteristics of the OPTIMIZER INTEGRA CCM-D IPG. Some of the information is also presented in the IFU in text form.

Physical Characteristics

Model	CCM X12
Height (mm)	95.4 ± 2.0
Width (mm)	53.0 ± 0.5
Thickness (mm)	13.8 ± 0.5
Volume (cm^3)	49.5 ± 0.5
Mass (g)	85 ± 9
Area of Exposed Metal Can[a] (cm^2)	99.8
Radiopaque ID	**ID.OI.y**[b]
Materials in Contact with Human Tissue[c]	Titanium Epoxy resin Silicone rubber
Lead Connectors	V1: DF4-LLHO V2: 3.2 mm; IS-1 BI

[a] When using unipolar ventricular sensing for CCM, the case of the OPTIMIZER INTEGRA CCM-D device serves as an indifferent electrode.

[b] "ID" is the manufacturer code for Impulse Dynamics; "OI" is the model code for OPTIMIZER INTEGRA CCM-D; "y" is replaced by the year code: "A" for 2019, "B" for 2020, "C" for 2021, etc...

[c] Tests have revealed that these materials are biocompatible. The OPTIMIZER INTEGRA CCM-D IPG does not cause any temperature elevation capable of damaging the surrounding tissue.



Figure 4: OPTIMIZER INTEGRA CCM-D IPG

Electrical Characteristics

Implantable Pulse Generator Modes	VVE-VVI	
Antitachycardia Pacing (ATP) Pulse Amplitude	7.0 V	
Available Energy Settings for Cardioverter Defibrillator Pulses (J)	6, 11, 16, 21, 26, 31, 36	
Delivered Cardioverter Defibrillator Biphasic Pulse Energy with 50Ω Defibrillation Impedance[a]	@ Maximum Energy Setting of 36 J:	33.2 J
	@ Minimum Energy Setting of 6 J:	5.8 J
	@ Mean Energy Setting of 21 J:	19.3 J
Delivered Cardioverter Defibrillator Monophasic Pulse Energy with 50Ω Defibrillation Impedance[a]	@ Maximum Energy Setting of 36 J:	33.5 J
	@ Minimum Energy Setting of 6 J:	5.9 J
	@ Mean Energy Setting of 21 J:	19.5 J
Peak ICD Output Voltage for Biphasic Pulse Energy[a]	@ Maximum Energy Setting of 36 J:	670 V
	@ Minimum Energy Setting of 6 J:	275 V
	@ Mean Energy Setting of 21 J:	515 V
Peak ICD Output Voltage for Monophasic Pulse Energy[a]	@ Maximum Energy Setting of 36 J:	670 V
	@ Minimum Energy Setting of 6 J:	275 V
	@ Mean Energy Setting of 21 J:	515 V
Typical Charge Time for Cardioverter Defibrillator Pulse at Maximum Energy Setting of 36 J[a]	Beginning of Service (BOS):	12 s
	Recommended Replacement Time (RRT):	19s

[a] Values shown are nominal. Exact values will vary between devices and operating conditions.

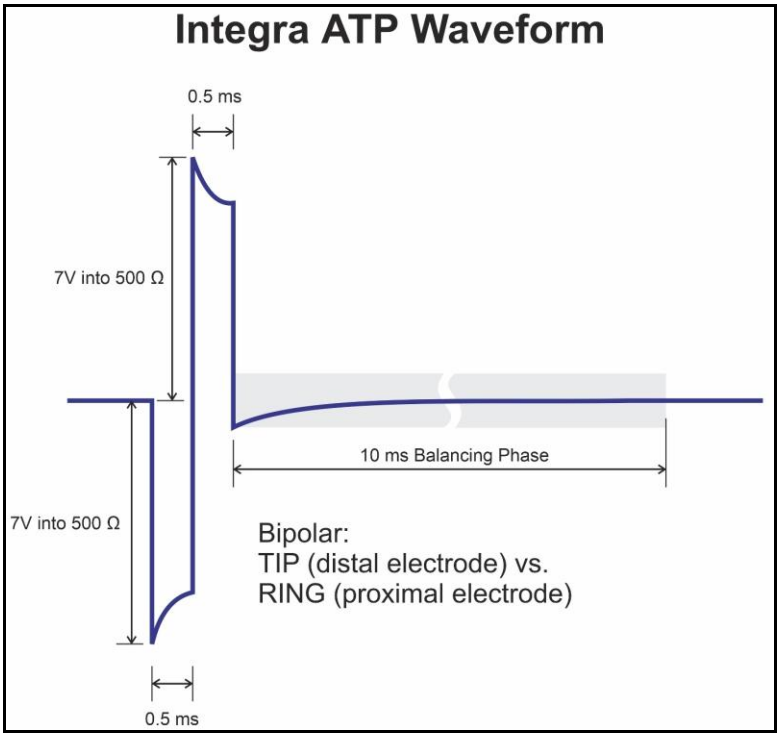


Figure 5: Illustration of the OPTIMIZER INTEGRA CCM-D IPG's ATP Waveform

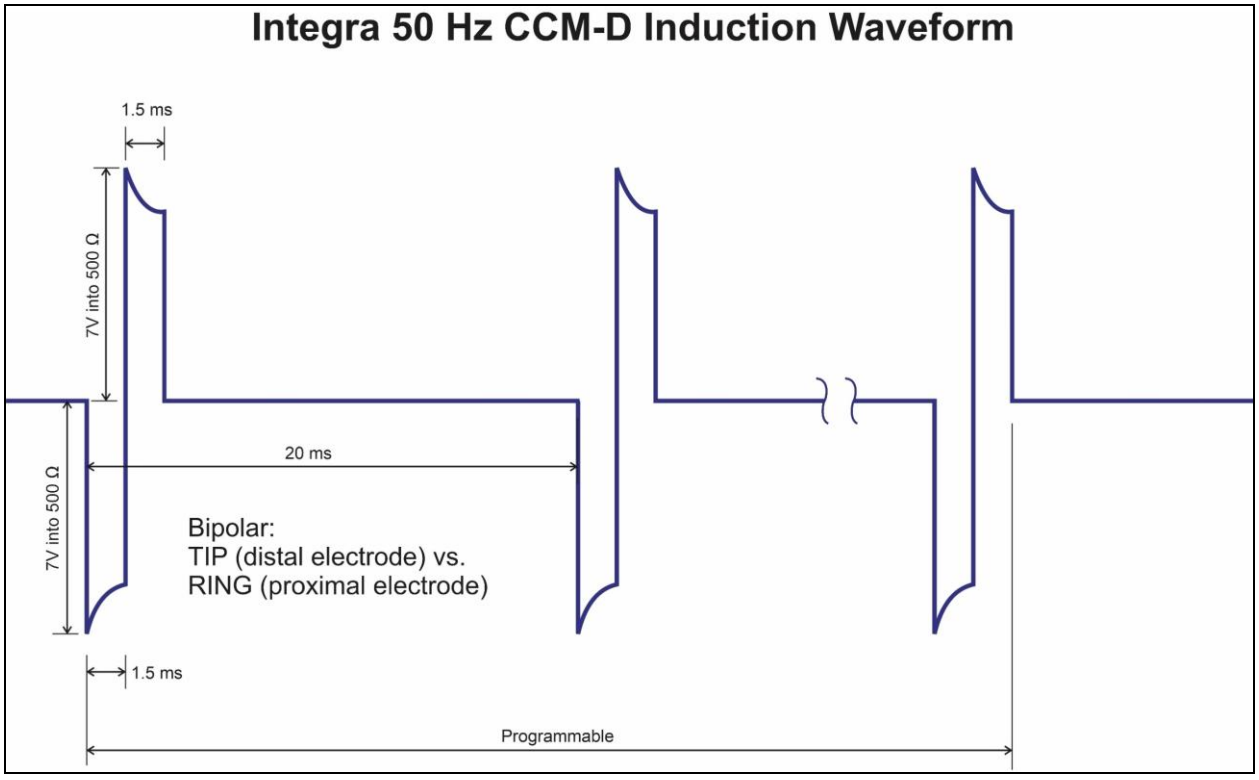


Figure 6: Illustration of the OPTIMIZER INTEGRA CCM-D IPG's 50 Hz Induction Waveform

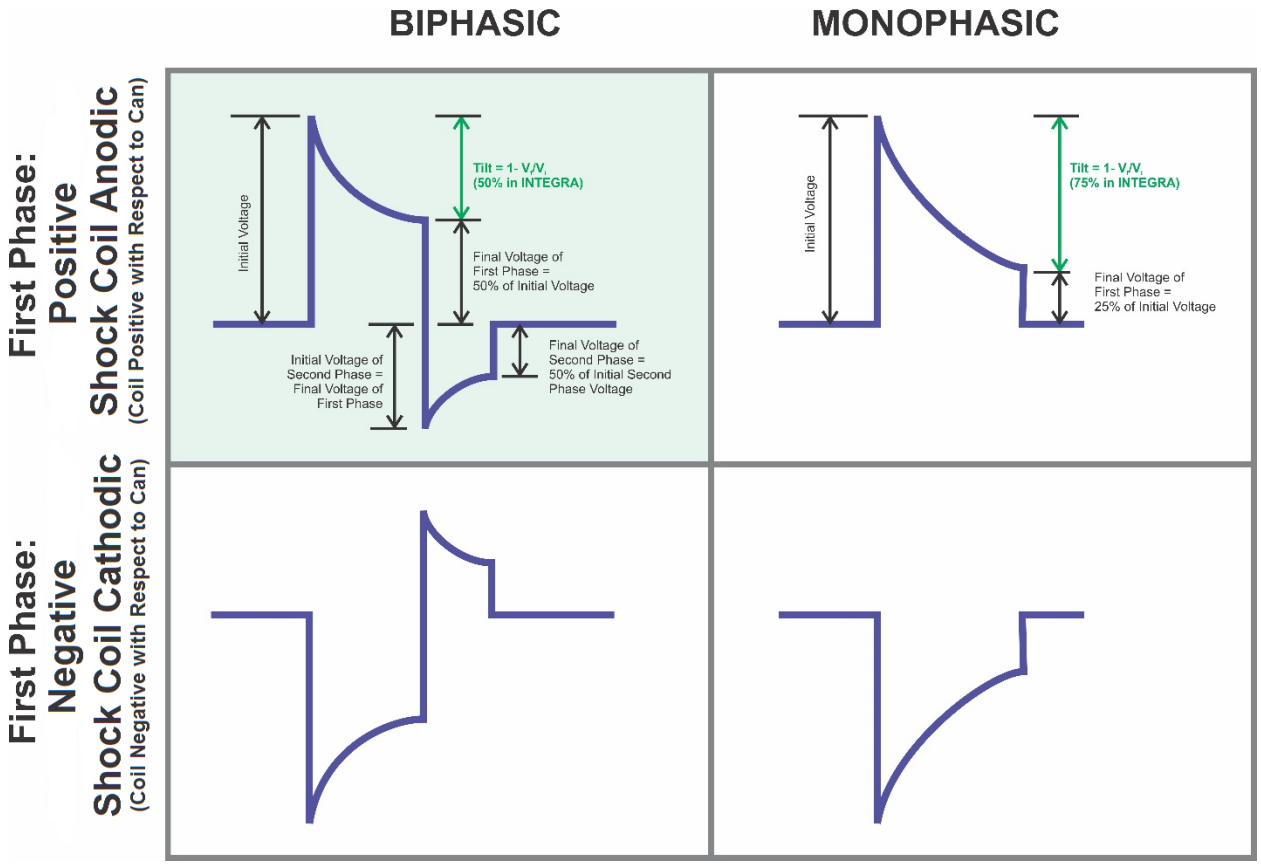


Figure 7: Illustration of the OPTIMIZER INTEGRA CCM-D IPG's Defibrillation Waveforms

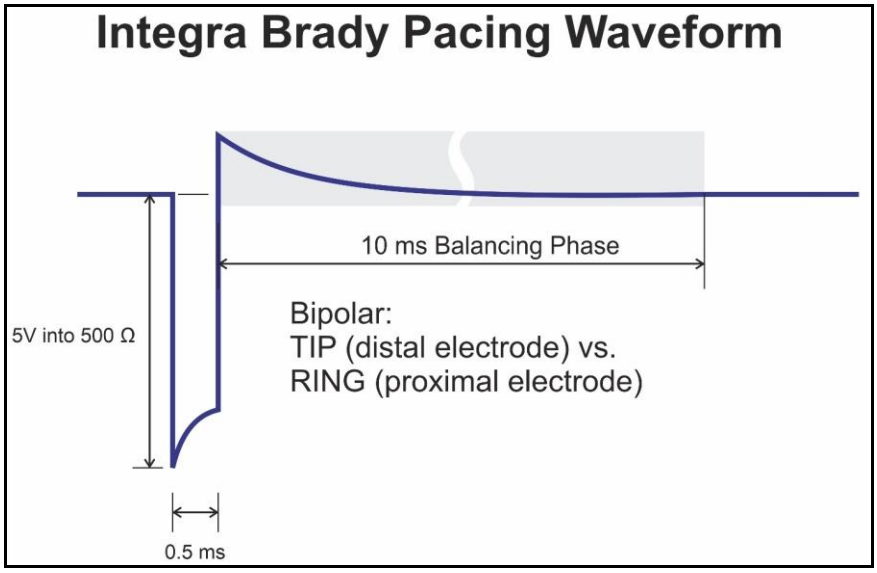


Figure 8: Illustration of the OPTIMIZER INTEGRA CCM-D IPG's Brady Pacing Waveform

Current Consumption from Rechargeable Battery

Mode	Current Consumption
OOO, ICD Mode: OFF	Less than 41 µA
OVO-LS-CCM ON, ICD Mode: OFF	130 µA[a]
OVO-LS-CCM ON, ICD Mode: ON, EGM Pre-trigger OFF	160 µA[a]
OVO-LS-CCM ON, ICD Mode: ON, EGM Pre-trigger ON	260 µA[a]

[a] Value when the OPTIMIZER INTEGRA CCM-D IPG is not actively delivering CCM therapy

Rechargeable Battery Specifications

Model and IEC Type	2993, rechargeable
Manufacturer	Greatbatch Medical
Chemistry	Lithium-ion
Battery Voltage Range	2.8 V to 4.4 V
Battery Service Life[a]	> 20 years
Nominal Capacity	215 mAh

[a] Battery service life conditions:

- Combined (parallel) lead impedance of enabled CCM channel(s): 250 Ω (either singular impedance if one CCM channel is enabled or parallel impedance if both CCM channels are enabled – e.g., 500 Ω lead impedance for both the V1 and V2 leads, with both channels enabled, would result in a parallel CCM impedance of 250 Ω)
- CCM therapy delivery: 5 hours per day
- Heart rate and CCM delivery percentage equating to a CCM therapy delivery rate of 60 CCM trains per minute
- ICD mode programmed ON (monitoring state), pre-trigger EGM recording programmed OFF
- Weekly recharging of the OPTIMIZER INTEGRA CCM-D IPG's rechargeable battery

Note: Deviations from the conditions listed above may decrease the service life of the rechargeable battery in the OPTIMIZER INTEGRA CCM-D IPG.

Non-Rechargeable Battery Specifications

Model and IEC Type	3340, primary
Manufacturer	Greatbatch Medical
Chemistry	Li/CFx-SVO Hybrid
Nominal Battery Voltage	3.2 V
Battery Service Life[a]	20 years
Nominal Capacity at BOL	1.784 Ah

[a] Battery service life conditions:

- The IPG has been on the shelf for no more than 1 year after manufacture.
- At most, 44 full-energy defibrillation capacitor charges have been conducted between BOL and RRT. These include 2 shocks at implant and 2 shocks per year for 20 years (defibrillation shocks or capacitor reform every 6 months).
- The patient has been fully compliant throughout the life of the device with charging the IPG. Thus, sensing, VT/VF detection and housekeeping operations have always been powered from its rechargeable battery.
- Rescue Brady Pacing has not been delivered to the patient
- The IPG has been operating normally throughout its service life.

Safe Modes

Mode	Description
CCM Safe Mode	Occurs when the device encounters conditions considered to be the result of faulty device hardware or firmware. In this mode, CCM therapy is not delivered and cardiac events are not sensed.
ICD Safe Mode	Occurs when the ICD module encounters conditions considered to be the result of faulty device hardware or firmware. In this mode, ICD therapies (includes all antiarrhythmic therapies) are not delivered and cardiac events are not sensed.

Programmable Parameters

CCM THERAPY PARAMETERS

Parameters Name	Values	Characteristics
Mode	OOO	Standby mode: no events are sensed and no CCM pulse trains are delivered
	OVO-LS-CCM	Active mode where the device senses ventricular and local sense events and is capable of CCM therapy delivery
CCM Therapy Mode	OFF	No pulse train enabled
	ON	As defined by the parameter values below
CCM Therapy (hs/day)	1 hs/day to 24 hs/day in 1 hs/day increments	
Start Time (hour)	00 h to 23 h in 1 h increments	
Start Time (minute)	00 m to 59 m in 1 m increments	
End Time (hour)	00 h to 23 h in 1 h increments	
End Time (minute)	00 m to 59 m in 1 m increments	
CCM Magnet Mode	Off 1 day or Off	
Extend on Low CCM%	ON or OFF	

V SENSING PARAMETERS

Parameter Name	Values
Ventricle 1 Sensitivity	14 possible between 1.0 mV and 10 mV
Ventricle 1 Polarity (CCM only)	Bipolar
Ventricle 2 Sensitivity	14 possible between 1.0 mV and 10 mV
Ventricle 2 Polarity (CCM only)	Bipolar

RV REFRACTORY PARAMETERS

Parameter Name	Values
Post-V RV Refractory Period	148 ms to 452 ms in 8 ms increments

CCM INHIBIT PARAMETERS

Parameter Name	Values
CCM Inhibit Cycles	1 to 16 in increments of 1
Tracking Rate	25 possible between 62 bpm and 110 bpm
After ATP	1 to 24 in increments of 1 hour
After HV Shock	1 to 24 in increments of 1 hour

CCM TIMING PARAMETERS

Parameter Name	Values
LS Assignment	V1 or V2
LS Alert Start	- 40 ms to 80 ms in 2 ms increments
LS Alert Width	1 ms to 40 ms in 1 ms increments

LS BLANKING REFRACTORY PARAMETERS

Parameter Name	Values
Pre RV LS Refractory Period	0 ms to 55 ms in 5 ms increments
Post RV LS Refractory Period	0 ms to 39 ms in 1 ms increments
Post LS Refractory Period	15 ms to 250 ms in 5 ms increments

CCM TRAIN PARAMETERS

Parameters Name	Values
CCM Train Delay	3 ms to 45 ms in 1 ms increments
CCM Amplitude	4.5 V to 7.5 V in 0.5 V increments
Number of Biphasic Pulses	1, 2, or 3
Balancing	40 ms to 100 ms in 10 ms increments
First Phase Polarity	“Positive” or “Negative”
Phase Duration	4 possible between 5.13 ms and 6.60 ms.
Interval	0 ms to 7 ms in 1 ms increments
CCM Channels	RV and/or LS

ICD GENERAL PARAMETERS

Parameters Name	Values
ICD Mode	ON or OFF
Sense Slope Filter	ON or OFF
Long/Short Filter	ON or OFF
Onset	ON or OFF
Onset (Δ rate)	30% to 85% in 5% increments
Morphology Threshold Percentage	60% to 95% in 5% increments
ICD Highest Sensitivity	9 possible between 0.3 mV and 3.5 mV
Conduction Velocity History	3 cycles to 6 cycles in 1 cycle increments
EHR (timeout)	ON or OFF
Pre-trigger EGM Recording	ON or OFF
Stored EGM Waveform Source	Bipolar or Unipolar

ICD DETECTION PARAMETERS

Parameters Name	Category	Values
Zone	Monitor	ON or OFF
	VT	ON or OFF
	FVT	ON or OFF
	VF	ON or OFF
Rate [Interval]	Monitor	110 bpm to 240 bpm in 5 bpm increments
	VT	110 bpm to 240 bpm in 5 bpm increments
	FVT	110 bpm to 240 bpm in 5 bpm increments
	VF	150 bpm to 300 bpm in 5 bpm increments
Binning	Monitor	Short (6 of 8), Regular (18 of 24), or Extended (30 of 40)
	VT	Short (6 of 8), Regular (18 of 24), or Extended (30 of 40)
	FVT	Short (6 of 8), Regular (18 of 24), or Extended (30 of 40)
	VF	Short (6 of 8), Regular (18 of 24), or Extended (30 of 40)
Stability (Δ variability)	VT	ON or OFF
	FVT	ON or OFF
Stability Window	VT	30 ms to 80 ms in 10 ms increments
	FVT	30 ms to 80 ms in 10 ms increments
AF gap	VT	ON or OFF
	FVT	ON or OFF
AF Gap threshold	VT	50 ms to 200 ms in 10 ms increments
	FVT	50 ms to 200 ms in 10 ms increments
AF-Gap persistence intervals	VT	OFF or 10 cycles to 30 cycles in 2 cycle increments
	FVT	OFF or 10 cycles to 30 cycles in 2 cycle increments
Conduction Velocity	VT	ON or OFF
	FVT	ON or OFF
Morphology Binning	VT	ON or OFF
	FVT	ON or OFF
Morphology Binning Count	VT	Short (6 of 8), Regular (18 of 24), or Extended (30 of 40)
	FVT	Short (6 of 8), Regular (18 of 24), or Extended (30 of 40)

ICD THERAPY PARAMETERS (General)

Parameters Name	Values
Magnet Mode	“Disabled” or “Therapy OFF when applied”
Shock Waveform	“Biphasic” or “Monophasic”
Shock Waveform Polarity	“Positive” or “Negative”
Inverting Shock Polarity	ON or OFF
Rescue Brady Pacing	ON or OFF
Post-Shock Brady	ON or OFF
Post-Shock Brady Pacing Duration	15 possible between 10 s and 600 s
ATP Initial Train	5 pulses to 10 pulses in 1 pulse increments
ATP Start from last successful	ON or OFF
ATP R-S1 (%RR)	70% to 90% in 1% increments

ICD THERAPY PARAMETERS (Zone-Specific)

Parameters Name	Category	Values
Zone	Monitor	ON or OFF
	VT	ON or OFF
	FVT	ON or OFF
	VF	ON or OFF
HV Shocks	VT	OFF or 6 J to 36 J in 5 J increments
	FVT	OFF or 6 J to 36 J in 5 J increments
	VF	OFF or 6 J to 36 J in 5 J increments
Therapy Delay	VT	26 possible between 0 s and 1200 s
	FVT	26 possible between 0 s and 1200 s
ATP Bursts	VT	0, 1, 2, 3, 4, 5, or 6
	FVT	0, 1, 2, 3, 4, 5, or 6

Nominal Settings

CCM THERAPY

Parameter Name	Nominal Value
Mode	OOO
CCM Therapy Mode	OFF (when Mode enabled)
Timed	5 hs/day (when CCM Therapy Mode enabled)
CCM Magnet Mode	Off 1 day (when CCM Therapy Mode enabled)
Extend on low CCM%	ON (when CCM Therapy Mode enabled)

CCM SCHEDULE

Parameter Name	Nominal Value
Start Time	00:00
End Time	23:59

V SENSING

Parameter Name	Nominal Value
Ventricle 1 Sensitivity	2 mV
Ventricle 1 Polarity (CCM only)	Bipolar
Ventricle 2 Sensitivity	2 mV
Ventricle 2 Polarity (CCM only)	Bipolar

RV REFRACTORY

Parameter Name	Nominal Value
Post-V RV Refractory Period	249 ms

CCM INHIBIT

Parameter Name	Nominal Value
CCM Inhibit Cycles	1 beat
Tracking	110 bpm
After ATP	24 hours
After HV Shock	24 hours

TIMING ALGORITHM

Parameter Name	Nominal Value
LS Assignment	V1
LS Alert Start	0 ms
LS Alert Width	15 ms

LS BLANKING REFRACTORIES

Parameter Name	Nominal Value
Pre RV LS Refractory Period	0 ms
Post RV LS Refractory Period	0 ms
Post LS Refractory Period	30 ms

CCM TRAIN

Parameters Name	Nominal Value
CCM Train Delay	30 ms
CCM Amplitude	7.5 V
Number of Biphasic Pulses	2
Balancing	40 ms
First Phase Polarity	Positive
Phase Duration	5.13 ms
Interval	2 ms
CCM Channels	RV (enabled), LS (enabled)

ICD GENERAL

Parameters Name	Nominal Value
ICD Mode	OFF
Sense Slope Filter	ON (when ICD Mode enabled)
Long/Short Filter	OFF
Onset	ON (when ICD Mode enabled)
Onset (∆ rate)	80%
Morphology Threshold Percentage	80% (when Morphology Binning enabled)
ICD Highest Sensitivity	0.3 mV
Conduction Velocity History	5 cycles
EHR (timeout)	OFF
Pre-trigger EGM Recording	ON (when ICD Mode enabled)
Stored EGM Waveform Source	Unipolar

ICD DETECTION

Parameters Name	Category	Nominal Value
Zone	Monitor	OFF
	VT	OFF
	FVT	OFF
	VF	OFF
Rate [Interval]	Monitor	150 bpm [400 ms] (when Zone enabled)
	VT	170 bpm [353 ms] (when Zone enabled)
	FVT	190 bpm [316 ms] (when Zone enabled)
	VF	250 bpm [240 ms] (when Zone enabled)
Binning	Monitor	Regular (18 of 24) (when Zone enabled)
	VT	Regular (18 of 24) (when Zone enabled)
	FVT	Regular (18 of 24) (when Zone enabled)
	VF	Short (6 of 8) (when Zone enabled)
Stability (Δ variability)	VT	ON (when Zone enabled)
	FVT	ON (when Zone enabled)
Stability Window	VT	70 ms (when Zone enabled)
	FVT	70 ms (when Zone enabled)
AF gap	VT	ON (when Zone enabled)
	FVT	ON (when Zone enabled)
AF Gap threshold	VT	150 ms (when Zone enabled)
	FVT	150 ms (when Zone enabled)
AF-Gap persistence intervals	VT	20 cycles (when Zone enabled)
	FVT	20 cycles (when Zone enabled)
Conduction Velocity	VT	ON (when Zone enabled)
	FVT	ON (when Zone enabled)
Morphology Binning	VT	OFF
	FVT	OFF
Morphology Binning Count	VT	Short (6 of 8) (when enabled)
	FVT	Short (6 of 8) (when enabled)

ICD THERAPY (General)

Parameters Name	Nominal Value
Magnet Mode	Therapy OFF when applied
Shock Waveform	Biphasic
Shock Waveform Polarity	Positive
Inverting Shock Polarity	ON
Rescue Brady Pacing	OFF
Post-Shock Brady	ON
Pacing Duration	60 s
ATP Initial Train	8 pulses (if ATP Bursts > 0)
ATP Start from last successful	ON (if ATP Bursts > 0)
ATP R-S1 (%RR)	90% (if ATP Bursts > 0)

ICD THERAPY (Zone-Specific)

Parameters Name	Category	Nominal Value
Zone	VT	OFF
	FVT	OFF
	VF	OFF
HV Shocks	VT	OFF (when Zone enabled)
	FVT	OFF (when Zone enabled)
	VF	4 shocks at 36 J each (when Zone enabled)
Therapy Delay	VT	30 s (when Zone enabled)
	FVT	10 s (when Zone enabled)
ATP Bursts	VT	0
	FVT	0

LOW-PRIORITY ALERTS **(See Intelio Programmer IFU for more information)**

Parameters Name	Nominal Value
Alert Delivery Mode	Scheduled
Alert Delivery Mode Start Time, End Time	09:00, 21:00
Charger Battery Low	ON
Charger Failure	ON
Rechargeable Battery Low	ON
Battery Recharge Reminder	ON
Battery Recharge Reminder days	10 days
Long time without communicating with the IPG	ON
Long time without communicating with the IPG days	3 days
Long time without transmitting data to the remote monitor	OFF
Long time without transmitting data to the remote monitor days	7 days (when alert enabled)
Minimum CCM%	ON
Minimum CCM% Percentage	70%
Maximum lead impedance change	ON
Maximum lead impedance change Percentage	50%
CCM Not Sensing/Noise	ON
CCM therapy suspended	ON
CCM Safe Mode	ON
ICD battery RRT	ON
ICD Not Sensing	ON
ICD battery EOS	ON
HV lead impedance not OK	ON
ICD Safe Mode	ON
ICD Anomaly	ON

HIGH-PRIORITY ALERTS **(See Intelio Programmer IFU for more information)**

Parameters Name	Nominal Value
Detected VF Event	ON
Detected FVT Event	ON
Detected VT Event	ON
Detected Monitor Event	ON
Delivered HV Shock	ON
Delivered ATP	ON
Delivered Rescue Brady Pacing	ON

APPENDIX II

Battery Charge Longevity

The battery charge longevity for the rechargeable battery in the OPTIMIZER INTEGRA CCM-D IPG can be estimated from the following table.

Note: The battery charge longevity data below are conservative estimates.

Table 1 show the charge longevity for the rechargeable battery in the OPTIMIZER INTEGRA CCM-D IPG as a function of parallel lead impedance when tested under the following conditions:

- CCM therapy delivery: 5 hours per day
- Number of pulses per CCM train: 2
- Phase duration: 5.13 ms
- Heart rate: 75 bpm
- 100% CCM therapy delivery
- Nominal Rechargeable Battery Voltage: 3.8 V

Table 1

Parallel Lead (V1‖V2) Impedance (Ω)	CCM Amplitude (V)	Battery Charge Longevity (days)		
		CCM Therapy: ON ICD Therapy: OFF	CCM Therapy: ON ICD Therapy: ON	
			Pre-trigger EGM: OFF	Pre-trigger EGM: ON
220	4.5	27	23	18
220	6	18	17	14
220	7.5	13	12	11
250	4.5	28	26	19
250	6	20	19	15
250	7.5	14	13	11
300	4.5	31	26	21
300	6	22	20	16
300	7.5	16	15	13
600	4.5	41	35	25
600	6	32	27	21
600	7.5	23	23	18
900	4.5	47	41	27
900	6	38	32	23
900	7.5	30	27	21
1200	4.5	50	41	28
1200	6	42	34	25
1200	7.5	32	31	22

Battery Current Consumption

The current consumption from the rechargeable battery in the OPTIMIZER INTEGRA CCM-D IPG is highly dependent on the amount of energy used when CCM therapy is delivered to the patient.

Table 2 shows the average measured current consumption from the rechargeable battery in the OPTIMIZER INTEGRA CCM-D IPG during CCM therapy delivery under the following conditions:

- Number of pulses per CCM train: 2
- Phase duration: 5.13 ms
- Heart rate: 75 bpm
- 100% CCM therapy delivery
- Nominal Rechargeable Battery Voltage: 3.8 V

Table 2

Parallel Lead (V1‖V2) Impedance (Ω)	CCM Amplitude (V)	Battery Current Consumption (mA)		
		CCM Therapy: ON ICD Therapy: OFF	CCM Therapy: ON ICD Therapy: ON	
			Pre-trigger EGM: OFF	Pre-trigger EGM: ON
220	4.5	1.0	1.1	1.2
220	6	1.7	1.7	1.9
220	7.5	2.6	2.6	2.7
250	4.5	0.9	1.0	1.1
250	6	1.5	1.5	1.7
250	7.5	2.3	2.4	2.6
300	4.5	0.8	0.9	0.9
300	6	1.4	1.4	1.5
300	7.5	2.0	2.0	2.2
600	4.5	0.5	0.5	0.6
600	6	0.8	0.9	0.9
600	7.5	1.2	1.2	1.2
900	4.5	0.4	0.4	0.5
900	6	0.6	0.6	0.8
900	7.5	0.8	0.9	1.0
1200	4.5	0.3	0.4	0.5
1200	6	0.5	0.6	0.6
1200	7.5	0.7	0.7	0.8

APPENDIX III

Electromagnetic Immunity

GUIDELINES AND MANUFACTURER'S DECLARATION – ELECTROMAGNETIC IMMUNITY OF THE OPTIMIZER INTEGRA CCM-D IMPLANTABLE PULSE GENERATOR

The OPTIMIZER INTEGRA CCM-D IPG, part of the OPTIMIZER INTEGRA CCM-D System is intended for use in an electromagnetic environment as specified below. The patient implanted with the OPTIMIZER INTEGRA CCM-D IPG must ensure that it is used within the specified environment.

The Optimizer INTEGRA CCM-D IPG **is** a life-support device. Essential Performance of the OPTIMIZER INTEGRA CCM-D IPG:

- The IPG shall be able to detect and discriminate ventricular tachyarrhythmias.
- The IPG shall be able to deliver anti-tachycardia therapy, including ATP and defibrillation shocks.
- No changes in the settings of tachycardia arrhythmia detection or discrimination shall occur unless programmed.
- No changes in the settings of anti-tachycardia therapies shall occur unless programmed.
- ATP and/or shocks shall not be inappropriately delivered.
- The IPG shall be able to detect profound ventricular bradycardia (< 40 bpm) and post-shock bradycardia (< 60 bpm).
- The IPG shall be able to deliver anti-bradycardia pacing therapy.
- No changes in the settings of anti-bradycardia therapies shall occur unless programmed.
- Pacing shall not be inappropriately delivered.

CCM therapy is **not** life-support. CCM shall be delivered with safe settings. It is allowable that these settings disable CCM stimulation.[a]

Note: In case of emergency, placing a pacemaker magnet over the implant site of the OPTIMIZER INTEGRA CCM-D IPG and maintaining it in close proximity to the device, sets the OPTIMIZER INTEGRA CCM-D IPG into Magnet Mode, suspending CCM therapy and inhibiting the delivery of antiarrhythmic therapies.

Immunity test[b]	Test level	Compliance level	Electromagnetic environment – guidelines[c, d]
ISO 14117:2019 Clause 4.2 – Induced lead current – 16.6 Hz to 20 kHz	Test 1 and Test 2 per standard	Induced lead current does not exceed limits for Test 1 and Test 2 per standard	See section on **Cautions → Environmental Conditions** in this manual. • Exercise caution in the vicinity of equipment that generates strong electrical or electromagnetic fields. • Do not enter an area with posted warnings advising pacemaker patients (or patients with other types of implantable devices) not to approach. • Interference may occur in the vicinity of equipment marked with the following symbol: 
ISO 14117:2019 Clause 4.3 - Protection from persisting malfunction attributable to ambient electromagnetic fields	Per clauses 4.3.2.1, 4.3.2.2, and 4.3.2.3 of standard	Does not exhibit malfunction which persists after the removal of the electromagnetic test signal per clauses 4.3.2.1, 4.3.2.2, and 4.3.2.3 of standard	
ISO 14117:2019 Clause 4.4 - Protection from malfunction caused by temporary exposure to CW sources	Per standard	Maintains essential performance[a] per standard	

ISO 14117:2019 Clause 4.5 - Protection from sensing EMI as cardiac signals	Per clauses 4.5.2, 4.5.3, 4.5.4	Maintains essential performance[a] per clauses 4.5.2, 4.5.3, 4.5.4	
ISO 14117:2019 Clause 4.6 - Protection from static magnetic fields of flux density up to 1 mT	Per standard	Device operation is unaffected per standard	Maintain 6 inches (15 cm) distance between household magnets or items containing magnets (e.g., headphones, mobile phones, exercise equipment containing magnets, etc.) and implant
ISO 14117:2019 Clause 4.7 - Protection from static magnetic fields of flux density up to 50 mT	Per standard	Does not exhibit malfunction which persists after the removal from the field per standard	See section on **Warnings → Nuclear Magnetic Resonance (NMR), Magnetic Resonance Imaging (MRI)** in this manual
ISO 14117:2019 Clause 4.8 - Protection from AC magnetic field exposure in the range of 1 kHz to 140 kHz	Per standard	Does not exhibit malfunction which persists after the removal from the field per standard	See section on **Cautions → Environmental Conditions**, **Cautions → Industrial Machinery**, and **Cautions → Home Appliances** in this manual. • Exercise caution in the vicinity of equipment that generates strong AC magnetic fields. • Do not enter an area with posted warnings advising pacemaker patients (or patients with other types of implantable devices) not to approach.
ISO 14117:2019 Clause 4.9 - Test requirements for the frequency range of 385 MHz ≤ f ≤ 3000 MHz	Per standard	Functions as it did before the test without further adjustment after application of the test signal per standard	See section on **Cautions → Transmitting Devices** and **Cautions → Cellular and Mobile Phones** in this manual • Exercise caution in the vicinity of equipment that generates strong radio-frequency fields. • Do not enter an area with posted warnings advising pacemaker patients (or patients with other types of implantable devices) not to approach. • Interference may occur in the vicinity of equipment marked with the following symbol: 

ISO 14117:2019 Clause 5 - Testing above frequency of 3000 MHz	Standard does not require testing of devices above 3 GHz[e]	N/A	Avoid direct exposure to the main lobe of high-power radar and microwave communication beams.
ISO 14117:2019 Clause 6.1 - Protection of the device from damage caused by high-frequency surgical exposure	Per standard	Does not exhibit malfunction which persists after the removal of the electromagnetic test signal per standard	See section on **Warnings → Electrocautery** and **Warnings → RF Ablation** in this manual
ISO 14117:2019 Clause 6.2 Protection of the device from damage caused by external defibrillators	Per standard	Does not exhibit malfunction which persists after the removal of the electromagnetic test signal per standard	See section on **Warnings → Defibrillation and Cardioversion** in this manual
GTRI E3 Representative Security and Logistical Systems (Electronic article surveillance, metal detectors, RFID)	Per E3 protocol	Per E3 protocol	See section on **Cautions → Store Anti-Theft Systems/Airport Security Screening Systems** in this manual Electronic Article Surveillance (EAS) systems, such as those found at department stores: • Do not linger near an EAS system longer than is necessary. • Be aware that EAS systems are often hidden or camouflaged near the exits for businesses such as retailers. • Do not lean against the system's sensors. Metal detector archways: • Do not stop or linger in a walk-through archway; simply walk through the archway at a normal pace. Radiofrequency identification (RFID) readers: • Maintain separation from wall unit (reader) and the implanted device. • Do not lean against the reader. Radiofrequency identification (RFID) and checkout counter tag deactivators: • Maintain an arm's length separation from the deactivator's surface. • Do not lean against the deactivator.

Notes:

[a] No inappropriate stimulation shall be delivered by the OPTIMIZER INTEGRA CCM-D IPG. Normal CCM delivery or inhibition of CCM delivery due to interference is permissible, but inappropriate triggering of CCM delivery by interference is not allowed.

[b] The OPTIMIZER INTEGRA CCM-D IPG does not fall within the clear definitions of ISO 14117:2019. As such, the criteria of ISO 14117:2019 were adapted to be applicable to CCM-D.

[c] See sections on **WARNINGS** and **CAUTIONS** in this manual

[d] This guidance shall not be considered the exclusive or only source for this information. It is best practice to consult the original manufacturer of the item with potential electromagnetic interference to verify any specific guidance concerning operation and compatibility with implantable devices. Always seek the advice of your physician or other qualified health provider with any questions you may have regarding the OPTIMIZER INTEGRA CCM-D IPG.

[e] Electromagnetic fields > 3 GHz are not expected to interfere with device operation because of the increased device protection afforded by the attenuation of the enclosure and body tissue at microwave frequencies, the expected performance of EMI control features implemented to meet lower-frequency requirements, and the reduced sensitivity of circuits at microwave frequencies.

Electromagnetic Emissions

The OPTIMIZER INTEGRA CCM-D must emit electromagnetic energy in order to perform its intended function when communicating with the INTELIO Programmer or the GUARDIO/VESTA Charger. Nearby electronic equipment may be affected.

FCC 47 CFR 95 Subpart I - Medical Device Radio Communications Service

GUIDELINES AND MANUFACTURER'S DECLARATION – ELECTROMAGNETIC EMMISSIONS OF THE OPTIMIZER INTEGRA IPG PURSUANT TO: **FCC 47 CFR 95 Subpart I - Medical Device Radio Communications Service**		
The OPTIMIZER INTEGRA CCM-D Implantable Pulse Generator, part of the OPTIMIZER INTEGRA CCM-D System, is intended for use in an electromagnetic environment as specified below. The patient implanted with the OPTIMIZER INTEGRA CCM-D Implantable Pulse Generator must ensure that it is used within the specified environment.		
Emissions Test	**Compliance**	**Electromagnetic environment - guidelines**
Duration of Transmissions	Complies with clause 95.2557	The OPTIMIZER INTEGRA CCM-D IPG must emit electromagnetic energy in order to perform their intended function when communicating with the Intelio Programmer or the Guardio/Vesta Charger. Nearby electronic equipment may be affected.
Frequency Monitoring	Complies with clause 95.2559	
Frequency Accuracy	Complies with clause 95.2565	
EIRP	Complies with clause 95.2567(a)	
Field Strength	Complies with clause 95.2569	
Bandwidth	Complies with clause 95.2573	
Unwanted Emissions	Complies with clause 95.2579	
Permissible Exposure Evaluation	Complies with clause 95.2585	

ETSI EN 301 839

GUIDELINES AND MANUFACTURER'S DECLARATION – ELECTROMAGNETIC EMMISSIONS OF THE OPTIMIZER INTEGRA CCM-D IPG PURSUANT TO: **ETSI EN 301 839 V2.1.1 - Ultra Low Power Active Medical Implants (ULP-AMI) and associated Peripherals (ULP-AMI-P) operating in the frequency range 402 MHz to 405 MHz; Harmonised Standard covering the essential requirements of article 3.2 of the Directive 2014/53/EU**		
The OPTIMIZER INTEGRA CCM-D Implantable Pulse Generator, part of the OPTIMIZER INTEGRA CCM-D System, is intended for use in an electromagnetic environment as specified below. The patient implanted with the OPTIMIZER INTEGRA CCM-D Implantable Pulse Generator must ensure that it is used within the specified environment.		
Emissions Test	**Compliance**	**Electromagnetic environment - guidelines**
Frequency Error	Complies with clause 4.2.1.1	The OPTIMIZER INTEGRA CCM-D IPG must emit electromagnetic energy in order to perform their intended function when communicating with the Intelio Programmer or the Guardio/Vesta Charger. Nearby electronic equipment may be affected.
Occupied Bandwidth	Complies with clause 4.2.1.2	
Power Output	Complies with clause 4.2.1.3	
Transmitter Spurious Emissions (30 MHz to 6 GHz)	Complies with clause 4.2.1.4	
Frequency Stability Under Low Voltage Conditions	Complies with clause 4.2.1.5	
Spurious Radiation of Receivers	Complies with clause 4.2.2.1	

ETSI EN 301 489-1 and ETSI EN 301 489-27

GUIDELINES AND MANUFACTURER'S DECLARATION – ELECTROMAGNETIC EMMISSIONS OF THE OPTIMIZER INTEGRA CCM-D IPGs PURSUANT TO:

ETSI EN 301 489-1 V2.2.3 - ElectroMagnetic Compatibility (EMC) standard for radio equipment and services; Part 1: Common technical requirements; Harmonised Standard for ElectroMagnetic Compatibility

ETSI EN 301 489-27 - ElectroMagnetic Compatibility (EMC) standard for radio equipment and services; Part 27: Specific conditions for Ultra Low Power Active Medical Implants (ULP-AMI) and related peripheral devices (ULP-AMI-P) operating in the 402 MHz to 405 MHz bands; Harmonised Standard covering the essential requirements of article 3.1(b) of Directive 2014/53/EU

The OPTIMIZER INTEGRA CCM-D is intended for use in an electromagnetic environment as specified below. The patient implanted with the OPTIMIZER INTEGRA CCM-D Implantable Pulse Generator must ensure that it is used within the specified environment.

Emissions Test	Compliance	Electromagnetic environment - guidelines
Radiated Emissions EN 55032:2012/AC:2013	Class B	The OPTIMIZER INTEGRA CCM-D IPG must emit electromagnetic energy in order to perform their intended function when communicating with the Intelio Programmer or the Guardio/Vesta Charger. Nearby electronic equipment may be affected.

APPENDIX IV

Wireless Technology

RF wireless technology is used in the communication between an OPTIMIZER INTEGRA CCM-D Implantable Pulse Generator (IPG) and an Intelio Programmer. It occurs through an encrypted channel over an RF link that complies with the requirements of the Medical Implant Communication System (MICS) (range specified to 2 m, 402–405 MHz) of the MedRadio Band. The "OPTI*link*" encrypted MICS channel is established after the IPG is positively identified and encryption keys are exchanged via a very-short-range (<4 cm) communication over the 13.56 MHz recharge channel.

RF wireless technology is also used to transcutaneously transmit energy from the Guardio Charger to recharge the OPTIMIZER INTEGRA CCM-D IPG at the 13.56 MHz ISM frequency. The transmission range is specified at a maximum of 4 cm between the Charger's coil and the IPG's receiving coil. Control over the recharge process, as well as the communications of alert messages from the IPG to the Charger take place over an encrypted MICS channel.

OPTIMIZER INTEGRA CCM-D IPG Wireless Nominal Specifications

Characteristic	Nominal
OPTI*link* MICS MedRadio	
Frequency Band	402 – 405 MHz Medical Implant Communication Service (MICS) Medical Device Radio Communication Service (MedRadio)
Bandwidth	< 145 kHz
Modulation	FSK
Radiated Power	< 25 µW E.I.R.P.
Range	0 to at least 1.5 m

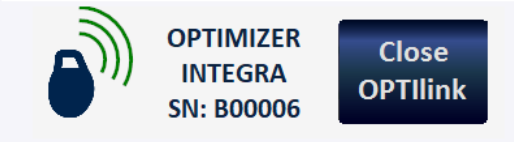
Quality of Service (QoS) for Wireless Technology

QoS for Communications between the Intelio Programmer and the OPTIMIZER INTEGRA CCM-D IPG

MedRadio in the MICS sub-band (402 to 405 MHz) wireless technology enables communication between the OPTIMIZER INTEGRA CCM-D IPG and the Intelio Programmer.

Before the Intelio Programmer can be used to program the OPTIMIZER INTEGRA CCM-D IPG, an OPTI*link* communication session must first be established between the Intelio Programmer and the IPG. This is accomplished by means of the Intelio Programming Wand, which must be placed over the implant site and within 4 cm of the IPG. Once the Intelio Programming Wand is over the patient's implant site, the communication link is established by initiating the Start OPTI*link* command. Encryption keys are exchanged through a proprietary process using the 13.56 MHz Recharge Channel, after which the Intelio Programming Wand can be placed at a distance of up to 1.5 m away from the implant site, with communications taking place over MedRadio.

The OPTI*link* Signal Strength Indicator dynamically displays the Quality of Service (QoS) for the link between the Intelio Programming Wand and the OPTIMIZER INTEGRA CCM-D IPG. Depending on the quality of the link, the curved "waves" of the Signal Strength Indicator are displayed in the following manner:

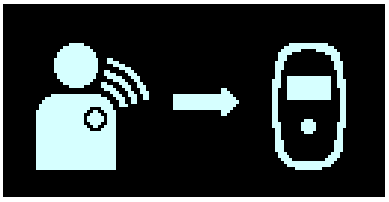


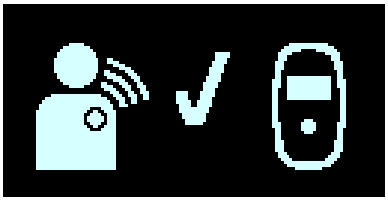
- Good quality link – 3 green signal waves
- Medium quality link – 2 yellow signal waves
- Low quality link – 1 red signal wave

QoS for Communications between the Guardio/Vesta Charger and the OPTIMIZER INTEGRA CCM-D IPG

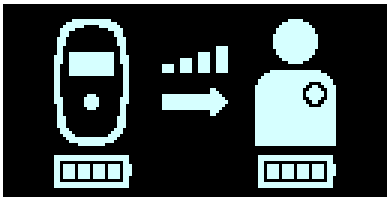
MedRadio in the MICS sub-band (402 to 405 MHz) wireless technology enables communication between the OPTIMIZER INTEGRA CCM-D IPG and the Guardio/Vesta Charger. The requirements for the Quality of Service (QoS) vary depending on the use environment (operating room, recovery room, clinic, and home environment).

The Guardio/Vesta Charger will begin by displaying the IPG Data Download and IPG Data Download Success screens:





After the data download has been completed, the Charging IPG Status screen is displayed by the Guardio/Vesta Charger:

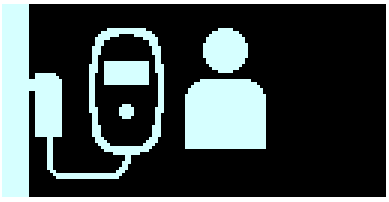


The Charging IPG Status screen's Coupling Level icon (), whose number of illuminated bars is proportional to the proximity of the charging wand to the implanted OPTIMIZER INTEGRA CCM-D IPG, is indicative of the Quality of Service (QoS) for the transcutaneous energy transmission wireless link. The charging wand should be repositioned until at least 2 bars of the Charging IPG Status screen's Coupling Level icon are illuminated, indicating sufficient QoS for charging the OPTIMIZER INTEGRA CCM-D IPG.

One illuminated bar indicates degraded QoS which may require a longer charging time. Zero illuminated bars on the Charging IPG Status screen's Coupling Level icon accompanied by an audible beeping tone indicates poor placement of the charging wand. If the charging wand is not repositioned onto the implant site within 20 seconds, the Guardio/Vesta Charger will emit 3 long beeping tones, display the Charging IPG Coupling Error screen, and then shut off.

Besides charging the OPTIMIZER INTEGRA CCM-D, the Guardio/Vesta Charger also serves as a way of messaging the patient about alerts and other conditions. The Guardio/Vesta Charger is configured to communicate with the OPTIMIZER INTEGRA CCM-D IPG at least once a day. This communication occurs whenever the IPG is within 1.5 m (5 ft) of the Guardio/Vesta Charger for a few minutes.

If the Guardio/Vesta Charger and the OPTIMIZER INTEGRA CCM-D IPG do not communicate within a programmable time period, the patient may see the “Long Time Without Downloading Data From IPG” alert screen displayed by the Guardio/Vesta Charger:



In this case, instruct the patient to attempt to charge their OPTIMIZER INTEGRA CCM-D IPG with their Guardio/Vesta Charger. If the patient is able to charge their implanted device successfully, then the alert screen should no longer be displayed by the Guardio/Vesta Charger. If the attempt to charge the OPTIMIZER INTEGRA CCM-D IPG with the Guardio/Vesta Charger is unsuccessful, instruct the patient to please call the 24-hour Support Hotline (866-312-5370).

Troubleshooting for Wireless Coexistence Issues

Troubleshooting OPTIlink Connection between the OPTIMIZER INTEGRA CCM-D IPG and the Intelio Programmer

If you experience issues with establishing an OPTI*link* session between the OPTIMIZER INTEGRA CCM-D IPG and the Intelio Programmer, try the following:

- Reposition the Intelio Programming Wand so that it lays parallel to the IPG’s plane and its center is coaxial with the center of the IPG’s header.
- Decrease the distance between the devices.
- Move the devices away from other devices that may be causing interference.
- Do not operate other wireless devices (i.e., programmers for other devices, laptop, tablet, mobile phone, or cordless phone) at the same time.

If you experience issues with maintaining an OPTI*link* session between the OPTIMIZER INTEGRA CCM-D IPG and the Intelio Programmer, try the following:

- Decrease the distance between the devices.
- Move the devices so they share line of sight.
- Move the devices away from other devices that may be causing interference.
- Do not operate other wireless devices (i.e., programmers for other devices, laptop, tablet, mobile phone, or cordless phone) at the same time.
- Wait a few minutes and try connecting again

Note: Wireless communications equipment, such as wireless home network devices, mobile and cordless telephones, and tablets, could affect the quality of the OPTI*link* connection.

Troubleshooting Wireless Connection between OPTIMIZER INTEGRA CCM-D IPG and Guardio/Vesta Charger

If you experience issues with establishing a wireless connection between the OPTIMIZER INTEGRA CCM-D IPG and the Guardio/Vesta Charger, try the following:

- Whenever the Guardio/Vesta Charger is not being used to charge the OPTIMIZER INTEGRA CCM-D IPG, place it in an area that is frequented by the patient (e.g., bedside table in the bedroom), connected to its AC Adapter, and the AC Adapter plugged into the wall outlet. This will ensure regular communications between the OPTIMIZER INTEGRA CCM-D IPG and the Guardio/Vesta Charger.
- Remain stationary during the charging or data transfer process.
- Decrease the distance between the devices.
- Move the devices so they share line of sight.
- Move the devices away from other devices that may be causing interference.
- Do not operate other wireless devices (i.e., programmers for other devices, laptop, tablet, mobile phone, or cordless phone) at the same time.
- Wait a few minutes and try connecting again.

Note: Wireless communications equipment, such as wireless home network devices, mobile and cordless telephones, and tablets, could affect the quality of the wireless connection.

APPENDIX V

Scientific Background About Heart Failure and Cardiac Contractility Modulation

Heart failure is a condition wherein the heart muscle does not pump blood as well as it should, generally resulting in reduced cardiac output, possibly due to reduced contraction force or impaired relaxation or other deficiencies. Chronic heart failure is associated with cardiac muscle remodeling, which is the result of abnormal genomic, molecular, cellular, and structural changes that typically manifest clinically as changes in size, shape, and function of the heart's ventricles. The reduced cardiac function is associated with multiple symptoms, such as fatigue, shortness of breath (dyspnea), co-morbidities, and limited ability to walk, exercise, or tolerate effort. The severity of symptoms is often classified by the physician in accordance with New York Heart Association (NYHA) classification (for example, NYHA class II represents moderate symptoms and class IV represents severe symptoms). Over time, chronic heart failure is a leading cause for hospitalizations and mortality. There are several medications that are used for treating heart failure according to the guidelines. In patients that are symptomatic despite appropriate medication, further evaluation of left ventricular ejection fraction (usually valuated by echocardiography) and QRS duration (evaluated by ECG) are useful in determining the possible need for an ICD, in cases having low ejection fraction, or a CRT, in cases with wide QRS, respectively.

Cardiac Contractility Modulation therapy is based on the delivery of non-excitatory electrical signals to the ventricles during the ventricular absolute refractory period. Published scientific research on cardiac contractility modulation therapy in animals and in humans explored various properties and effects. Some data suggests that cardiac contractility modulation has immediate effects on heart failure tissue, including potentially increasing the contraction force (contractility) of the muscle, possibly by immediate (i.e. less than a minute) improvement in the activity of the intracellular proteins that are associated with calcium cycling, for example by increased phosphorylation of the phospholamban protein, which is believed to modify the activity level of SERCA-2a, a protein responsible for intracellular calcium handling. Other data in heart failure animals and in humans suggest that after treating with cardiac contractility modulation for several hours, there may be normalization of mRNA expression levels of plurality of cardiac genes that are associated with heart failure (e.g. SERCA-2a, ANP, BNP, a-MHC, and others). Some data suggest that these changes and improvements in contraction are not associated with increase in myocardial oxygen consumption. Other data in animals over a period of a few months of cardiac contractility modulation delivery suggest the potential for improvements in the expression levels of several proteins that are associated with heart failure. In addition, some data suggest that with a few months of cardiac contractility modulation delivery, cardiac dimensions, structure, function (e.g. LVEDD, LVESD, and LVEF), cellular function, and/or tissue behavior may improve, providing the potential for reverse remodeling. Other studies explored clinical benefits with cardiac contractility modulation therapy in chronic heart failure patients, typically with a narrow QRS and New York Heart Association (NYHA) class of at least II, and suggest that several months (e.g. at least 3 months) of treatment potentially result in improvements in exercise tolerance (e.g. by six minute walk tests or by peak oxygen consumption in cardio pulmonary tests) and in quality of life (e.g. by NYHA classification or by questionnaire), which could be indicative of clinically significant improvements in cardiac function. Various studies explored effects of cardiac contractility modulation in patients with NYHA classes II, III, and IV, some with EF up to 35%, some with higher EF (e.g. 40%, 45%). The studies usually included population with a range of age, gender, etiology (e.g. ischemic, idiopathic) and other characteristics.

With regard to use of cardiac contractility modulation outside the United States, the 2016 European Society of Cardiology practice guidelines has reviewed clinical studies of cardiac contractility modulation in heart failure patients and mentioned cardiac contractility modulation as a treatment option that may be considered in selected patient population. Summaries of some of these studies are available on Impulse Dynamics' website (http://www.impulse-dynamics.com/int/for-physicians/clinical-data/).

Over the years of evaluation of cardiac contractility modulation therapy and use of the therapy outside the USA in countries that accept the CE Mark, CCM was delivered using various models of the OPTIMIZER System, which includes an implantable pulse generator (IPG) that is programmable and has a rechargeable battery. In principle, the OPTIMIZER System is implanted in a procedure which is similar to a pacemaker implantation. Unlike pacemakers or defibrillators, the OPTIMIZER System does not have integrated pacing or defibrillation capabilities, and is only used for delivering cardiac contractility modulation therapy. Often a patient may have concomitant implantable devices, as may be indicated per patient. The OPTIMIZER is connected to the heart's ventricles using leads, typically with the electrodes fixated to the right ventricular septum. For example, the ventricular leads may be spaced apart by a few centimeters and positioned on the septum, at or adjacent to an intersection of the septum and right ventricular free wall. The electrodes are used for sensing electrical activity of the heart and for delivery of CCM signals to the ventricular muscle at the proper timing and signal configuration. The OPTIMIZER can be programmed to deliver cardiac contractility modulation therapy for several hours every day: typically 5 hours per day in the US studies, and 7 or more hours per day in other countries. As part of the OPTIMIZER algorithm, the circuitry records one or more local electrical activity (i.e. activity in the vicinity of the electrode measured using the bipolar electrode configuration) or non-local electrical activity (i.e. wide-field electrogram using unipolar sensing between the electrode and the distant IPG can). The timing of the CCM delivery is determined to be at a certain delay and duration from the sensing, designed to deliver the CCM during the absolute refractory period of the muscle within the current beat cycle; this may maintain the CCM signal non-excitatory. If the patient has a concomitant pacing or defibrillation device, the OPTIMIZER can be configured to apply the CCM signals during a paced cardiac cycle, within the refractory period which follows the pacing. The OPTIMIZER can also be configured to apply the CCM signal during a non-paced cardiac cycle. The algorithm also applies criteria for delivery of the CCM signal or inhibiting the delivery of the CCM signal according to the relative timing of events, for example using criteria for minimum and maximum acceptable heart rate (R-R intervals), minimum and maximum acceptable time between sensed events in two locations on the RV septum, inhibition if signals are detected at an unexpected timing, and/or the use of an alert window in order to detect unexpected events and potentially block CCM delivery. Thus, the OPTIMIZER may deliver the non-excitatory CCM signal during the absolute refractory period of hundreds or thousands of beats out of 50,000 consecutive beats, taking into account the detection of any conditions that inhibit the CCM signal delivery (such as, for example, a detected arrhythmia). The parameters of the algorithm are configured per patient, with the purpose of enabling the normal delivery of the contractility modulating signal when the trace of events is indicative of an expected activation sequence of the heart.

APPENDIX VI

Current Clinical Summary: FIX-HF-5C

Study Design

FIX-HF-5C was a prospective, randomized, third-party blinded, multicenter study involving 160 patients. Key inclusion criteria included EF ≥ 25% and ≤ 45%, normal sinus rhythm, QRS duration <130 ms and NYHA Class III or ambulatory IV heart failure despite GDMT (including ICD when indicated). Main exclusion criteria included baseline peak VO_2 < 9 or > 20 mL/min/kg, hospitalization for heart failure 30 days before enrollment, clinically significant ambient ectopy (> 8,900 premature ventricular contractions [PVCs] / 24 hours), PR interval > 375 ms, and chronic atrial fibrillation or atrial flutter within 30 days of enrollment.

A device implant date was scheduled for all eligible patients, which served as the study start date (SSD) for all patients. Patients were then randomized 1:1 to either continued OMT alone (control group) or OMT plus CCM (CCM group). Patients randomized to the CCM group were implanted with the device and the implant date was canceled for patients randomized to the control group. Patients returned to the clinic for evaluation at 2 weeks, 12 weeks, and 24 weeks. Follow-up visits included 2 CPX tests, a blinded NYHA assessment, MLWHFQ quality of life assessment, and an assessment of adverse events (AEs).

Blinding of NYHA and CPX

NYHA was assessed by a blinded on-site clinician according to their standard clinical practice.

CPX tests were assessed by an independent core laboratory blinded to the randomization assignment of individual patients.

Primary Effectiveness Endpoint

The primary effectiveness endpoint was defined as the change in peak VO_2 from baseline at 24-weeks between the control and CCM groups as evaluated by the blinded core laboratory. The primary effectiveness analysis employed a Bayesian repeated measures linear model to estimate group differences in mean peak VO_2 at 24 weeks from baseline, with fixed 30% borrowing of information (70% down-weighting) from the corresponding treatment group difference observed in the FIX-HF-5 study subgroup defined as EF ≥ 25%.

Secondary Effectiveness Endpoints

Because there were multiple secondary hypotheses being tested, the method of alpha control was the closed form hierarchical method. For these analyses, if the one-sided p-value for the secondary endpoint was ≤ 0.025, the null hypothesis was rejected, and the next secondary endpoint was tested. The hierarchy for testing the secondary endpoints is the following:

- Minnesota Living with Heart Failure Questionnaire
- NYHA classification
- Peak VO_2 with a peak respiratory equivalent ratio (RER) ≥ 1.05

Safety Endpoints

The primary safety endpoint was the proportion of patients experiencing an OPTIMIZER device- or procedure-related complication through the 24-week follow up period as determined by the events adjudication committee (EAC). The primary safety endpoint was evaluated against a prespecified performance goal of 70% which was derived from several prior studies involving CRT (PMAs P010012: Contak CD CRT D, P030005: Contak Renewal TR, P030035: St. Jude Frontier, and P010012/S37: Contak Renewal 3AVT; Van Rees, 2011).

Other safety endpoints included all-cause death, cardiovascular death, composite rate of all-cause death or all-cause hospitalizations, composite rate of cardiovascular death or worsening heart failure-related hospitalizations, and overall rate of AEs and SAEs.

Demographics and Baseline Characteristics

Of the 160 eligible patients, 74 were randomized to the CCM group and 86 were randomized to the control group. In the CCM group, 6 patients did not receive the device and 2 patients died prior to the 24-week visit (including 1 patient who died prior to randomization). In the control group, 4 patients died, and 3 patients withdrew prior to the 24-week visit.

The groups were well-balanced with regards to demographic and baseline characteristics (**Table 3**). Overall, the mean age was approximately 63 years. The majority of patients were white and male, and the etiology was predominantly ischemic cardiomyopathy, characteristics which are typical of recent heart failure studies. Average peak VO_2 at baseline was approximately 15 mL/kg/min, which is moderately reduced compared to the normal population. Characteristics of the prospectively enrolled FIX-HF-5C patients were similar to those of the FIX-HF-5 subgroup used for Bayesian analysis (**Table 3**).

Table 3: Demographic and Baseline Characteristics

	FIX-HF-5C		FIX-HF-5 Subgroup (25% ≤ EF ≤ 35%)	
	CCM (N=74)	Control (N=86)	CCM (N=117)	Control (N=112)
Mean Age (years)	63	63	59	60
Male	73%	79%	71%	74%
White	74%	71%	75%	72%
Ischemic Heart Failure	62%	59%	72%	69%
Prior MI	49%	59%	67%	59%
Prior PM/ICD System	88%	85%	80%	79%
Diabetes	51%	49%	49%	52%
NYHA Class III Class IV	 87% 14%	 91% 9%	 93% 7%	 87% 13%
QRS Duration (ms)	103	104	99	101
LVEF (%)	33	33	31	32
LVEDD (mm)	58	60	57	56
Peak VO_2 (mL/kg/min)	15.5	15.4	14.6	14.8
Exercise Time (minutes)	11.4	10.6	11.3	11.7
6MHW (meters)	317	324	326	324
MLWHFQ (total score)	56	57	60	56

Mean or % (n/N)

Effectiveness Results

Primary Effectiveness Endpoint

The primary effectiveness endpoint was met. The model-based estimated mean difference in peak VO_2 at 24 weeks between CCM and control groups was 0.84 mL/kg/min with a 95% Bayesian credible interval of (0.12, 1.55) mL/kg/min. The probability that CCM is superior to control was 0.989, which exceeds the 0.975 criterion required for statistical significance of the primary endpoint.

Figure 9 shows that the Bayesian model's point estimate is very similar to the estimate from just the FIX-HF-5C study. However, the model further incorporates the high quality data from the previous randomized, blinded trial which increases the precision of the estimate. If FIX-HF-5C were a standalone trial, the middle CI would be appropriate. However, the Bayesian model allows us to incorporate the totality of the clinical experience which is an increased precision in the effect size estimate and is shown by the narrower 95% CI with the Bayesian estimate.

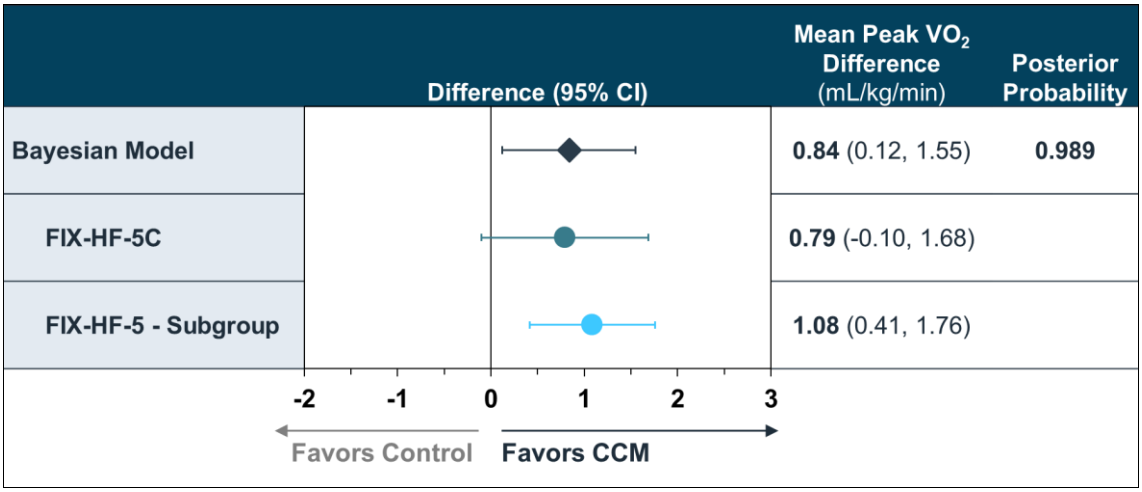


Figure 9: Peak VO_2 by Study

The improvement in peak VO_2 built up over time, from 3 to 6 months (**Figure 10**). The treatment effect can be seen in this graph to be a result of a significant decrease in VO_2 for the control group with relatively little increase in VO_2 for the treatment group.

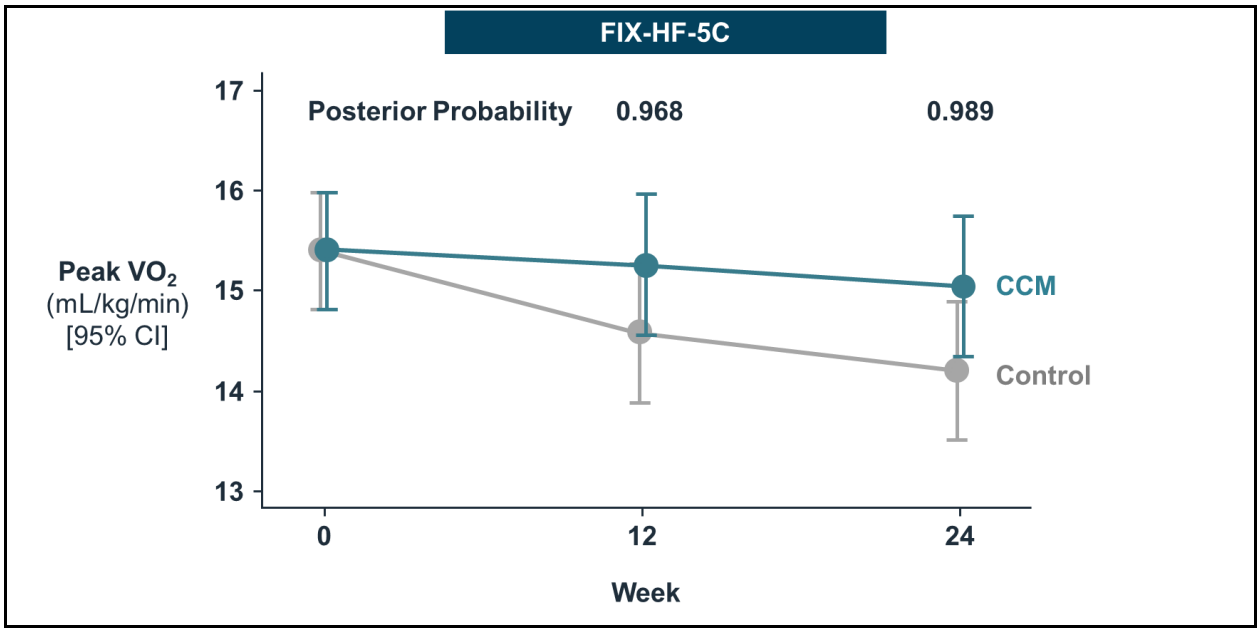


Figure 10: Time Course of Treatment Effect on Peak VO_2 (FIX-HF-5C)

Sensitivity analyses involving the primary effectiveness endpoint were conducted in which missing data were handled with different mechanisms or modifications (**Table 4**). Method of imputation affected the results and the VO_2 estimate varied from 0.48 to 0.84 depending on method. The conclusion of CCM superiority with respect to mean peak VO_2 was consistent across all sensitivity analyses. In addition, the primary analysis would achieve statistical significance with any borrowing weight of 0.11 or larger (as noted above, 0.30 was pre-specified in the analysis plan).

Table 4: Peak VO_2 Treatment Effect Across Studies

Study	Population	Bayesian VO_2 Estimate	Bayesian Posterior Probability
Primary Analysis with Borrowing FIX-HF-5C & FIX-HF-5	Imputation (Death = 0)	0.836	0.989
	Imputation (Death = lowest peak VO_2)	0.693	0.988
	Completed Cases (No Imputation)	0.603	0.978
Pooled FIX-HF-5C & FIX-HF-5	Completed Cases (No Imputation)	0.749	0.999
FIX-HF-5C Alone	Imputation (Death = 0)	0.799	0.960
	Imputation (Death = lowest peak VO_2)	0.611	0.957
	Completed Cases (No Imputation)	0.480	0.916
FIX-HF-5 Alone	Imputation (Death = 0)	1.074	1.00
	Completed Case (No Imputation)	1.080	1.00

Secondary Effectiveness Endpoints

MLWHFQ results at 24 weeks are presented in **Table 5** and show that the CCM group was statistically significantly superior over the control group ($p < 0.001$) in each study.

Table 5: Change in MLWHFQ at 24 Weeks by Study

	Difference (95% CI) in MLWHFQ Total Score Between Groups	p-value (1-sided)
Pooled data	-10.9 (-14.6, -7.2)	< 0.001
FIX-HF-5C	-11.7 (-17.6, -5.9)	< 0.001
FIX-HF-5 Subgroup	-10.8 (-15.6, -6.1)	< 0.001

The percentage of patients improving by 1 or more NYHA class by study was statistically significantly superior in the CCM group compared to the control group ($p < 0.001$ in each study; **Table 6**).

Table 6: Patients Achieving ≥ 1 Class Improvement in NYHA at 24 Weeks by Study

Change in ≥ 1 Class in NYHA Class	CCM	Control	p-value (1-sided)
Pooled data	104/173 (60.1%)	59/169 (34.9%)	< 0.001
FIX-HF-5C	57/70 (81.4%)	32/75 (42.7%)	< 0.001
FIX-HF-5 Subgroup	47/103 (45.6%)	27/94 (28.7%)	< 0.001

In the FIX-HF-5C study, the p-value for the comparison of mean peak VO_2 at 24 weeks for CCM compared to control among observations with RER > 1.05 was 0.1100. Therefore, this secondary effectiveness endpoint was not met with FIX-HF-5C data alone. When data were pooled from the FIX-HF-5 and FIX-HF-5C studies, the treatment effect was estimated as 0.62 mL/kg/min with a p-value of 0.009. In addition, the endpoint was met in the FIX-HF-5 subgroup (**Table 7**).

Table 7: Change in Peak VO_2 in Tests with RER ≥ 1.05 at 24 Weeks by Study

	Difference (95% CI) in Peak VO_2 (mL/kg/min) Between Groups	p-value (1-sided)
Pooled data	0.62 (0.11. 1.14)	0.009
FIX-HF-5C	0.43 (-0.25, 1.11)	0.1100
FIX-HF-5 - Subgroup	0.83 (0.06, 1.61)	0.017

Safety Results

The incidence of AEs in this study was relatively low. Comparisons between the groups did not show any statistical differences between CCM and control groups with respect to any AE tabulated for the analysis.

Primary Safety Endpoint

The primary safety endpoint was met as shown in **Table 8**. The complication-free proportion in the CCM group cohort was 89.7% (61/68) with lower confidence limit of 79.9% (one-sided alpha=0.025), which was greater than the pre-defined threshold of 70%. The majority of complications (5/7, 71.4%) were lead dislodgements.

Table 8: Primary Safety Endpoint (FIX-HF-5C, As Treated CCM Group Only)

Complication Free Rate n/N (%)	95% LCL	95% UCL
61/68 (89.7%)	79.9%	95.8%

Secondary Safety Endpoints (FIX-HF-5C)

As shown in **Table 9**, the freedom from death, freedom from cardiovascular death, and freedom from all-cause death or all-cause hospitalization at 24 weeks were similar in both groups.

Table 9: Secondary Safety Endpoints at 24 Weeks (FIX-HF-5C)

Freedom from	CCM	Control	p-value
All-cause death	98.3%	95.3%	0.2549
Cardiovascular death	100%	96.5%	0.1198
All-cause death or all-cause hospitalization	78.1%	77.7%	0.9437

Current Clinical Summary: FIX-HF-5C2

Introduction

Prior versions of the OPTIMIZER device used under the current US IDE have required sensing of atrial depolarization via an atrial lead to properly time the delivery of CCM pulses. Accordingly, the presence of atrial fibrillation or flutter imposed a technical limitation to the delivery of CCM signals. The current version of the OPTIMIZER, the 2-Lead OPTIMIZER Smart, has overcome the need for atrial sensing while maintaining safe and effective delivery of CCM to the ventricle. The 2-Lead OPTIMIZER Smart reduces the total lead requirement from 3-leads to 2-leads enabling CCM therapy to be delivered to a broader range of symptomatic HF patients while reducing the total hardware burden and corresponding lead-related adverse events on all patients receiving CCM.

The most frequent complications observed in the FIX-HF-5 and FIX-HF-5C trials were lead dislodgment, lead insulation breech, and lead fracture requiring an additional surgery to revise or replace the lead. Similarly, such lead-related complications are the most frequently cited complications for CRT, ICD, and pacemaker devices. Therefore, the ability to reduce the total number of leads needed for any given device, such as the OPTIMIZER Smart, has the potential to reduce the overall complication rate of that device. Improving the inherent safety of the OPTIMIZER Smart will allow physicians to expand its use thereby helping more patients with chronic heart failure.

Overview of Study Design

The FIX-HF-5C2 study was a multicenter, prospective, single-arm treatment only study of the 2-Lead configuration of the OPTIMIZER Smart System. Sixty patients were enrolled and implanted with the OPTIMIZER Smart System. The primary effectiveness endpoint was an improvement in exercise tolerance as measured by peak VO_2 obtained on cardiopulmonary exercise testing (CPX). CPX data were evaluated by an independent core laboratory. Results for subjects implanted with the OPTIMIZER Smart were compared to the peak VO_2 results for the subjects in the control group of the FIX-HF-5C study with respect to mean change in peak VO_2 at 24-weeks from baseline.

The secondary effectiveness endpoint for the FIX-HF-5C2 study was an assessment of the average daily amount of CCM therapy provided over the 24-week study. A comparison between the OPTIMIZER 2-lead device subjects in the FIX-HF-5C2 study was made to the OPTIMIZER 3-lead device subjects of the FIX-HF-5C study to determine whether or not there was a difference between the therapy provided by the two device configurations.

The primary safety endpoint in the FIX-HF-5C2 study was the percentage of subjects experiencing an OPTIMIZER device or procedure related complication through the 24-week follow up period. Complications were adjudicated by an independent events committee.

Overview of Methodology

Sites identified potential patients from their clinic's chronic heart failure population. The target patient population consisted of subjects with ejection fractions from 25 to 45% (inclusive) whose symptoms were consistent with NYHA functional class III or ambulatory NYHA Class IV. Informed consent was obtained from potential subjects who were then enrolled in the study to undergo baseline screening testing to determine eligibility for the study. Baseline screening exams included: a medical history, physical examination, medication history, blood testing, cardiopulmonary exercise testing (CPX) to determine peak VO_2, echocardiography to determine left ventricular ejection fraction (LVEF), 12-Lead ECG, and an NYHA Class assessment. The CPX and echocardiography tests were evaluated by an independent core laboratory.

Subjects that passed baseline testing and eligibility criteria were scheduled to have the OPTIMIZER Smart with 2-leads implanted as soon as possible. Subjects then returned to the clinic for evaluation at 2 weeks, 12 weeks, and 24 weeks following the initial implantation. At the 12-week and 24-week visits, subjects completed a physical examination, medication evaluation, blood testing, CPX test, NYHA assessment, and an

assessment of adverse events. Data collection for assessment of the study endpoints was concluded with the 24-week visit.

Results

Number of Investigators and Number of Sites

There were 8 sites participating in the FIX-HF-5C2 study and 8 principal investigators are shown in **Table 10** below.

Table 10: List of Sites

Investigator/Investigational Site	Screened	Enrolled
Site A	7	4 (6.7%)
Site B	33	18 (30.0%)
Site C	3	1 (1.7%)
Site D	43	12 (20.0%)
Site E	8	3 (5.0%)
Site F	14	3 (5.0%)
Site G	6	1 (1.7%)
Site H	39	18 (30.0%)
TOTAL	**153**	**60**

Accountability of Subjects with Study Visits

Table 11 contains patient disposition. There were 153 subjects screened. Of these 60 subjects were enrolled and all 60 subjects were implanted with the study device. One subject withdrew prior to 24 weeks. There were no deaths. Follow-up by study visit is presented in the table along with the number and percent of subjects who successfully completed exercise testing for the primary endpoint. A total of 53 subjects returned for exercise testing at 12 weeks while 55 subjects completed the exercise testing visit at 24 weeks. One (1) subject had his testing deemed inadequate at 12 weeks while 3 subjects had inadequate tests at 24 weeks, leaving 52 evaluable tests at 12 weeks and 52 evaluable tests at 24 weeks. One subject withdrew from the study prior to 24 weeks.

Table 11: Patient Disposition

Variable	FIX-HF-5C2 OPTIMIZER
Screened	153
Enrolled / Implanted	60 (39.2%)
Per Protocol (PP)	59 (98.3%)
Died[1]	0 (0.0%)
Withdrawn[1]	1 (1.7%)
12 Week Visit Completed	59 (98.3%)
12 Week Exercise Tolerance Test Completed	53 (88.3%)
12 Week Exercise Tolerance Test Evaluable[2]	52 (86.7%)
24 Week Visit Completed	59 (98.3%)
24 Week Exercise Tolerance Test Completed	55 (91.7%)
24 Week Exercise Tolerance Test Evaluable[2]	52 (86.7%)

[1]Prior to 24 Week Visit
[2]Includes only subjects with valid Peak VO_2, as determined by the core lab, at the indicated visit.

Baseline Characteristics

Baseline characteristics of subjects in the FIX-HF-5C2 study are presented in **Table 12** along with baseline characteristics of the FIX-HF-5C study groups. Of primary note are the comparisons between the OPTIMIZER group in the FIX-HF-5C2 study and the Control group from the FIX-HF-5C study, as these groups form the primary comparison groups for the efficacy analyses. At a nominal 0.05 level of significance, FIX-HF-5C2 subjects were older (66.3 ± 8.9 vs. 62.8 ± 11.4), had a lower prevalence of diabetes (30% vs. 48.8%), and a lower LVEDD value (57.7 ± 6.8 vs. 60.2 ± 7.0) than subjects in the FIX-HF-5C Control group. Although FIX-HF-5C2 subjects had a smaller LVEDD, LVEF between the two groups (34.1 + 6.1 vs. 32.5 + 5.2%) was not statistically significantly different. Peak VO_2 on CPX testing at baseline was similar between the two groups, but the FIX-HF-5C2 subjects exercised for a full minute longer on average than the FIX-HF-5C control group subjects (11.6 + 2.9 vs. 10.6 + 3.1 minutes). This difference was statistically significant ($p<0.04$).

Consistent with the study purpose and design, significantly more subjects in the FIX-HF-5C2 study had permanent atrial fibrillation at baseline as evidenced by the presence of atrial fibrillation on the baseline ECG tracing. Although it did not reach statistical significance, there was only 1 NYHA Class IV subject in FIX-HF-5C2 while 8 subjects were NYHA Class IV in FIX-HF-5C. This difference reflects clinical practice. It is not a regulatory limitation as the protocol was established before the Indications for Use were narrowed to NYHA III subjects and NYHA IV subjects were allowed in the FIX-HF-5C2 study. The clear clinical practice selection of NYHA Class III subjects in the FIX-HF-5C2 study confirms that the NYHA III functional class group is the appropriate target for CCM therapy. All other characteristics were similar between the two groups.

Baseline medication usage is presented in **Table 13**.

Table 12: Baseline Characteristics: ITT Population

	FIX-HF-5C2	FIX-HF-5C			
Variable	**OPTIMIZER**	**OPTIMIZER**	**P-value[1]**	**Control**	**P-value[1]**
Age (yrs)	66.3 ± 8.9 (60)	63.1 ± 10.9 (74)	0.071	62.8 ± 11.4 (86)	0.049
Male	53 (88.3%)	54 (73.0%)	0.032	68 (79.1%)	0.182
Ethnicity (White)	40 (66.7%)	55 (74.3%)	0.346	61 (70.9%)	0.590
CHF Etiology (Ischemic)	41 (68.3%)	46 (62.2%)	0.473	51 (59.3%)	0.299
Prior MI	36 (60.0%)	36 (48.6%)	0.224	51 (59.3%)	1.000
Prior CABG	13 (21.7%)	18 (24.3%)	0.837	23 (26.7%)	0.560
Prior ICD or PM System	55 (91.7%)	67 (94.4%)	0.731	73 (85.9%)	0.432
Prior ICD (ICD,CRT-D,S-ICD)	53 (88.3%)	66 (93.0%)	0.382	73 (85.9%)	0.804
Prior PM	2 (3.3%)	1 (1.4%)	0.593	0 (0.0%)	0.170
Angina	2 (3.3%)	5 (6.8%)	0.459	6 (7.0%)	0.471
Diabetes	18 (30.0%)	38 (51.4%)	0.014	42 (48.8%)	0.027
Baseline Permanent Atrial Fibrillation	9 (15.0%)	0 (0%)	0.0005	0 (0%)	0.0002
History of Atrial Arrhythmias	34 (56.7%)	25 (33.8%)	0.009	35 (40.7%)	0.065
Atrial Flutter	5 (8.3%)	8 (10.8%)	0.772	6 (7.0%)	0.761
Atrial Fibrillation	28 (46.7%)	20 (27.0%)	0.029	27 (31.4%)	0.082
Frequent PACs	3 (5.0%)	3 (4.1%)	1.000	1 (1.2%)	0.306
Other Atrial Abnormalities	2 (3.3%)	2 (2.7%)	1.000	3 (3.5%)	1.000
History of Ventricular Arrhythmias	17 (28.3%)	26 (35.1%)	0.459	28 (32.6%)	0.716
Ventricle Fibrillation	5 (8.3%)	5 (6.8%)	0.752	8 (9.3%)	1.000
Ventricular Tachycardia	13 (21.7%)	19 (25.7%)	0.685	19 (22.1%)	1.000
Frequent PVCs	5 (8.3%)	8 (10.8%)	0.772	7 (8.1%)	1.000
NYHA					
Class III	59 (98.3%)	64 (86.5%)	0.023	78 (90.7%)	0.082
Class IV	1 (1.7%)	10 (13.5%)	0.023	8 (9.3%)	0.082

[1]Compared to FIX-HF-5C2 OPTIMIZER Group via Fishers exact test for binary variables and two-sample t-test for continuous variables.

Table 13: Baseline Medications: ITT Population

	FIX-HF-5C2	FIX-HF-5C			
Variable	**OPTIMIZER**	**OPTIMIZER**	**P-value[1]**	**Control**	**P-value[1]**
ACEi/ARB/ARNi	45 (75.0%)	61 (82.4%)	0.393	72 (83.7%)	0.212
ACE inhibitor	29 (48.3%)	40 (54.1%)	0.603	49 (57.0%)	0.317
ARB	8 (13.3%)	18 (24.3%)	0.128	22 (25.6%)	0.096
ARNi	9 (15.0%)	3 (4.1%)	0.035	3 (3.5%)	0.028
Beta Blocker	57 (95.0%)	72 (97.3%)	0.656	82 (95.3%)	1.000
Diuretic	44 (73.3%)	57 (77.0%)	0.689	67 (77.9%)	0.558
Secondary Diuretic	5 (8.3%)	6 (8.1%)	1.000	8 (9.3%)	1.000
Ivabradine	3 (5.0%)	2 (2.7%)	0.656	4 (4.7%)	1.000
Digoxin	4 (6.7%)	10 (13.5%)	0.260	8 (9.3%)	0.762
Aldosterone Inhibitor	25 (41.7%)	26 (35.1%)	0.477	33 (38.4%)	0.733
Hydralazine	3 (5.0%)	5 (6.8%)	0.731	10 (11.6%)	0.240
Nitrates	11 (18.3%)	18 (24.3%)	0.527	26 (30.2%)	0.124
Calcium Channel Blocker	6 (10.0%)	9 (12.2%)	0.787	8 (9.3%)	1.000
Anti-arrhythmic	19 (31.7%)	14 (18.9%)	0.108	12 (14.0%)	0.013
Anti-platelet	41 (68.3%)	54 (73.0%)	0.572	59 (68.6%)	1.000
Anticoagulant	27 (45.0%)	19 (25.7%)	0.028	18 (20.9%)	0.003

[1]Compared to FIX-HF-5C2 OPTIMIZER Group via Fishers exact test.

Baseline heart failure medications are summarized in **Table 13**. The only significant differences were a greater use of ARNi's, anti-arrhythmics, and anticoagulants in FIX-HF-5C2 subjects. The greater ARNi use reflects the fact that they were introduced toward the end of the FIX-HF-5C study. The greater use of anti-arrhythmics and anticoagulants likely represents the inclusion of patients with atrial fibrillation; those patients were excluded in the FIX-HF-5C study. **Table 14** breaks down the anti-arrhythmic medication usage in FIX-HF-5C2 and FIX-HF-5C studies for comparison.

Table 14: Baseline Anti-arrhythmic Medications

	FIX-HF-5C2	FIX-HF-5C	
Variable	**OPTIMIZER**	**OPTIMIZER**	**Control**
Anti-arrhythmic	19 (31.7%)	14 (18.9%)	12 (14.0%)
Amiodarone	12 (20.0%)	11 (14.9%)	6 (7.0%)
Sotalol	5 (8.3%)	3 (4.1%)	2 (2.3%)
Mexiletine	1 (1.7%)	0	3 (3.5%)
Dofetilide	1 (1.7%)	0	1 (1.2%)

Primary Effectiveness Endpoint

Bayesian Analysis

A Bayesian repeated measures model was used to estimate group differences in the mean peak VO_2 at 24 weeks from baseline in FIX-HF-5C2 device patients compared to FIX-HF-5C control patients, with 30% borrowing of information (70% down-weighting) from the corresponding group difference observed in the FIX-HF-5 subgroup data.

In the FIX-HF-5C2 device group, 55 of the 60 patients provided at least one post-baseline peak VO_2 measurement, and 52 patients provided 24-week peak VO_2 measurements. There were no deaths in FIX-HF-5C2 subjects at the 24-week assessment period, and there were no missing observations due to heart failure hospitalizations. However, patients in the FIX-HF-5C control group who are missing peak VO_2 observations due to death are imputed as zeros per the FIX-HF-5C protocol. There are a total of 146 patients and 397 non-missing peak VO_2 observations in the combined FIX-HF-5C2 device and FIX-HF-5C control groups for this analysis.

Tables 15 and 16 provide results of the Bayesian analyses while **Figures 11 and 12** show the peak VO2 results graphically.

Table 15: Number of Observations, Mean, SD of Peak VO_2 by Group and Time

	Nobs (observed)		Nobs (missing)		Mean		Standard Deviation	
	Control	**Device**	**Control**	**Device**	**Control**	**Device**	**Control**	**Device**
Baseline	86	60	0	0	15.36	15.01	2.81	2.94
12 Weeks	73	52	13	8	14.59	16.01	4.29	3.34
24 Weeks	74	52	12	8	14.34	16.22	4.69	3.09

Table 16: Bayesian Primary Analysis Results (with Borrowing)

		Borrowing (Bayes)			
Time	**TmtDiff**	**LL**	**UL**	**SE**	**P(Superior)**
12 Weeks	1.079	0.381	1.776	0.356	0.999
24 Weeks	1.722	1.021	2.417	0.356	1.000

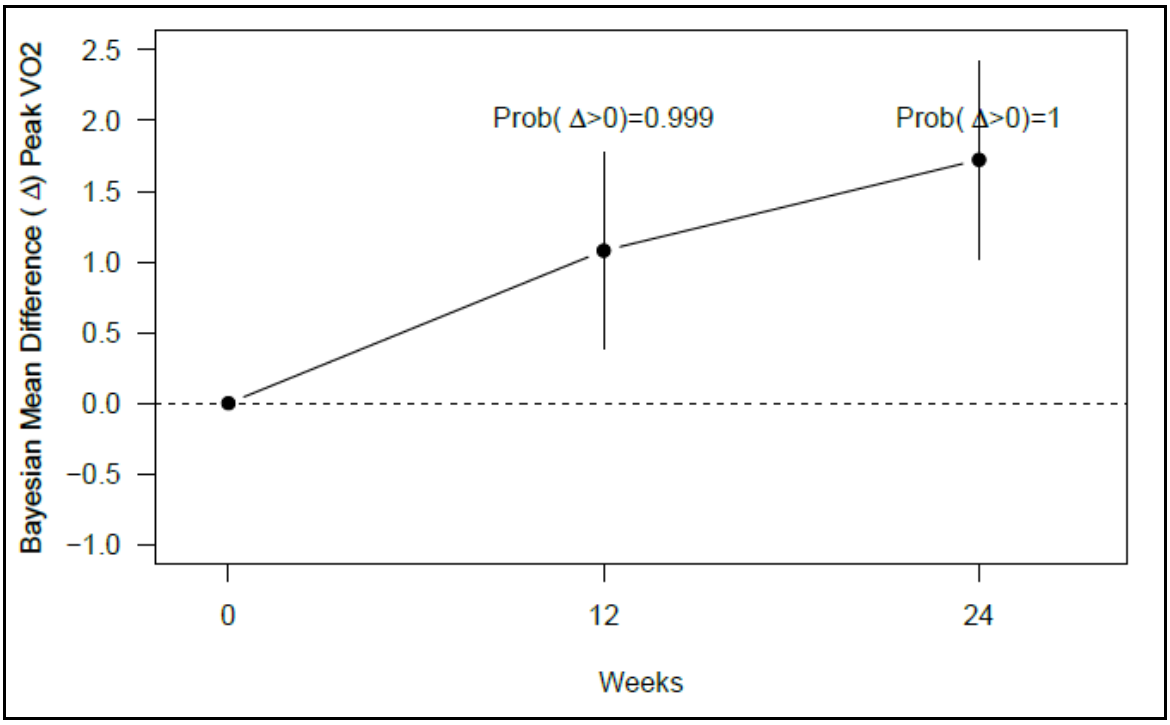


Figure 11: Bayesian Modeled Treatment Mean Difference (Δ) Peak VO_2 by Time

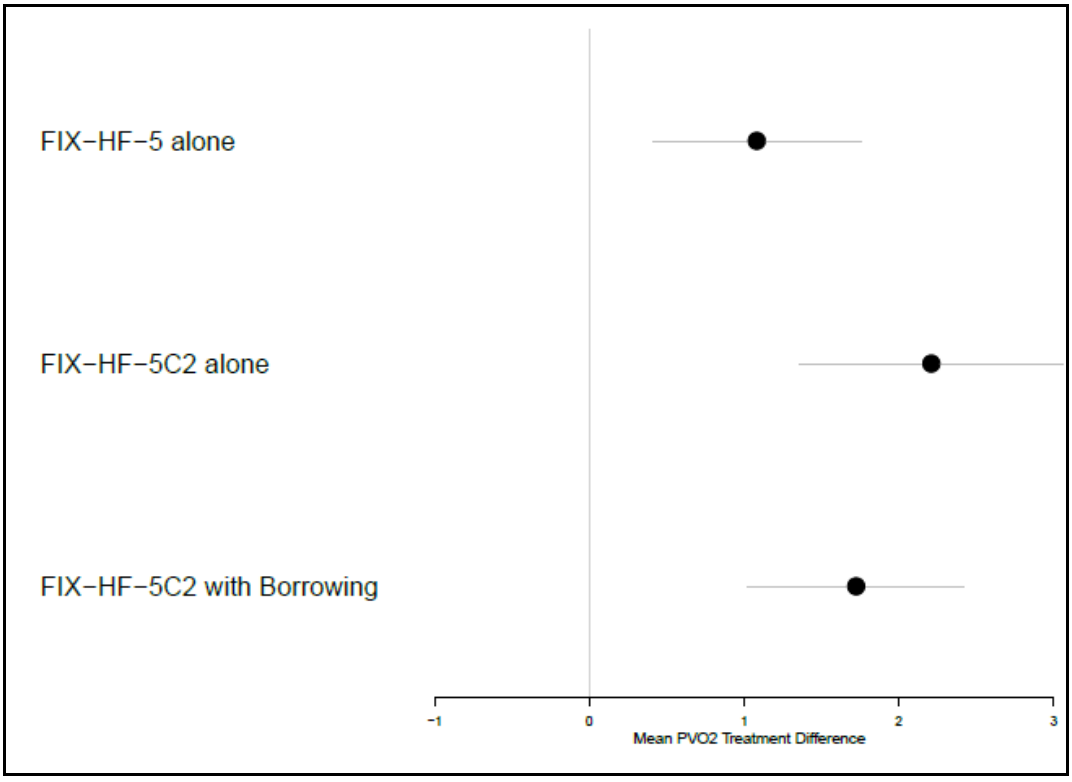


Figure 12: 24-Week Modeled Mean PVO_2 Treatment Difference by Study

The Bayesian Posterior Probability that Δ_3 is greater than 0 (indicating superiority of FIX-HF-5C2 device to FIX-HF-5C control) is 1. Because this exceeds 0.975, the null hypothesis is rejected and superiority is claimed with respect to the primary endpoint.

Frequentist Analysis

The Bayesian analysis indicates that the FIX-HF-5C2 OPTIMIZER group had a superior increase in Peak VO_2 over the FIX-HF-5C Control group with a posterior probability which exceeds the 0.975 required for statistical significance.

A supporting, non-Bayesian analysis of Peak VO_2 appears in **Table 17** overall summaries).

Eleven (11) subjects were missing evaluable Peak VO_2 results at weeks 12 or 24. Five (5) subjects were missing at both visits.

There were no deaths or missingness due to heart failure hospitalizations so there were no imputations of zeros or lowest value in the FIX-HF-5C2 data. Previous study results are presented for comparative purposes including differences between the current OPTIMIZER results and results from the FIX-HF-5C study. Peak VO_2 was significantly increased at both 12 and 24 weeks in the FIX-HF-5C2 OPTIMIZER group and the change from baseline was significantly different from the control group in the FIX-HF-5C study. This was confirmed in the frequentist mixed model results compared to the FIX-HF-5C study control.

In total, we observed an improvement in peak VO_2 for the device subjects in the FIX-HF-5C2 study which was not dependent on a decrease in VO_2 for the control group.

Table 17: Efficacy Summary: ITT Population

		FIX-HF-5C2	FIX-HF-5C			
Variable		**OPTIMIZER**	**OPTIMIZER**	**Difference[1]**	**Control**	**Difference[1]**
Peak VO_2 (ml/kg/min)						
Baseline	Mean ± SD (n)	15.0 ± 2.9 (60)	15.5 ± 2.6 (73)	-0.48 ± 2.76	15.4 ± 2.8 (86)	-0.36 ± 2.87
	(min, max)	(9.8, 19.9)	(9.8, 19.7)		(9.1, 19.9)	
	[95% CI]	[14.2,15.8]	[14.9,16.1]	[-1.44, 0.47]	[14.8,16.0]	[-1.31, 0.60]
	P-value[2]			0.317		0.462
12 Weeks	Mean ± SD (n)	16.0 ± 3.3 (52)	15.6 ± 3.2 (67)	0.43 ± 3.25	15.2 ± 3.1 (70)	0.80 ± 3.20
	(min, max)	(10.2, 22.2)	(9.0, 23.3)		(8.5, 21.9)	
	[95% CI]	[15.1,16.9]	[14.8,16.4]	[-0.76, 1.62]	[14.5,15.9]	[-0.36, 1.96]
	P-value[2]			0.478		0.174
Change Baseline to 12 Weeks	Mean ± SD (n)	0.77 ± 1.64 (52)	0.10 ± 2.34 (67)	0.67 ± 2.06	-0.35 ± 2.11 (70)	1.13 ± 1.92
	(min, max)	(-5.30, 4.60)	(-7.35, 5.95)		(-6.10, 4.80)	
	[95% CI]	[0.32,1.23]	[-0.47,0.67]	[-0.09, 1.42]	[-0.86,0.15]	[0.43, 1.82]
	P-value[2]	0.001	0.716	0.082	0.164	0.002
24 Weeks	Mean ± SD (n)	16.2 ± 3.1 (52)	15.5 ± 3.5 (66)	0.73 ± 3.33	15.2 ± 3.3 (70)	1.06 ± 3.20
	(min, max)	(10.2, 23.9)	(8.9, 23.2)		(8.8, 22.7)	
	[95% CI]	[15.4,17.1]	[14.6,16.3]	[-0.49, 1.95]	[14.4,15.9]	[-0.10, 2.21]
	P-value[2]			0.239		0.074
Change Baseline to 24 Weeks	Mean ± SD (n)	1.13 ± 1.50 (52)	-0.027 ± 2.745 (66)	1.15 ± 2.28	-0.50 ± 2.36 (70)	1.63 ± 2.04
	(min, max)	(-2.60, 4.20)	(-7.30, 5.90)		(-6.85, 4.90)	
	[95% CI]	[0.71,1.54]	[-0.701,0.648]	[0.32, 1.99]	[-1.07,0.06]	[0.89, 2.37]
	P-value[2]	<.001	0.938	0.007	0.078	<.001

[1]Compared to FIX-HF-5C2 OPTIMIZER Group.
[2]Values are compared to baseline using the paired t-test, and differences are compared using the two-sample t-test without taking into account other time points.

Secondary Effectiveness Analyses

Since the primary endpoint was met, the secondary endpoint of total CCM delivery could be formally tested. Total CCM delivery is presented in **Table 18** for the IP populations. Results are presented for all available data and for the multiple imputation approach as described previously. Although all subjects in FIX-HF-5C2 were implanted, 1 subject in the FIX-HF-5C OPTIMIZER group died prior to study start and an additional 5 subjects were not implanted, so the IP population differs for the FIX-HF-5C study used in comparison. As can be seen in **Table 18,** for all available data and imputed data, the total CCM delivery at 24 weeks is equivalent between the OPTIMIZER groups of the FIX-HF-5C2 and FIX-HF-5C studies since the 95% confidence interval of the difference between the 2 groups lies wholly within the interval defined by (Θ_L,Θ_U).

Table 18: Secondary Efficacy - OPTIMIZER Interrogation: IP Population

		FIX-HF-5C2	FIX-HF-5C		FIX-HF-5C2 Bsl Permanent AFIB
Variable		**OPTIMIZER (N=60)**	**OPTIMIZER (N=60)**	**Difference[1]**	**OPTIMIZER (N=9)**
Total CCM Delivery					
24 Weeks	Mean ± SD (n)	19892 ± 3472 (59)	19583 ± 4998 (67)	310 ± 4352	19734 ± 4187 (9)
	(min, max)	(11618, 28284)	(3645, 31009)		(12787, 24578)
	[95% CI]	[18988,20797]	[18364,20802]	[-1228, 1847]	[16515,22952]
	P-value[2]			0.691	
	(Θ_L,Θ_U)			(-2448,2448)	
Total CCM Delivery (IMPUTED)					
24 Weeks	Mean ± SE	19897 ± 463	19618 ± 610	279 ± 783	
	(min, max)	(19811, 20037)	(19553, 19722)		
	[95% CI]	[18988,20805]	[18421,20814]	[-1256,1813]	
	P-value[2]			0.722	
	(Θ_L,Θ_U)			(-2452,2452)	

[1] Bioequivalence is conceded if the two-sided 95% confidence interval, for the difference, is completely contained within the interval (Θ_L,Θ_U).
[2] P-value for mean from the two-sample t-test for the difference between groups.

Primary Safety Endpoint

The primary safety endpoint was the composite endpoint of the percentage of subjects in the OPTIMIZER group who experienced either an OPTIMIZER device or OPTIMIZER procedure related complication through the 24-week follow-up period, as determined by an independent events adjudication committee (EAC). The EAC reviewed all serious adverse event reports (SAEs), confirmed the classification of “serious”, and adjudicated the relationship of the event to the OPTIMIZER System device or procedure. SAEs that the EAC determined to be definitely related to either the OPTIMIZER System or the OPTIMIZER Procedure were considered a Complication.

There was only 1 complication observed in the FIX-HF-5C2 subjects. This was in a subject who had a minor hematoma at the OPTIMIZER IPG implant site and was kept in the hospital overnight for observation following the device implantation. The hematoma resolved without treatment, and there were no further complications in this case. The EAC adjudicated the event as a procedure related complication to account for the index hospital stay being prolonged an additional day for observation. There was no OPTIMIZER device-related SAE reported in the 2-lead device subjects.

Thus, the complication rate in FIX-HF-5C2 study ITT group was 1.7% (1/60) with exact 95% CI (0.0%, 8.9%). As can be seen in **Table 19**, the rate of complications in the FIX-HF-5C2 study was nominally lower than seen in the previous study although not statistically significant. The small sample size for the FIX-HF-5C2 study renders it difficult to show a statistical difference in percentage points. However, the absolute difference between the complication rate for the FIX-HF-5C2 study (1.7%) and the FIX-HF-5C study (10.3%) is clinically relevant.

We can therefore conclude that the primary safety endpoint of the FIX-HF-5C2 study was met and that delivery of CCM through a 2-Lead device is just as safe as delivery of CCM therapy through a 3-Lead device. These results may, in part, be due to a reduction in the number of leads implanted with the 2-Lead device as well as the reduction in the total volume of leads introduced in the venous vasculature.

Table 19: Safety: ITT Population

		FIX-HF-5C2	FIX-HF-5C	
Variable		**OPTIMIZER 2-lead**	**OPTIMIZER 3-lead**	**P-value[1]**
Primary Safety				
OPTIMIZER device- or procedure-related complication through 24 Weeks	N (%)	1 (1.7%)	7 (10.3%)	0.0660
	[95% CI]	(0.0%, 8.9%)	(4.2%, 20.1%)	
Secondary Safety				
PVC or VT SAEs	N (%)	0 (0.0%)	0 (0.0%)	
PVC	N (%)	0 (0.0%)	0 (0.0%)	
VT	N (%)	0 (0.0%)	0 (0.0%)	

[1]Compared to FIX-HF-5C2 OPTIMIZER Group via Fishers exact test.
*Values are number and percent of subjects. Subjects are counted only once within each category.

Adverse Events

All sites reported non-serious adverse events and adjudicated serious adverse events from study start date to 24 weeks; are tabulated in **Table 20** and **Table 21** in the ITT population. The total number of events and the number and percent of subjects having at least one event of the type listed is given. Event rates were similar to those seen in both the FIX-HF-5C OPTIMIZER and control groups. At a nominal 0.05 level of significance, there were fewer percentage of subjects that had a serious OPTIMIZER System malfunction in the FIX-HF-5C2 study than in the previous study (p=0.03).

Table 20: Adjudicated Serious Adverse Events, Day 0-168: ITT Population

	FIX-HF-5C2 OPTIMIZER		FIX-HF-5C OPTIMIZER			FIX-HF-5C Control		
Variable	**# Events**	**Subjects[2]**	**# Events**	**Subjects**	**P-value[1]**	**# Events**	**Subjects**	**P-value[1]**
All	26	19 (31.7%)	29	20 (27.0%)	0.572	27	19 (22.1%)	0.250
		(20.3%, 45.0%)		(17.4%, 38.6%)			(13.9%, 32.3%)	
General Medical	8	7 (11.7%)	7	7 (9.5%)	0.779	8	7 (8.1%)	0.571
		(4.8%, 22.6%)		(3.9%, 18.5%)			(3.3%, 16.1%)	
Arrhythmia	3	2 (3.3%)	3	3 (4.1%)	1.000	2	2 (2.3%)	1.000
		(0.4%, 11.5%)		(0.8%, 11.4%)			(0.3%, 8.1%)	
Worsening Heart Failure	7	5 (8.3%)	4	3 (4.1%)	0.466	8	7 (8.1%)	1.000
		(2.8%, 18.4%)		(0.8%, 11.4%)			(3.3%, 16.1%)	
General Cardiopulmonary	2	2 (3.3%)	4	3 (4.1%)	1.000	2	2 (2.3%)	1.000
		(0.4%, 11.5%)		(0.8%, 11.4%)			(0.3%, 8.1%)	
Bleeding	1	1 (1.7%)	0	0 (0.0%)	0.448	1	1 (1.2%)	1.000
		(0.0%, 8.9%)		(0.0%, 4.9%)			(0.0%, 6.3%)	
Neurologic	1	1 (1.7%)	0	0 (0.0%)	0.448	0	0 (0.0%)	0.411
		(0.0%, 8.9%)		(0.0%, 4.9%)			(0.0%, 4.2%)	
Thromboembolism	1	1 (1.7%)	1	1 (1.4%)	1.000	1	1 (1.2%)	1.000
		(0.0%, 8.9%)		(0.0%, 7.3%)			(0.0%, 6.3%)	
Local Infection	1	1 (1.7%)	1	1 (1.4%)	1.000	4	4 (4.7%)	0.649
		(0.0%, 8.9%)		(0.0%, 7.3%)			(1.3%, 11.5%)	
Sepsis	1	1 (1.7%)	1	1 (1.4%)	1.000	1	1 (1.2%)	1.000
		(0.0%, 8.9%)		(0.0%, 7.3%)			(0.0%, 6.3%)	
ICD or Pacemaker System Malfunction	1	1 (1.7%)	2	2 (2.7%)	1.000	0	0 (0.0%)	0.411
		(0.0%, 8.9%)		(0.3%, 9.4%)			(0.0%, 4.2%)	
OPTIMIZER System Malfunction	0	0 (0.0%)	6	6 (8.1%)	0.033		-	
		(0.0%, 6.0%)		(3.0%, 16.8%)				

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[1]Compared to FIX-HF-5C2 OPTIMIZER Group via Fishers exact test.

[2]Number and percent of subjects. Subjects are counted only once within each category.

Table 21: Non-Serious Adverse Events, Day 0-168: ITT Population

	FIX-HF-5C2 OPTIMIZER		FIX-HF-5C OPTIMIZER			FIX-HF-5C Control		
Variable	**# Events**	**Subjects[2]**	**# Events**	**Subjects**	**P-value[1]**	**# Events**	**Subjects**	**P-value[1]**
All	39	26 (43.3%)	41	21 (28.4%)	0.101	35	23 (26.7%)	0.050
		(30.6%, 56.8%)		(18.5%, 40.1%)			(17.8%, 37.4%)	
General Medical	23	19 (31.7%)	22	14 (18.9%)	0.108	23	13 (15.1%)	0.025
		(20.3%, 45.0%)		(10.7%, 29.7%)			(8.3%, 24.5%)	
Arrhythmia	1	1 (1.7%)	1	1 (1.4%)	1.000	4	4 (4.7%)	0.649
		(0.0%, 8.9%)		(0.0%, 7.3%)			(1.3%, 11.5%)	
Worsening Heart Failure	3	3 (5.0%)	6	5 (6.8%)	0.731	4	4 (4.7%)	1.000
		(1.0%, 13.9%)		(2.2%, 15.1%)			(1.3%, 11.5%)	
General Cardiopulmonary	4	4 (6.7%)	3	3 (4.1%)	0.700	3	3 (3.5%)	0.446
		(1.8%, 16.2%)		(0.8%, 11.4%)			(0.7%, 9.9%)	
Bleeding	2	2 (3.3%)	2	2 (2.7%)	1.000	0	0 (0.0%)	0.167
		(0.4%, 11.5%)		(0.3%, 9.4%)			(0.0%, 4.2%)	
Neurologic	0	0 (0.0%)	1	1 (1.4%)	1.000	0	0 (0.0%)	
		(0.0%, 6.0%)		(0.0%, 7.3%)			(0.0%, 4.2%)	
Thromboembolism	1	1 (1.7%)	0	0 (0.0%)	0.448	0	0 (0.0%)	0.411
		(0.0%, 8.9%)		(0.0%, 4.9%)			(0.0%, 4.2%)	
Local Infection	5	5 (8.3%)	3	3 (4.1%)	0.466	1	1 (1.2%)	0.043
		(2.8%, 18.4%)		(0.8%, 11.4%)			(0.0%, 6.3%)	
Sepsis	0	0 (0.0%)	0	0 (0.0%)		0	0 (0.0%)	
		(0.0%, 6.0%)		(0.0%, 4.9%)			(0.0%, 4.2%)	
ICD or Pacemaker System Malfunction	0	0 (0.0%)	0	0 (0.0%)		0	0 (0.0%)	
		(0.0%, 6.0%)		(0.0%, 4.9%)			(0.0%, 4.2%)	
OPTIMIZER System Malfunction	0	0 (0.0%)	3	2 (2.7%)	0.502		-	
		(0.0%, 6.0%)		(0.3%, 9.4%)				

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[1]Compared to FIX-HF-5C2 OPTIMIZER Group via Fishers exact test.

[2]Number and percent of subjects. Subjects are counted only once within each category.

The incidence of overall non-serious adverse events was significantly higher in the OPTIMIZER subject cohort of the FIX-HF-5C2 study than for the control group of the FIX-HF-5C study. It was not significantly greater than the incidence on non-serious adverse events in the OPTIMIZER group for the FIX-HF-5C study. The higher rate between the FIX-HF-5C2 OPTIMIZER subjects and subjects in the control group for FIX-HF-5C can be attributed to differences in general medical events and localized infection. General medical events include a wide range of adverse events such as sore throats to more serious events like cholelithiasis. Clinically, it is difficult to interpret the meaning of any differences in general medical events. Only 1 of the 5 non-serious localized infections was device related (IPG pocket). The important point is that the localized infection rate was not high to begin with and was not significantly different between the OPTIMIZER subjects for the FIX-HF-5C2 study and the OPTIMIZER subjects for the FIX-HF-5C study.

Discussion

The study met its primary effectiveness endpoint based on the Bayesian analysis presented which was supported by frequentist analyses. With respect to safety, there were no device-related complications and only 1 procedure-related complication (<2%). This was significantly lower than the rate observed in the FIX-HF-5C 3-lead device study. There was no evidence of a difference between study groups with respect to adverse events or adjudicated serious adverse events, although the FIX-HF-5C2 OPTIMIZER group appeared to have a lower rate of serious OPTIMIZER System related events than was seen previously.

Thus, it can be concluded that the FIX-HF-5C2 study met its pre-specified endpoints and that the 2-Lead configuration of the OPTIMIZER Smart is at least as safe and effective as the 3-Lead configuration of the OPTIMIZER Smart approved by FDA in P180036.

Peak VO_2 improved more in the OPTIMIZER patients of the present FIX-HF-5C2 study than in the prior FIX-HF-5C study control group for both Bayesian and frequentist statistical analyses.

Risk-Benefit

The benefits of the 2-Lead configuration of the OPTIMIZER Smart are an improvement in peak VO_2, improved functional status as evidenced by improvements in NYHA functional class and a reduced incidence of procedural complications as compared to the 3-Lead configuration of the OPTIMIZER Smart (FIX-HF-5C study). Risks associated with the OPTIMIZER Smart system are similar to those associated with ICDs and pacemakers; which are well documented in the literature. In the FIX-HF-5C2 study, lead dislodgments were the primary complication reported. There were no lead dislodgments reported in the FIX-HF-5C2 study. Thus, it is clear that the potential benefits of the 2-Lead configuration of the OPTIMIZER Smart outweigh the potential risks.

Conclusions

Based on the results of the FIX-HF-5C2 study described herein, we conclude the following:

1. The 2-Lead configuration of the OPTIMIZER Smart System is safe and effective for the delivery of CCM therapy in patients with NYHA class III heart failure symptoms.
2. Exercise tolerance as evidenced by improved peak VO_2, is improved by CCM therapy delivered by the 2-Lead configuration of the OPTIMIZER Smart system.
3. CCM therapy delivery with the 2-Lead system is clinically effective and the same as delivery with the 3-Lead device.
4. Complication rates are lower with the 2-Lead device possibly due to the reduction in the number of implanted leads.
5. The serious adverse event profile for the 2-Lead device is not significantly different from that with the 3-Lead device.

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