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Revo MRI™ SureScan™ Pacing System

Sponsor Panel Briefing Package

Volume 1 of 1

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1 Executive Summary of the Program

This section provides an overview of the benefits of MRI and clinical need and the strategy for demonstrating safety and effectiveness, which includes the interactions between a pacemaker system and the MRI environment, the hazards associated with those interactions, and the clinical impacts. In addition, an overview of the development process is presented, along with a document map.

Since the information in this document spans two medical specialties (Cardiology and Radiology), a basic overview of pacemakers and MRI are provided in Appendices 1 and 2, respectively. Furthermore, due to the extensive and diverse nature of the testing conducted in this program, additional appendices were created to provide an in-depth description of these activities.

Note: Footnotes are indicated with Roman numerals, while endnotes are indicated with Arabic numerals.

1.1 Benefits of MRI and Clinical Need

Magnetic resonance imaging (MRI) is commonly used as an imaging tool for detecting and diagnosing abnormalities and diseases in soft tissue. In 2007, there were approximately 30 million MRI scans performed in the US, and its use continues to grow.[1] MRI makes earlier detection of medical conditions possible and offers important advantages over other imaging technologies, which include the absence of ionizing radiation, superior soft-tissue resolution, and discrimination in any imaging plane.[2] Because of the benefits it provides, MRI is the imaging modality of choice for many types of neurological, oncological, and musculoskeletal diseases and disorders. For example, the following are just a few of the medical conditions for which patients can benefit from MRI diagnoses:

- Cancer
  - Estimated prevalence of over 11 million people in the US[3]
  - MRI for diagnosis, mapping, and monitoring response to therapy is especially prevalent for brain tumors
- Stroke
  - Approximately 800,000 strokes are diagnosed annually in the US[4]
- Dementia
  - Approximately 30% of the population over age 80 will be diagnosed with dementia in the US[5]
- Spinal stenosis
  - Most common indication for surgery in patients over age 60 in the US[6]

However MRI examinations are currently contraindicated in the US for patients who have implanted pacemakers. This is due to concerns that the strong static, gradient, and radiofrequency magnetic and electromagnetic fields generated by an MRI scanner may interfere with pacemaker operation, damage system components, or cause safety risks for patients, such as

inappropriate therapy, lead or pacemaker dislodgement, or change in pacing capture threshold.[7,8,9,10] As a result, many patients receive additional computed tomography (CT) scans, undergo interventional procedures, experience delayed diagnoses, and may not receive optimal treatment for their condition.

Considering that many pacemaker patients today also have other comorbidities, many of these patients would benefit from having access to MRI in order to optimally treat and manage their conditions and avoid the risks due to ionizing radiation from CT scans, delays in treatment, and interventional procedures.

Safe access to MRI scanning for pacemaker patients is a significant and growing unmet medical need. Currently, it is estimated that well over 200,000 patients (annually) in the US have to forego an MRI scan because of the presence of their implanted pacemaker system.[11] Moreover, the number of patients with pacemakers is growing at the same time that the use of MRI is increasing. It has been estimated that there is a 50-75% probability that cardiac device patients will be indicated for an MRI over the lifetime of their devices[10]. Increased MRI adoption, multi-specialty physician demand, and clear patient benefit are driving the critical need for pacemaker patients to have safe access to MRI.

In response, Medtronic Cardiac Rhyhm Disease Management (CRDM) has been engaged for more than a decade in research and development, along with rigorous and comprehensive testing, to understand the risks associated with pacemaker/MRI scanner interactions. The knowledge gained from this analysis has provided a solid foundation for the design of a safe and effective MR Conditional pacing system – the Revo™ MRI SureScan™ pacing system. (The term *MR Conditional* is defined as an item that has been demonstrated to pose no known hazards in a specified MR environment with specified conditions of use.[12])

1.2 Strategy for Demonstrating Safety and Effectiveness

The information that follows describes Medtronic CRDM's development program for the Revo MRI SureScan pacing system. These elements will be discussed in more detail in Section 1.2.1 (Analysis), Section 1.2.2 (Design), and Section 1.2.3 (Testing).

Current standards to demonstrate compatibility between MR scanners and implantable medical devices address testing only for passive implants (e.g., stents, aneurysm clips). Portions of these standards may be applicable to some hazards of active implantable medical devices (AIMDs) such as force and torque; however, these standards do not comprehensively address all the potential patient hazards presented by active implants such as cardiac pacemakers. Regulatory agencies, the MR scanner industry and the medical device industry recognized this shortcoming, and established an international joint working group in 2007 between the International Organization for Standardization (ISO)[i] and the International Electrotechnical Commission (IEC)[ii] to address the unique safety issues of AIMDs in MRI.

The objective of the ISO/IEC MRI Joint Working Group was to develop a technical specification with the goal of defining test methods and conditions to aid in assessing the performance of AIMDs in the MRI environment. The initial draft of this technical specification is expected to be available in 2010. The test methods proposed in the technical specification can be used to aid in

[i] ISO groups TC150/SC6 on active implants

[ii] IEC group SC 62B MT40 on magnetic resonance equipment for medical diagnosis

the analysis of interactions between MRI and AIMDs. Patient safety evaluation criteria will not be established in the initial draft.

Since the inception of the Joint Working Group, Medtronic has been actively participating and contributing to the development of the technical specification based on the years of experience Medtronic has invested in researching and understanding compatibility concerns between AIMDs and MR scanners. Medtronic has proposed many of the test methods that have been implemented in the technical specification, and the test methods and procedures that Medtronic has used to analyze the Revo MRI system are aligned with those laid out in the ISO/IEC Joint Working Group Technical Specification draft.

1.2.1 Analysis

The analysis stage of the development effort focused on understanding and characterizing the MRI environment. Medtronic CRDM conducted multiple assessments and analyses to:

- Identify all hazards associated with interactions of implantable pacemaker systems with the MRI environment, and
- Translate the hazards into clinical impacts for the patient (i.e., patient risk).

These assessments included 1) a literature review and 2) MRI environment characterizations.

Literature Review

A comprehensive literature review was conducted to obtain an understanding of the issues related to pacing systems in an MRI environment and risks associated with MRI scans of pacemaker patients. The literature identified a number of hazards in the MRI environment and risks to the patient, including:[9, 13, 14, 15, 16, 17, 18, 19, 20, 21]

- device or lead movement or dislodgment,
- pacing inhibition or inappropriate therapy,
- change in pacing capture threshold due to tissue heating near the lead electrodes, and
- induction of electrical currents within leads that could cause arrhythmias.

Based on the literature review, the hazards that pose the highest risk to the patient are lead heating, unintended cardiac stimulation, and device interactions. These interactions are complex, and there are no standard test methods for evaluating patient risk due to lead heating, unintended cardiac stimulation, and device interactions.[iii] For this reason, the Food and Drug Administration (FDA) requires "…thorough evaluation of concerns related to heating, arrhythmogenesis and [electromagnetic compatibility (EMC)]-related proper device function during and after MRI…"[22] before a manufacturer demonstrates safety and effectiveness of an MR Conditional active cardiac device.

MRI Environment Characterization and Hazard Identification

In order to thoroughly understand the MRI environment and identify any other hazards that have not been previously identified in the literature, Medtronic CRDM performed comprehensive

[iii] "Device interactions" is a generic term that refers to any other adverse interactions between the MRI fields and the device, which may impact the electrical operation of the device.

MRI scanner characterization of several different scanner models from the leading MRI manufacturers (GE, Siemens, and Philips). The specific clinical scanners were chosen based on performance and installed base. The evaluation included 1) measurements of the gradient electromagnetic fields, 2) pulse sequence characterization, and 3) identification of parameters that affect the average radio frequency power absorbed by the patient during an MRI scan. These evaluations helped Medtronic CRDM:

- understand the MRI environment,
- identify the similarities and differences among different clinical scanners,
- establish the applicability of the evaluations to all other scanners on the market,
- identify the hazards and associated patient risk for each field during an MRI scan, and
- learn what is necessary to design a pacemaker system that will be safe in the current clinical environment and remain safe given evolving scanner capabilities.

Furthermore, Medtronic CRDM identified applicable standards, such as the IEC standard that sets requirements for safety of MR scanners.[23] These standards were used in developing the appropriate test methods.

The hazards, field interactions, and clinical impact identified by Medtronic CRDM are consistent with those published in the peer-reviewed literature, but also include interactions not previously identified in the literature. Furthermore, all evaluated hazards are consistent with those identified by the MRI Joint Working Group. The breadth and depth of the completed characterizations lend Medtronic CRDM confidence that the evaluated hazards are appropriate and complete.

Table 1-1 summarizes the potential MRI interactions between the MRI environment and implanted pacemaker systems, the hazards, and the potential clinical impacts, identified in the literature and through Medtronic CRDM's characterization testing. Refer to Appendix 2 for an overview of fields in an MRI environment.

Table 1-1. Summary of MRI Hazards and Potential Clinical Impacts

Hazard	Field Interaction	Mechanism and Source of Hazard	Potential Clinical Impact	Sample Literature References
Lead Heating	Radiofrequency	The conductive pacing lead acts as an antenna, picking up radiofrequency energy. A portion of this energy is dissipated as heat in the cardiac tissue near the tip electrode.	Tissue heating near the electrode may result in thermal cardiac tissue damage and affect pacing therapy.	14, 24, 25
Unintended Cardiac Stimulation	Gradient Radiofrequency	The gradient and radiofrequency fields will induce voltages in pacemaker leads that will be applied to the pacing lead electrodes. If these voltage pulses are large enough, they may directly stimulate the heart.	Cardiac stimulation may lead to a single or intermittent stimulation or a sustained tachycardia.	26, 27, 37

Hazard	Field Interaction	Mechanism and Source of Hazard	Potential Clinical Impact	Sample Literature References
Device Interactions	Static Gradient Radiofrequency	The gradient, radiofrequency, and static fields may adversely impact the electrical operation of the pacemaker system if its operation is not protected from the effects of those fields.	Pacemaker malfunction may affect pacing therapy.	14, 28
Case Heating	Gradient Radiofrequency	Electrical currents on the conductive surface of the pacemaker case are dissipated as heat.	Tissue heating near the pacemaker case may lead to patient discomfort or tissue damage.	--
Force and Torque	Static	The static magnetic field will act on any ferromagnetic material in a pacemaker or lead, producing a translation or rotation of the device or lead.	Pacemaker or lead movement may lead to patient discomfort or affect pacing therapy.	14, 29
Vibration	Static Gradient	Gradient magnetic field induces electrical currents in the conductive surfaces of pacemaker components. Interaction of these currents with the static magnetic field causes the component to vibrate.	Pacemaker malfunction may affect pacing therapy.	--

1.2.2 Design

System requirements were defined based on MRI characterization work during the analysis phase and on input from customers (physicians, radiologists, electrophysiologists, and cardiologists). While maintaining pacemaker feature functionality before and after an MRI scan was essential, minimum pacing therapy for supporting patients during the scans was also defined.

Medtronic CRDM research and development activities toward an MR Conditional pacing system were conceptualized in 1997. The product development program began in 2004. During this period, design changes began to be implemented in Medtronic CRDM products (such as the EnRhythm pacemaker) as hazards and mitigation techniques were understood. Platforms for both device and lead were carefully assessed based on these design features and proven field reliability experience.

The EnRhythm device was selected as the baseline pacemaker for the first MR Conditional pacing system based on features such as flexible architecture that allowed incorporation of new firmware, a Hall sensor to mitigate the effects of the static magnetic field, advanced pacing therapies, and other features (see **Table 2-2** for a complete list).

The CapSureFix MRI 50868MRI lead design was based on a high volume Medtronic CRDM pacing platform with proven reliability in the field (99% lead survival probability over 5 years in 2005). Medtronic re-designed the lead body to mitigate the hazard due to lead tip heating. This design approach provided the most robust option to address the MRI hazards and still utilize existing lead manufacturing technology and material construction techniques approved for current pacing leads on the market (see Table 2-3).

Further enhancements to both the pacemaker and lead were undertaken with the goal of designing for inherent safety by mitigating the risks due to MRI-related hazards. In addition, the MRI SureScan application software was added, which simplifies programming steps to provide appropriate therapy during an MRI scan (see Section 2.4 for a more complete description of the MRI SureScan feature).

Testing was used to demonstrate that the design changes met the specified requirements with low risk to the system or patient, and that the risk due to the MRI hazards was mitigated. In certain cases, testing was used to demonstrate that the existing EnRhythm design met the specified requirements with low risk to the system or patient, and thus no further design changes were required. More details regarding the testing are given in the next section. In addition, based on the identified environment and possible hazards, Medtronic CRDM defined the proposed conditions of use (see Section 3).

1.2.3 Testing

In order to demonstrate safety and effectiveness of the Revo MRI SureScan pacing system when used according to the proposed labeling conditions, both pre-clinical and clinical evaluations were performed.

Extensive pre-clinical MRI testing was necessary in order to fully evaluate potential patient hazards at environmental conditions (e.g., radiofrequency (RF) fields, gradient fields, and MRI exposure durations) beyond those that can be obtained using currently available MRI scanners. In addition, the pre-clinical testing demonstrated safety and effectiveness for a wide range of system implant and patient anatomy configurations, beyond those reasonable to assess in a human clinical study.

The purpose of the clinical study was to confirm the results of the pre-clinical testing and to assess the clinical implementation and usability of the system.

Pre-Clinical Testing

Pre-clinical test methods included in vitro (bench) testing, in vivo (animal) testing, and computer simulations (modeling).

- In vitro testing was used to identify performance concerns or device failures and to demonstrate device reliability and integrity during and post MRI exposure. In vitro test environments included traditional bench testing, as well as testing in clinical MRI scanners to provide the appropriate electromagnetic environment.
- In vivo testing was used to understand and confirm the clinical manifestation of identified MRI hazards (e.g., gradient-induced cardiac stimulation, and radiofrequency-induced lead heating). In addition, in vivo evaluations were required to assess the system performance beyond the clinical labeling conditions using an animal model.
- Computer simulations (modeling) were used to predict hazard probabilities and performance for a broad patient population and wide range of clinical scenarios. The modeling approach was necessary for cases where the interactions between the MRI environment and the human body and implanted pacing system were too complex to be evaluated using only in vitro or in vivo methods.

In addition, standard (non-MRI environment) testing was conducted to ensure that the system met all pacing system requirements. For additional details on the pre-clinical testing, refer to Section 4.2, Pre-Clinical Evaluation.

Confirmatory Clinical Study

The primary safety objective of the clinical study was to assess MRI-related complications in the month following MRI. The primary effectiveness objective was to compare changes in pacing capture threshold and sensing amplitudes before and after MRI between the MRI and control groups. This objective was designed to evaluate the effect, if any, of MRI-induced lead tip heating on pacing therapy. An additional objective was to characterize the occurrence of MRI-induced sustained ventricular arrhythmias and asystole. This objective was designed to evaluate the occurrence of MRI-induced unintended cardiac stimulation. The sample size of the clinical study was based on the primary endpoints of the study, each powered at 90% to reject the null hypothesis under certain assumptions.

The MRI scanning protocol represented one MRI scan procedure, which was approximately 30 minutes active scan time (60 minutes in MRI bore) and included 14 head and lumbar clinically relevant scans which were modified to maximize the effects of the gradient or radiofrequency fields. For additional details on the clinical study, refer to the Confirmatory Clinical Study, in Section 4.3.

1.3 Development Timeline

Throughout this document, several devices will be referenced. The devices are described in Table 1-2 below; the rest of the document reflects the device name as appropriate.

Table 1-2. Device Naming Convention

Device Name	Description
EnRhythm Pacemaker	Previous device used as the baseline platform for the EnRhythm MRI SureScan pacemaker. This *non*-MR Conditional pacemaker was approved for US market release on April 28, 2005.
EnRhythm MRI SureScan Pacemaker	Device name used during the development process, clinical study, and for release outside of the US.
Revo MRI SureScan Pacemaker	To avoid confusion surrounding previous product platforms, the EnRhythm MRI SureScan pacing system was renamed the Revo MRI SureScan pacing system after completion of the clinical study.

1.3.1 Clinical Study

Beginning in 2004, Medtronic CRDM initiated discussion with the FDA to obtain input on the clinical study and pre-market approval (PMA) requirements prior to submitting a formal Investigational Device Exemption (IDE) application. After constructive collaboration, the IDE application was submitted in March 2007. The FDA granted conditional IDE approval in November 2007, allowing Medtronic CRDM to begin enrolling patients in the US clinical study. Full IDE approval was granted in March 2008.

The clinical study was a global study, requiring regulatory approval for the study sites outside the US. Approval was obtained from the appropriate Competent Authorities and medical ethics committees, allowing the clinical study to be initiated outside of the US in February 2007.

1.3.2 Pre-Market Approval (PMA) Application

The FDA granted Medtronic CRDM expedited review of the PMA on the grounds that the MR Conditional system has the potential to offer patients a significant clinical advantage for which there is no alternative currently available.

Medtronic CRDM and the FDA agreed to use the modular review approach for the PMA. In general, the modular review approach provides a mechanism by which pre-clinical data and manufacturing information can be submitted to the FDA for review while allowing collection, compiling, and analyzing of the clinical data. This allows for resolution of deficiencies noted by the FDA in the review process of the earlier submitted information.[iv] This PMA consists of eight modules, filed from September 2008 to June 2009.

1.3.3 Market Approval Outside the US

Marketing approval in Europe (CE Mark) for the EnRhythm MRI system was obtained in September 2008, which allowed sales of the system in Europe. Following CE Mark approval, applications and/or registrations in other geographies followed. The system has been approved for sale in 23 geographies (Austria, Belgium, Central America, Czech Republic, Denmark, Finland, Germany, Greece, Hong Kong, India, Ireland, Italy, Malaysia, Netherlands, Portugal, Saudi Arabia, Singapore, Slovakia, South Africa, Spain, Sweden, Switzerland, and United Kingdom).

Figure 1-1 provides an illustration of the program timeline discussed in this section.

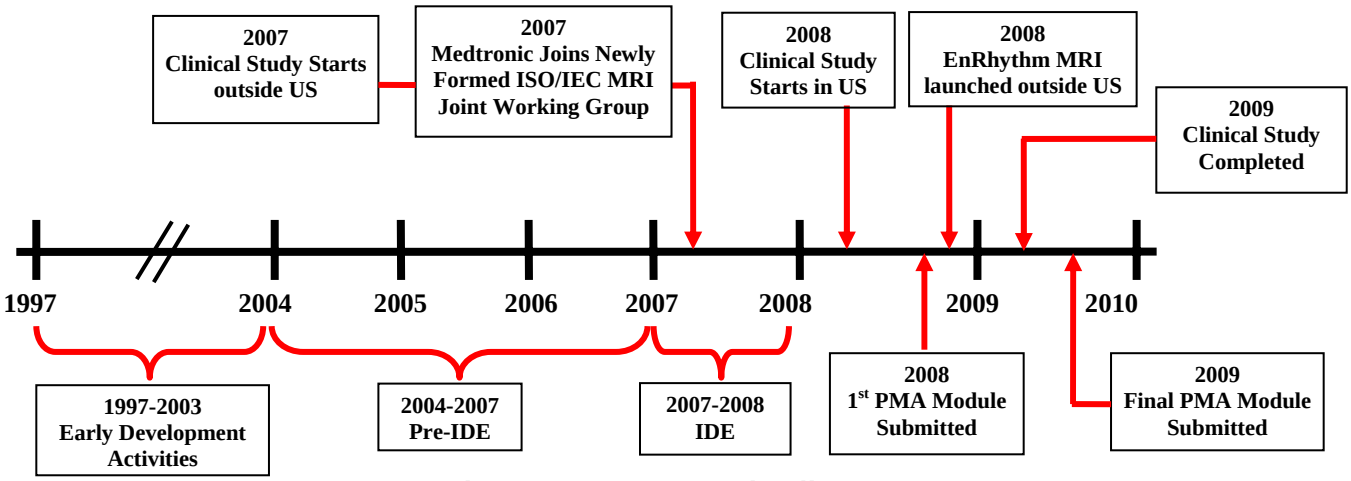


Figure 1-1. Program Timeline

[iv] Due to the extensive pre-clinical evaluation, a portion of pre-clinical testing for the Revo MRI system was conducted in parallel with the clinical study.

1.4 Document Map

This document is organized as shown in Figure 1-2.

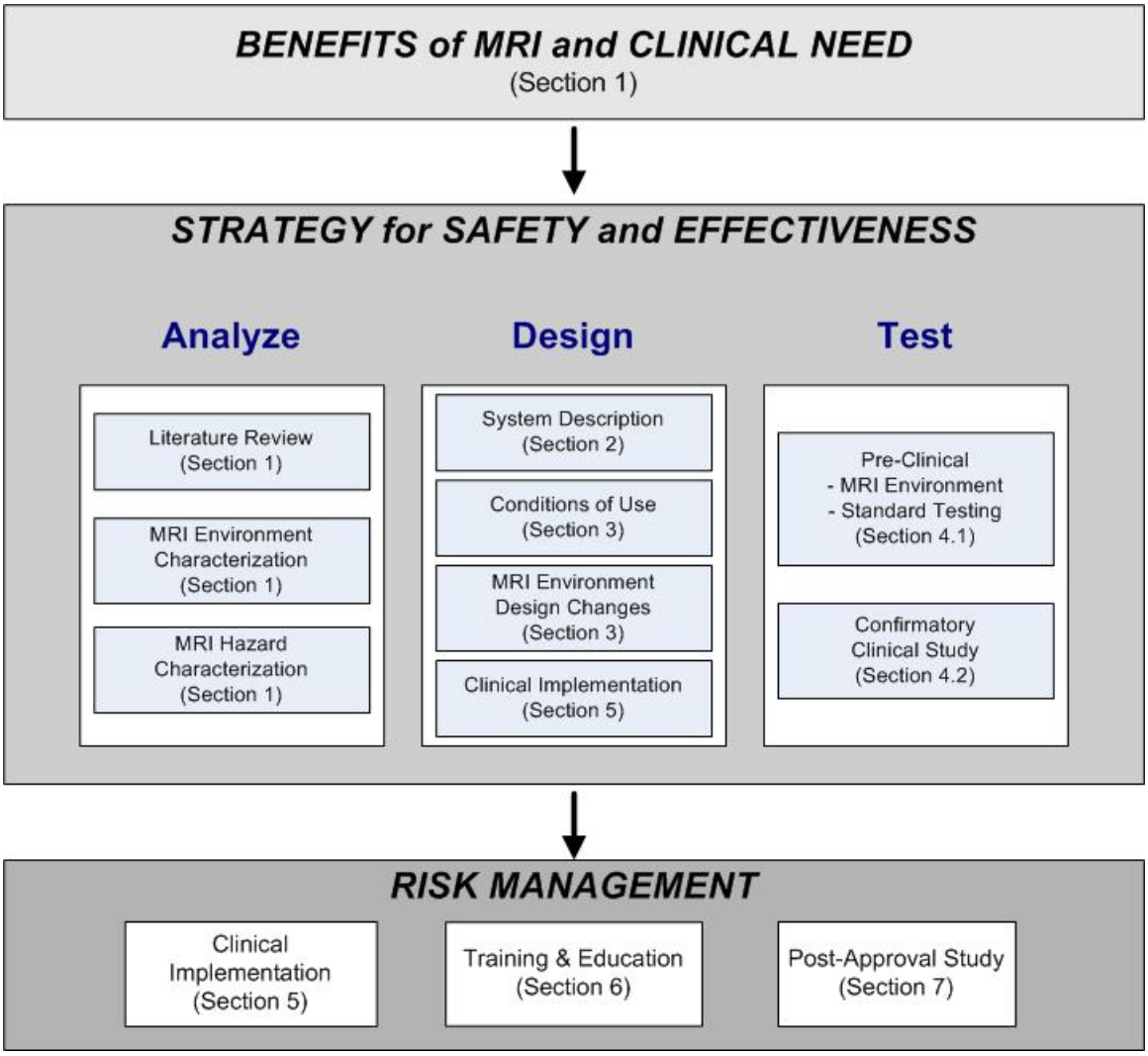


Figure 1-2. Overview of the Revo MRI SureScan Pacing System Development Strategy

In addition, a number of appendices are attached. The content of the appendices is shown in Table 1-3.

Table 1-3. Outline of Appendix Contents

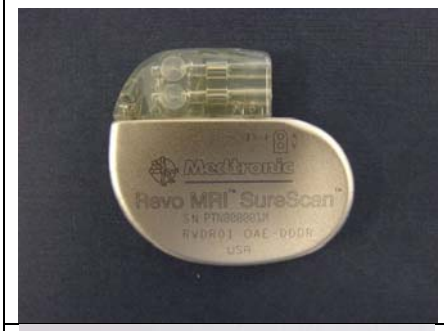
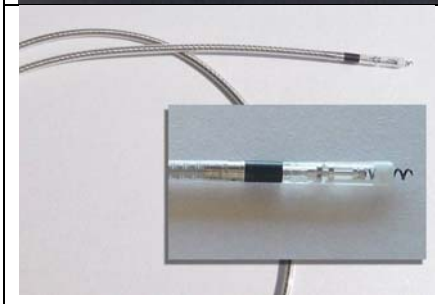
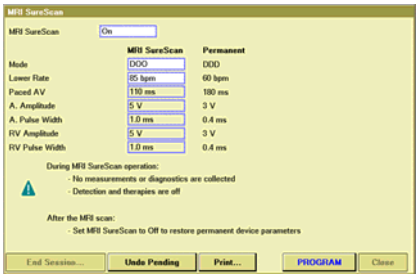
Appendix #	Title
Appendix 1	**Basic Pacing Information**
Appendix 2	**Basic MRI Information**
Appendix 3	**Pre-Clinical Evaluation**
Appendix 4	**Confirmatory Clinical Study**
Appendix 5	**List of Acronyms**
Appendix 6	**Summary of Literature**
Appendix 7	**Proposed Labeling**
Appendix 8	**Proposed Summary of Safety and Effectiveness Data**

2 Revo MRI System Description

2.1 Revo MRI SureScan Pacing System Description

The Revo MRI SureScan pacemaker and the CapSureFix MRI SureScan Model 5086MRI pacing leads comprise the implantable portion of the Revo MRI SureScan pacing system. Refer to Table 2-1 below for a summary of the system components.

Table 2-1. Summary of System Components

	The **Medtronic Revo MRI SureScan Model RVDR01** pacemaker is a multi-programmable, bipolar, implantable cardiac device that manages a patient's heart rate by providing rate responsive pacing. The Revo MRI pacemaker is designed for use in the MRI environment when used with the CapSureFix MRI 5086MRI pacing leads.
	The **Medtronic CapSureFix MRI 5086MRI** pacing lead is designed for use in the MRI environment when used in combination with the Revo MRI pacemaker. The CapSureFix MRI 5086MRI lead is a steroid-eluting, bipolar, implantable, screw-in, ventricular/atrial, transvenous lead designed for pacing and sensing applications. For this system, these leads are required in both the right atrium and ventricle. The leads are available in 45, 52, and 58 cm lengths.
	The **SW018 Revo MRI SureScan Application Software** (the SureScan software) allows the commercially available Medtronic CareLink Model 2090 programmer to be used with the Revo MRI pacemaker. The SureScan software contains the programmer application for the Revo MRI pacemaker, including the MRI SureScan feature, a mode of operation that allows pacemaker patients to undergo MRI scans while being safely supported with appropriate pacing therapy. The SureScan software is designed to: • Provide appropriate therapy during an MRI scan • Verify system integrity prior to an MRI scan • Mitigate MRI-induced interference • Provide ease of use • Provide a communication aid

2.2 Indications for Use

2.2.1 Revo MRI SureScan RVDR01 Indications for Use

The device is indicated for the following:

- Rate adaptive pacing in patients who may benefit from increased pacing rates concurrent with increases in activity.
- Accepted patient conditions warranting chronic cardiac pacing include:
    - Symptomatic paroxysmal or permanent second- or third-degree AV block
    - Symptomatic bilateral bundle branch block
    - Symptomatic paroxysmal or transient sinus node dysfunctions with or without associated AV conduction disorders
    - Bradycardia-tachycardia syndrome to prevent symptomatic bradycardia or some forms of symptomatic tachyarrhythmia

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

- Various degrees of AV block to maintain the atrial contribution to cardiac output
- VVI intolerance (for example, pacemaker syndrome) in the presence of persistent sinus rhythm

Antitachycardia pacing (ATP) is indicated for termination of atrial tachyarrhythmia in bradycardia patients with one or more of the above pacing indications.

Atrial rhythm management features such as Atrial Rate Stabilization (ARS), Atrial Preference Pacing (APP), and Post Mode Switch Overdrive Pacing (PMOP) are indicated for the suppression of atrial tachyarrhythmia in bradycardia patients with atrial septal lead placement and one or more of the above pacing indications.

The Revo MRI SureScan pacemaker has been designed for use in the MRI environment when used with the specified conditions of use.

2.2.2 5086MRI Indications for Use

The Medtronic CapSureFix MRI Model 5086MRI steroid-eluting, bipolar, implantable, screw-in, ventricular/atrial, transvenous lead is designed to be used with a pulse generator as part of a cardiac pacing system. The lead has been designed for use in the MRI environment, but only when used with a Medtronic SureScan IPG. The lead has application where implantable atrial or ventricular, single chamber or dual chamber pacing systems are indicated.

2.3 Comparison of Baseline Platform to Revo MRI

As stated in Section 1.2.2, the EnRhythm MRI SureScan pacemaker was based on the EnRhythm pacemaker that has state of the art features, while the CapSureFix MRI 5086MRI pacing lead

was based on highest sold Medtronic pacing lead with proven long term reliability and customer satisfaction (CapSureFix Novus 5076).

The changes to the lead were the modification of the inner conductor coil to reduce lead tip heating, and the addition of a radiopaque MRI symbol. The modified coil was designed which reduces the transfer of radiofrequency energy to the lead tip.

Extensive bench testing was successfully completed on the CapSureFix MRI 5086MRI, and includes coil and lead body stress fatigue and flex performance. The radiopaque MRI symbol, which is a non functional component and does not impact pacing or sensing, was tested for flex and fatigue. The coil components and full lead assembly successfully passed all design verification and qualification testing.

All remaining lead components used on the CapSureFix MRI 5086MRI lead are currently designed in the CapSureFix Novus 5076 lead, which has 99% long term survivability rates since its launch in 2000, with over 1 million implants. The bench testing and common lead component construction on the CapSureFix MRI 5086MRI lead provide confidence that its reliability performance will be equivalent to it predecessors.

The EnRhythm device platform has shown solid reliability performance since its launch in 2004 (99.9% device survival probability). Since several components were upgraded for the Revo MRI pacemaker, component and process qualifications were completed on each component to determine design robustness and repeatability. In addition, relevant device and system level testing was conducted with the new components. The results on the component and device level qualifications provide confidence that the Revo MRI pacemaker will have equivalent reliability performance as predecessor devices.

The changes to the device and lead to mitigate MRI hazards do not impact reliability as supported by bench testing results. The design characteristics and their impact on MRI environment hazards will be addressed in more detail in Section 4.2.

Table 2-2. Comparison of Device Design Characteristics

Design Characteristic	Baseline platform (EnRhythm)	Revo MRI
Pacing Functionality		
State of the art pacing capabilities (e.g., managed ventricular pacing & atrial therapies and diagnostics)	✓	✓
Firmware		
Extensible firmware architecture to allow incorporation of future firmware updates	✓	✓

MRI Environment Design Features		
Minimal ferromagnetic content to minimize forces due to the static magnetic field	✓	✓
Hall sensor to mitigate the effects of the magnetic fields	✓	✓
Optimized input circuitry to balance the risks of unintended cardiac stimulation and electromagnetic interference		✓
Circuit component upgrade to prevent the gradient-induced current from affecting the internal circuitry and pacing output		✓
Radiopaque MRI symbol for system identification		✓
MRI SureScan Application Software to facilitate safe scanning		✓
Labeling to describe conditions of use and guidelines for health care professionals		✓

Table 2-3. Comparison of Lead Design Characteristics

Design Characteristic	Baseline platform (CapSureFix Novus 5076)	CapSureFix MRI 5086MRI
Long-Term Reliability		
Long-term reliability	99% lead survival probability (2000 - 2009) >1 million implanted	2 years of implant experience with comparable performance
MRI Environment Design Features		
Minimal ferromagnetic content to minimize forces due to static magnetic field	✓	✓
Inner coil design for lead heating reduction		✓
Radiopaque MRI symbol for system identification		✓
Labeling to describe conditions of use and guidelines for health care professionals		✓

2.4 MRI SureScan Feature Description

The MRI SureScan feature was designed to:

- provide appropriate pacing therapy in the MRI environment,
- verify the integrity of the pacing system before allowing the user to initiate MRI SureScan operation,
- mitigate the risk due to hazardous effects of MRI-induced interference,
- provide ease of use, and
- provide a communication aid for the clinicians.

A summary of the major design elements of the MRI SureScan feature is provided in Table 2-4. For more detailed information on MRI SureScan feature operation, refer to the SureScan Technical Manual.

Table 2-4. Purpose of MRI SureScan Feature

Purpose	MRI SureScan Feature Design
Provide appropriate therapy during an MRI scan	• Allows the user to select appropriate therapies for the MRI environment, i.e., a pacing-only mode (AOO, VOO, or DOO) or a non pacing mode (ODO), based on whether the patient needs pacing support. • Sensed events are ignored to ensure the pacemaker does not falsely detect MRI-induced noise and deliver inappropriate therapy or withhold appropriate therapy.
Verify system integrity prior to an MRI scan	• Verifies the integrity of the pacing leads prior to initiating MRI SureScan operation. • Verifies the battery voltage prior to initiating MRI SureScan operation.
Mitigate MRI-induced interference	• Suspends magnet mode. • Suspends all diagnostic processing to eliminate the possibility of acquiring data that is corrupted by the MRI-induced interference.
Provide ease of use	• Simplifies programming steps. • Restores permanent parameters after an MRI scan.
Provide a communication aid	• Provides a pre-MRI scan checklist to help ensure safe scanning. • Allows the user to print out the MRI SureScan Checklist and the MRI SureScan Settings.

3 Conditions of Use

The conditions of use for the Revo MRI system, along with the rationale for each condition of use, are listed in Table 3-1 below.

Table 3-1. SureScan Conditions of Use

Condition of Use	Rationale	Clinical Impact
1. Cylindrical bore magnet, clinical MRI systems with a static magnetic field of 1.5 Tesla (T) must be used.	This Condition of Use was selected because hazards and risks vary by magnet strength, and the effects of scanners other than 1.5 T have not been evaluated.	**Minimal –** This condition has little or no clinical impact due to the large percentage of 1.5 T scanners present in clinical facilities. (In 2007, 1.5 T units accounted for 68% of clinical scanner configurations in all settings and 83% of clinical scanner configurations in hospitals.)
2. Gradient systems with maximum gradient slew rate performance per axis of ≤ 200 T/m/s must be used.	This Condition of Use was selected because the maximum dB/dt any particular gradient system could expose the patient to is generally unknown by MR clinical professionals since manufacturers do not publicize dB/dt performance. As a result, product labeling that simply restricts patient gradient field dB/dt exposure to 100 T/s would be ineffective. Product labeling restricting the scanning of patients to scanners with a gradient slew rate (T/m/s) specification of 200 T/m/s was selected as a practical means of limiting dB/dt exposure to 100 T/s or less.	**Minimal –** This condition has little or no clinical impact due to the fact that 100 T/s or 200 T/m/s is the worst case gradient field strength among all clinical 1.5 T MRI scanners.
3. Whole body averaged specific absorption rate (SAR) as reported by the MRI equipment must be ≤ 2.0 W/kg; head SAR as reported by the MRI equipment must be < 3.2 W/kg.	This Condition of Use was selected because the 2.0/3.2 W/kg limits conform to SAR limitations for normal operating mode imposed on MRI equipment manufacturers defined in IEC 60601-2-33.	**Minimal –** This condition has little or no clinical impact since all 1.5 T diagnostic scans can be completed within these SAR limits without significant impact to image quality.
4. Patients and their implanted systems must be screened to meet the following requirements.	This Condition of Use was selected because screening is essential for ensuring the safety of all MRI patients.	**Minimal –** This condition has little or no clinical impact due to the fact that the radiology community recognizes patient screening procedures as one of the most critical components of a program that guards the safety of all those preparing to undergo magnetic resonance (MR) procedures or to enter the MR environment.[18,9]
a. No previously implanted (active or abandoned) medical devices, leads, lead extenders, or lead	This Condition of Use is an added safety precaution to ensure that there are no MRI-interactions due to multiple implanted devices (active or abandoned). Lead extenders or adaptors may change	**Minimal –** The Condition of Use regarding active medical devices has little or no clinical impact due to the fact that these patients are currently contraindicated

Condition of Use	Rationale	Clinical Impact
adaptors.	important parameters that are designed to prevent lead tip heating due to RF energy and unintended cardiac capture due to the gradient magnetic fields. Medtronic has characterized the performance of a single Revo MRI IPG and 5086MRI leads that are fully functional and electrically intact (one in the atrium and one in the ventricle). Revo MRI performance in the presence of other devices has not been studied.	by MRI manufacturers, and because it is more restrictive than current MRI screening guidelines which allow a case-by-case MR scanning determination if a patient has active implanted medical devices. The Condition of Use regarding abandoned medical devices is consistent with current MRI screening guidelines which state that, "*Pacemaker and/or ICD leads may also present a hazard in the absence of any implant connected to them*."
b. No broken or intermittent leads.	This Condition of Use is an added safety measure to ensure that no MRI interactions arise due to a broken/intermittent lead. Medtronic has characterized the performance of the 5086MRI leads that are fully functional and electrically intact. Lead fractures or other damage to the leads may cause changes in the electrical properties of the Revo MRI SureScan pacing system that could make the system unsafe for an MRI scan.	**Minimal –** This condition has little or no clinical impact since the SureScan feature has checks in place to ensure the patient has impedance values within an appropriate range before SureScan feature can be initiated.
c. A SureScan pacing system that has been implanted for a minimum of 6 weeks.	This Condition of Use was selected to minimize the possibility of the lead dislodging during positioning of the patient in the MRI scanner, and to allow the lead to stabilize electrically. After lead implantation, arm motion is initially restricted to prevent lead dislodgement. It takes approximately 4-6 weeks for the fibrous encapsulation to surround and anchor the lead, which minimizes the possibility of lead dislodgement due to patient positioning during the MRI scan. Also, it takes about six weeks for the lead thresholds to stabilize and allow the device to be programmed to chronic settings.[30, 31, 32]	**Minimal –** This condition has little or no clinical impact since six weeks is recognized in the medical community as an adequate maturation period.[18,9]
d. A SureScan pacing system implanted in the left or right pectoral region.	This Condition of Use was selected because the potential hazards arising from abdominal implants were not evaluated for Revo MRI. The increased variability in lead path for an abdominal implant results in more uncertainty in lead electrode heating and unintended cardiac stimulation. Therefore, these types of implants are contraindicated.	**Minimal –** This condition has little or no clinical impact since the 5086MRI lead is available in 45, 52 and 58 cm lengths. Use of these lead lengths for an abdominal implant is not practical in most cases and therefore is not a clinical issue.
e. Pacing capture threshold values of $\leq$ 2.0 V at a pulse width of 0.4 ms.	This Condition of Use was selected as a conservative measure to allow for an adequate pacing safety margin. Pacing capture thresholds are typically much less than 2.0 V, and if the pacing capture threshold is greater than 2.0 V, it may be an indication of a	**Minimal –** This condition has little or no clinical impact since typical pacing capture threshold values are less than or equal to 2.0 V.

Condition of Use	Rationale	Clinical Impact
	potential issue with the lead.	
f. No diaphragmatic stimulation at a pacing output of 5.0 V and at a pulse width of 1.0 ms in patients whose device will be programmed to an asynchronous mode when MRI SureScan is on.	This Condition of Use was selected because diaphragmatic stimulation is uncomfortable for the patient and is another possible manifestation of lead malposition. Additionally, this movement can negatively impact the quality of MRI.	**Minimal –** This condition has little or no clinical impact since the EnRhythm MRI SureScan Pacing System clinical study showed that out of 244 patients in the MRI group, 2 did have diaphragmatic stimulation.
g. A lead impedance value of ≥ 200 Ω or ≤ 1500 Ω.	This Condition of Use was selected because if the measured lead impedance falls outside of the specified range for either of the leads then the patient may be subjected to intermittent or loss of capture. This Condition of Use was selected because the effects of MR scans on a lead with a lead impedance value of < 200 Ω or > 1500 Ω have not been evaluated. Therefore, these patients are contraindicated.	**Minimal –** This condition has little or no clinical impact since the EnRhythm MRI SureScan Pacing System clinical study showed that out of 244 patients in the MRI group, all patients had impedance values of greater than 200 ohms or less than 1500 ohms. This is a nominal lead impedance range. Prior to entering the SureScan mode, the Revo MRI SureScan system requires in-range lead impedance measurements to confirm the electrical integrity of implanted leads. A SW interlock message appears if one or both of the most recent lead impedance measurements is out of range and the user attempts to program MRI 'On'. The MRI SureScan feature cannot be programmed 'On' if either of the lead impedance measurements falls below 200 Ohms or above 1500 Ohms.
5. The patient must be positioned within the bore such that the isocenter (center of the MRI bore) is superior to the C1 vertebra or inferior to the T12 vertebra.	This Condition of Use was selected as a conservative approach for the first generation MR Conditional IPG. There is potential for an MR scan of the thoracic region to increase the amount of RF coupling to the implanted lead, thereby increasing the amount of lead electrode heating.	**Moderate –** This Condition of Use may have some impact in a clinical scenario in order to identify this region. Physicians may need to reference the technical manual to address any questions. The EnRhythm MRI Clinical Study did not specifically collect data on how easily this Condition of Use can be followed. Additionally, scans of this region of the body account for approximately 10-20% of all scan procedures. Therefore, this Condition of Use may have some impact.
6. Proper patient monitoring must be provided during the MRI procedure.	This Condition of Use was selected because these patients are cardiac patients and because there is a rare potential for the	**Minimal –** Current MR scanning guidelines as well as the MR safety community recognize the importance of

Condition of Use	Rationale	Clinical Impact
	induction of arrhythmia due to the interaction between the MRI fields and the implanted system. If an arrhythmia is detected, there may be the need to defibrillate back into normal rhythm.	patient monitoring for ICD/IPG patients as well as those patient populations with underlying health problems or patients who are sedated, unconscious or anesthetized.[18, 33] If an asynchronous MRI SureScan pacing feature is selected, be aware that some patients may be susceptible to cardiac arrhythmia induced by competitive pacing. For these patients, it is important to first select an MRI SureScan pacing rate that avoids competitive pacing and then minimize the duration of the asynchronous pacing operation. There is relatively little clinical impact since there are publications available regarding asynchronous pacing causing arrhythmias. This is not incongruent with other medical procedures (placing a magnet in surgery) and cardiologists seem well aware of the competitive pacing risk. Additionally, Medtronic representatives will be trained and fully able to answer any questions, if they arise.
a. This includes continuous monitoring of the patient's hemodynamic function. Since the MR environment may interfere with the patient monitoring system, it is recommended that more than one of the following monitoring systems be used: • electrocardiography • pulse oximetry • noninvasive blood pressure measurements Keep an external defibrillator available during the MRI scan. **Note:** If the patient's hemodynamic function is compromised during the MRI scan, discontinue the MRI scan	See above.	See above.

Condition of Use	Rationale	Clinical Impact
and take the proper measures to restore the patient's hemodynamic function.		
7. There are no restrictions on the placement of any receive-only coils.	This Condition of Use was selected because receive-only coils do not impact the performance of the Revo MRI SureScan System since they do not radiate RF or gradient frequency energy.	**Minimal –** This Condition of Use will have little impact in a clinical setting since receive-only coils do not radiate RF or gradient fields.
8. There are no restrictions on the use of local transmit or local transmit/receive coils for imaging of the head or the extremities.	This Condition of Use was selected because the most common forms of local transmit coils are either head coils for neurological imaging or extremity coils for imaging of joints such as the knee or ankle. These local transmit coils will operate at much lower power levels than the whole body coil and the radiated field of a local transmit coil will not radiate much past the volume contained by the coil. In addition, these specific local transmit coils would not be used within the C1-T12 thoracic region.	**Minimal –** This Condition of Use will have little impact in a clinical setting since the radiated field of these kinds of local transmit coils will not extend far beyond the coil. In addition, current technology trends show a shift towards the use of multiple receive coils for improved image quality and away from the use of local transmit coils.
9. The implanted system must consist solely of a Medtronic Revo MRI SureScan Model RVDR01 device and 2 CapSureFix MRI SureScan Model 5086MRI leads.	This Condition of Use was selected because no other device/lead combination was tested nor is another combination within the scope of this submission. Therefore, patient safety may be compromised if other devices are present.	**Minimal –** This Condition of Use has relatively little clinical impact since the tools described in the Care Pathway section (also referred to as clinical implementation) support the ease of identifying and verifying a complete system (SureScan checklist, patient ID card, awareness of the system, etc.)

4 Safety and Effectiveness

4.1 Introduction

This section summarizes the pre-clinical and clinical evaluations for demonstrating safety and effectiveness of the Revo MRI SureScan pacing system when used according to the conditions of use. The pre-clinical testing is described in Section 4.2, and the confirmatory clinical study is described in Section 4.3. See Appendix 3 and Appendix 4 for a more detailed discussion of the pre-clinical and clinical studies, respectively.

4.2 Pre-Clinical Evaluation

This section provides a summary of the pre-clinical testing for the MRI-environment hazards. Requirements for the MRI-induced lead heating and unintended stimulation hazards could not be defined due to the complex interactions between the associated fields and pacemaker system. In addition, no standards or test requirements exist that define the evaluation methodology. Therefore, probabilistic analyses were performed to address the risk due to these two hazards. On the other hand, the hazards of case heating, force, torque, vibration and device interactions have requirements that were defined based on relevant literature and standard test methods (e.g., applicable ASTM standards for passive devices were used or modified).

Discussion of these hazards is organized as follows:

- Lead tip heating: Section 4.2.1
- Unintended cardiac stimulation: Section 4.2.2
- Device interactions: Section 4.2.3
- Case heating: Section 4.2.4
- Force and Torque: Section 4.2.5
- Vibration: Section 4.2.6
- Effects of multiple MRI scans: Section 4.2.7

The design changes implemented in the Revo MRI SureScan pacing system are discussed as appropriate for specific hazards. In addition, all design changes to the Revo MRI SureScan pacemaker and CapSureFix MRI 5086MRI lead are summarized in Section 4.2.8. Finally, standard testing and qualification are summarized in Section 4.2.9.

See Appendix 3 for a more detailed discussion of the pre-clinical test methods and results.

4.2.1 MRI-Induced Lead Heating

Mechanism

The conductive pacing lead acts as an antenna, picking up radiofrequency energy that is radiated by the body coil of the MRI scanner. A portion of this energy is dissipated as heat in the cardiac tissue near the tip electrode, which may result in thermal damage to the tissue, changes in pacing capture threshold, and, in extreme cases, loss of pacing therapy.

Design change

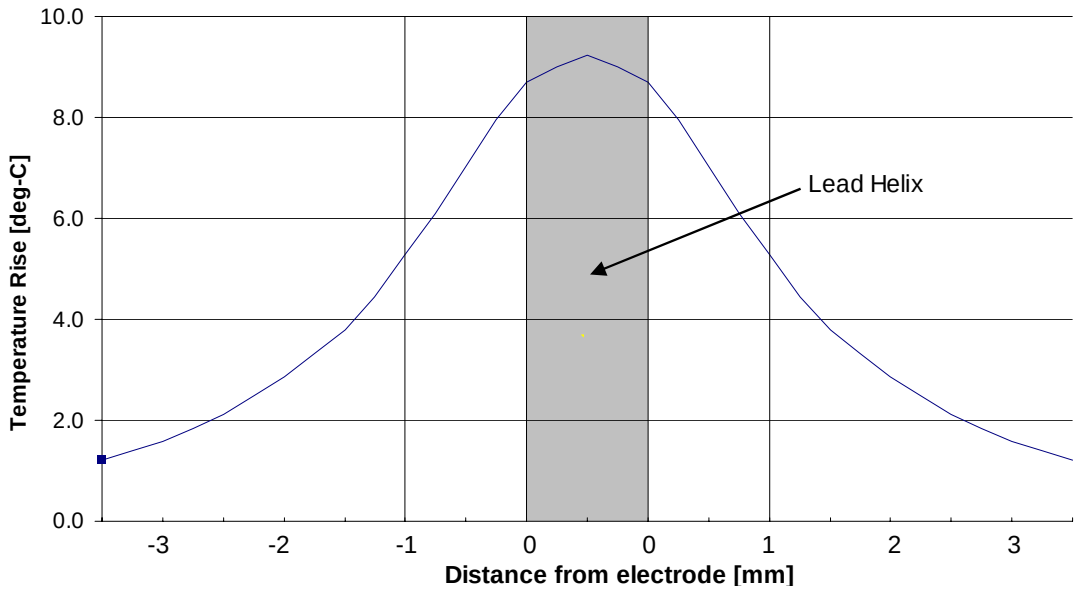
As stated in Section 1.2.2, the EnRhythm MRI SureScan pacemaker was based on the EnRhythm pacemaker that has state of the art features, while the CapSureFix MRI 5086MRI pacing lead was based on highest sold Medtronic pacing lead with proven long term reliability and customer satisfaction.

In Vitro Temperature Profile

In vitro measurements were performed to characterize the spatial temperature distribution in the vicinity of the lead tip helix. The test results showed that the measured temperature is strongly dependant on the exact location of the temperature probe with respect to the lead tip electrode (see Figure 4-1). t This in vitro data shows the lead tip heating is localized to the immediate vicinity of the lead helix and that the actual temperature is highly dependant on location relative to the helix.

Tip-Tissue Interface

As part of the body's natural inflammatory response, a fibrotic capsule (collagenous/fibrous scar tissue) forms around the lead tip electrode within several weeks after lead implantation. The The location of the viable cardiac tissue with respect to the helix determines the pacing capture threshold.



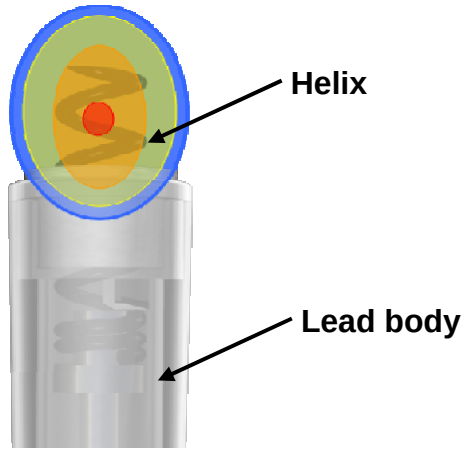


Figure 4-1. (top) In vitro CapSureFix MRI 5086MRI lead tip helix temperature profile as a function of distance. The dark gray shaded region shows the width of the lead helix. (bottom) A two-dimensional illustration of the temperature profile around a CapSureFix MRI 5086MRI lead tip. The red circle in the center represents the location of the highest measured temperature rise. The colored ellipses represent zones of decreasing heating (red: highest temperature; blue: lowest temperature).

Histological Evaluation of Thermal Tissue Damage

Medtronic CRDM performed histological evaluations as part of several studies to determine the correlation between tissue change due to lead tip heating and changes in pacing parameters. The conclusions from the histological analysis were:

Lead Heating Assessment

Since histopathology is not a reliable indicator of RF-induced cardiac tissue damage, temperature is highly dependant on the measurement position and impractical to measure in vivo, and pacing capture threshold is the most clinically relevant pacing parameter, Medtronic CRDM used pacing capture threshold to evaluate the patient risks associated with RF-induced lead heating.

No standard test methods or requirements exist for evaluating the safety impact of lead tip heating; therefore, Medtronic CRDM developed the necessary methodology. This methodology is consistent with that being proposed by the ISO/IEC Joint Working Group.

Historically, simple body phantoms (such as the ASTM phantom[vi]) have been used to evaluate lead tip heating. However, human bodies are highly diverse, irregular, and electrically heterogeneous, while a simple body phantom is geometrically and electrically homogeneous. This difference will result in different levels of RF-induced temperature rise near the lead electrodes. Therefore, phantom testing alone is insufficient to make a lead heating safety assessment for a broad patient population.

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[v]

[v] A rectangular phantom filled with a homogeneous medium, as described in ASTM F2182 - 02a "Standard Test Method for Measurement of Radio Frequency Induced Heating Near Passive Implants During Magnetic Resonance Imaging."

The amount of RF energy coupled to the leads depends on a number of parameters, and therefore is highly variable. Accordingly, the tissue heating near the lead electrode is also highly variable. For example, a lead of a given length and design may experience different levels of heating in different human bodies depending on the lead routing (lead path) and patient anatomy. Due to the large number of independent variables that affect lead tip heating, Medtronic CRDM chose to conduct a probabilistic (statistical) analysis to evaluate the MRI-induced change in pacing capture threshold. This modeling strategy allowed for analysis of numerous variables in order to evaluate lead heating effects at the extremes of the MRI environment and patient parameters. In addition, this analysis allowed the MRI-induced changes in pacing capture threshold to be separated from other sources of pacing capture threshold variability, which is not possible when evaluating pacing capture threshold changes in a clinical study.

To thoroughly assess the risk associated with lead heating, Medtronic CRDM developed a robust modeling framework using well-established electromagnetic methods. The simulation framework includes an electromagnetic model of several MRI scanner RF body coils, 22 human body models that represent the 2nd - 97th percentile of the adult population, and CapSureFix MRI 5086MRI leads. The simulations of the RF body coils and human body models were performed using a widely-used off-the-shelf electromagnetic simulation package; the electromagnetic lead model was developed in-house. The modeling approach allowed Medtronic CRDM to simulate a large number of combinations of human body models, positioned at different locations in the MRI scanner bore, for several MRI RF coil designs. The analyses were performed for thousands of combinations corresponding to clinically-relevant scan scenarios.

The probability for pacing capture threshold change was obtained by combining (see Figure 4-2):

- the prediction for power dissipated at the tip-tissue interface obtained via the above simulations, with
- a prediction for pacing capture threshold change as a function of the same dissipated power obtained via an in vivo study.

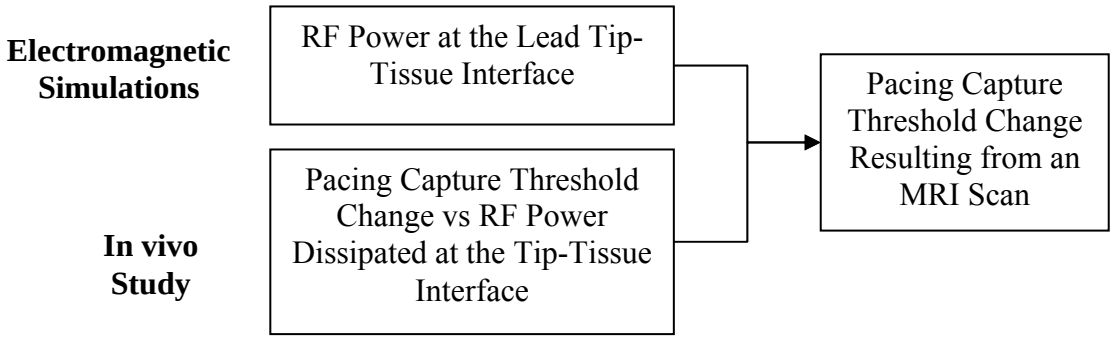

Figure 4-2. Strategy for evaluating the effect of MRI-induced lead tip heating.

The results of the final analysis predict that under the maximum proposed labeling conditions, the probability of a 0.5 V MRI-induced change in pacing capture threshold is approximately 1/71,000, and the probability of a 1.0 V MRI-induced change in pacing capture threshold is approximately 1/2,900,000. It is important to note that these results are for MRI-induced pacing capture threshold changes only, and do not take into account any other sources of pacing capture threshold variability.

A change in pacing capture threshold greater than or equal to 1.0 V was chosen as a clinically significant change in pacing capture threshold because changes less than 1.0 V may be related to normal variation in cardiac electrophysiology.[34,35] The lead tip heating analysis shows that CapSureFix MRI 5086MRI lead tip heating will not result in clinically significant changes in pacing performance, and that there is minimal risk to the patient from the lead tip heating hazard. The maximum pacing output of the Revo MRI SureScan pacemaker is 6.0 V. Therefore, if an MRI-induced change in PCT of 1.0 V were to occur in a patient with an initial PCT of 2.0 V (which is a very low probability), the system would still be capable of delivering a pacing stimulus with a voltage that is two times higher than the pacing capture threshold (a standard pacing safety margin).

It should be noted that this analysis includes a number of conservative factors. The most significant factor was that all simulations were performed at the maximum allowed 2 W/kg whole body SAR (or 3.2 W/kg head SAR). In clinical practice, the majority of scans are performed at SAR levels below this maximum limit. The impact of this conservative assumption is discussed in more detail in Appendix 3.

MRI-Induced In Vivo Temperature Rise

While the primary analysis of patient safety with respect to the MRI-induced lead tip heating hazard was performed using dissipated power at the tip-tissue interface and the resulting change in pacing capture threshold, the simulation and in vitro temperature measurement results can also be used to estimate tissue temperatures in the vicinity of the lead tip.

Methodology Validation

The lead heating modeling and study methodology has been validated as follows:

- The human body models used by Medtronic CRDM have been used by researchers in various fields (e.g. cell phone industry, MRI manufacturers, AIMDs with telemetry) for many years. Electrical parameters of tissues used in these models are also widely accepted in the field.
- The computer model (used to compute the power dissipated in human bodies) was validated by conducting simulations of a phantom (tank filled with a homogeneous conductive solution) and leads for a wide range of varying conditions. Identical

conditions were replicated in an experimental phantom, and measurements corresponding to the same cases were performed. The results of simulations and measurements (1538 cases) show excellent agreement (correlation coefficient = 0.98) between the measured and simulated values (see Appendix 3 for details).

- Influence of the heating at the tip-tissue interface was analyzed via a [redacted] by applying RF energy directly to the leads. [redacted] in many studies of pacing and defibrillation as good predictors of performance in humans. They are accepted by the FDA for pre-clinical pacing lead studies.
- The modeling predicts the pacing capture threshold change only due to MRI exposure, and does not take into account any other sources of pacing capture threshold variability. As will be shown in the clinical study results (Section 4.3), there is no statistical difference in the pacing capture threshold changes between the MRI and control groups. This is consistent with the extremely small probabilities for MRI-induced pacing capture threshold change predicted by the modeling.

MRI-Induced Lead Heating Conclusion

The Revo MRI SureScan pacing system modeling and in vivo evaluation show that the probability of a clinically significant change in pacing capture threshold is low, not a risk to pacing performance, and does not lead to patient harm. The testing and modeling demonstrate safety and effectiveness in relation to the lead heating hazard of the Revo MRI SureScan pacing system.

4.2.2 MRI-Induced Unintended Cardiac Stimulation

The gradient and radiofrequency (RF) fields produced by MRI scanners will induce voltages in pacemaker leads that will be applied to the pacing lead electrodes. If these MRI-induced voltage pulses are large enough, they may directly stimulate the heart. The clinical manifestations[37] and possible interventions[38] of unintended cardiac stimulation are as follows:

- Single or intermittent stimulation of the atrium or ventricle, which may result in symptomatic extra contractions, but does not require immediate intervention.
- Intermittent or continuous low rate (much lower than unperturbed heart rate) stimulation of the atrium or ventricle, which may result in symptomatic extra contractions, but does not require immediate intervention.
- Multiple or continuous high rate (much higher than unperturbed heart rate) stimulation of the atrium or ventricle may result in cardiac output reduction (hemodynamic collapse) and a drop in systolic blood pressure. In this situation, cessation of the stimulus by terminating the MRI scan will restore normal cardiac function.
- In rare cases, the extra stimuli could introduce sustained (persisting after scan is stopped) ventricular tachycardia, which may require cardiopulmonary resuscitation, including application of external defibrillators.

Medtronic CRDM assessed the risk due to unintended cardiac stimulation from both sources – radiofrequency and gradient fields. No standard test methods or requirements exist for evaluating unintended cardiac stimulation; therefore, Medtronic CRDM developed the necessary methodology.

Gradient-induced unintended cardiac stimulation

Mechanism

The time-varying gradient magnetic fields will induce a time-varying voltage along the pacing leads. These voltage pulses will stimulate adjacent cardiac tissue if the amplitude and pulse width are sufficiently large.

Design change

The characteristics of the pacemaker lead interface (circuitry connected to the leads) play a critical role on the pulse width of the gradient-induced voltage pulse. The circuitry of the Revo MRI pacemaker was modified to reduce the width of the gradient-induced voltage pulse, mitigating the risk of gradient-induced unintended cardiac stimulation. This design change has no impact on the long-term reliability of the Revo MRI pacemaker.

Gradient-induced unintended cardiac stimulation analysis

The voltage across the cardiac tissue due to the gradient magnetic field is a function of many independent variables, such as the patient's position within the bore, scan settings, performance of the scanner, implant location and patient size. The strategy for evaluating the MRI-induced unintended cardiac stimulation was to conduct a probabilistic analysis due to the large number of variables that affect stimulation. The probability for stimulation was computed by combining:

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The analysis shows that approximately 1 in 29,000 patients will be susceptible to a gradient-induced unintended cardiac stimulation event during an MRI session. An unintended cardiac stimulation event can manifest as described above. A number of risk factors must add up in order to reach a condition where unintended cardiac stimulation might occur. In the above analysis, several factors were set conservatively, resulting in a higher predicted probability of stimulation than expected in clinical practice. Refer to Appendix 3 for further details.

The results of this evaluation show that the probability of gradient-induced unintended cardiac stimulation for the Revo MRI pacing system is low.

Radiofrequency-induced unintended cardiac stimulation

Mechanism

The high frequency voltage pulses from the radiofrequency fields in MRI scanners will not directly cause electrical stimulation of cardiac tissue. However, there is the potential for the pacemaker circuitry connected to pacing leads to rectify the radiofrequency pulses (i.e., convert the high frequency voltage pulses into low frequency voltage pulses). The rectified pulses are similar in duration to pacing pulses, and may stimulate the cardiac tissue if their amplitude is sufficiently large.

Radiofrequency-induced unintended cardiac stimulation analysis

The minimum stimulation threshold for rectified pulses was determine
Analysis of the results showed that the minimum stimulation threshold

Since the maximum measured RF rectification voltage was approximately 25x below the conservative requirement, the test results indicate that the risk of radiofrequency-induced unintended cardiac stimulation is negligible. Refer Appendix 3 for further details.

Unintended Cardiac Stimulation Conclusion

The Revo MRI SureScan pacing system pre-clinical evaluation confirmed that the patient safety risk due to UCS caused by voltage induced on the lead by MRI RF and gradient fields is low and has been mitigated to an acceptable level.

vii

The hazards of device interactions, case heating, force, torque, and vibration are summarized in tabular format in the following sections. Refer to Appendix 3 for further details.

4.2.3 MRI-Induced Device Interactions

Table 4-1 briefly summarizes the testing methodology and results for investigating safety of the Revo MRI SureScan pacing system with respect to the device interactions hazard.

Table 4-1. MRI Induced Device Interactions

MRI-Induced Device Interactions	
Field interaction	Static, gradient, and radiofrequency
Mechanism and source of hazard	The gradient, radiofrequency, and static fields present in the MRI environment may adversely impact the electrical operation of the pacemaker system if its operation is not protected from the effects of those fields.
Clinical impact	Loss of pacing therapy and syncope.
Design change	A circuit component was changed to prevent the gradient-induced current from affecting the internal power supplies and pacing output. This design change has no impact on the long-term reliability of the Revo MRI pacemaker.
Evaluation method	Medtronic CRDM developed bench test systems to accurately deliver gradient or radiofrequency energy at higher levels than could be achieved in an MRI scanner, and with accurate control over the exposure level. In addition, tests in clinical MRI scanners were also performed to identify any combined field interactions, and to evaluate the effects of the static field on the pacemaker. Critical pacing parameters (e.g., pacing pulse amplitude, pulse width, and pacing rate) were monitored during MRI scans to ensure that the pacemaker delivered the programmed therapy to the patient. Non-critical parameters (e.g., activity sensor and telemetry) were evaluated before and after each test to ensure that the pacemaker functions within specification after MRI exposure, and that MRI exposure does not substantially impact the reliability or longevity of the pacemaker. Testing was completed for more than 1700 device-hours, at worst-case exposure settings and positions.

MRI-Induced Device Interactions	
Requirement	During and after MRI exposure: • No device resets occur. • No damage occurs to the pacemaker or components. • The pacemaker delivers appropriate therapy during an MRI scan. • Sub-systems necessary to support proper operation during an MRI scan are within specification. • The pacemaker functions within specification after exposure to an MRI scan. • MRI exposure does not substantially impact the reliability or longevity of the pacemaker.
Results	No device resets were observed during testing. Testing demonstrated that the reliability of the Revo MRI pacing functionality (pulse amplitude, pulse width, and pacing rate) during and after an MRI scan met the required specifications. All tested subsystems (e.g., clock and oscillator frequencies, output capacitance) were within specification.
Conclusion	The Revo MRI SureScan Pacemaker in vitro evaluation confirmed that the system meets the requirements for the device interactions hazard. Thorough analysis and testing has demonstrated that the Revo MRI SureScan pacing system will deliver appropriate therapy during an MRI and that MRI exposure does not compromise subsequent operation, pacemaker reliability, or longevity. This demonstrates safety and effectiveness in relation to the device interactions hazard of the Revo MRI SureScan pacing system.

4.2.4 MRI-Induced Case Heating

Table 4-2 briefly summarizes the testing methodology and results for investigating safety of the Revo MRI SureScan pacing system with respect to the case heating hazard.

Table 4-2. MRI-Induced Case Heating

MRI-Induced Case Heating	
Field interaction	Gradient and radiofrequency (RF)
Mechanism and source of hazard	The time-varying gradient and RF magnetic fields will induce circulating electrical currents on the conductive surface of the pacemaker case, which are dissipated in the form of heat.
Clinical impact	Patient discomfort or damage to tissue in contact with the pacemaker case. The extent of the hazard depends on the temperature increase and the duration of the increase, i.e., the time-temperature profile of the heating.
Design change	The design of the previous EnRhythm pacemaker met the requirements for case heating. No further design changes were required.
Evaluation method	Case heating was evaluated in vitro at the maximum labeling conditions, and at worst-case scan conditions.
Requirement	
Results	
Conclusion	The Revo MRI SureScan Pacemaker in vitro evaluation confirmed that the pacemaker meets the requirements for case heating. The testing confirmed that even at worst-case test conditions, there is minimal heating of the pacemaker case, resulting in no tissue damage. This demonstrates safety in relation to the case heating hazard of the Revo MRI SureScan Pacemaker.

4.2.5 MRI-Induced Force and Torque

Table 4-3 briefly summarizes the testing methodology and results for investigating safety of the Revo MRI SureScan pacing system with respect to the force and torque hazards.

Table 4-3. MRI-Induced Force and Torque

MRI-Induced Force and Torque		
Field interaction	Static field	
Mechanism and source of hazard	The static magnetic field may translate or rotate the pacemaker and leads if ferromagnetic material is present in the pacemaker or leads.	
Clinical impact	Tugging sensation, pacemaker dislodgement, or tissue injury at the implant location. Since all of the ferromagnetic material of the CapSureFix MRI 5086MRI lead is located in the connector, and there is no ferromagnetic material in the lead body or at the lead tip, there is no risk of lead dislodgement.	
Design change	The design of the previous EnRhythm pacemaker met the requirements for force and torque. No further design changes were required.	
Evaluation method	Force and torque were measured at worst-case conditions for: • pacemakers alone, • pacemakers with leads attached, • leads alone.	
	Force: Test methodology based on ASTM F2052-02, "Standard Test Method For Measurement of Magnetically Induced Displacement Force On Medical Devices in the Magnetic Resonance Environment".[41]	Torque: Test methodology based on ASTM F2213-02, "Standard Test Method for Measurement of Magnetically Induced Torque on Passive Implants in the Magnetic Resonance Environment".[42]
Requirement	The requirements were developed by Medtronic CRDM based on the forces or torques applied to implanted pacemaker systems during daily activities (e.g., sitting, sneezing, etc.), and provide a significant margin compared to other environments to which the pacemaker is frequently exposed.	
Results	Force: The largest measured force was approximately 25% of the requirement.	Torque: The largest measured torque was approximately 65% of the requirement.
Conclusion	The in vitro test confirmed that the Revo MRI SureScan Pacemaker and CapSureFix MRI 5086MRI leads meet the requirements for magnetically-induced force and torque. This demonstrates safety in relation to the magnetically-induced force and torque hazards of the Revo MRI SureScan pacing system.	

4.2.6 MRI-Induced Vibration

Table 4-4 briefly summarizes the testing methodology and results for investigating safety of the Revo MRI SureScan pacing system with respect to the vibration hazard.

Table 4-4. MRI-Induced Vibration

MRI-Induced Vibration	
Field interaction	Static and gradient
Mechanism and source of hazard	Time-varying gradient magnetic field induces time-varying currents in the conductive surfaces of pacemaker components. When these currents interact with the static magnet field, a time-varying force is applied to the component, causing the component to vibrate.
Clinical impact	MRI-induced vibration can affect internal pacemaker components and may result in pacemaker failure, leading to loss of pacing therapy and syncope.
Design change	The design of the previous EnRhythm pacemaker met the requirements for vibration. No further design changes were required.
Evaluation method	Medtronic CRDM developed a vibration test method using an MRI scanner to vibrate the components in the pacemaker just as they would vibrate during a scan, at and above the proposed labeling conditions. Testing was conducted in vitro for a total of 1475 device-hours at clinically-relevant and worst-case scan conditions.[viii]
Requirement	Upon exposure to the MRI environment, pacemaker operations shall be within the system specifications, all components shall remain intact, and no device resets or replacement indicators shall be observed.
Results	The test results showed no missing pacing pulses during the testing, as well as proper operation following testing. No device resets or battery replacement indications were observed.
Conclusion	The in vitro evaluation confirmed that the Revo MRI SureScan Pacemaker meets requirements for vibration. This demonstrates safety and effectiveness in relation to the vibration hazard of the Revo MRI SureScan pacing system.

[viii] Note that a pacemaker subjected to a single 30-minute MRI scan is equivalent to 0.5 device-hours.

4.2.7 Effects of Multiple MRI scans

When considering the potential cumulative effects of multiple MRI scans, Medtronic CRDM considered each hazard independently. Based on a technical understanding of the mechanisms for the hazards, only vibration and lead tip heating were found to be dependent on the number of performed scans.

Vibration

As described above in Section 4.2.6, vibration testing was conducted at vibration stress levels above what a device would reasonably be exposed to during its lifetime. Since testing met the established requirements, there is no patient safety risk associated with multiple MRI scans due to the vibration hazard.

Lead Tip Heating

Medtronic CRDM conducted a [redacted] to evaluate the effect of multiple MRI scans on change in pacing capture threshold. [redacted]

Conclusion

In conclusion, cumulative exposure testing for vibration met the established requirements, demonstrating no risk due to multiple scans. In addition, cumulative exposure testing for lead heating in [redacted] demonstrated that there is no cumulative effect due to repeated exposure.

ix [redacted]

4.2.8 Revo MRI SureScan Pacing System Design Features

In addition to the existing design features of the EnRhythm pacemaker and CapSureFix Novus 5076 lead, additional MRI-environment design features were incorporated in the Revo MRI SureScan pacemaker and the CapSureFix MRI SureScan 5086MRI pacing lead to allow for safe use in the MRI environment. These design features were described in the previous sections, and are summarized in

Table 4-5 and Table 4-6, respectively.

Table 4-5. Revo MRI SureScan Pacemaker MRI Environment Design Features

Design Feature	Rationale
Mechanical	
Radiopaque MRI Symbol	A radiopaque MRI symbol is unique to distinguish the MR Conditional system. This symbol assists the user in the identification of the MR Conditional system.
Electrical	
Optimized Input Capacitor	The input capacitance was optimized to minimize MRI-induced unintended cardiac stimulation. This capacitance: 1) minimizes the pulsed charge passing through the pacemaker and lead electrodes as a result of the induced voltage caused by the gradient magnetic field without degrading electromagnetic immunity performance of the device, and 2) decreases the chances of stimulating the heart during MRI.
Circuit Component Upgrade on Hybrid	It was found that the gradient field-induced current affected pacemaker circuitry, which affected pacing output. A circuit component upgrade was incorporated to prevent the gradient-induced current from affecting the internal circuitry and pacing output.
Firmware /Software	
MRI SureScan	Firmware: • In the MRI environment, the gradient magnetic field is the primary source of electrical noise, which may cause the pacemaker to inhibit (i.e., failure to deliver pacing therapies) or deliver inappropriate therapies. To mitigate these risks, the MRI SureScan feature was added to ensure reliable pacing operation during MRI. Software: • Added MRI SureScan feature interface to the programmer software.
Labeling	
Labeling	Developed labeling to describe appropriate information such as conditions of use and guidelines for health care professionals.

Table 4-6. CapSureFix MRI 5086MRI Lead MRI Environment Design Features

Design Feature	Rationale
Inner Coil Design/Diameter	
Radiopaque MRI Symbol	The radiopaque MRI symbol is visually recognizable under X-ray, indicating that it is a lead designed to be used in the MRI environment. The CapSureFix MRI 5086MRI connector sleeve is larger to accommodate the radiopaque MRI symbol.

4.2.9 Standard Testing and Qualification

Apart from the unique MRI testing, all required standard testing was conducted for the Revo MRI SureScan pacing system for use outside the MRI environment. The standard testing conducted on the Revo MRI SureScan pacing system consisted of the following:

- Biocompatibility
- Packaging
- Sterilization
- Pacemaker Hardware – Component, Electrical, and Mechanical Testing
- Software Testing
- Firmware Testing
- System Validation Testing
- Lead Mechanical and Electrical Testing

The standard lead and pacemaker testing met all of the rigorous lead and device requirements for pacing systems and their respective product specification documents. Changes made to the lead and device to eliminate the MRI hazards were selected based on historical performance in other commercialized products and thoroughly characterize within the design. The verification/qualification testing provides confidence that the system will meet the high standards that Medtronic places on its system for reliable performance and quality.

4.2.10 Pre-Clinical Conclusion

Medtronic CRDM follows rigorous Quality Assurance and Control procedures throughout the life of a product, from the business analysis phase through development, market release, and post-market surveillance. The formal risk analysis and risk assessment for the Revo MRI SureScan pacing system is conducted according to ISO 14971,[43] which specifies the process to identify, control, and evaluate the risks associated with medical devices in the anticipated environment. All risks due to identified system hazard scenarios have been either eliminated or mitigated to a low and acceptable level.

4.3 EnRhythm MRI SureScan Confirmatory Clinical Trial

The EnRhythm MRI SureScan pacing system confirmatory clinical study was designed to confirm the results of pre-clinical testing, which demonstrated that the EnRhythm MRI system was safe and effective for human use in the MRI environment in the specified conditions of use. Note that after completion of the clinical study enrollments, the EnRhythm SureScan pacing system was renamed the "Revo MRI SureScan pacing system."

4.3.1 Study Design

The confirmatory clinical study was a prospective, randomized, controlled, unblinded, global multi-center investigational study.

Randomization of subjects to control (no MRI) and MRI groups (MRI at 9-12 weeks post-implant) was used to provide treatment effect information.

The primary and secondary safety and effectiveness objectives in the clinical study are stated below. Study success required all five safety and effectiveness results to be met:

Safety (MRI group only)

- MRI procedure-related complication-free rate

Effectiveness (MRI group vs. control group)

- Atrial pacing capture thresholds
- Ventricular pacing capture thresholds
- Atrial sensed amplitudes
- Ventricular sensed amplitudes

Secondary objectives included characterization of system safety, lead handling, and lead performance, amongst others.

Up to 470 subjects were planned for implant and follow-up. Enrollment began February 2007 and the last subject was enrolled July 2008. Study subjects from all geographies will be followed until approval is granted from the FDA or official study closure, whichever is first. At the time of database lock, subjects were followed through November 2008 for an average of 11.2 months with some subjects implanted for as long as 21.5 months. The results presented in this clinical summary were submitted to the FDA on 05 June 2009 in the clinical report in support of PMA version 1, dated 17 March 2009.

The clinical study had oversight from three external committees, including a Data Monitoring Committee, an Adverse Event Advisory Committee and a Scan Advisory Committee. See Appendix 4 Confirmatory Clinical Study Summary Table 4-1 for committee, membership and purpose.

See Table 4-7 for an overview of the study visits.

Table 4-7. Visit Schedule

Visit	Time	Procedure
1	Baseline	Enrollment, informed consent, eligibility
2	Implant	Implant, randomization
3	2 month post-implant	Follow up; pacemaker measurements
4	9-12 weeks post-implant	MRI scan/control waiting period follow-up; pre-post pacemaker measurements
5	1 week post 9-12 weeks (3 months post-implant)	Follow-up; pacemaker measurements
6	1 month post 9-12 weeks (4 months post-implant)	Follow-up; pacemaker measurements
7	6 months post-implant	Follow-up; pacemaker measurements
	Every 6 months post-implant thereafter	Follow-up; pacemaker measurements

Data collected at all follow-up visits included adverse event assessment, system modifications, study exits and deaths. All follow-up visits consisted of pacemaker measurements, which included evaluation of pacing capture threshold at a pulse duration of 0.5ms, sensed electrogram amplitude and lead impedance.

Visit 1 - Baseline
Confirmed eligibility, as well as collection of demographic and cardiovascular history data.

Visit 2 - Implant
After a successful implantation of the EnRhythm MRI SureScan pacemaker Model EMDR01 and CapSureFix MRI SureScan Model 5086MRI leads (right atrial and right ventricular), randomization was performed to either undergo an MRI scan (MRI group) or not to undergo an MRI scan (Control group).

Visit 3 – 2 months post implant
All subjects underwent pacemaker measurements, which included evaluation of pacing capture threshold, sensed electrogram amplitude and lead impedance.

Visit 4 – 9-12 weeks post implant (MRI scan visit for MRI group patients)
All subjects underwent pacemaker measurements at two time points, which included assessment of pacing capture threshold, sensed electrogram amplitude, and lead impedance. The MRI group underwent pacemaker measurements immediately before the MRI (pre-MRI) and directly after the MRI (post-MRI), while the control group underwent pacemaker measurements at corresponding time points (i.e., pre-waiting period and post-waiting period, respectively). Adverse events were evaluated, including sustained ventricular arrhythmias, asystole and pacemaker function during and after the MRI scan. Unique to each randomization assignment were the following procedures at this visit:

MRI group: This visit required collaborative subject oversight by a cardiology and radiology provider at each center. Cardiology staff provided initial clearance, while radiology provided final clearance to undergo the MRI scan procedure. The prescribed MRI scan procedure was performed on 1.5T MRI systems from one of three MRI manufacturers (General Electric, Philips, and Siemens). The MRI scanning protocol represented one MRI scan procedure, which was approximately 30 minutes active scan time (60 minutes in MRI bore) and included 14 head and lumbar clinically relevant scans which were modified to maximize gradient dB/dt or maximize transmitted RF power to achieve whole body SAR levels of 2W/kg (upper limit of Normal Operating Mode). See Appendix 4 Confirmatory Clinical Study Summary, Section 4.3.2. for additional MRI scanning methods.

There was both monitoring and IPG programming requirements.

- Monitoring: During the entire MRI scan, the subject's cardiac function was required to be monitored using pulse oximetry by an study trained center electrophysiologist, cardiologist, or Advanced Cardiac Life Support (ACLS) trained clinician who is capable of delivering external cardiac pacing defibrillation and advanced cardiac life support. Verbal communication with the subject was required to assess or confirm any clinically significant changes. It was required that all Zone 3 radiology areas had an emergency code cart with an external defibrillator, as well as a programmer. It was further recommended that all means of subject monitoring were used (e.g., ECG).
- IPG Programming: After confirmation of the pre-MRI checklist for MRI scan, pacemakers were required to be programmed pre-MRI scan as follows: 1) pacing capture output programmed to 5V at 1.0ms, 2) MRI SureScan feature programmed ON, with selection of asynchronous pacing or sensing only mode. Pacing mode and rate (if applicable) were programmed per physician's discretion. Post-MRI scan, pacemakers were required to be programmed as follows: 1) MRI SureScan feature OFF (pacemaker returns to pre-MRI programmed settings) and 2) pacing capture outputs remain programmed to 5V at 1.0ms. The subject was required to remain at this output until the 3 month post-implant follow-up visit (1 week post-MRI scan).

Cardiology staff concluded the visit with pacemaker measurements.

Control group: No MRI scan. 60 minute waiting period between the two sets of pacemaker measurements (the equivalent duration of the MRI group).

Visit 5 – Follow-up one week post 9-12week visit (MRI scan/control visit)
All subjects underwent pacemaker measurements, which included assessment of pacing capture threshold, sensed electrogram amplitude, and lead impedance.

Visit 6 – Follow-up one month post 9-12 week visit (MRI scan/control visit)
All subjects underwent pacemaker measurements, which included assessment of pacing capture threshold, sensed electrogram amplitude, and lead impedance.

Visit 7 – Follow-up six months post implant (and every six-months thereafter)
All subjects underwent pacemaker measurements, which included assessment of pacing capture threshold, sensed electrogram amplitude, and lead impedance.

4.3.2 Study Results

Of 484 subjects enrolled, 464 subjects were successfully implanted with EnRhythm MRI SureScan pacing system. Of the 464 subjects, 258 patients were randomized to the MRI group (EnRhythm MRI SureScan pacing system with MRI scan) and 206 were randomized to the control group (EnRhythm MRI SureScan system without MRI scan).

Within the MRI group, 226 patients underwent a full or partial MRI scan, 211 of whom were scanned according to MR scanning protocol requirements. See Appendix 4 Confirmatory Clinical Study Summary, Figure 4-1 for full listing of subject distribution.

There were 5 primary safety and effectiveness objectives in the study, all of which had to be met for study success. These endpoints were measured at the 9-12 week MRI/control visit (immediately prior to when the MR scan was performed for the MRI group subjects and the control subjects waited for one hour), and at the one-month post-MRI/control visit. These results are presented in Tables 4-8, 4-10, and 4-12.

There were a number of pre-specified exclusions for each primary objective which resulted in smaller sample sizes than the 258 (MRI) and 206 (control) randomized. For the safety primary objective, it was pre-specified that only subjects undergoing an MRI scan per protocol design would be included. For the pacing capture threshold and sensed amplitude objectives, a number of exclusions were pre-specified to keep out data that might confound the results. In addition, some subjects had atrial arrhythmias which made collection of atrial data impossible. These exclusions can be found in Appendix 4 Confirmatory Clinical Study Summary.

Primary Safety Objective: MRI-Related Complications

Objective: To assess the MRI-related complication-free rate in the month following MRI.

A complication was defined as an adverse event that resulted in invasive intervention or the termination of significant device function regardless of other treatments. The complication-free rate was calculated as a ratio. The denominator was all subjects implanted with the EnRhythm MRI system that underwent an MRI scan per protocol and completed their one-month post-MRI visit, or had an MRI-related complication before the end of the one-month post-MRI visit date. The numerator was the subjects included in the denominator who were free from MRI-related complications at the end of the one-month post-MRI visit date. Subjects who were lost to follow-up, or withdrew for other reasons prior to the one-month post-MRI visit, were not included in the analysis unless an MRI-related complication was recorded.

Table 4-8: Safety Objective

Success Criteria	Subjects	Complications	P-value	Conclusion
The MRI-related complication-free rate is greater than 90%	211	0	$p < 0.001$	Objective Met

A total of 211 subjects underwent an MRI per protocol and completed the one-month post-MRI visit. No subjects experienced MRI-related complications through the one-month post-MRI visit. Therefore, no invasive interventions or termination of device function was needed or observed as a result of the MRI procedure.

In addition, none of the additional 15 subjects whose MR scans were not performed per protocol design (see Appendix 4 Confirmatory Clinical Study Summary), or the one additional control subject who underwent an MRI scan, experienced MRI-related complications.

While there were no MRI-related complications, the adverse events committee classified 4 events as MRI-procedure related observations: paraesthesia (n=3) and palpitations (n=1). In all cases, the adverse events advisory committee classified the events as not related to the pacing system and no actions were taken or required as a result of these events.

Table 4-9 shows the 4 observations that occurred in which relatedness to the MRI procedure was unknown.

Table 4-9. Observations with unknown relatedness to MRI

Observation	Action
Chest Discomfort	No action taken/required
Dyspnea	No action taken/required
Atrial Flutter	MRI SureScan feature was reprogrammed
Atrial Fibrillation	Subject medications changed

In all cases, the adverse events committee classified the events as not related to the pacing system.

Primary Effectiveness Objective #1: Pacing Capture Threshold

Objective: To compare the changes in 1) atrial and 2) ventricular voltage thresholds at 0.5 ms before and after an MRI scan between the MRI and control groups.

The objective focused on whether a significant change in ventricular and atrial voltage thresholds at 0.5 ms occurs following an MRI scan. The hypothesis tested whether the proportion of subjects who experienced threshold increases less than or equal to 0.5 V was clinically equivalent between the MRI and control groups. Post-MRI/control visit measurements were calculated at the one-month post-MRI/control visit.

A success was defined as a subject who experienced a change in pacing capture threshold less than or equal to 0.5 V. The equivalence margin of 10% is an upper bound for the absolute difference in success rates. Exclusions from the analysis were pre-defined in the clinical investigational plan (CIP) or statistical analysis plan. Subjects who were unable to capture at 0.5 ms were assigned a value of 6.0 V.

Table 4-10: Pacing Capture Thresholds

Success Criteria	Comparison		Success/ n	Success Rates	P-value	Conclusion
The proportions of subjects who experienced an increase less than or equal to 0.5 V are clinically equivalent, defined as within 10%.	Atrial	MRI Control	165 / 165 164 / 164	100% 100%	NA*	Objective Met
	Ventricular	MRI Control	190 / 190 183 / 184	100% 99.5%	$p < 0.001$	Objective Met

* Since the success rates were both 100%, the one-sided 97.5% confidence boundary and p-value could not be calculated.

A pre-defined sensitivity analysis was performed to include analysis-ineligible subjects (refer to Table 4-11). This included MRI subjects whose scans were not performed according to protocol but who had at least a partial MRI scan, subjects whose visits fell outside of the visit window at the one-month post-MRI/control visit, and subjects with data missing at the one-month post-MRI/control visit but for whom one-week post-MRI/control follow-up data could be used for the one-month post-MRI/control values. For atrial pacing capture thresholds, 35 MRI subjects and 13 control subjects were added to the primary analysis cohort for the sensitivity analysis. For ventricular pacing capture thresholds, 35 MRI subjects and 11 control subjects were added. The failure in the MRI group experienced a pacing capture threshold increase of 1.0 V.

Table 4-11. Sensitivity Analysis of Pacing Capture Threshold Primary Objective

	Primary Analysis			Sensitivity Analysis		
Comparison	Group	Success/ n	Success Rates	Group	Success/ n	Success Rates
Atrial	MRI Control	165 / 165 164 / 164	100% 100%	MRI Control	200 / 200 177 / 177	100% 100%
Ventricular	MRI Control	190 / 190 183 / 184	100% 99.5%	MRI Control	224 / 225 194 / 195	99.6% 99.5%

In addition a tipping point analysis was conducted. In a tipping point analysis, the missing data is examined to see at what point results would become not statistically significant. For the atrial pacing capture thresholds, where 165 / 165 MRI group subjects were successful, and 164 / 164 control group subjects were successful, if the remaining 42 randomized control group subjects were all successful, the endpoint would still be achieved as long as at least 77 of the 93 (83%) remaining MRI group subjects were successful. For the ventricular pacing capture threshold, if the 22 excluded control subjects were all successful, then the objective would have still been met if at least 51 of the 68 (75%) missing MRI group subjects were successes.

Primary Effectiveness Objective #2: Sensed Amplitude

Objective: To compare the changes in 1) atrial and 2) ventricular sensed amplitudes before and after MRI between the MRI and control groups.

The hypothesis tested whether the proportion of subjects who experienced a decrease in sensed amplitude less than or equal to 50% and whose sensed amplitude remained above an acceptable

minimum at one-month post-MRI/control visit (four-months post-implant) was clinically equivalent between the MRI and control groups.

A success was defined as meeting both of the following criteria: a sensed amplitude decrease not exceeding 50%, and a one-month post-MRI/control visit sensed amplitude not less than 5.0 mV for ventricular measurements and not less than 1.5 mV for atrial measurements. The equivalence margin of 10% was an upper bound for the absolute difference in success rates between the MRI and control groups. Subjects with a pre-MRI/control visit sensed amplitude less than 5.0 mV in the ventricle or less than 1.5 mV in the atrium were excluded from the primary analysis but were included in a sensitivity analysis. Exclusions from the analysis were pre-defined in the protocol or statistical analysis plan.

Table 4-12. Sensed Amplitudes

Success Criteria	Comparison		Success/ n	Success Rates	P-value	Conclusion
The proportion of subjects who experienced a sensing amplitude decrease not exceeding 50%, and a one-month post-MRI/waiting period sensing amplitude not less than 1.5 mV for atrial measurements and not less than 5.0 mV for ventricular measurements, are clinically equivalent, defined as within 10%.	Atrial	MRI Control	124 / 131 129 / 139	94.7% 92.8%	p <0.001	Objective Met
	Ventricular	MRI Control	130 / 134 129 / 136	97.0% 94.9%	p < 0.001	Objective Met

A pre-defined sensitivity analysis was performed to include analysis-ineligible subjects, including MRI subjects whose scans were not performed according to protocol but who had at least a partial MRI scan, subjects whose visits fell outside of the visit window at the one-month post-MRI/control visit, and subjects with data missing at the one-month post-MRI/control visit but for whom one-week post-MRI/control visit follow-up data could be used for the one-month post-MRI/control values. Results are in Table 4-13**.** For atrial pacing capture thresholds, 41 MRI subjects and 12 control subjects were added to the primary analysis cohort for the sensitivity analysis. For ventricular pacing capture thresholds, 34 MRI subjects and 11 control subjects were added.

The subjects excluded due to low sensed amplitude values, defined in the protocol as less than 5.0 mV in the ventricle and less than 1.5 mV in the atrium, were included in an additional sensitivity analyses, where success was defined as a sensed amplitude decrease not exceeding 50%. All subjects with low sensed amplitude values were successful according to this definition.

Table 4-13. Sensitivity Analysis of Sensed Amplitude Primary Objective

	Primary Analysis			Sensitivity Analysis		
Comparison	**Group**	**Success/ n**	**Success Rates**	**Group**	**Success/ n**	**Success Rates**
Atrial	MRI Control	124 / 131 129 / 139	94.7% 92.8%	MRI Control	162 / 172 141 / 151	94.2% 93.4%
Ventricular	MRI Control	130 / 134 129 / 136	97.0% 94.9%	MRI Control	172 / 178 140 / 147	96.6% 95.2%

In addition a tipping point analysis was conducted. In a tipping point analysis, the missing data is examined to see at what point results would become not statistically significant. For the atrial sensed amplitude, if all 67 missing control subjects were successes the null hypothesis would still be rejected if at least 109 of the 127 (86%) missing MRI group subjects were successes. For the ventricular sensed amplitude, if all 70 missing control subjects were successes the null hypothesis would still be rejected if at least 106 of the 124 (85%) missing *MRI group subjects* were successes.

Adverse Events

All adverse events were reviewed and classified by the adverse events committee. There were 260 subjects who experienced a total of 527 adverse events in this study. Fifty-nine percent of all of the adverse events were clinical observations which required no invasive action. Seventy-seven percent of the adverse events were not related to the system, the study procedures, the implant procedure, or the MRI procedure. Adverse events and incidence rates are similar in comparison to the Medtronic EnRhythm clinical study results as reported in the EnRhythm clinical study P980035/S038 approved by FDA.
For additional details on the EnRhythm MRI SureScan pacing system Confirmatory Clinical Study adverse events, refer to Appendix 4 Confirmatory Clinical Study Summary.

Deaths

There were 11 subject deaths during the study. Nine of the deaths occurred in the MRI group and two occurred in the control group. Of the nine that occurred in the MRI group, three occurred before the MRI and six occurred after the MRI. Of the six that occurred after the MRI, the closest in time to the MRI procedure was a pulmonary edema which occurred 10 days post MRI. Other events occurred no earlier than six months post MRI and further out to one year. The adverse event advisory committee adjudicated that none of the 11 subject deaths were related to the pacing system, to the implant procedure, or to the MRI procedure. For additional details on the EnRhythm MRI SureScan pacing system Confirmatory Clinical Study subject deaths, refer to Appendix 4 Confirmatory Clinical Study Summary, Clinical Summary.

4.3.3 Conclusion

The EnRhythm MRI clinical study evaluated and confirmed the following:

- The EnRhythm MRI system is safe for use in the MRI environment when used in accordance with its labeling as determined by the MRI-related complication-free rate and no occurrences of sustained ventricular arrhythmias or asystole.

- The EnRhythm MRI system is effective for use in the MRI environment when used in accordance with its labeling as determined by:
  - The clinical equivalence of the atrial and ventricular pacing capture threshold results between the MRI group and the control group.
  - The clinical equivalence of the atrial and ventricular sensed amplitude results between the MRI group and the control group.

In summary, all five primary safety and effectiveness objectives were met. All secondary objectives were met when performance criteria was predefined. Overall, there was no difference in performance between the MRI group and the control group. In the MRI environment under specific guidelines at 1.5 T field strength, the EnRhythm MRI pacing system performance was commensurate with MR-Conditional labeling requirements. As noted previously, the total adverse event rates are similar in comparison to other Medtronic clinical investigations of pacemakers and leads.

The Data Monitoring Committee chair wrote on behalf of the board, “We concur that the study met its objectives”. The study has confirmed the safety and effectiveness of the EnRhythm MRI SureScan Pacing System in the clinical MRI environment.

4.3.4 Summary of Safety and Effectiveness (Pre-Clinical and Clinical)

The results of the pre-clinical MRI environment testing and evaluation demonstrated that the Revo MRI SureScan pacing system is safe and effective in the MRI environment when used per the conditions specified in the labeling. The MRI hazards were evaluated and tested according to each environment hazard category. Lead heating and unintended cardiac stimulation were evaluated at the extremes of the MRI environment and for the extremes of the patient population and were determined to pose low risk to the patient. Case heating, force, torque, vibration, and device interactions were evaluated at clinically reasonable conditions, as well as beyond the extremes of the proposed labeling conditions, and determined to be of minimal concern. The results of the pre-clinical standard testing showed that the Revo MRI SureScan pacing system meets all the established requirements, and demonstrates the safety and effectiveness outside of the MRI environment. The overall risk of the Revo MRI SureScan pacing system, which is defined in accordance with ISO 14971, is predicted to be low and acceptable.

The results of the confirmatory clinical study showed that all primary safety and effectiveness objectives were met. All secondary objectives were met or, where no performance criteria were predefined, achieved favorably. Overall, there was no difference in performance between the MRI group and the control group. The study has confirmed the safety and effectiveness of the EnRhythm MRI SureScan pacing system in the clinical MRI environment. The results of all MRI-related pre-clinical and clinical evaluations are summarized for each hazard in Table 4-14.

Table 4-14. Summary of Safety and Effectiveness

Analyze			Design	Tests		Clinical Study	
Hazard	**Field Interactions**	**Clinical Impact**	**Design Element**	**Pre-clinical Evaluation Testing**	**Pre-clinical Test Results**	**Clinical Evaluation**	**Clinical Result**
Lead Heating	RF	• Thermal tissue damage • Change in pacing capture threshold • Loss of therapy	The inner coil of the CapSureFix MRI 5086MRI lead was designed to dissipate more RF energy, reducing heating at the tip-tissue interface.	Conducted in vivo studies to determine lead tip heating impact on pacing capture threshold and tissue. Modeled RF coil, lead, and human bodies to determine clinically relevant lead tip heating levels. Combined modeling and in vivo results to predict the likelihood of changes in pacing capture threshold.	MRI-induced changes in pacing capture threshold are unlikely to occur.	Primary effectiveness objective: To compare the changes in atrial and ventricular pacing capture thresholds before and after MRI between the MRI and control groups.	The proportion of subjects who experienced an increase in atrial or ventricular pacing capture thresholds ≥0.5 V are clinically equivalent, defined as within 10% ($p<0.001$).
Unintended Cardiac Stimulation	Gradient and RF	• Single/intermittent stimulation • Multiple/continuous stimulation (hemodynamic collapse) • Sustained ventricular tachycardia	The input circuitry of the Revo MRI pacemaker was optimized to balance the risk of gradient-induced unintended cardiac stimulation with electromagnetic interference rejection.	Calculated the potential MRI-induced voltages and pulse widths on the lead. Conducted in vivo studies to determine stimulation thresholds. Combined results to determine the likelihood of unintended cardiac stimulation. Conducted study to demonstrate design margin.	Patient harm due to unintended cardiac stimulation is unlikely to occur.	Primary safety objective: To assess the MRI-related complication-free rate in the month following MRI.	The MRI-related complication-free rate between the MRI procedure and one-month post-MRI is greater than 90% ($p<0.001$)*
Device Interactions	Static, Gradient and RF	• Pacemaker malfunction or failure • Loss of therapy • Syncope	A circuit protection component of the Revo MRI pacemaker was upgraded to prevent the gradient-induced current from affecting the internal power supplies and pacing output.	Evaluated potential electromagnetic device interactions in vitro for a total of over 1700 device-hours. Pacing, electromagnetic interference, and functional tests performed during and after MRI exposure.	Zero failures detected during in vitro and clinical MRI scanner testing.	System-related adverse events and technical observations related to MRI Dislodgements related to MRI	No patients with system-related complication adverse events (associated with discomfort or tissue damage) or technical observations, related to MRI** No patients with dislodgements related to MRI
Pacemaker Case Heating	Gradient and RF	• Discomfort • Tissue damage	The design of the previous EnRhythm pacemaker met the requirements for case heating. No further design changes were required.	Evaluated pacemaker case temperature rise in vitro at the maximum labeling conditions. Evaluated the time-temperature profile of case heating	All case heating measurements met requirements.		
Force and Torque	Static	• Tugging • Pacemaker or lead dislodgement • Tissue injury	The design of the previous EnRhythm pacemaker met the requirements for force and torque. No further design changes were required.	Used ASTM test methods to measure MRI-induced force and torque. Measurements taken at worst-case magnetic field locations in clinical MRI scanners for the pacemaker and lead. Compared measurement results to the force and torque exerted on a pacemaker due to everyday activities.	All force and torque measurements met requirements.		
Vibration	Static and Gradient	• Pacemaker malfunction or failure • Loss of therapy • Syncope	The design of the previous EnRhythm pacemaker met the requirements for vibration. No further design changes were required.	Pacemakers tested in vitro for a total of 1475 device hours in the worst-case MRI environment. Functional tests performed during and after testing.	Zero failures detected during and after exposure to worst-case vibration conditions.		

* The independent Adverse Event Committee classified two events in two subjects as observations of atrial flutter and atrial fibrillation with unknown relatedness to MRI and unknown relatedness to the pacing system. Subject 317620506 reported Atrial flutter during the MRI procedure. Baseline history indicated the following atrial arrhythmias: persistent atrial fibrillation, atrial tachycardia, sinus arrest, and sinus bradycardia. Subject 451320012 reported atrial fibrillation during the MRI procedure. Baseline history indicated the following atrial arrhythmias: paroxysmal atrial fibrillation, atrial tachycardia, premature atrial contraction, and sinus bradycardia.

** One observation of chest discomfort with unknown relatedness to MRI.

5 Clinical Implementation

5.1 Introduction

There is a need not only to develop the pacing system, but to ensure that it is designed and delivered in a manner to ease the clinical implementation aspects and ensure patient safety during the process. During the development of the Revo MRI SureScan pacing system, "clinical implementation" was the term used to refer to the following:

- Assumptions and recommendations regarding the MRI patient referral or MRI exam processes
- Assumptions and recommendations regarding use of the Revo MRI SureScan pacing system
- Tools supporting the proper and safe use of the Revo MRI SureScan pacing system

This section summarizes the key elements of the clinical implementation that support the safe and appropriate use of the Revo MRI SureScan pacing system in the MRI environment.

The American College of Radiology (ACR), which is recognized for its work in the radiology industry, has developed a guidance document for safe MR practices. This white paper includes recommendations and considerations on screening, scanning, and monitoring patients with implantable medical devices, including cardiac pacemakers and implantable cardioverter defibrillators. The design and clinical implementation of the Revo MRI SureScan pacing system is consistent with these ACR MR Safe Practice Guidelines.

The radiology community currently assesses patients for MRI safety when presented with an MR Safe, MR Conditional, or MR Unsafe implantable medical device, as defined below.

ASTM F2503-08: Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment provides the following definitions for medical devices:

- *MR Safe* – an item that poses no known hazards in all MR environments (e.g., a plastic Petri dish).
- *MR Conditional* – an item that has been demonstrated to pose no known hazards in a specified MR environment with specified conditions of use. Field conditions that define the specified MR environment include field strength, spatial gradient, dB/dt (time rate of change of the magnetic field), radio frequency (RF) fields, and specific absorption rate (SAR). Additional conditions, including specific configurations of the item, may be required.
- *MR Unsafe* – an item that is known to pose hazards in all MR environments (e.g., a pair of ferromagnetic scissors).

The Revo MRI SureScan pacing system is not unique among the broader category of implantable medical devices with MR Conditional labeling (e.g., implantable loop recorders, stents, vagus nerve stimulators, and aneurysm clips), and specific care has been taken in designing a system that fits into current protocols in standard radiology and cardiology practices. There are several fundamental steps to the Revo MRI SureScan System clinical implementation. These steps can occur with many different variations and in many different sequences, depending upon the patient condition, urgency of the MRI exam, type and size of the medical facility and medical judgment of the involved medical staff. It should be noted that from a cardiology perspective, the clinical implementation will be similar to the current process utilized for the reprogramming of patients undergoing elective surgery. An overview of the clinical implementation for the Revo MRI SureScan pacing system is illustrated in Figure 5-1.

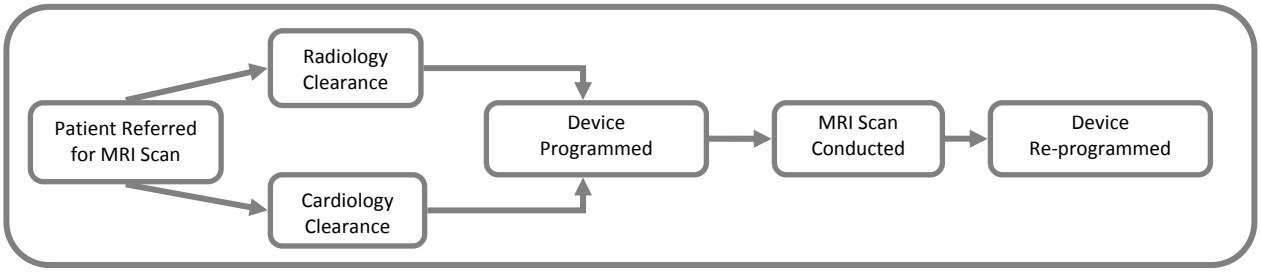


Figure 5-1. Clinical Implementation Overview

The design and clinical implementation of the Revo MRI SureScan pacing system focus on three primary areas:

- Awareness and Education – creating awareness of the availability of an MR Conditional pacing system.
- System Identification – correctly identifying that a patient has a system labeled for use in an MRI environment.
- Labeling Implementation – applying the appropriate conditions of use as prescribed by the product's labeling.

Medtronic CRDM's approach to addressing each issue is summarized in Table 5-1 and discussed in detail in the sections that follow.

Table 5-1. ACR MR Safe Practice Guidelines / Revo MRI SureScan Clinical Implementation

ACR MR Safe Practice Guidelines	Revo MRI SureScan Clinical Implementation
MRI SYSTEM AWARENESS AND EDUCATION (see Section 5.2.1)	
Patients with implanted cardiac pacemakers are precluded from undergoing an MRI exam.	Create awareness of the availability of an MR Conditional pacing system: • Directing users to central repository on website (www.MRISureScan.com) for access to technical manuals and other tools and resources related to Revo MRI SureScan pacing system. • Upon market approval and commercialization, create awareness at congress activities and scientific sessions, and through journal advertising, key opinion leader activities, and publications.
MRI SYSTEM IDENTIFICATION (see Section 5.2.2)	
All patients with a history of potential ferromagnetic foreign object penetration must undergo further investigation prior to undergoing an MRI exam (e.g., patient history, X-ray, prior computed tomography (CT) or MR studies, written documentation).	Correctly identify that a patient has a system labeled for use in an MRI environment: • Patient ID card identifies the presence of a Revo MRI SureScan pacing system. • Radiopaque MRI symbols verify, through an X-ray image, whether components are designed for use in the MRI environment; symbols are located on lead connector block of pacemaker and on CapSureFix MRI 5086MRI lead near pacemaker case and lead connector. • Programmer interface/printout provides MRI SureScan checklist and programmed parameters for key radiology considerations and confirmation of proper programming.
MRI SYSTEM LABELING IMPLEMENTATION (see Section 5.2.3)	
Once positive identification has been made as to the type of implant that is within a patient, an assessment should be made to identify the MR safety of the implant (e.g., written records of the results of formal testing, product labeling regarding the implant, and review of peer-reviewed publications regarding the MR safety testing of the implant).	Identify MR safety through: • Central repository on website (www.MRISureScan.com). • Revo MRI SureScan product labeling. • *Reference Manual for Magnetic Resonance Safety, Implants and Devices* by Dr. Frank Shellock. • Dr. Shellock's website (www.mrisafety.com).

5.2 Revo MRI SureScan Clinical Implementation

5.2.1 Awareness and Education

The ACR MR Safe Practice Guidelines state that patients with implanted cardiac pacemakers are precluded from undergoing an MRI exam, and there are several ways in which an implanted pacemaker can potentially be identified in the current screening processes. The radiology community recognizes patient screening procedures as one of the most critical components of a program that guards the safety of all patients preparing to undergo an MRI exam, and this will not change with the introduction of the Revo MRI SureScan pacing system.

Medtronic CRDM's fundamental focus for radiology and MRI referrers (oncology, orthopedic surgery, neurology, neurosurgery, general medicine, family practice, etc.) consists of establishing and promoting awareness of the Revo MRI SureScan pacing system. This includes directing users to a central repository (a website: www.MRISureScan.com) that provides tools, resources, and access to the Revo MRI SureScan technical manual to understand the system's labeling and methods of applying it. Upon market approval and commercialization, Medtronic CRDM will implement a program to create clinical awareness of the system, including tools and activities such as congress activities and scientific sessions, journal advertising, key opinion leader activities, and publications (discussed further in Section 6).

5.2.2 System Identification

In accordance with the ACR MR Safe Practice Guidelines, all patients with a history of potential ferromagnetic foreign object penetration must undergo further investigation prior to undergoing an MRI exam. Examples of acceptable methods of screening include:

- Patient history.
- Plain X-ray films.
- Prior imaging studies of the questioned anatomic area.
- Access to written documentation as to the type of implant that might be present.

Throughout the development of the Revo MRI SureScan pacing system, three primary tools were implemented in the system's design to ensure its proper identification in accordance with the ACR MR Safe Practice Guidelines:

- Patient ID Card
- Radiopaque MRI Symbols
- Programmer Interface / Printout

The intended use and examples of each of the primary identification tools is described in detail in the sections that follow.

Patient ID Card

According to the ACR MR Safe Practice Guidelines, MR safety information about an implant should never be assumed if it is not clearly documented in writing. Like all Medtronic CRDM pacemaker patients, those implanted with a Revo MRI SureScan pacing system will receive an identification card to help track their system. The patient ID card (shown in Figure 5-2 and Figure 5-3) will be used to identify the presence of the Revo MRI SureScan pacing system, including model information, and will direct the user to the central repository for further information (discussed further in Section 6). The

patient ID card and the referenced MRI SureScan website are two methods of providing MR safety documentation in accordance with the ACR MR Safe Practice Guidelines. An additional method of providing documentation containing MR safety information is also available via the programmer (discussed further below).

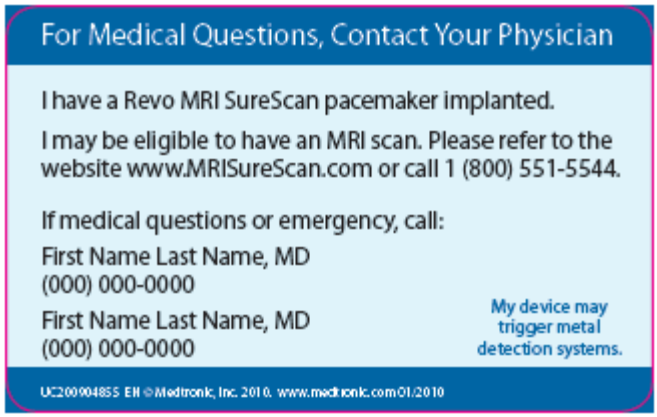


Figure 5-2. Front of Patient ID Card

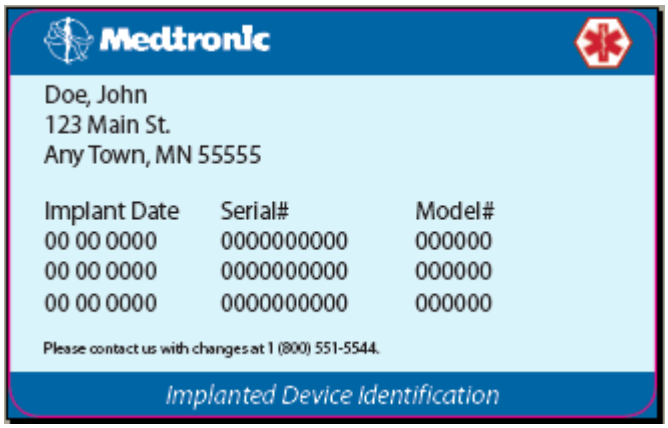


Figure 5-3. Back of Patient ID Card

Radiopaque MRI Symbols

According to the ACR MR Safe Practice Guidelines[18], plain X-ray films are one of the acceptable methods for screening patients suspected of having an implant in their bodies. Therefore, in consultation with radiologists, Medtronic CRDM developed a unique radiopaque MRI symbol as a means of easily and uniquely identifying the Revo MRI SureScan pacemaker and the CapSureFix MRI 5086MRI leads. The MRI radiopaque symbols help the user verify, through an X-ray image of the implanted system, whether the components are Revo MRI SureScan pacing system components that are designed for use in the MRI environment.

The unique radiopaque MRI symbol is present on all Revo MRI SureScan pacing system components. On the Revo MRI SureScan pacemaker, the radiopaque MRI symbol is located in the lead connector block of the pacemaker, indicated by a wavy line located in the upper portion of the full pacemaker's

radiopaque. A similar indicator is visible on the CapSureFix MRI 5086MRI lead, adjacent to the case and lead connector. On the leads, the radiopaque is a short loop of coil wrapped around the lead near the connector end. The radiopaque MRI symbols and their locations are illustrated in Figure 5-4.

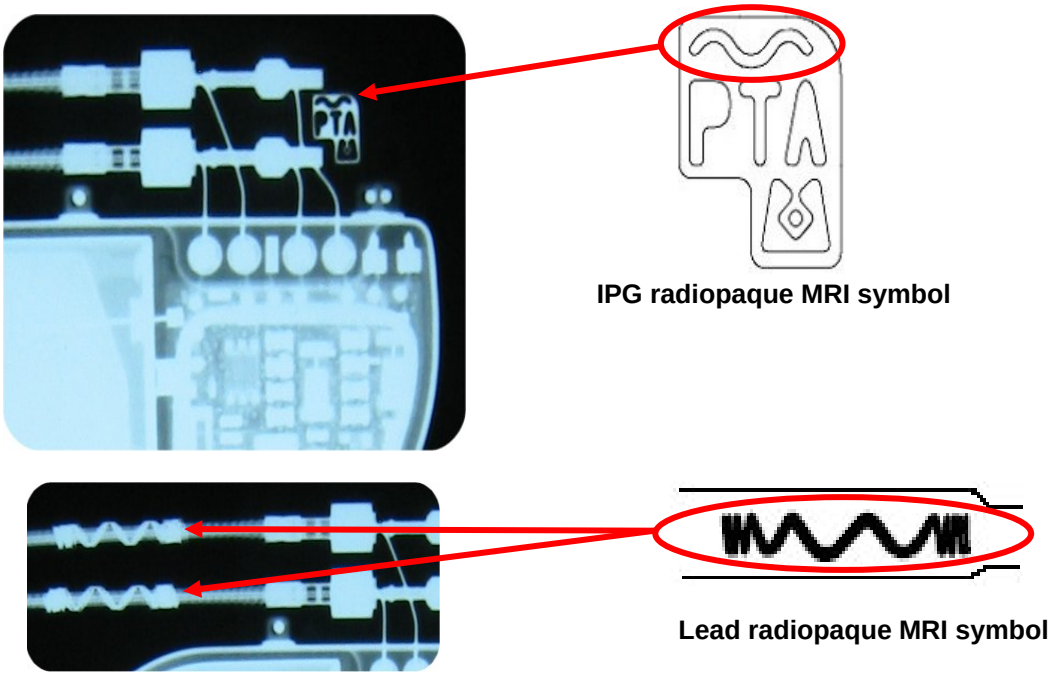


Figure 5-4. Radiopaque MRI Symbols

Physicians were asked to assess the ease of identifying the radiopaque MRI symbols as part of the EnRhythm MRI clinical study, and both cardiologists and radiologists found that the identification markings were "above their expectations" (data in Appendix 4 Confirmatory Clinical Study Summary).

Programmer Interface / Printout

The MRI SureScan feature allows the user to print out the MRI SureScan checklist and the MRI SureScan parameter programming screen from the programmer. Cardiologists will be guided to include this printout in the patient's file as part of Medtronic CRDM's field introduction of the MRI SureScan feature. Printing the MRI SureScan parameter programming screen may also serve as a communication tool for radiologists to confirm the Revo MRI SureScan pacemaker is programmed properly for an MRI exam. Additionally, the printout provides an overview of the key radiology considerations for safe use of the system and directs the user to the MRI SureScan technical manual for detailed instructions. Figure 5-5 and Figure 5-6 provide examples of the programmer user interface screens and Figure 5-7 is a sample printout.

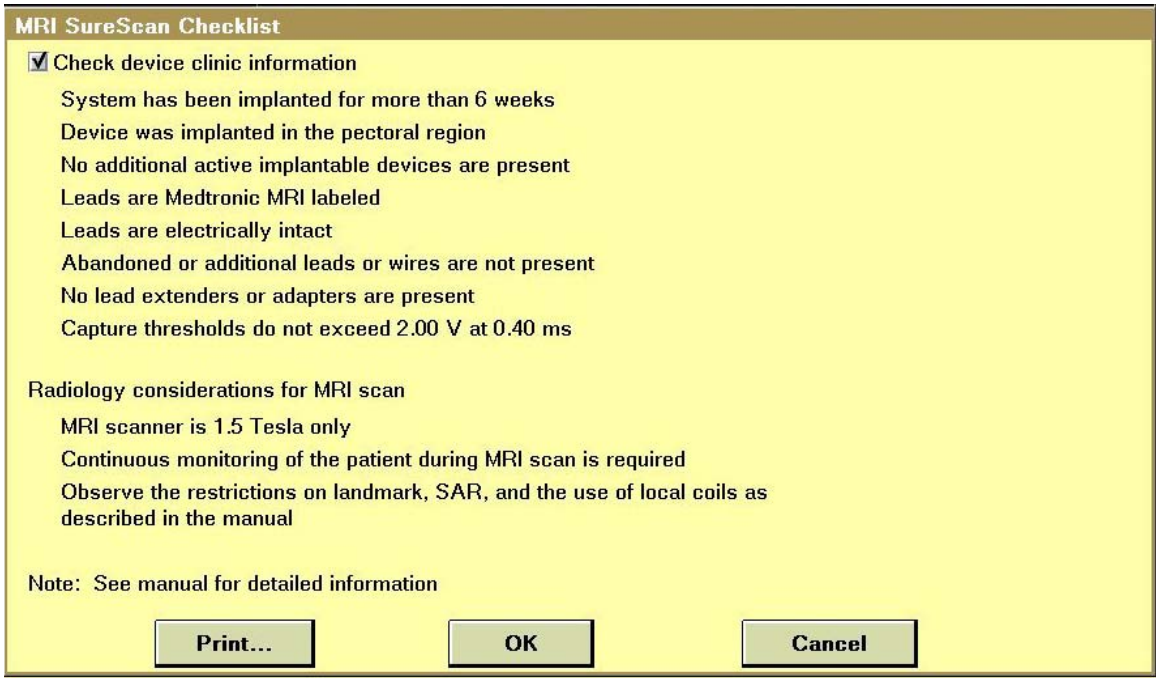


Figure 5-5. MRI SureScan Checklist

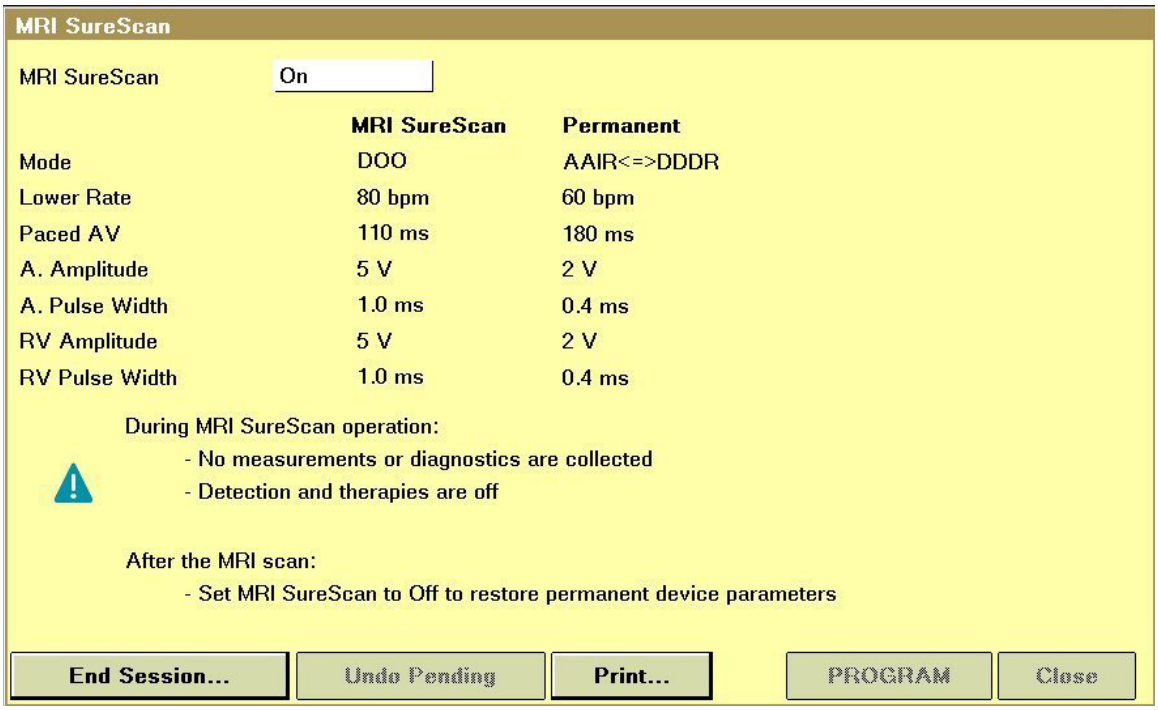
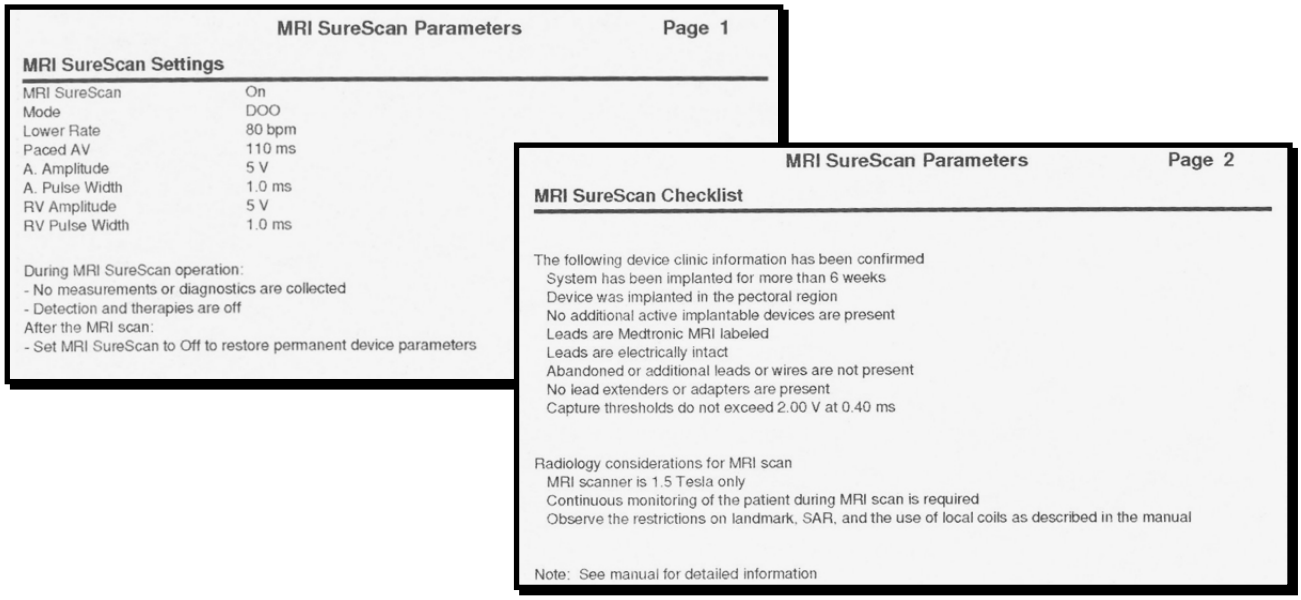


Figure 5-6. MRI SureScan Programming Screen



MRI SureScan Parameters Page 1

MRI SureScan Settings

MRI SureScan	On
Mode	DOO
Lower Rate	80 bpm
Paced AV	110 ms
A. Amplitude	5 V
A. Pulse Width	1.0 ms
RV Amplitude	5 V
RV Pulse Width	1.0 ms

During MRI SureScan operation:
- No measurements or diagnostics are collected
- Detection and therapies are off

After the MRI scan:
- Set MRI SureScan to Off to restore permanent device parameters

MRI SureScan Parameters Page 2

MRI SureScan Checklist

The following device clinic information has been confirmed
System has been implanted for more than 6 weeks
Device was implanted in the pectoral region
No additional active implantable devices are present
Leads are Medtronic MRI labeled
Leads are electrically intact
Abandoned or additional leads or wires are not present
No lead extenders or adapters are present
Capture thresholds do not exceed 2.00 V at 0.40 ms

Radiology considerations for MRI scan
MRI scanner is 1.5 Tesla only
Continuous monitoring of the patient during MRI scan is required
Observe the restrictions on landmark, SAR, and the use of local coils as described in the manual

Note: See manual for detailed information

Figure 5-7. MRI SureScan Programmer Printout

The cardiac staff was asked to assess the MRI SureScan feature performance as part of the EnRhythm MRI clinical study, and the data indicates that they found these tools “easy to use” (data in Appendix 4 Confirmatory Clinical Study Summary).

5.2.3 Labeling Implementation

In accordance with the ACR MR Safe Practice Guidelines, once positive identification has been made as to the type of implant that is within a patient, an assessment should be made to identify the MR safety of the implant. Efforts at identification include written records of the results of formal testing, product labeling regarding the implant, and review of peer-reviewed publications regarding the MR safety testing of the implant. Even though the Revo MRI SureScan pacing system is unique among pacemakers because of its MR Conditional labeling, the radiology community is already well-equipped and trained to screen all patients, and two key resources currently used by the radiology community in identifying the MR safety of the implant are the manufacturer's website and Dr. Frank Shellock's reference manual (*Reference Manual for Magnetic Resonance Safety, Implants and Devices*) and/or website (www.mrisafety.com). The Revo MRI SureScan clinical implementation fits into this previously existing radiology framework and mirrors the recommendations provided in the ACR MR Safe Practice Guidelines. Specifically, the Revo MRI SureScan product labeling will be made available via the MRI SureScan website (www.MRISureScan.com), as well as via Dr. Shellock's reference manual and website (discussed further in Section 6).

Actual clinical experience has also demonstrated that the Revo MRI SureScan clinical implementation fits into the current protocols in standard radiology and cardiology practices. This was confirmed by data collected in the EnRhythm MRI clinical study, which showed that the coordination between cardiology and radiology was perceived as "easy" and the information included in the labeling was "clear" (data in Appendix 4 Confirmatory Clinical Study Summary). In addition, no subjects experienced a system-related adverse device effect related to insufficiencies in or incorrect following of the EnRhythm MRI SureScan pacing system labeling (data in Appendix 4 Confirmatory Clinical Study Summary). To date, there have also been no reported complications resulting from the clinical implementation of the EnRhythm MRI SureScan pacing system.

5.3 Foreseeable Off-Label Clinical Use

Medtronic CRDM studied the clinical use of the Revo MRI SureScan pacing system, and identified foreseeable off-label clinical use scenarios related to the proposed labeling. The foreseeable off-label clinical use scenarios that are considered most likely are identified in Table 5-2. Refer to Appendix 3 for additional details.

Table 5-2. Foreseeable Off-Label Clinical Use

Off-Label Clinical Use Scenario	Clinical Impact
Failure to observe patient positioning restriction	• Only affects the system performance in relation to the lead heating hazard. • Results demonstrate the probability of a pacing capture threshold change increases. • A patient receiving an MRI scan with the isocenter within the C1-T12 thoracic region is unlikely to experience a clinically significant change in pacing capture threshold levels.

Off-Label Clinical Use Scenario	Clinical Impact
Failure to observe 2 W/kg SAR limit	• Only affects the system performance in relation to the lead heating hazard. • The results demonstrate the probability of a change in pacing capture threshold increases. • A patient receiving an MRI scan at a whole body average SAR of 4 W/kg is unlikely to experience a clinically significant change in pacing capture threshold levels.
MRI SureScan not enabled prior to MRI exam	• Hall sensor reliably detects strong magnetic fields and switches to magnet mode (asynchronous pacing at 85 beats per minute). • Once the patient exits the MRI environment, normal pacemaker operation will resume. • Risk of patient harm is considered low and acceptable
MRI SureScan not disabled following MRI exam	• Patient may experience asynchronous pacing during this period of time • Risk of patient harm is considered low and acceptable

5.4 Conclusion

Medtronic's approach to the Revo MRI SureScan clinical implementation has been to focus on creating awareness of the Revo MRI SureScan pacing system and providing the necessary tools to identify, understand, and apply the requirements for safe utilization of the Revo MRI SureScan pacing system. The design and clinical implementation of the Revo MRI SureScan pacing system aligns with the ACR MR Safe Practice Guidelines and fits into current protocols in standard radiology and cardiology practices. The clinical implementation offers a variety of tools supporting the proper and safe use of the Revo MRI SureScan pacing system, which will allow physicians to implement the various elements based on the needs at their own clinical centers. Based on feedback from physicians, as well as the additional analyses included in the EnRhythm MRI clinical study report, the Revo MRI SureScan clinical implementation supports the safe and effective use of this system in the clinical environment.

6 Training and Education

6.1 Introduction

Upon FDA approval, the introduction of the Revo MRI SureScan pacing system into the market place will be accomplished through awareness, education, and/or training for the following audiences:

- **Internal**
  - Medtronic CRDM Field Representatives
  - Medtronic CRDM Technical Services
- **External**
  - Electrophysiologists and Cardiologists
  - MR Referrers (Oncologists, Neurologists, Orthopedic Surgeons, etc.)
  - MR Radiologists and Technologists

Following is a description of the audiences, their needs, and the related training tools and activities that will drive the understanding and safe implementation of the Revo MRI SureScan pacing system.

6.2 Internal Audiences

6.2.1 Medtronic CRDM Field Representatives

- **Description**: There are approximately 2,000 Medtronic CRDM Field Representatives in the US. These individuals are typically Technical Field Engineers, Sales Representatives, or Clinical Specialists. They frequently have a close relationship with the physician customers (Electrophysiologists and/or Cardiologists), and Allied Health Professionals. They provide technical support and education to these customers on a regular, ongoing basis.
- **Needs**: This group must have a detailed understanding of the system, all elements of its labeling, and how to appropriately follow that labeling.
- **Tools and Activities**: Prior to product launch, Medtronic CRDM Field Representatives will undergo extensive training on MRI safety, system identification, and safe clinical implementation of the technology. This training will include an on-line, technical tutorial portion with a related examination, a large group training session, and local team training. Conditions of use will be the primary emphasis of each of these training sessions. Medtronic CRDM field personnel are very familiar with the pacing therapies available in the Revo MRI SureScan pacemaker; however, a technical review will also be provided.

6.2.2 Medtronic CRDM Technical Services

- **Description**: Medtronic CRDM Technical Services personnel are trained to answer technical issues and questions from customers and Medtronic CRDM Field Representatives. Users of Medtronic CRDM technologies are very aware of Medtronic CRDM Technical Services and

frequently rely on this group for answers to questions arising from the use of Medtronic CRDM products.

- **Needs**: The training needs of this group are similar to those of the Medtronic CRDM Field Representatives as mentioned above.
- **Tools and Activities**: This group will receive the same training provided to the Medtronic CRDM Field Representatives.

6.3 External Audiences

6.3.1 Cardiology and Electrophysiology

- **Description**: Medtronic CRDM has a long and consistent history of delivering training through the Medtronic CRDM Field Representatives to our Cardiology and Electrophysiology customers.
- **Needs**: This group must understand the system's labeling and how to appropriately implement this labeling. In particular, they must understand the required components, including the Revo MRI SureScan feature, as well as the electrical parameters and programming to comply with the MR Conditional labeling.
- **Tools and Activities**: As with other product introductions, Medtronic will provide training to customers. The Cardiology and Electrophysiology customer training for the Revo MRI SureScan pacing system will be developed and delivered according to established Medtronic CRDM customer training goals and standards. Resources (brochures, presentations, job aids, and manuals) will be made available to Medtronic CRDM Field Representatives to assist in this education. Additionally, reference materials, clinical/technical manuals, and other tools will be made available on-line (www.medtronic.com, www.MRISureScan.com, and Medtronic Connect). For example, an interactive demo on programming the Revo MRI SureScan feature 'on' and 'off' will be provided, in which the user can view and/or attempt programming the Revo MRI SureScan feature, as well as receive immediate feedback.

6.3.2 Radiology

- **Description**: The radiology community is a new, and significant, audience for Medtronic CRDM. This group is comprised of both Radiologists and MR Technologists.
- **Needs**: Collectively, this group is responsible for patient safety in the MRI environment, and as such, it is critical to reach them as part of our education and training program. As in Cardiology, this group also needs to understand the system's labeling and how to safely implement the labeling. However, for the Radiology audience, there will be a specific emphasis on system identification, existence of the pre/post programming requirements, and scanning considerations (i.e., magnet strength, gradient slew rate, specific absorption rate [SAR], and patient positioning). It is important to note that one of the fundamental elements Radiology employs to ensure patient safety – the rigorous screening process outlined in the ACR (American College of Radiology) Guidelines – will not change with the introduction of the Revo MRI SureScan MR Conditional pacing system. This screening process includes multiple opportunities to identify a pacemaker patient. As such, it is critical to 1) create awareness within this group that an MR Conditional pacing system exits, and 2) provide education and

tools that fit within their current system for safely addressing patients with MR Conditional implants.

- **Tools and Activities**: As mentioned above, the Radiology program will focus on awareness of the existence of an MR Conditional pacing system, and education and tools on how to apply that system's labeling. Each is described below:
  - **Awareness**: Medtronic CRDM will embark on a robust program to create awareness that an MR Conditional pacing system exists. The program will include national and local PR, journal advertising, website advertising, partnerships with key associations, relationships with thought leaders, incorporation in key websites and resource sites (www.mrisafety.com), professional congresses, and symposia. All of these efforts will direct the recipients to one location (www.MRISureScan.com), which is described in detail below.
  - **Education and Training**: In an attempt to understand the needs and current practice of these new stakeholders, Medtronic CRDM has performed extensive market research (quantitative, qualitative, and ethnographic). This research, as well as the ACR Guidelines, indicates there are two key resources that are leveraged by Radiology in determining appropriate conditions for an MR Conditional (or MR Safe) implant: the manufacturer's website (www.mrisafety.com) and Dr. Frank Shellock's *Reference Manual for Magnetic Resonance Safety, Implants and Devices*[33].

    Every initiative described in the Awareness section above, as well as the Patient ID card itself, will direct the recipient to www.MRISureScan.com. This site will serve as a definitive resource for Radiology and include: a central repository for Revo MRI SureScan pacing system information, technical manuals, and multiple paths to search for products (model look-up; device type). This website will include the following:

    a. A description of the Revo MRI SureScan pacing system.

    b. The Revo MRI SureScan MR Conditional criteria for Radiology and Cardiology (e.g., MRI conditions of use).

    c. Illustrations with guidance on recognizing Revo MRI SureScan pacing systems.

    d. An electronic tutorial on identifying the Revo MRI SureScan pacing system and MR Conditional criteria, similar to what will be delivered to the Medtronic CRDM Field Representatives.

    e. A description of the Revo MRI SureScan pacing system clinical implementation.

    f. A series of interactive case studies (from Radiology and Cardiology perspectives) on the application of the Revo MRI SureScan pacing system clinical implementation. For example, the user is provided a case situation and asked to execute the appropriate clinical implementation steps. Immediate feedback is provided regarding the choices made.

    g. Job aids covering the system description, system identification, MRI conditions of use, programming summary, and clinical implementation steps will be available for download.

h. Contact information for Medtronic CRDM Technical Services and the national answering service will also be provided.

6.3.3 MR Referrers

- **Description**: This group comprises any physician who uses MRI in the care and treatment of patients. Oncologists, Neurologists, and Orthopedic Surgeons represent more than 50% of all MR referrals. The balance of referrals comes from Emergency Room physicians, General/Family physicians and Cardiology. Today, these groups typically assume a patient is ineligible for an MRI exam given the presence of a pacing system.
- **Needs**: Awareness that an MR Conditional pacing system exists.
- **Tools and Activities**: The awareness program described under the Radiology section above will address the needs of this audience.

7 SureScan Post-Approval Clinical Study

7.1 Introduction

Medtronic is proposing a global, prospective, non-randomized, multi-center post-approval study to meet the FDA conditions of product approval. The purpose of this Post-Approval Study (PAS) is to demonstrate acute and chronic performance of the SureScan™ Pacing System when used in an MRI environment according to product labeling.

7.2 Study Design

The SureScan pacing system PAS is designed to monitor long-term performance of the SureScan pacing system and identify individual system failure modes when used in an MRI environment. Sample size determination must satisfy both primary objective analysis requirements and provide reliable estimates of individual failure mode rates for the general population.

A minimum enrollment of subjects is estimated to be required in order to achieve the desired sample size for the all primary objective analyses. Subjects will be followed for at least 5 years from their implant date. It is expected to take months to enroll subjects. The month enrollment period estimate is due to anticipated challenges resulting from requiring an in-office visit every and the complexity of activating centers with both a Cardiology and Radiology component.

It is anticipated approximately centers globally will support the SureScan pacing system PAS. The number of participating centers will be regularly assessed to ensure appropriate expertise and capacity exists to meet study objectives. The study will limit the enrollment of subjects outside of US to no more than 50% of the cohort.

Subjects will be asked to notify their cardiologist if they are scheduled for an MRI. Additional steps, such as those listed below, will be taken to further mitigate challenges associated with ensuring cardiologist awareness of a subject MRI and data collection before, during, and after the MRI if conducted at a radiology clinic unaffiliated with the study. These mitigation steps include:

- Select sites with affiliated radiology capabilities willing to contractually agree to direct data access
- Review of CareLink transmissions, if available, for enrolled SureScan pacing system to determine if the SureScan software was enabled since subjects' last in-office visit
- Letters to enrolled subjects reminding them to notify the center if they have had an MRI since their last in-office visit.

An overview of the design is shown in Figure 7-1.

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7.3 Objectives

7.3.1 Primary Objective

The SureScan pacing system PAS will have 3 primary objectives:

Primary Objective #1: To demonstrate MRI-related complication rate will be less than

The Adverse Event Adjudication Committee will classify the relatedness to MRI of a complication that occurred within one-month of the MRI scan.

The analysis of this primary objective will include all complications adjudicated as MRI-related. A final list of MRI-related complications that contributed to the primary objective will be presented when the primary objective is analyzed.

Primary Objective #2: To demonstrate that the complication free survival probability for Model 5086MRI lead placed in the right atrium (RA) is greater than 92.5% at 5 years post-implant.

Primary Objective #3: To demonstrate that the complication free survival probability for Model 5086MRI lead placed in the right ventricle (RV) is greater than 92.5% at 5 years post-implant.

For Primary Objective #2 and #3, complications related to lead hardware or design failure regardless of MRI scans will be included in the analysis.

7.3.2 Secondary Objectives

There are four secondary objectives:

Secondary Objective #1: Characterize chronic SureScan pacing system electrical performance by MRI exposure

- Atrial and ventricular pacing capture threshold measurement changes for each scheduled visit will be summarized by MRI scans: i.e., no MRI, Single MRI, Multiple MRIs.
- Atrial and ventricular sensing measurement changes for each scheduled visit will be summarized by MRI scans: i.e., no MRI, Single MRI, Multiple MRIs
- Atrial and ventricular pacing capture threshold measurement changes for subjects with follow-up due to an observed clinically significant change between pre and post MRI will be summarized
- Atrial and ventricular sensing measurement changes for subjects with follow-up due to an observed clinically significant change between pre and post MRI will be summarized.

Secondary Objective # 2: Summarize all MRI system and scan conditions collected at time of MRI.

Secondary Objective # 3: Summarize all SureScan pacing system related adverse device effects including failure modes by key term (including lead failure modes) occurring up to five years post-implant.

Secondary Objective # 4: Characterize atrial and ventricular lead impedance

7.3.3 Statistical Analysis Method & Sample Size Justification

This study is designed to confirm the safety performance of MRI exposed SureScan pacing systems, to monitor long term performance of the pacing system and to identify individual failure modes. Sample size determination must satisfy primary objective analysis requirements and provide reliable estimates on individual failure mode rates for the general population.

Sample sizes have been calculated for Primary Objectives #1, #2, #3, and for Secondary Objective #3. The overall enrollment for this study is driven by the objective requiring the largest sample size. For this study, the overall enrollment is driven by Primary Objective #1.

For Primary Objective #1, the MRI-related complication rate will be calculated by dividing the number of subjects with an MRI-related complication by the total number of subjects who experience at least one MRI scan. The Exact Binomial method will be used to calculate the 1-sided 95% confidence interval upper bound for the MRI related complication probability.

7.4 Data Collection

Electrical measurements and Adverse Device Effect event data collection will be completed via in-office visits every Data collection for subjects receiving an MRI include: electrical measurements pre and post scan (if a clinically significant difference between pre- and post-scan electrical measurements and/or an adverse event is observed, the subject is required to be seen by the cardiologist, recommended within 30 days of the MRI scan visit), MRI equipment and scan acquisition conditions (if MRI scan is at affiliated radiology clinic) and clinical implementation information. .

Data collection includes, but is not limited to, the following:

- Subject Baseline & Medical History (example: demographics, primary indication for implant, cardiovascular history)
- Implant Data (Implant date, device information, electrical measurements)
- Electrical Data (Sensing, Impedance and Threshold):
  Pacing Threshold Testing: Perform pacing threshold measurements for the atrium and ventricle using a pacing threshold test. It is recommended to conduct the test at a 0.4 ms pulse-width setting, and decreasing amplitude until capture is lost. The lowest amplitude where capture still consistently occurred is the pacing threshold value.

  Electrical data collection completed at:
  - Implant
  - Before and After MRI
  - Within one-month of MRI if there is a clinically significant change in the pre- and post electricals or an adverse event.
  - Follow-up visits throughout the 5-year study duration

- Adverse Device Effect and MRI status assessment via device interrogation. If there have been any unreported SureScan pacing system MRI-related adverse events since the last visit or any changes i.e. actions to previously reported events will be updated.

MRI Data Collection Includes but not limited to:

- Equipment and Scan acquisition condition data collection: Magnet field strength, specific absorption rate (SAR), peripheral nerve stimulation (PNS), scan duration, indication for scan, patient monitoring method during scan
- Clinical Implementation data: Pre-Scan activities, SureScan programming, MRI facility information, system MRI conditional verification.

8 Risk - Benefit

The Revo MRI SureScan pacing system provides pacing therapies and diagnostics which are currently available in other approved pacemaker systems. The design changes required to make this system MR Conditional do not alter pacing functionality or affect system reliability. The following factors were considered in determining that the Revo MRI SureScan pacing system has a highly favorable risk-benefit profile:

1. Allowing pacemaker patients access to MRI technology with the Revo MRI SureScan system will:
    - Enable patients to benefit from MRI's superior soft-tissue imaging capabilities instead of less specific or sensitive testing. Precluding patients from MRI access may lead to delayed diagnosis and decreased accuracy in diagnosis, ultimately impacting appropriate and timely treatment.
    - Eliminate risks associated with alternate procedures, such as ionizing radiation from CT scans or interventional diagnostic procedures.
2. Potential patient risk resulting from failure to follow labeling or other misuse in a market release environment.

Patients implanted with the Revo MRI SureScan pacing system will have access to MRI technology with the knowledge that the environment has been thoroughly characterized and the system designed and tested to demonstrate that the risks have been sufficiently mitigated. The rigorous pre-clinical and confirmatory clinical investigation provide the valid scientific evidence that demonstrates the Revo MRI SureScan Pacing System is safe and effective under the specified conditions of use in an MRI environment.

- The breadth and depth of the pre-clinical testing fully evaluated the potential patient hazards at environmental conditions (e.g., radiofrequency [RF] fields, gradient fields, and MRI exposure durations) beyond those that can be obtained using clinically available MRI scanners. In addition, the pre-clinical testing demonstrated safety and effectiveness for a wide range of system implant and patient anatomy configurations, beyond those reasonable, or even possible, to assess in a human clinical study.
- The prospective, randomized, controlled, global multi-center human clinical study was performed to confirm the results of the pre-clinical testing and to assess the clinical implementation and usability of the system. The human clinical study met all five primary safety and effectiveness objectives with no MRI related complications.

Medtronic has designed the system to mitigate risks associated with clinical implementation in a diverse market release environment. The Revo MRI SureScan pacing system is not unique among the broader category of implantable medical devices with MR- Conditional labeling (e.g., implantable loop recorders, stents, vagus nerve stimulators, and aneurysm clips), and specific care has been taken in designing a system that fits into current protocols in standard radiology and cardiology practices.

Medtronic has designed education and training tools to support the proper and safe use of the system. As with all medical devices, medical judgment still applies in the use of the system. With this system, clinicians will need to employ standard screening processes prior to scanning patients and appropriately program the system for each individual patient.

Foreseeable misuse scenarios related to the proposed labeling were evaluated as part of the development process. The most likely misuse conditions are performing scans in the chest region and at SAR levels above 2 W/kg. The preclinical analysis indicated that there would be an increase in the probability of seeing a measureable change in capture threshold. There would be no effect for most patients and only a small increase in threshold for some patients, which would have a minimal effect on pacing functionality and no impact on safety (as shown in Appendix 3, Section 3.10.) This demonstrates that there is minimal additional risk resulting from inappropriate application of the labeling.

Lastly, Medtronic is committed to monitoring the performance of the system using standard Medical Device Reporting (MDR) processes and by conducting a robust post-approval clinical study to evaluate product performance and reliability in the market release environment.

MRI is a valuable and powerful diagnostic tool and the benefit that the Revo MRI pacing system brings by allowing patients access to MRI technology is clear. Pacemaker patients will now be afforded the option of using MRI technology to make more accurate diagnosis of medical conditions possible. MRI offers important advantages over other imaging technologies, including the absence of ionizing radiation, superior soft-tissue resolution, and discrimination in any imaging plane.

The need for access to MRI is large and increasing due to the growth in the pacemaker population and the use of MRI to aid in the diagnosis and treatment of additional medical conditions. The Revo MRI SureScan Pacing System demonstrated safety, effectiveness and a low risk profile in extensive pre-clinical and human clinical evaluation, resulting in an overall highly favorable benefit to risk profile. Approval of this system will allow pacemaker patients to benefit from MRI technology and avoid unfavorable trade-offs in diagnostic imaging options in order to receive pacing therapy.

9 Summary and Conclusions

MRI is a powerful imaging tool for detecting and diagnosing abnormalities and diseases in soft tissue. However, pacemaker patients have not had access to MRI scans because of the potential safety concerns due to the interactions between pacemakers and the MRI environment. Thorough characterization and mitigation of potential safety risks are required to allow routine use of MRI scanning in a pacemaker patient population.

The Medtronic Revo MRI SureScan pacing system was designed to mitigate the risk due to potential hazardous interactions between the pacemaker and the MRI environment. The Medtronic Revo MRI SureScan pacing system was comprehensively tested at and beyond conditions typically found in the clinical environment. Bench testing, animal studies, computer simulations, as well as a clinical study all demonstrate that the Revo MRI SureScan pacing system, when used in accordance with the specified conditions of use, is immune to the MRI environment, thereby allowing pacemaker patients to be scanned safely.

In addition, Medtronic CRDM developed a clinical implementation program that fits into current protocols in standard radiology and cardiology practice, and which incorporates a number of tools designed to mitigate the risk due to potential errors or deviations from the labeling.

The thorough characterization of the Revo MRI SureScan pacing system demonstrates that it is safe and effective when used in accordance with the specified conditions of use as defined in the labeling. Given the low overall risk of the Revo MRI SureScan pacing system, it is apparent that the risk of denying a patient this treatment option becomes the critical issue. The lack of ability to scan a pacemaker patient is a currently unmet clinical need, and Medtronic CRDM firmly asserts that the Revo MRI SureScan pacing system mitigates potential hazardous interactions in the MRI environment and provides a medical benefit that outweighs the associated risks.

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Appendix 1 - Basic Pacing Information

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1.1. Introduction to Pacing

Note: This section describes pacing systems in general.

The first implantable cardiac pacemaker was introduced in 1958. It was a relatively simple device, designed to provide an electrical pulse to the right ventricle at a steady rate, approximately 72 beats per minute, in a patient diagnosed with symptomatic bradycardia.

Since then, pacemakers have evolved into sophisticated "mini-computers," capable of sensing and pacing in either or both chambers of the heart, providing patient diagnostics and device information to physicians, varying the patient's heart rate in response to activity and other physiological parameters, and allowing long-distance follow-up via the Internet.

The American Heart Association (AHA) and American College of Cardiology (ACC) have defined the indications for a pacemaker by the underlying arrhythmia, including: [1]

- Sinus node disease or sick sinus syndrome
- AV conduction disease / complete heart block
- Chronotropic incompetence
- Neurocardiogenic syndrome
- Chronic heart failure

Pacemakers are battery-powered, noninvasively programmable, and offer battery longevity of 5-10 years. Pacemakers are usually implanted subcutaneously in the pectoral region with the patient under conscious sedation or light anesthesia during an outpatient or overnight procedure.

Pacing leads -- thin insulated wires -- are inserted into a vein, implanted in one or more cardiac chambers and then connected to the pacemaker. An external programmer is used to adjust pacing parameters non-invasively. Single chamber pacemakers can pace and sense in either the atrium or ventricle. Dual chamber pacemakers pace and sense in both cardiac chambers. Because Revo MRI SureScan system is a dual pacemaker system, we will focus on this type of design. **Figure 1-1** shows a schematic diagram of dual chamber system.

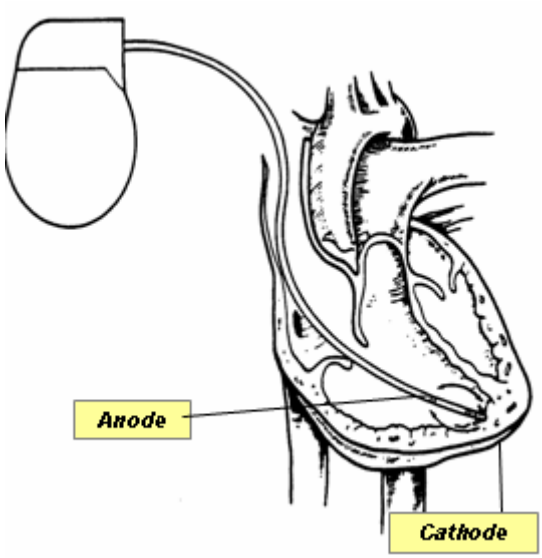

Figure 1-1. Dual Chamber Pacing Systems

1.1.1. Pacing System Components

Today's pacing system consists of an external programmer, the pacemaker (device), and one or more pacing leads.

Programmer

The external programmer resembles a laptop computer and is used to noninvasively adjust pacemaker parameters and functions and retrieve patient and device information from the pacing system. Communication between the pacemaker and the programmer is performed with a "programming head" via a radio frequency telemetry link.

Pacemaker

The pacemaker is about the size of a pocket watch and includes:

- A battery (power source)
- Hybrid circuitry microprocessor that controls sensing, output, telemetry, and diagnostic circuits
- A device connector (where pacing leads are inserted)

The battery and circuitry are hermetically sealed within a titanium case. **Figure 1-2** shows a schematic diagram of a pacing system, including the pacemaker and leads.

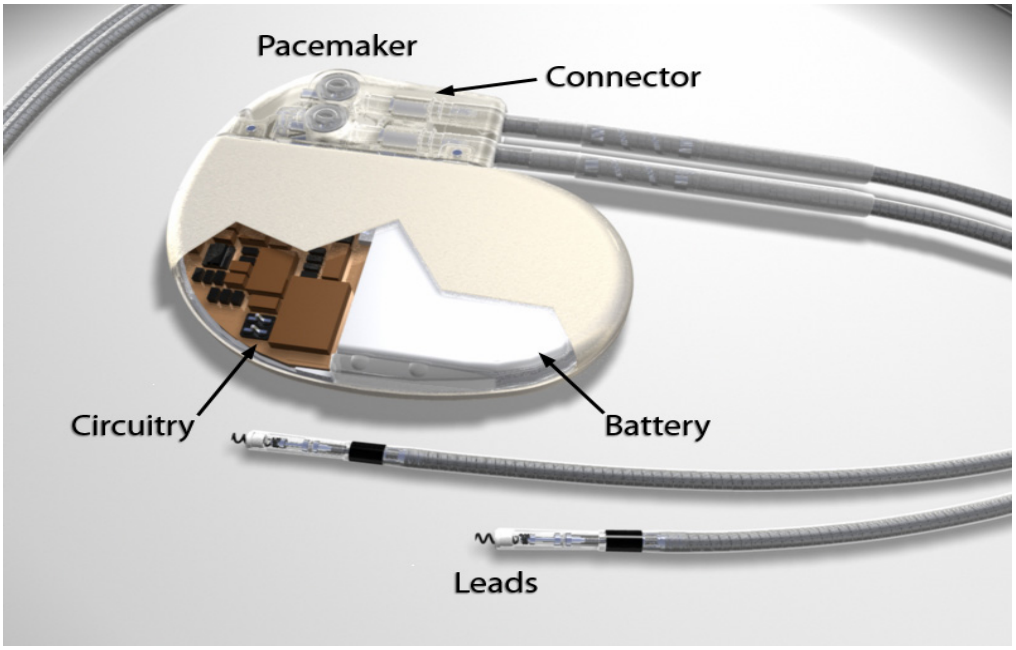

Figure 1-2. Schematic Diagram of Pacing System

Pacing leads deliver electrical impulses from the pacemaker to the heart. Leads also are designed to sense intrinsic cardiac activity and relay this information back to the pacemaker. Pacing leads are usually inserted transvenously through the subclavian or cephalic vein.

A pacing lead (**Figure 1-3**) consists of:

- **Conductor coils:** The coils conduct the electrical current between the pacemaker and heart tissue. A common conductor material is MP35N (a nickel alloy) because it has good conductivity, corrosion resistant, and mechanical properties.
- **Insulation:** Non-conducting insulation material protects the conductor from exposure to body tissue and fluids. Insulation is typically made of silicone or polyurethane.
- **Electrodes:** Electrodes are small metallic components at or near the lead tip that contact the cardiac tissue. Intrinsic cardiac activity is sensed at the electrodes, and the pacing pulses are delivered to the tissue through the electrodes.
- **Fixation mechanism:** Active-Fix: The lead tip is fixated into the endocardial cardiac tissue via a retractable helix (active fixation) which allows lead positioning anywhere in the heart's chamber as compared to a passive-fix lead which has soft pliable tines which lodges in the traveculae (fibrous meshwork) to help secure the lead in cardiac tissue.
- **Connector pin:** Connector pins on the leads are inserted into the device connector of the pacemaker to complete the conduction pathway.

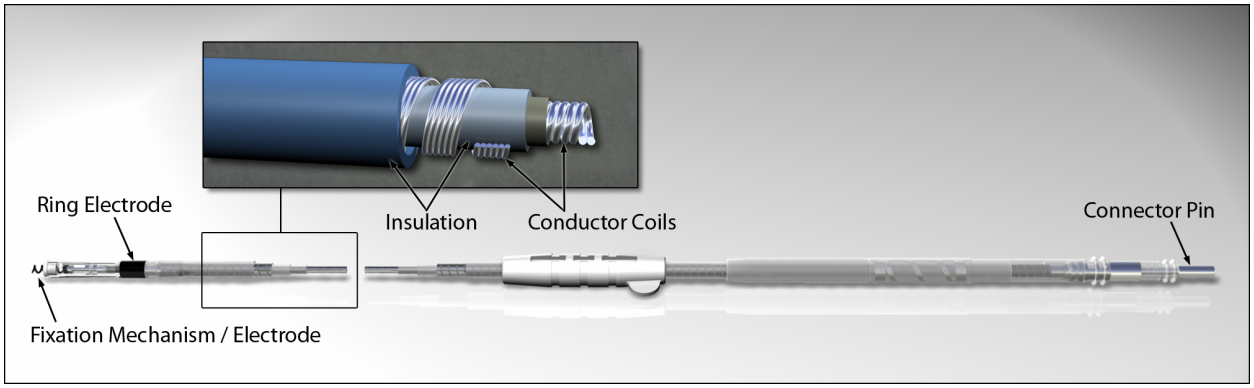

Figure 1-3. Components of an Active Fixation Pacing Lead

Lead Maturation Process

When the pacing electrode comes into contact with the blood pool in cardiac tissue, the inflammatory system is activated in response to a foreign substance in the body.

In the chronic inflammatory phase, fibrous tissue develops around the electrode, creating a layer of "scar" tissue that increases the distance between the electrode and excitable cardiac tissue. This fibrotic build-up may result in the need to adjust pacemaker parameters to maintain an adequate pacing capture threshold (PCT).

Steroid Elution

Pacing leads often contain minute doses of a steroid at the lead tip which is eluted into cardiac tissue to reduce tissue inflammation and fibrosis that may occur at the electrode-tissue interface after implant. Steroid eluting leads reduce the inflammatory process and thus exhibit little to no acute stimulation threshold peaking and low chronic thresholds

1.1.2. Pacemaker Operation and Electrical Parameters

Understanding pacemaker operation depends on understanding how an electrical circuit is created between the pacing system components.

In every electrical circuit, the current must flow in a closed-loop path between a positive pole (the anode) and a negative pole (the cathode) through conductive material. In a pacing system, the circuit consists of the pacemaker, the pacing lead, and heart tissue. In a bipolar system, the tip electrode is the cathode, and a second, small metal ring electrode near the tip electrode serves as the anode (**Figure 1-1**).

Pacing occurs when the pacemaker sends an electrical pulse through the lead and to the heart, causing the heart to beat (called "capture"). The pulse then returns to the pacemaker, completing the circuit.

A pacing circuit can be defined in terms of voltage, current, and impedance:

Voltage (V) – is the force or "push" that causes current to move through a circuit. Voltage is measured in volts (V). Voltage reflects the strength or intensity of a pacing pulse.

Current (I) – is the movement of electrons through a circuit over time. In a pacing system, current is measured in milliamps (mA).

Impedance (R) – is the sum of all the factors that resist the flow of current. The main sources of impedance in a pacing circuit are the lead conductor(s), electrode(s), and the electrode-tissue interface. Impedance is measured in ohms (Ω).

Pacing Capture Threshold

Pacing capture threshold (PCT) is defined as the minimum electrical pulse needed to consistently capture the heart (reference **Figure 1-4**). PCT is a function of:

- **Amplitude (V):** The strength of the impulse must be large enough to achieve capture.
- **Pulse width:** The duration of the current flow, expressed in milliseconds (ms), must be long enough to achieve capture.

Amplitude and pulse width are interrelated. When making programming decisions, clinicians must always balance amplitude and pulse width to ensure capture, while also optimizing pacemaker longevity. An increase in either the amplitude or the pulse width will reduce battery longevity.

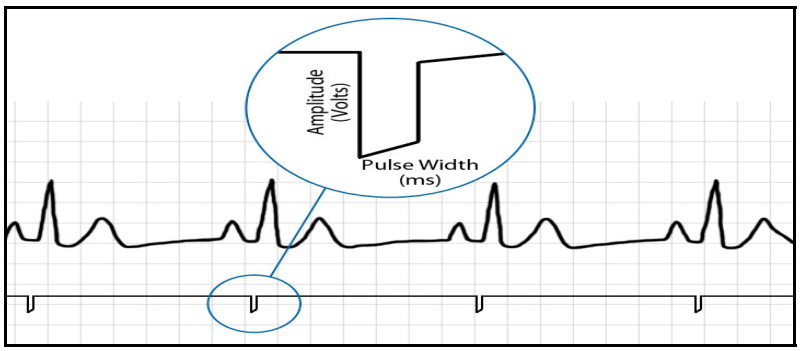

Figure 1-4. Relationship Between Pulse Width and Pacemaker Amplitude. A Pacing Pulse to the Ventricle Is Depicted in This Example

Strength-Duration Curve

The strength-duration curve is used to determine the patient's stimulation threshold. The strength-duration curve shows the lowest combinations of pulse amplitude and pulse width that capture the patient's heart (**Figure 1-5**).

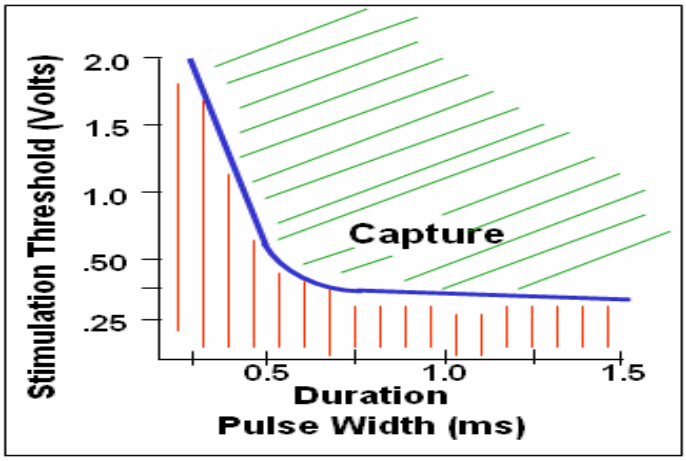

Figure 1-5. Strength Duration Curve

A safety margin is added to the stimulation threshold to prevent loss of capture due to threshold variations.

After pacemaker implantation, the stimulation threshold rises, peaks (acute phase), and then settles into a stable pattern (chronic phase). The stable threshold *or chronic threshold* is achieved three to six weeks after implant.

A typical example of the pacing capture threshold over time is illustrated in **Figure 1-6**. To cope with acute and chronic thresholds variations, the output pulse is programmed with a *safety margin*. A 3:1 safety margin is usually needed immediately after implantation and a 2:1 safety margin is used when the threshold stabilizes (chronic phase).

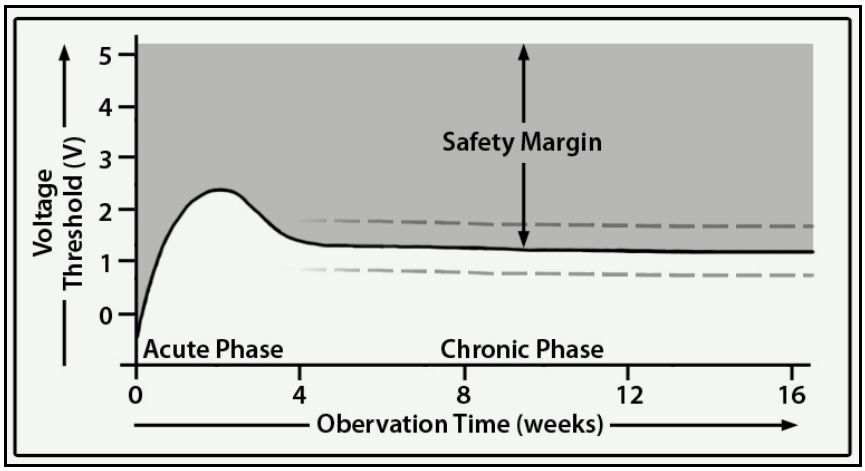

Figure 1-6. Pacemaker Safety Margin

Also, a patient with an acute pacing system will typically be programmed to a setting allowing a higher safety margin, due to the lead maturation process, which can occur within the first 6-8 weeks following implant.

Pacemaker Sensing

Sensing is the ability of the pacemaker to recognize an electrical signal on its leads. Appropriate sensing helps to ensure that appropriately timed pacing pulses are delivered in the absence of intrinsic activity, and inhibited when the heart is beating on its own.

To sense, the pacemaker uses the same electrodes it uses to pace. The intrinsic intracardiac signal is transmitted to a sensing circuit in the device. There, signals are processed and compared with the programmed sensing threshold.

Under sensing (the failure of the sensing circuit to detect intrinsic activity) can lead to competitive pacing, a condition in which the pacemaker competes with the heart by delivering an unnecessary pacing impulse.

Over sensing is the sensing of events other than intrinsic activity and may result in the inappropriate delay or inhibition of a pacing pulse. One example of over sensing is the sensing of muscle signals (called myopotentials) that originate from the depolarization of muscles near the heart or pacemaker.

1.1.3. Physiological Effect on Pacing Parameters

Among many other diagnostic functions, pacemakers can monitor and notify the clinician on lead integrity (pacing impedance), sensed electrical signals from the heart, and PCT. The significance of these parameters and their sensitivity to change are important when trying to discern changes that are occurring in the heart and pacing system.

Pacing Lead Impedance

Pacing lead impedance provides information about the integrity of the lead and the lead-pacemaker connection, as well as information about the physiological environment in the vicinity of the electrodes. One of the challenges of using pacing lead impedance for diagnostic purposes is that it can fluctuate under normal conditions for a variety of reasons, such as:

- Body motion, body position, and respiration.
- Variations in impedance between blood and myocardium, changes in cardiac wall tension, and orientation of the blood cells influenced by laminar flow.
- Disturbances at the microscopic electrode-electrolyte surface.[2]

Therefore, it is important to focus on relative trends in lead impedance rather than relying on absolute values for diagnostic purposes.

Sensing

The heart's electrical signals are sensed between the anode and cathode (in a bipolar pacing system the tip and ring electrodes). The sensed waveform depends on the viability of 1-2 cm^3 of myocardium around the electrodes. Additionally, the signal includes the "far field depolarization" of myocardium at distances greater than 1-2 cm^3. Therefore, the sensed signal reflects tissue changes directly under the electrodes, along with changes that occur over a much larger volume of tissue within the cardiac chamber.

Pacing Capture Threshold

Pacing capture threshold (PCT) reflects the status of the tissue directly in contact with the electrode (e.g., scar tissue, cardiac myocytes, etc.), and is sensitive to changes in the tip-tissue interface and surrounding cardiac tissue.[3, 4, 5, 6] Clinical factors that affect PCT include proximity of the electrode to the myocardium, pathology of the underlying cardiac tissue, size and shape of the electrode, and the effects of drugs, hormones, and electrolytes on the underlying cardiac tissue. Therefore, PCT is a reflection of the tissue directly beneath the electrode and is not confounded by other, global, variables.

Figure 1-7 shows the influence of right ventricular tissues on pacing electrical parameters. PCT is shown in blue (inset), and reflects only the tissue in the immediate vicinity of the tip helix. Sensing is shown in yellow, and reflects the tissue beneath the helix, as well as tissue far from the helix. Pacing impedance is shown in red, and reflects both the blood impedance, as well as the tissue impedance.

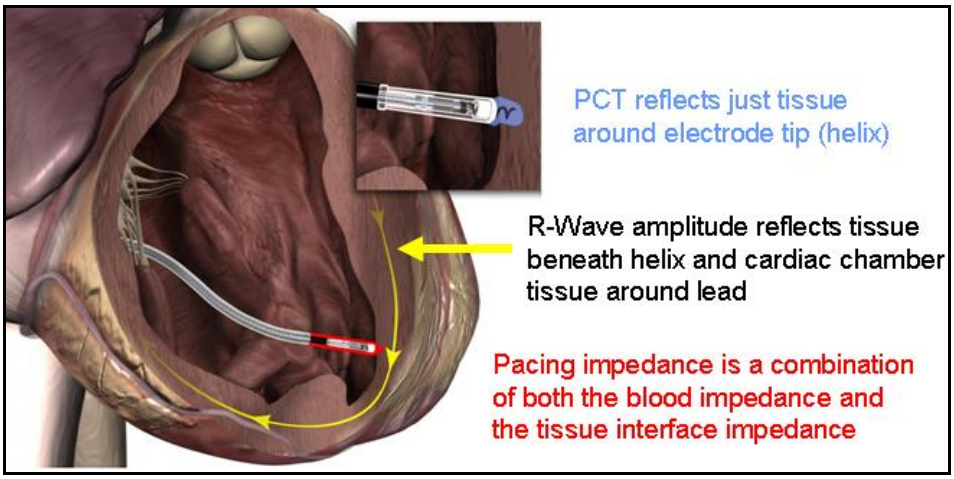

Figure 1-7. Right Ventricular Tissue Influence on Pacing Electrical Parameters

1.1.4. Pacing Modes

- Pacemaker modes define the capabilities and actions of a specific pacemaker model. The standard NBG (NASPE/BPEG)[7] Code is used as a shorthand for mode identification.

Table 1-1 defines the various codes.

Table 1-1. NBG Code for Pacing Mode

Position I	Position II	Position III
Chamber(s) Paced	**Chamber(s) Sensed**	**Response to Sensing**
O = None **A** = Atrium **V** = Ventricle **D** = Dual (A + V)	**O** = None **A** = Atrium **V** = Ventricle **D** = Dual (A + V)	**O** = None **T** = Triggered **I** = Inhibited **D** = Dual (T + I)

Position I: the chamber(s) paced. Pacing can occur in the atrium (A), ventricle (V), or both chambers (D for dual).

Position II: the chamber(s) sensed.

Position III: what the pacemaker's response is to sensed intrinsic signals (trigger: pace, inhibit: do not pace).

Synchronous Pacing

The most common pacing modes in clinical practice today are synchronous pacing modes (modes in which the pacemaker senses the cardiac signal and responds accordingly): DDD, DDD, DDI, VVI, VVI, and AAI. The selection of a pacing mode for an individual patient depends on the arrhythmia being treated, the patient's medical and physical status, and other factors.

Asynchronous Pacing

In asynchronous pacing, there is no sensing of, or response to, intrinsic cardiac events. The pacemaker paces at a programmed fixed rate, independent of any underlying cardiac rhythm. Examples of asynchronous modes are AOO, VOO, and DOO. Asynchronous pacing is used to manage patients during medical/surgical procedures when they require pacing support. Asynchronous pacing minimizes the chance that the patient's device may sense signals other than intrinsic cardiac events, which could lead to inappropriate pacemaker inhibition or pacing.

1.1.5. Pacemaker Standards

Per industry standards, today's pacemakers are designed, qualified, and manufactured in accordance with well established and recognized standards for safety, electromagnetic compatibility, biological testing, labeling, etc.

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Appendix 2 - Basic MRI Information

Appendix 2 - Basic MRI Information

2.1. Introduction to MRI

Magnetic resonance imaging (MRI) is an imaging tool used to diagnose and/or examine a wide range of disease conditions and internal body structures. This noninvasive technology provides soft tissue imaging with spatial resolution and multiplanar three-dimensional analysis. With MRI scanning, patients avoid exposure to ionizing radiation[1]. MRI scanners use static, gradient, and radio frequency (RF) magnetic fields to form images of parts of the human body.

MRI systems are differentiated based on the strength of the static magnetic field they produce, measured in units of Tesla (T). MRI equipment used in today's clinical settings have static magnetic field strengths ranging from less than 1.0 T to 3.0 T, with the majority of MRI systems at 1.5 T, commonly called "1.5 T MRI scanners[2]."

2.1.1. Electromagnetic Fields

Variations in strength of electromagnetic fields in the MRI environment depend on the manufacturer and model of the MRI scanner. These variations must be characterized and understood in order to fully evaluate potential risks associated with MRI/pacemaker interactions.

MRIs use three different types of magnetic fields to produce an image:

- Static magnetic field
- Gradient magnetic fields
- Radiofrequency (RF) field

Static Magnetic Field

The static magnetic field strength in an MRI scanner is produced by magnets surrounding a tube-shaped scanner "bore" where the patient is placed for imaging (**Figure 2-1**). The static magnetic field aligns the magnetic dipoles produced by spinning protons in the body's hydrogen atoms.

The static magnetic field for a 1.5 T MRI system is approximately 30,000 times stronger than the earth's magnetic field.[3] To put this into perspective, an adult using both hands cannot easily hold a pair of standard ferromagnetic pliers near the opening of the scanner bore without having them pulled into the scanner.

Figure 2-1. A Typical 1.5 T MRI System.
Note the Cylindrical Bore the Patient Enters for Scanning

The center of the bore, both longitudinally (along the length of the bore) and transversely (across the diameter of the bore), is known as the "isocenter." (**Figure 2-2)**.

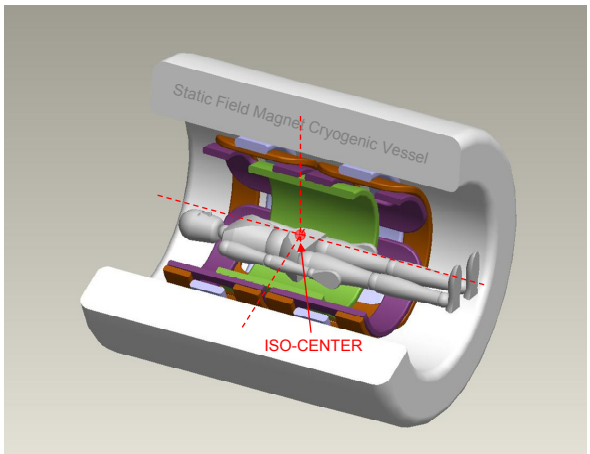

Figure 2-2. A Patient within the Bore of an MRI Scanner.
The Red Dot Represents the Isocenter of the Scanner

Gradient Magnetic Fields

Gradient magnetic fields are used to select the location and orientation of the image plane or "slice" through the patient's anatomy. Three independent gradient magnetic fields are active during MRI set-up (pre-scan) and image acquisition. When active, the gradient fields are pulsed on and off at a rapid rate, typically hundreds or thousands of times per second.

A variety of gradient pulse sequences is used for different imaging applications. A gradient pulse sequence may also be modified to optimize slice thickness, image resolution, and other imaging parameters.

Gradient magnetic field characteristics can be described and quantified by amplitude, slew rate, and duty cycle.

Gradient Amplitude
Gradient amplitude, referring to the spatial variation of the gradient field, is measured in units of milli-Tesla per meter (mT/m). The maximum gradient amplitude capability of 1.5 T MRI scanners ranges from approximately 10 to 100 mT/m. In general, larger gradient amplitudes provide higher image resolution.

Gradient Slew Rate
The gradient slew rate defines the rate at which the gradient fields can change when adjusting from one gradient amplitude to another (e.g., from zero to maximum gradient amplitude), and is measured in units of Tesla per meter per second (T/m/s). In general, larger gradient slew rates allow faster image acquisition.

The maximum gradient slew rate capability of 1.5 T MRI scanners ranges from approximately 30 to 200 T/m/s. Patient physiological considerations limit the maximum allowable gradient slew rate.

Gradient Pulse Sequence
The gradient pulse sequence is characterized by the repetition rate, gradient pulse amplitude, gradient slew rate, and other parameters.

dB/dt
Magnetic field rate of change with time (units of T/s). This term will be used frequently in discussion about gradient field interaction with pacemaker systems.

Any significant variations in gradient magnetic field characteristics in 1.5 T MRI scanners will be caused by the maximum amplitude and slew rate of a specific gradient system and to the pulse sequence being used to acquire the image.

RF Field

MRI scanners apply a pulsed RF magnetic field in order to change the alignment of the magnetic fields of protons relative to the static magnetic field. Energy absorbed by the protons during the RF pulse is released in the form of RF electromagnetic radiation, which is received by the MRI system and processed to obtain a diagnostic image.

The frequency of RF energy radiated by a 1.5 T MRI scanner is approximately 64 MHz (64 million cycles per second).[4] Some of this RF energy is absorbed in the patient's body tissues as heat. The measure of the absorption of this energy in the body is indicated by the specific absorption rate (SAR), measured in watts per kilogram (W/kg).

The RF field is active during image set-up and image acquisition. When active, the RF field is pulsed on and off at a rapid rate, typically hundreds of times per second.

Significant variations in the RF field environment will be caused by the pulse sequence being used to acquire the image, the choice and characteristics of the RF coil being used to transmit the RF power into the patient, the portion of the patient's anatomy being imaged, and the patient's size and shape. Each of these factors can affect the peak and average strength of the RF magnetic field, and the amount of RF energy absorbed by the body.

2.1.2. Applicable MRI Equipment Standards

All MRI equipment manufacturers design and test their systems to meet the requirements defined in IEC 60601-2-33 "Particular Requirements for the Safety of Magnetic Resonance Equipment for Medical Diagnosis." The IEC standard takes a three-tier approach to controlling patient exposure to gradient and RF fields that may cause different levels of physiological stress to patients undergoing an MRI scan. This list highlights key points and is not intended to be an exhaustive description:

Normal Operating Mode: routine patient monitoring. The MRI equipment has no outputs with a value that may cause physiological stress to the patient.

First Level Controlled Operating Mode: One or more outputs from the MRI equipment may reach a value that may cause physiological stress to patients; needs medical supervision.

Second Level Controlled Operating Mode: One or more outputs from MRI equipment may produce significant risk for patients; explicit ethical approval is required before proceeding.

MRI equipment standards include but are not limited to the following:

Document Number	Title
IEC 60601-2-33	Particular requirements for the safety of magnetic resonance equipment for medical diagnosis
ASTM F2052	Standard Test Method for Measurement of Magnetically Induced Displacement Force on Medical Devices in the Magnetic Resonance Environment
ASTM F2213	Standard Test Method for Measurement of Magnetically Induced Torque on Medical Devices in the Magnetic Resonance Environment
ASTM F2182	Standard Test Method for Measurement of Radio Frequency Induced Heating Near Passive Implants During Magnetic Resonance Imaging
ASTM F2503	Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment

[1] Semelka RC, et al. Imaging Strategies to Reduce the Risk of Radiation in CT Studies, Including Selective Substitution With MRI. Journal of Magnetic Resonance Imaging 2007; 25:900-909.
[2] IMV, "Benchmark Report: MRI 2007," IMV Medical Information Division 2008.
[3] Duru F, et al, Pacing in magnetic resonance imaging environment: Clinical and technical considerations on compatibility. European Heart Journal 2001; 22:113-124.
[4] Duru F, et al. Pacing in magnetic resonance imaging environment: Clinical and technical considerations on compatibility. European Heart Journal 2001; 22: 113-124.

Appendix 3 -
Pre-Clinical Evaluation

Appendix 3 - Pre-Clinical Evaluation

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Appendix 4 -
Confirm. Clin. Study

Appendix 4 - Confirmatory Clinical Study Summary

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4.1. Purpose

The purpose of the EnRhythm MRI SureScan pacing system study was to confirm the results of earlier pre-clinical bench and animal testing, which indicated that the investigational SureScan pacing system was safe and effective for human use in the MRI environment in the specified conditions of use.

Note that after completion of the clinical study enrollments, the EnRhythm MRI SureScan pacing system was renamed the "Revo MRI SureScan Pacing System." This name change is reflected throughout the main document, except in this clinical section where it is referred to as the EnRhythm MRI system, as this is the nomenclature used during the clinical study.

4.2. Design

The confirmatory clinical study was a prospective, randomized, controlled, unblinded, global multi-center investigational study.

All subjects followed the clinical Investigational Plan (CIP) following approval by an Institutional Review Board (IRB) or Medical Ethics Committee (MEC). A multi-center design was used because it ensured a representative sample of the population as well as a reasonable enrollment period. Randomization of subjects to control (no MRI) and MRI groups was used to provide treatment effect information. The study was initiated with subjects randomized in a 1:1 ratio to the MRI group or to the control group. Subsequently, the FDA requested a minimum of 200 subjects to undergo an MRI scan. The randomization ratio was then adjusted to a 2:1 ratio (MRI group: control group) in order to facilitate new sample size requirements for the MRI group.

Up to 470 subjects were planned for implant and follow-up. Enrollment began February 2007 and the last subject was enrolled July 2008. Study subjects from all geographies will be followed until approval is granted from the FDA or official study closure, whichever is first. At

the time of database closure for report analysis, subjects were followed through November 2008 for an average of 11.2 months, with some subjects implanted for as long as 21.5 months. The results presented in this clinical summary were submitted to the FDA on 05 June 2009 in the clinical report in support of Pre Market Application version 1, dated 17 March 2009.

The clinical study had external oversight from the Data Monitoring Committee, Adverse Event Committee and Scan Advisory Committee. See **Table 4-1** for committee, membership and purpose.

Table 4-1. External Committees

External Oversight		
Committee	Membership	Purpose
Data Monitoring Committee (DMC)	• U.S. membership. • Represented cardiology, radiology and statistics. • Three non-Medtronic-employed members. • Members were not associated with study centers.	• Review aggregate safety and effectiveness data. • Responsible for safeguarding interests of subjects. • Oversight of conduct of study.
Adverse Event Advisory Committee (AEAC)	• Global membership: U.S., Canada, and Europe. • Represented cardiology and radiology. • Seven non-Medtronic-employed physicians (5 study investigators, 2 non-study investigators).	• Review all adverse events, including deaths and technical observations and determine relatedness.
Scan Advisory Committee (SAC)	• Global membership: US and Europe. • Represented MRI systems from three manufacturers used in the study. • Five non-Medtronic-employed physicians/physicists (5 study investigators).	• Developed prescribed MRI scan sequences. • Review all MRI data from subject scans.

The Data Monitoring Committee met on 21 March 2009 to review the Clinical Report in Support of Pre-Market Approval, Version 1, dated 17 March 2009. Following this final DMC meeting, the DMC chair wrote on behalf of the board, “We concur that the study met its objectives”.

4.3. Methods

Patients who met all inclusion and no exclusion criteria were eligible. Enrollment was defined as the time at which a patient signed and dated the informed consent form. The baseline visit confirmed eligibility, as well as collection of demographic and cardiovascular history data. Inclusion and exclusion criteria are described in **Table 4-2**.

Table 4-2. Study Inclusion/Exclusion Criteria

Inclusion criteria
Subjects who had a Class I or II indication for implantation of a dual chamber pacemaker according to the ACC/AHA/NASPE guidelines.[1]
Subjects had to be able to undergo a pectoral implant.
Subjects who were able and willing to undergo elective MRI scanning without sedation.
Subjects who were geographically stable and available for follow-up at the study center for the length of the study.
Exclusion criteria
Subjects with a mechanical tricuspid heart valve.
Subjects with a history of tricuspid valvular disease.
Subjects who had a previously implanted pacemaker or implantable cardioverter defibrillator (ICD) (abandoned pacemaker and/or defibrillator leads not permitted; however, subjects with complete system explants were not excluded).
Subjects who were immediate candidates for an ICD.
Subjects currently indicated or expected to be indicated for another MRI scan procedure other than those specifically described in the study during the period of required study follow-up.
Subjects with previously implanted active medical devices.
Subjects with non-MRI compatible device (such as ICDs or neurostimulators) or material implant (e.g., non-MRI compatible sternal wires, neurostimulator, biostimulator, metals, or alloys).
Pregnant women, or women of child bearing potential and who were not on a reliable form of birth control.[2]
Subjects with exclusion criteria required by local law (e.g. age, breastfeeding).
Subjects who required a legally authorized representative to obtain consent.
Subjects for whom a single dose of 1.0 mg dexamethasone acetate might be contraindicated.

4.3.1. Statistical Methods

The primary and secondary safety and effectiveness objectives in the clinical study are stated below. Study success required all five safety and effectiveness results to be met.

Safety (MRI group only)

- MRI procedure-related complication-free rate

Effectiveness (MRI group vs. control group)

- Atrial pacing capture thresholds
- Ventricular pacing capture thresholds
- Atrial sensed amplitudes
- Ventricular sensed amplitudes

Safety and Effectiveness Objectives
Primary Safety Objective:

Hypothesis

The MRI-related complication-free rate between the MRI procedure and one month post-MRI is greater than 90%.

H_0: MRI-related complication-free rate ≤ 0.90

H_a: MRI-related complication-free rate > 0.90

Analysis Methods
The objective was evaluated using a one-sided one-sample exact test of binomial proportions along with a one-sided 97.5% confidence interval.

Subjects randomized to the MRI group who underwent MRI scans per protocol design and had completed their one-month post-MRI follow-up, or had an MRI-related complication before the end of the follow-up date were included in the analysis.

Sample Size
Assumptions used were:

- alpha, the Type I error rate, was 0.025.
- Power, 1-beta, was 90%.
- The assumed true proportion of success was 0.975.

Based on the above assumptions, 114 MRI group subjects were needed.

Primary Effectiveness Objective #1: Pacing Capture Threshold (Atrial and Ventricular)

Hypothesis (same hypothesis for both atrial and ventricular endpoints)

H_0: | MRI group success rate - Control group success rate | ≥ 10%

H_a: | MRI group success rate - Control group success rate | < 10%

Each subject had pacing capture thresholds (atrial and ventricular) measured just prior to the MRI scan (or control) 9-12 week visit. Pacing capture thresholds were also measured one month after the MRI (or control) visit. If the change in pacing capture threshold between these two visits was less than or equal to 0.5 V, the subject was considered a success.

Analysis Methods
This objective was evaluated using a two-sample one-sided 97.5% confidence interval for proportions. The Farrington-Manning test for statistical equivalence of proportions was used to calculate the p-value.

Only subjects with measured threshold values at 0.5 ms were used in this analysis. Pre-defined exclusions from this analysis included; subjects whose scans were deemed not performed according to the protocol by the scan advisory committee, subjects with atrial arrhythmias at either time (atrial endpoint only), subjects with lead dislodgments, subjects with no printed threshold testing strips, and subjects with a pacing threshold difference exceeding 0.5 V between the two-month and the 9-12 week post-implant (pre-MRI/control) since such short-term variability in pacing performance can be indicative of an abnormal lead/tissue interface.

Sample size
Assumptions used (for both atrial and ventricular capture thresholds) were:

- The expected proportion of successes was 0.96 in both the MRI and control groups.
- alpha, the Type I error rate, was 0.025.
- Power, 1-beta, was 80%.

Based on the above assumptions, 89 MRI subjects and 89 control group subjects were required.

Primary Effectiveness Objective #2: Sensed Amplitudes (Atrial and Ventricular)

Hypothesis (same hypothesis for both atrial and ventricular endpoints)

H_0: | MRI group success rate - Control group success rate | ≥ 10%

H_a: | MRI group success rate - Control group success rate | < 10%

Each subject had sensed amplitudes (atrial and ventricular) measured just prior to the MRI scan or control 9-12 week visit. Sensed amplitudes were also measured one-month after the MRI or control visit.

For atrial sensed amplitudes, a success was declared if the sensed amplitude one-month post-MRI/control remained above 1.5 mV and above 50% of the pre-MRI/control sensed amplitude.

For ventricular sensed amplitudes, a success was declared if the sensed amplitude one-month post-MRI/control remained above 5.0 mV and above 50% of the pre-MRI/control sensed amplitude.

Analysis Methods
This objective was evaluated using a two-sample one-sided 97.5% confidence interval for proportions. The Farrington-Manning test for statistical equivalence of proportions provides a p-value from the test statistic.

Pre-defined exclusions from this analysis included: subjects whose scans were deemed not performed according to the protocol by the scan advisory committee, subjects with atrial arrhythmias at either time (atrial endpoint only), subjects with pre-MRI/waiting period sensed amplitudes less than 5.0 mV in the ventricle or less than 1.5 mV in the atrium; and subjects with a pacing threshold difference exceeding 0.5V between the two-month and the 9-12 week post-implant (pre-MRI/control) visit (since such short-term variability in pacing performance can be indicative of an abnormal lead/tissue interface).

Sample size
Assumptions used (for both atrial and ventricular capture thresholds) were:

- The expected proportion of successes was 0.93 in both the MRI and control groups.
- alpha, the Type I error rate, was 0.025.
- Power, 1-beta, was 80%.

Based on the above assumptions, 122 MRI subjects and 122 control group subjects were required.

Sample Size Summary

The largest number required to meet each of the endpoints was 122 MRI group subjects and 122 control group subjects. With an estimated 25% of subjects lost for attrition or indeterminate tests, and in order to enroll a sufficient number of subjects such that at least 200 subjects with MR scans would be included in the study, up to 470 subjects were planned for implantation in the study.

Secondary Objectives
A statistical test was performed for the following 3 secondary objectives:

Secondary Objective #1: Pacing System-Related Complications: H_0: $p \leq 80\%$, evaluated using a one-sided one-sample exact test of binomial proportions along with a one-sided 95% confidence interval. As pre-specified, all subjects implanted with the EnRhythm MRI SureScan Pacing System who had four-month post-implant follow-up visits, or a complication before the end of the 4 month post-implant follow-up date were included.

Secondary Objective #6: Lead Handling: H_0: Mean (5076) – Mean (5086) $\geq$ 1.5, A two-sample t-test for clinical equivalence was used to calculate the p-value.

Secondary Objective #7: Lead Performance: pacing threshold tests H_0: Mean (5086) – Mean (5076) $\geq$ 0.5V, sensed amplitude tests H_0: Mean (5076) – Mean (5086) > Δ, where Δ is 0.9mV for atrial sensed amplitude, and 2.5mV for ventricular sensed amplitude. A two-sample t-test for clinical equivalence was used to calculate the p-value.

4.3.2. MR Scanning Methods

Scan sequences were designed with guidance of an external scan advisory committee. See **Table 4-1** for scan advisory committee details. The 14 head and lumber scan sequences were defined with the following objectives:

- Maximize gradient field interaction with the implanted system
- Maximize RF field interaction with the implanted system
- Sequences should be clinically relevant or a modification thereof
- Total scan duration should be 30 minutes

The prescribed MRI scan procedure was performed on 1.5T MRI systems from one of three MRI manufacturers (General Electric, Philips, and Siemens). Each subject randomized to the MRI group was assigned to one MRI scan procedure. Each subject randomized to the MRI group was subjected to one MRI scan procedure, which included 14 head and lumbar spine sequences.

Interactions with the gradient magnetic field were maximized by choosing clinically relevant sequences as a base, typically using Echo Planar Imaging (EPI) techniques. Sequence parameters were then modified, as per the protocol, beyond what would be optimal in clinical imaging, to maximize interactions. This was done by minimizing the dimension of the slice thickness and field of view, ensuring that each gradient function was operating on the worst case gradient axis[1], and by increasing the number of slices to extend the scan time.

To maximize the interaction between the implanted system and the RF field the sequence parameters were modified such that the whole body SAR was near or equal to 2 W/kg without exceeding. The majority of the RF intensive scan sequences used a variation of Fast Spin Echo (FSE, also known as rapid acquisition with relaxation enhancement, RARE, or Turbo Spin Echo, TSE). The sequence parameters were then modified to increase the number of RF pulses per unit time by decrease TE and TR, maximize the energy within each RF pulse by increasing the flip angle, and extending the scan time by increasing the number of slices.

The 14 head and lumber sequences performed a total study time of approximately 60 minutes, 30 minutes consisting of imaging. Scan sequences can be found in **Table 4-3**.

[1] The gradient magnetic field is produced by three coils: X, Y, and Z. Each coil produces a unique spatially varying magnetic field. The hazards identified in section X are worse when the implanted system interacts with the Y gradient.

Table 4-3. Scan Sequences

Location	Scan sequence
brain	3D Plane Loc
brain	SAG FSE T1
brain	AX FSE T2
brain	AX FSE T2 Flair
brain	AX Diffusion EPI
brain	AX 3D TOF MRA
brain	COR 3D Bolus MRA
brain	AX Perfusion EPI
lumbar	3 Plane Loc
lumbar	SAG FSE T1
lumbar	SAG FSE T2
lumbar	AX FSE T1
lumbar	AX FSE T2
lumbar	SAG Diffusion EPI

4.3.3. Visit Schedule

Table 4-4. Visit Schedule

Visit	Time	Procedure
1	Baseline	Enrollment, informed consent, eligibility
2	Implant	Implant, randomization
3	2 month post-implant	Follow up; pacemaker measurements
4	9-12 weeks post-implant	MRI scan/control waiting period follow-up; pre-post pacemaker measurements
5	1 week post 9-12 weeks (3 months post-implant)	Follow-up; pacemaker measurements
6	1 month post 9-12 weeks (4 months post-implant)	Follow-up; pacemaker measurements
7	6 months post-implant	Follow-up; pacemaker measurements
	Every 6 months post-implant thereafter	Follow-up; pacemaker measurements

Data collected at all follow-up visits included adverse event assessment, system modifications, study exits and deaths. All follow-up visits consisted of pacemaker measurements, which included evaluation of pacing capture threshold at a pulse duration of 0.5ms, sensed electrogram amplitude and lead impedance.

Visit 1 - Baseline
Confirmed eligibility, as well as collection of demographic and cardiovascular history data.

Visit 2 - Implant
After a successful implantation of the EnRhythm MRI SureScan pacemaker Model EMDR01 and CapSureFix MRI SureScan Model 5086MRI leads (right atrial and right ventricular), randomization was performed to either undergo an MRI scan (MRI group) or not to undergo an MRI scan (Control group).

Visit 3 – 2 months post implant
All subjects underwent pacemaker measurements, which included evaluation of pacing capture threshold, sensed electrogram amplitude and lead impedance.

Visit 4 – 9-12 weeks post implant (MRI scan visit for MRI group patients)
All subjects underwent pacemaker measurements at two time points, which included assessment of pacing capture threshold, sensed electrogram amplitude, and lead impedance. The MRI group underwent pacemaker measurements immediately before the MRI (pre-MRI) and directly after the MRI (post-MRI), while the control group underwent pacemaker measurements at corresponding time points (i.e., pre-waiting period and post-waiting period, respectively). Adverse events were evaluated, including sustained ventricular arrhythmias, asystole and pacemaker function during and after the MRI scan. Unique to each randomization assignment were the following procedures at this visit:

MRI group: This visit required collaborative subject oversight by a cardiology and radiology provider at each center. Cardiology staff provided initial clearance, while radiology provided final clearance to undergo the MRI scan procedure. The prescribed MRI scan procedure was performed on 1.5T MRI systems from one of three MRI manufacturers (General Electric, Philips, and Siemens). The total MRI investigation time was approximately 60 minutes of static magnetic field exposure with a total active MRI scanning time of approximately 30 minutes of gradient and RF field exposure. There was both monitoring and IPG programming requirements.

- Monitoring: During the entire MRI scan, the subject's cardiac function was required to be monitored using pulse oximetry by an study trained center electrophysiologist, cardiologist, or Advanced Cardiac Life Support (ACLS) trained clinician who is capable of delivering external cardiac pacing defibrillation and advanced cardiac life support. Verbal communication with the subject was required to assess or confirm any clinically significant changes.
  It was required that all Zone 3 radiology areas had an emergency code cart with an external defibrillator, as well as a programmer. It was further recommended that all means of subject monitoring were used (e.g. ECG).

- IPG Programming: After confirmation of the pre-MRI checklist for MRI scan, pacemakers were required to be programmed pre-MRI scan as follows: 1) pacing capture output programmed to 5V at 1.0ms, 2) MRI SureScan feature programmed ON, with selection of asynchronous pacing or sensing only mode. Pacing mode and rate (if applicable) were programmed per physician's discretion. Post-MRI scan, pacemakers were required to be programmed as follows: 1) MRI SureScan feature OFF (pacemaker returns to pre-MRI programmed settings) and 2) pacing capture outputs remain programmed to 5V at 1.0ms. The subject was required to remain at this output until the 3 month post-implant follow-up visit (1 week post-MRI scan).

Cardiology staff concluded the visit with pacemaker measurements.

Control group: No MRI scan. 60 minute waiting period between the two sets of pacemaker measurements (the equivalent duration of the MRI group).

Visit 5 – Follow-up one week post 9-12week visit (MRI scan/control visit)
All subjects underwent pacemaker measurements, which included assessment of pacing capture threshold, sensed electrogram amplitude, and lead impedance.

Visit 6 – Follow-up one month post 9-12 week visit (MRI scan/control visit)
All subjects underwent pacemaker measurements, which included assessment of pacing capture threshold, sensed electrogram amplitude, and lead impedance.

Visit 7 – Follow-up six months post implant (and every six-months thereafter)
All subjects underwent pacemaker measurements, which included assessment of pacing capture threshold, sensed electrogram amplitude, and lead impedance.

4.4. Results

The first enrollment occurred 5 February 2007. These results include any visit or event that occurred on or before 21 November 2008 with data received by 18 December 2008. The database was closed for analysis on 30 December 2008.

A total of 484 subjects were enrolled at 42 centers, including 113 enrollments at 13 centers in the US and 371 enrollments at 29 centers outside of the US. The enrollments outside of the US included 302 enrollments at 21 centers in Europe, 68 enrollments at seven centers in Canada, and one enrollment at one center in Saudi Arabia. Of the 484 enrolled subjects, 464 subjects were successfully implanted with the EnRhythm MRI pacing system and randomized.

Figure 4-1 shows a study flow chart which accounts for subjects withdrawal due to death or exits and denotes missing follow-up visit data. (Note: although a subject can miss a follow-up visit, they can contribute to data at a subsequent follow-up visit). See Section 4.4.6 for a summary of subject accountability.

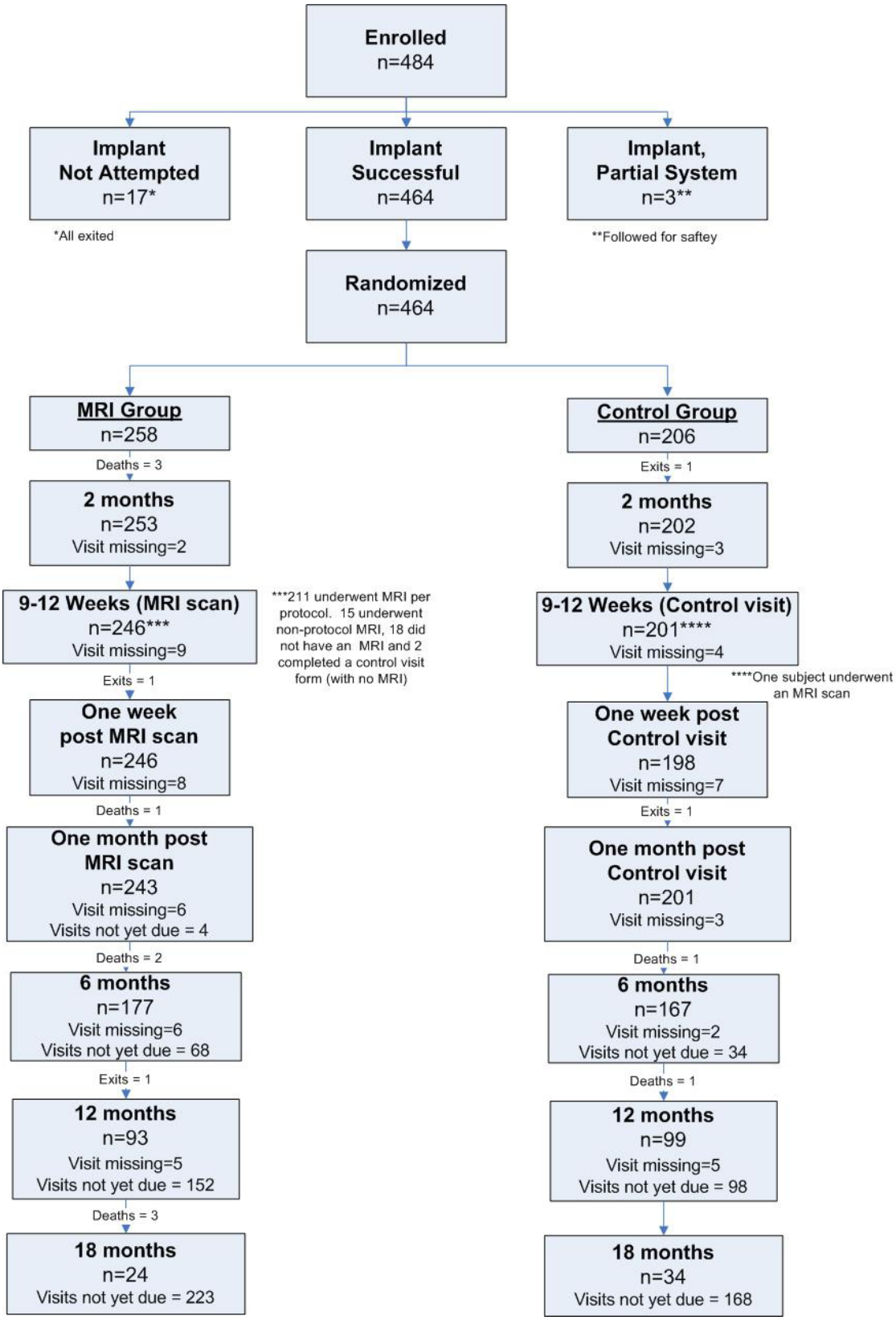

Figure 4-1. Subject Distribution

Study deviation case report forms were required for those visits that fell outside the follow-up window or were missed. Overall visit compliance was 97.8% of visits completed, with 95.9% of visits completed on time.

Table 4-5 and **Table 4-6** summarize baseline clinical characteristics, including subject demographics and the primary indication for successfully implanted subjects.

Table 4-5. Baseline Clinical Characteristics

Demographic	MRI Group (n=258)	Control Group (n=206)
Age at Implant (years) Mean ± SD	69.3 ± 12.9	68.0 ± 12.6
Male	154 (59.7%)	135 (65.5%)
Atrial Tachyarrhythmias	130 (50.4%)	82 (39.8%)

Table 4-6. Primary Indication for Implant

Primary Indication for Implant	MRI Group (n=258)	Control Group (n=206)
Atrial tachyarrhythmias	19 (7.4%)	15 (7.3%)
AV block	95 (36.8%)	84 (40.8%)
Cardial sinus hypersensitivity	5 (1.9%)	4 (1.9%)
Sinus node dysfunction	122 (47.3%)	90 (43.7%)
Vasovagal syncope	4 (1.6%)	4 (1.9%)
Sick Sinus Syndrome	2 (0.8%)	6 (2.9%)
Other*	11 (4.3%)	3 (1.5%)

* Includes His ablation with pacemaker implant (1 MRI group), AV ablation with pacemaker implant (1 MRI group), binodal disease (2 MRI group), bradycardia with junctional rhythm (1 MRI group), complete heart block (1 MRI group), observed asystole (1 MRI group), possible cardiac sarcoidosis (1 control group), rapid SVT (1 MRI group), sinus arrest (1 MRI group), symptomatic bradycardia (1 control group), syncope with bifascicular block (1 control group), AV node dysfunction (1 MRI group), and tachy-brady syndrome (1 MRI group).

4.4.1. Primary Objectives

All five primary safety and effectiveness objectives (MRI-related complications, atrial pacing capture threshold, ventricular pacing capture threshold, atrial sensed amplitude, and ventricular sensed amplitude) were met and are described in detail below.

Primary Safety Objective: MRI-Related Complications

Objective: To assess the MRI-related complication-free rate in the month following MRI.

A complication was defined as an adverse event that resulted in invasive intervention or the termination of significant device function regardless of other treatments. The complication-free rate was calculated as a ratio. The denominator was all subjects implanted with the EnRhythm MRI system that underwent an MRI scan per protocol and completed their one-month post-MRI visit, or had an MRI-related complication before the end of the one-month post-MRI visit date.

The numerator was the subjects included in the denominator who were free from MRI-related complications at the end of the one-month post-MRI visit date. Subjects who were lost to follow-up, or withdrew for other reasons prior to the one-month post-MRI visit, were not included in the analysis unless an MRI-related complication was recorded. Results are included in **Table 4-7**.

Table 4-7. Results of MRI-Related Complications Primary Objective

Success Criteria	Subjects	Complication-Free Rate	One-sided 97.5% Confidence Boundary and p-value	Conclusion
The MRI-related complication-free rate is greater than 90%	211	100%	98.3% $p < 0.001$	Objective Met

A total of 211 subjects underwent an MRI per protocol and completed the one-month post-MRI visit. No subjects experienced MRI-related complications through the one-month post-MRI visit. Therefore, no invasive interventions or termination of device function was needed or observed as a result of the MRI procedure.

In addition, none of the additional 15 subjects whose MR scans were not performed per protocol design (see Section 4.4.3), or the one additional control subject who underwent an MRI scan, experienced MRI-related complications.

While there were no MRI-related complications, the adverse events committee classified 4 events as MRI-procedure related observations: paraesthesia (n=3) and palpitations (n=1). In all cases, the adverse events committee classified the events as not related to the pacing system and no actions were taken or required as a result of these events.

Table 4-8 shows the 4 observations that occurred in which relatedness to the MRI procedure was unknown:

Table 4-8. Observations

Observation	Action
Chest Discomfort	No action taken/required
Dyspnea	No action taken/required
Atrial Flutter	MRI SureScan feature was reprogrammed
Atrial Fibrillation	Subject medications changed

In all cases, the adverse events committee classified the events as not related to the pacing system.

Primary Effectiveness Objective #1: Pacing Capture Threshold

Objective: To compare the changes in 1) atrial and 2) ventricular voltage thresholds at 0.5 ms before and after an MRI scan between the MRI and control groups.

The objective focused on whether a significant change in ventricular and atrial voltage thresholds at 0.5 ms occurs following an MRI scan. The hypothesis tested whether the proportion of subjects who experienced threshold increases less than or equal to 0.5 V was clinically equivalent between the MRI and control groups. Post-MRI/control visit measurements were calculated at the one-month post-MRI/control visit.

A success was defined as a subject who experienced a change in pacing capture threshold less than or equal to 0.5 V. The equivalence margin of 10% is an upper bound for the absolute difference in success rates. Exclusions from the analysis were pre-defined in the CIP or statistical analysis plan. Subjects who were unable to capture at 0.5 ms were assigned a value of 6.0 V. Results are included in **Table 4-9**.

Table 4-9. Results of Capture Threshold Primary Objective

Success Criteria	Comparison	Group	Success/ n	Success Rates	P-value	Conclusion
The proportions of subjects who experienced an increase less than or equal to 0.5 V are clinically equivalent, defined as within 10%.	Atrial	MRI Control	165 / 165 164 / 164	100% 100%	NA*	Objective Met
	Ventricular	MRI Control	190 / 190 183 / 184	100% 99.5%	$p < 0.001$	Objective Met

* Since the success rates were both 100%, the one-sided 97.5% confidence boundary and p-value could not be calculated.

For atrial and ventricular thresholds, the null hypothesis was rejected: the proportion of subjects who experienced an increase less than or equal to 0.5 V were clinically equivalent (defined as within 10%) between the MRI and control groups.

Figure 4-2 and **Figure 4-3** shows the frequency of pacing capture threshold changes from pre-MRI/control to one-month post-MRI/control visit for all subjects included in the success rate calculations. The figures show that approximately 90% of thresholds in both randomized groups either remained the same or decreased, with the remaining approximately 10% increasing by 0.5 V or, for one ventricular control subject, increasing by 1.0 V.

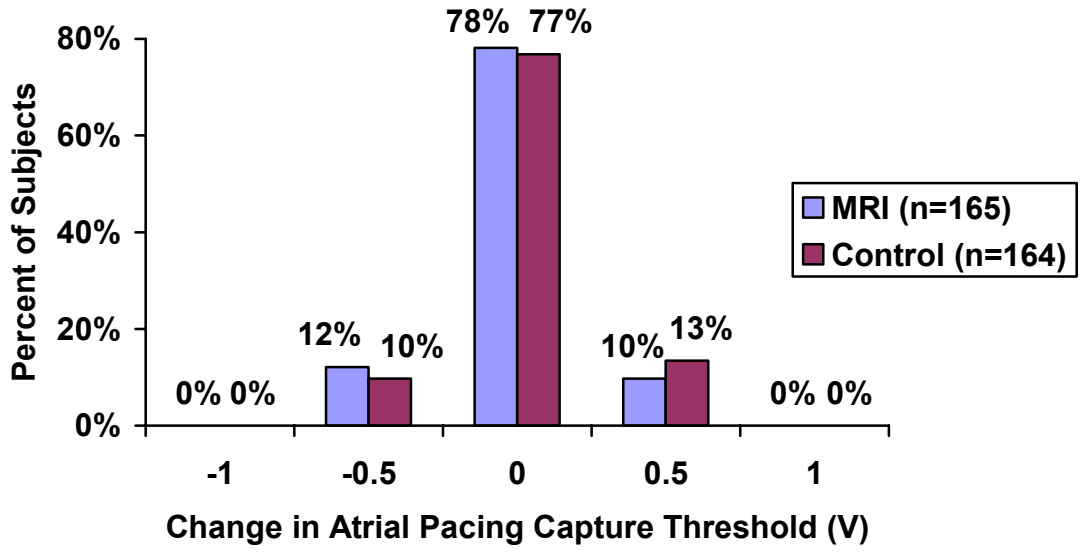

Figure 4-2. Atrial Pacing Capture Threshold Changes From pre-MRI (or control visit) to One Month Post-MRI

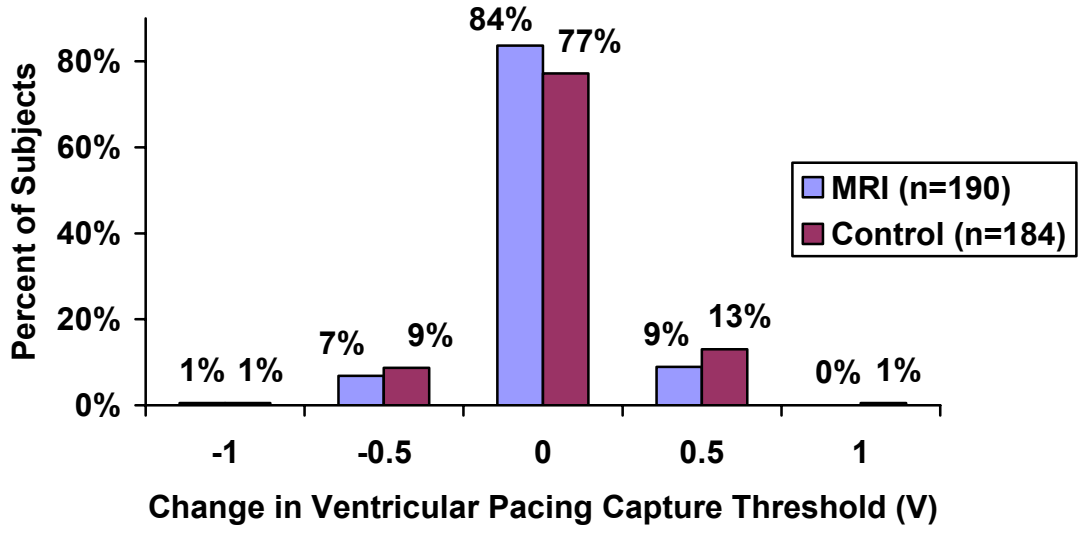

Figure 4-3. Ventricular Pacing Capture Threshold Changes From pre-MRI (or control visit) to One Month Post-MRI

Due to pre-specified analysis methods, of the 464 randomized subjects, 135 subjects were excluded from the atrial capture threshold analysis and 90 subjects were excluded from the ventricular capture threshold analysis. These reasons for exclusion are listed in **Table 4-10** and **Table 4-11**.

Table 4-10. Reasons for Exclusion from Primary Analysis of Atrial Capture Threshold Objective

Reason for Exclusion	n MRI Group	n Control Group
No one-month post-MRI/control visit follow-up	15	5
MR scans not performed per protocol	32	Not applicable
Atrial arrhythmia at 9-12 weeks or four-month visit	27	18
Early or late one-month post-MRI/control visits	10	8
Capture threshold increase exceeding 0.5 V from two months to 9-12 weeks	0	3
Missing data due to other reasons:		
Missed visits	6	2
Missing strips	3	4
Test performed at 0.4 ms instead of 0.5 ms	0	1
Lead dislodgment	0	1
Total excluded from the analysis	93	42
Included in the analysis	165	164
Randomized subjects	258	206

Table 4-11. Reasons for Exclusion from Primary Analysis of Ventricular Capture Threshold Objective

Reason for Exclusion	n MRI Group	n Control Group
No one-month post-MRI/control visit follow-up	15	5
MR scans not performed per protocol	32	Not applicable
Early or late one-month post-MRI/control visits	13	8
Capture threshold increase exceeding 0.5 V from two months to 9-12 weeks	1	1
Missing data due to other reasons:		
Missed visits	7	2
Missing strips	0	2
Test performed at 0.4 ms instead of 0.5 ms	0	1
Printer problems	0	1
Prior removal of RV lead	0	2
Total excluded from the analysis	68	22
Included in the analysis	190	184
Randomized subjects	258	206

A pre-defined sensitivity analysis was performed to include analysis-ineligible subjects. This included MRI subjects whose scans were not performed according to protocol but who had at least a partial MRI scan, subjects whose visits fell outside of the visit window at the one-month post-MRI/control visit, and subjects with data missing at the one-month post-MRI/control visit but for whom one-week post-MRI/control follow-up data could be used for the one-month post-MRI/control values. For atrial pacing capture thresholds, 35 MRI subjects and 13 control subjects were added to the primary analysis cohort for the sensitivity analysis. For ventricular pacing capture thresholds, 35 MRI subjects and 11 control subjects were added. The failure in the MRI group experienced a pacing capture threshold increase of 1.0 V.

Table 4-12. Sensitivity Analysis of Pacing Capture Threshold Primary Objective

	Primary Analysis			Sensitivity Analysis		
Comparison	**Group**	**Success/ n**	**Success Rates**	**Group**	**Success/ n**	**Success Rates**
Atrial	MRI Control	165 / 165 164 / 164	100% 100%	MRI Control	200/ / 200 177 / 177	100% 100%
Ventricular	MRI Control	190 / 190 183 / 184	100% 99.5%	MRI Control	224 / 225 194 / 195	99.6% 99.5%

In addition a tipping point analysis was conducted. In a tipping point analysis, the missing data is examined to see at what point results would become not statistically significant. For the atrial pacing capture thresholds, where 165 / 165 MRI group subjects were successful, and 164 / 164 control group subjects were successful, if the remaining 42 randomized control group subjects were all successful, the endpoint would still be achieved as long as at least 77 of the 93 (83%) remaining MRI group subjects were successful. For the ventricular pacing capture threshold, if the 22 excluded control subjects were all successful, then the objective would have still been met if at least 51 of the 68 (75%) missing MRI group subjects were successes.

Primary Effectiveness Objective #2: Sensed Amplitude

Objective: To compare the changes in 1) atrial and 2) ventricular sensed amplitudes before and after MRI between the MRI and control groups.

The hypothesis tested whether the proportion of subjects who experienced a decrease in sensed amplitude less than or equal to 50% and whose sensed amplitude remained above an acceptable minimum at one-month post-MRI/control visit (four-months post-implant) was clinically equivalent between the MRI and control groups.

A success was defined as meeting both of the following criteria: a sensed amplitude decrease not exceeding 50%, and a one-month post-MRI/control visit sensed amplitude not less than 5.0 mV for ventricular measurements and not less than 1.5 mV for atrial measurements. The equivalence margin of 10% was an upper bound for the absolute difference in success rates between the MRI and control groups. Subjects with a pre-MRI/control visit sensed amplitude less than 5.0 mV in the ventricle or less than 1.5 mV in the atrium were excluded from the primary analysis but were included in a sensitivity analysis. Exclusions from the analysis were pre-defined in the protocol or statistical analysis plan.

Table 4-13. Results of Sensed Amplitude Primary Objective

Success Criteria	Comparison		Success/ n	Success Rates	P-value	Conclusion
The proportion of subjects who experienced a sensed amplitude decrease not exceeding 50%, and a one-month post-MRI/waiting period sensed amplitude not less than 1.5 mV for atrial measurements and not less than 5.0 mV for ventricular measurements, are clinically equivalent, defined as within 10%.	Atrial	MRI Control	124 / 131 129 / 139	94.7% 92.8%	p <0.001	Objective Met
	Ventricular	MRI Control	130 / 134 129 / 136	97.0% 94.9%	p < 0.001	Objective Met

For both atrial and ventricular sensed amplitudes, the null hypothesis was rejected: the proportion of subjects who experienced a decrease in sense amplitude less than or equal to 50% and whose sense amplitude remained above an acceptable minimum at one-month post-MRI/waiting period were clinically equivalent (defined as within 10%) between the MRI and control groups.

Figure 4-4 shows the mean sensed amplitudes over times.

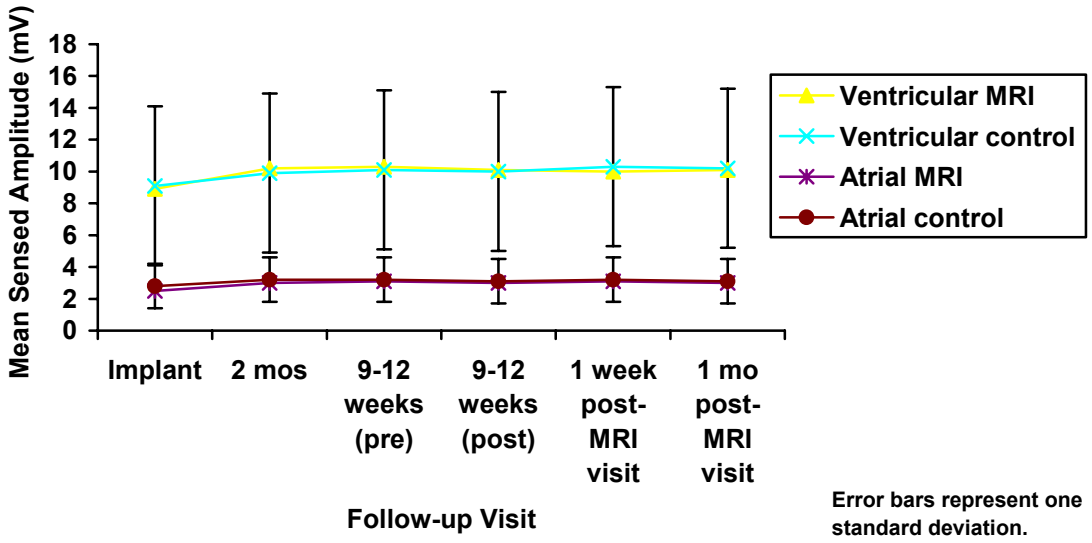

Figure 4-4. Sensed Amplitudes Over Time

Due to pre-specified analysis methods, many subjects were excluded from the primary analysis of sensed amplitudes. Of the 464 randomized subjects completing the one-month post-MRI/control visit, 194 subjects were not included in the atrial sensed amplitude primary analysis

and 194 subjects were not included in the ventricular sensed amplitude primary analysis. Reasons for exclusion are listed in **Table 4-14** and **Table 4-15**.

Table 4-14. Reasons for Exclusion from Primary Analysis of Atrial Sensed Amplitude Objective

Reason for Exclusion	n MRI Group	n Control Group
No one-month post-MRI/control visit follow-up	15	5
MR scans not performed per protocol	32	Not applicable
Atrial arrhythmia at 9-12 weeks or one-month post-MRI/control visit	27	18
Early or late one-month post-MRI/control visit	8	8
Capture threshold increase exceeding 0.5 V from two months to 9-12 weeks	0	2
Incomplete sensed test at 9-12 weeks or one-month post-MRI/control visit	14	12
Sensed values less than 1.5 mV at 9-12 weeks	22	16
Missing data due to other reasons: Missed visits Lead dislodgment Data unavailable	 6 0 3	 2 1 3
Total excluded from the analysis	127	67
Included in the analysis	131	139
Randomized subjects	258	206

Table 4-15. Reasons for Exclusion from Primary Analysis of Ventricular Sensed Amplitude Objective

Reason for Exclusion	n MRI Group	n Control Group
No one-month post-MRI/control visit follow-up	15	5
MR scans not performed per protocol	32	Not applicable
Early or late one-month post-MRI/control visit	10	5
Capture threshold increase exceeding 0.5 V from two months to 9-12 weeks	2	1
Incomplete sensed test at 9-12 weeks or one-month post-MRI/control visit	27	24
Sensed values less than 5.0 mV at 9-12 weeks	28	25
Missing data due to other reasons: Missed visits Prior removal of RV lead Data unavailable	 6 0 4	 2 2 6
Total excluded from the analysis	124	70
Included in the analysis	134	136
Randomized subjects	258	206

A pre-defined sensitivity analysis was performed to include analysis-ineligible subjects, including MRI subjects whose scans were not performed according to protocol but who had at least a partial MRI scan, subjects whose visits fell outside of the visit window at the one-month post-MRI/control visit, and subjects with data missing at the one-month post-MRI/control visit but for whom one-week post-MRI/control visit follow-up data could be used for the one-month post-MRI/control values. Results are in **Table 4-16**. For atrial pacing capture thresholds, 41 MRI subjects and 12 control subjects were added to the primary analysis cohort for the sensitivity analysis. For ventricular pacing capture thresholds, 44 MRI subjects and 11 control subjects were added.

The subjects excluded due to low sensed amplitude values, defined in the protocol as less than 5.0 mV in the ventricle and less than 1.5 mV in the atrium, were included in an additional sensitivity analyses, where success was defined as a sensed amplitude decrease not exceeding 50%. All subjects with low sensed amplitude values were successful according to this definition.

Table 4-16. Sensitivity Analysis of Sensed Amplitude Primary Objective

	Primary Analysis			Sensitivity Analysis		
Comparison	**Group**	**Success/ n**	**Success Rates**	**Group**	**Success/ n**	**Success Rates**
Atrial	MRI	124 / 131	94.7%	MRI	162 / 172	94.2%
	Control	129 / 139	92.8%	Control	141 / 151	93.4%
Ventricular	MRI	130 / 134	97.0%	MRI	172 / 178	96.6%
	Control	129 / 136	94.9%	Control	140 / 147	95.2%

In addition a tipping point analysis was conducted. In a tipping point analysis, the missing data is examined to see at what point results would become not statistically significant. For the atrial sensed amplitude, if all 67 missing control subjects were successes the null hypothesis would still be rejected if at least 109 of the 127 (86%) missing MRI group subjects were successes. For the ventricular sensed amplitude, if all 70 missing control subjects were successes the null hypothesis would still be rejected if at least 106 of the 124 (85%) missing MRI group subjects were successes.

4.4.2. Secondary Objectives

All secondary objectives with defined success criteria were met.

Secondary Objective #1: Pacing System-Related Complications

This objective involved characterizing all pacing system-related complications through the one-month post-MRI/control visit. (All adverse events are reported in Section 4.4.4.) The system consists of the EnRhythm MRI pacemaker and two CapSureFix MRI 5086MRI SureScan leads. There were 47 complications, 43 of which (in 37 subjects) occurred prior to the one-month post-MRI/control visit. None of these complications were related to the MRI scan procedure. Results are included in **Table 4-17.** While all complications through one-month post-MRI/control are included, only subjects with a one-month post-MRI/control visit or a system-related complication are included, hence the 447 subjects in the table. All adverse events were reviewed and classified by the adverse events committee.

Pacing system-related complication event rates are similar in comparison to the Medtronic EnRhythm clinical study results as reported in the EnRhythm clinical study P980035/S038 approved by FDA.

Table 4-17. Results of Pacing System-Related Complications Secondary Objective

Success Criteria	Subjects	Complication Free Rate	One-sided 95% Confidence Boundary and p-value	Conclusion
The pacing system-related complication-free rate is greater than 80%	447	91.7%	89.3% $p < 0.001$	Objective Met

The null hypothesis was rejected: the pacing system-related complication-free rate is greater than 80%. **Table 4-18** lists all complications and observations related to the system that occurred at any time during the study. As noted in Table **4-18**, the highest incidence rates were reported as lead dislodgements, elevated pacing threshold and failure to capture adverse events. Nineteen subjects reported 19 adverse events of lead dislodgements (12 MRI group subjects and 7 control group subjects). All lead dislodgement events occurring in MRI group subjects had occurred prior to the MRI procedure. Twelve subjects reported 12 adverse events of elevated thresholds (8 MRI group subjects and 4 control group subjects). Of the 8 MRI group subjects, 6 of these elevated thresholds events occurred and were resolved prior to MRI, 1 occurred after MRI (330 days post), and 1 resulted in no MRI occurring. Four subjects reported 4 adverse events of unable to capture (4 control group subjects). Lead dislodgement, elevated threshold and unable to capture event rates are similar in comparison to Medtronic studies using the predecessor 5076 lead (Medtronic EnRhythm, EnPulse, Adapta), approved by FDA.

Table 4-18. System-Related Adverse Events

Adverse Event	Observations (MRI / Control)	Complications (MRI / Control)	Total AEs (MRI / Control)
Lead dislodgement	0 / 1	12 / 6	12 / 7
Elevated pacing threshold	2 / 1	6 / 3	8 / 4
Failure to capture	0 / 1	0 / 3	0 / 4
Thrombosis	1 / 1	0 / 2	1 / 3
Inappropriate device stimulation of tissue	1 / 1	1 / 0	2 / 1
Pericardial effusion	0 / 0	2 / 1	2 / 1
Atrial fibrillation	1 / 0	0 / 1	1 / 1
Cardiac perforation	0 / 0	2 / 0	2 / 0
Heart rate increased	2 / 0	0 / 0	2 / 0
Implant site infection	0 / 0	1 / 1	1 / 1
Atrial flutter	0 / 1	0 / 0	0 / 1
Cardiac pacemaker revision	0 / 0	1 / 0	1 / 0
Chest pain	0 / 0	0 / 1	0 / 1
Endocarditis	0 / 0	1 / 0	1 / 0
Implant site discharge	0 / 1	0 / 0	0 / 1
Implant site pain	1 / 0	0 / 0	1 / 0
Implant site swelling	1 / 0	0 / 0	1 / 0
Medical device complication	0 / 0	1 / 0	1 / 0
Pain in extremity	0 / 0	0 / 1	0 / 1
Palpitations	1 / 0	0 / 0	1 / 0
Restlessness	1 / 0	0 / 0	1 / 0
Subclavian vein thrombosis	0 / 0	0 / 1	0 / 1
Swelling	1 / 0	0 / 0	1 / 0
Undersensing	0 / 1	0 / 0	0 / 1
Venous insufficiency	0 / 1	0 / 0	0 / 1
Total	12 / 9	27 / 20	39 / 29

Secondary Objective #2: Labeling Instructions

This objective confirmed that labeling instructions for completing the MRI scans were followed to ensure subject safety.

Table 4-19. Results of Labeling Instructions Secondary Objective

Success Criteria	Subjects	Subjects With a System-Related Adverse Device Effect That Occurred Due to Insufficiencies or Incorrect Following of MRI Labeling Instructions	Conclusion
None Defined	211	0	Analysis favorably achieved: no system-related Adverse Device Effects due to labeling instructions observed.

None of the subjects who underwent an MRI per protocol experienced a system-related adverse device effect related to insufficiencies or incorrect following of MRI labeling instructions.

In addition, none of the additional 15 subjects whose MR scans were not performed per protocol design, or the one additional control subject who underwent an MRI scan experienced a system-related adverse device effect related to insufficiencies or incorrect following of MRI labeling instructions.

Secondary Objective #3: Occurrence of Arrhythmias

This objective characterized the occurrence of sustained ventricular arrhythmias and asystole that were attributed to the MRI scan by the AEAC. (All adverse events are reported in Section 4.4.4)

Table 4-20. Results of Occurrence of Arrhythmias Secondary Objective

Success Criteria	Subjects (MRI Group)	Subjects With Sustained Ventricular Arrhythmias and Asystole Attributed to MRI Scan	Conclusion
None Defined	211	0	Analysis favorably achieved: no sustained ventricular arrhythmias or asystole observed.

No subjects experienced sustained ventricular arrhythmias or asystole episodes attributable to the MRI scan by the AEAC. In addition, none of the 16 subjects who either 1) underwent a MRI scan in deviation of the labeling, 2) failed to complete the MRI scan per protocol, or 3)

underwent an MRI scan in deviation of randomization experienced sustained ventricular arrhythmias or asystole episodes that were attributable to the MRI scan by the AEAC.

Secondary Objective #4: Adverse Events

This objective characterized all implant procedure-, pacing system-, and MRI procedure-related adverse events through the one-month post-MRI/control visit. See Section 4.4.4 for a description of all adverse events in the clinical study. A total of 89 subjects experienced 109 adverse events related to the implant procedure, pacing system, or MRI procedure prior to the one-month post-MRI/control visit. Though 467 subjects were implanted with at least a partial system (and all adverse events from these subjects are counted here), the denominator (452) used here conservatively includes only subjects who either completed the one-month post-MRI control visit, or had an adverse event prior to that time. All adverse events were reviewed and classified by the adverse events committee. Note that these adverse events include the system-related adverse events from secondary objective #1.

Implant procedure-, pacing system-, and MRI procedure-related event rates are similar in comparison to the Medtronic EnRhythm clinical study results as reported in the EnRhythm clinical study P980035/S038 approved by FDA.

Table 4-21. Results of Adverse Events Secondary Objective

Success Criteria	Subjects	System- and Procedure-Related Adverse Event-Free Rate	Conclusion
None Defined	452	80.3%	Analysis favorably achieved: all adverse events reported as per protocol; see Table 4-22

Table 4-22 lists the 120 implant procedure-, pacing system-, and MRI procedure-related complications and observations, 109 of which occurred prior to the one-month post-MRI follow-up.

Table 4-22. Implant- and/or System-Related Adverse Events

Adverse Event	Observations (MRI / Control)	Complications (MRI / Control)	Total AEs (MRI / Control)
Lead dislodgement	0 / 1	12 / 6	12 / 7
Pneumothorax	4 / 1	4 / 5	8 / 6
Elevated pacing threshold	2 / 1	6 / 3	8 / 4
Implant site infection	2 / 3	2 / 1	4 / 4
Implant site haematoma	2 / 3	0 / 0	2 / 3
Chest pain	1 / 0	1 / 2	2 / 2

Adverse Event	Observations (MRI / Control)	Complications (MRI / Control)	Total AEs (MRI / Control)
Failure to capture	0 / 1	0 / 3	0 / 4
Thrombosis	1 / 1	0 / 2	1 / 3
Inappropriate device stimulation of tissue	1 / 1	1 / 0	2 / 1
Paraesthesia	3 / 0	0 / 0	3 / 0
Pericardial effusion	0 / 0	2 / 1	2 / 1
Atrial fibrillation	1 / 0	0 / 1	1 / 1
Cardiac perforation	0 / 0	2 / 0	2 / 0
Heart rate increased	2 / 0	0 / 0	2 / 0
Palpitations	2 / 0	0 / 0	2 / 0
Pneumonia	0 / 0	0 / 2	0 / 2
Pyrexia	1 / 0	0 / 1	1 / 1
Anaemia	1 / 0	0 / 0	1 / 0
Atelectasis	1 / 0	0 / 0	1 / 0
Atrial flutter	0 / 1	0 / 0	0 / 1
Cardiac pacemaker revision	0 / 0	1 / 0	1 / 0
Cellulitis	1 / 0	0 / 0	1 / 0
Dizziness	0 / 1	0 / 0	0 / 1
Endocarditis	0 / 0	1 / 0	1 / 0
Erythema migrans	0 / 1	0 / 0	0 / 1
Implant site discharge	0 / 1	0 / 0	0 / 1
Implant site pain	1 / 0	0 / 0	1 / 0
Implant site swelling	1 / 0	0 / 0	1 / 0
Incision site erythema	0 / 1	0 / 0	0 / 1
Medical device complication	0 / 0	1 / 0	1 / 0
Musculoskeletal pain	0 / 1	0 / 0	0 / 1
Pain	0 / 1	0 / 0	0 / 1
Pain in extremity	0 / 0	0 / 1	0 / 1
Panic attack	0 / 1	0 / 0	0 / 1
Postoperative wound infection	0 / 0	1 / 0	1 / 0
Pulmonary oedema	0 / 0	1 / 0	1 / 0
Restlessness	1 / 0	0 / 0	1 / 0
Subclavian vein thrombosis	0 / 0	0 / 1	0 / 1
Swelling	1 / 0	0 / 0	1 / 0

Adverse Event	Observations (MRI / Control)	Complications (MRI / Control)	Total AEs (MRI / Control)
Syncope	0 / 0	1 / 0	1 / 0
Thrombophlebitis	0 / 1	0 / 0	0 / 1
Transient ischaemic attack	0 / 0	0 / 1	0 / 1
Undersensing	0 / 1	0 / 0	0 / 1
Venous insufficiency	0 / 1	0 / 0	0 / 1
Venous thrombosis	1 / 0	0 / 0	1 / 0
Viral infection	0 / 1	0 / 0	0 / 1
Total	30 / 24	36 / 30	66 / 54

Secondary Objective #5: Lead Impedance

This objective summarized atrial and ventricular lead impedance changes through the one-month post-MRI/control visit. For both atrial and ventricular impedance, the mean ± SD changes in ohms (Ω) from the 9-12 week follow-up pre-MRI/control visit to the one-month post-MRI/control visit are reported.

Table 4-23. Results of Lead Impedance Secondary Objective

Success Criteria	Comparison	Group	n	Mean ± SD Impedance (Ω)			Conclusion
				Pre-MRI/Control	One-month post-MRI/Control	changes from pre-MRI to one-month post-MRI	
None Defined	Atrial	MRI	201	516.0 ± 81.4	515.5 ± 78.1	-0.6 ± 61.8	Analysis favorably achieved: for all comparisons, the pre-MRI lead impedance was comparable to the post MRI lead impedance.
		Control	197	523.6 ± 92.8	530.9 ± 97.7	7.3 ± 50.4	
	Ventricular	MRI	201	570.3 ± 109.2	561.3 ± 104.8	-9.0 ± 48.5	
		Control	196	571.6 ± 103.0	565.9 ± 105.4	-5.7 ± 51.8	

Secondary Objective #6: Lead Handling

This objective characterized the lead handling of the CapSureFix MRI 5086MRI lead in relation to the commercially available Medtronic CapSureFix Model 5076 lead. The comparison group for this evaluation was from a different clinical study - the cohort reported in the clinical study report for PMA-S approval of the Medtronic Model 5076 lead (P930039S/009). This objective was evaluated by analyzing implanting physician responses regarding lead handling, and comparing the responses to the Medtronic Model 5076 lead study cohort.

The questionnaire scale was -3 (well below expectations) to +3 (well above expectations). A total of 212 surveys were completed, representing all 41 implanting centers. Lead handling either met or exceeded physician's expectations approximately 90% of the time. As demonstrated by the low p-values, atrial and ventricular lead handling were considered clinically equivalent, defined as within 1.5 questionnaire units, between the CapSureFix MRI 5086MRI SureScan lead and the Model 5076 lead.

Table 4-24. Results of Lead Handling Secondary Objective

Success Criteria	Comparison		Mean ± s.d. lead handling score (n)	Difference in Mean Lead Handling Scores	p-Value	Conclusion
Differences in overall lead handling characteristics are statistically equivalent (D=1.5 units on a scale of -3 to +3)	Atrial	5086 MRI 5076	0.53 ± 1.22 (212) 0.68 ± 1.16 (117)	0.15	p < 0.001	Objective Met
	Ventricular	5086 MRI 5076	0.58 ± 1.17 (211) 0.76 ± 1.06 (117)	0.18	p < 0.001	Objective Met

Secondary Objective #7: Lead Performance

This objective compared the one-month post-MRI/control visit (four-months post-implant) pacing thresholds and sensed amplitudes of the CapSureFix MRI 5086MRI leads in both the MRI and control groups to the three-month post-implant follow-up data from the commercially available Medtronic Model 5076 lead study. The top p-value in each cell compares MRI vs. 5076, and the bottom compares control vs. 5076. Low p-values indicate "equivalence" between the two comparison groups.

Table 4-25. Results of Lead Performance Secondary Objective

Pacing Capture Thresholds				
Success Criteria	**Comparison**	**Model 5086MRI Mean ± SD (V)**	**p-Value for equivalence between MRI or control and 5076**	**Conclusion**
Pacing thresholds are statistically equivalent (D=0.5 V)	Atrial	MRI: 0.78 ± 0.28 Control: 0.77 ± 0.66 5076: 0.61 ± 0.23	p < 0.001 p < 0.001	Objective Met
	Ventricular	MRI: 0.82 ± 0.30 Control: 0.90 ± 0.70 5076: 0.75 ± 0.77	p < 0.001 p < 0.001	Objective Met
Sensed Amplitude				
Sensed amplitudes are statistically equivalent (D=0.9 mV for atrial sensed amplitudes, 2.5 mV for ventricular sensed amplitudes)	**Lead Implant Site**	**Model 5086MRI Mean ± SD (mV)**	**p-Value for equivalence between MRI or control and 5076**	**Conclusion**
	Atrial	MRI: 3.0 ± 1.3 Control: 3.1 ± 1.4 5076: 3.2 ± 1.7	p < 0.001 p < 0.001	Objective Met
	Ventricular	MRI: 10.1 ± 5.0 Control: 10.2 ± 5.2 5076: 10.0 ± 4.3	p < 0.001 p < 0.001	Objective Met

Atrial and ventricular capture thresholds and sensed amplitudes were considered clinically equivalent, defined as within 0.5 V for capture thresholds, 0.9 mV for atrial sensed amplitudes, and 2.5 mV for ventricular sensed amplitudes, between the CapSureFix MRI 5086MRI lead (MRI and control groups) and the Model 5076 lead.

4.4.3. Additional Pre-Specified Analyses

Additional Analysis #1: Identification of Radiopaque Symbols

The purpose of this analysis was to demonstrate that the EnRhythm MRI system (both pacemaker and leads) can be identified as MRI-labeled via X-ray. The analysis was based on data collected from 240 cardiology staff and 239 radiologist questionnaires. The questionnaires rated the ease of identifying the pacemaker and lead radiopaque symbols using a scale of -3 (well below expectations) to +3 (well above expectations).

Table 4-26. Results of Identification of Radiopaque Additional Analysis

Radiopaque	Questionnaire	Results (Median Scores)	Conclusion
Pacemaker	Cardiology Staff	1 (Slightly above expectations)	Analysis favorably achieved: the identification of the radiopaque symbols met expectations
	Radiologists	2 (Moderately above expectations)	
Lead	Cardiology Staff	2 (Moderately above expectations)	
	Radiologists	2 (Moderately above expectations)	

Additional Analysis #2: SureScan Feature Performance

The purpose of this analysis was to summarize any aberrant or undesirable behavior of the SureScan MRI mode in the programmer application. The analysis was based on data collected from 82 questionnaires completed by cardiology staff. Using a scale of 1 (extremely difficult) to 7 (extremely easy), the cardiology staff were asked to rate the ease of locating the SureScan feature, verifying items on the software application's checklist, selecting the appropriate SureScan pacing mode, and identifying that the SureScan feature was turned on. The last question in the questionnaire, which required rating the clarity of the device's sensing and diagnostic features when in SureScan feature, used a scale of 1 (extremely unclear) to 7 (extremely clear) instead. The results of the questionnaire are listed in **Table 4-27** below.

Table 4-27. Results of SureScan Feature Performance Additional Analysis

Question	Median Score	Conclusion
Ease of locating the SureScan feature	6 (Easy)	Analysis favorably achieved: the SureScan MRI programmer application was easy to locate and utilize
Ease of verifying all of the items on the SureScan software application's check list	6 (Easy)	
Ease of selecting the appropriate SureScan pacing feature	6 (Easy)	
Ease of identifying that the SureScan feature was turned on	6 (Easy)	
Clarity of the device's sensing and diagnostic capabilities when in SureScan feature	6 (Clear)	

Additional Analysis #3: Analysis of Procedure

This analysis summarized whether safeguards and procedures were followed at the time of the MRI scans. The data were collected from 82 cardiology staff questionnaires and 84 radiology staff questionnaires. Questions pertained to patient monitoring, equipment availability, and communication between the radiology and cardiac teams. A scale of 1 to 7 was again used for the responses. Some of the key questions and their responses are summarized in the following table.

Table 4-28. Results of Analysis of Procedure Additional Analysis

Question	Results (Median Scores)	Conclusion
Cardiology staff's ease of scheduling the appointment with radiology	6 (Easy)*	Analysis favorably achieved: safeguards and procedures were easy to follow and staff were comfortable with patient monitoring procedure.
Radiology staff's ease of scheduling the appointment with cardiology	6 (Easy)*	
Radiology staff's level of comfort with monitoring and potentially resuscitating the patient if the staff was Advanced Cardiac Life Support (ACLS) trained	6 (Comfortable)**	
Radiology staff's opinion on the clarity of information in the manual if the manual was reviewed	6 (Clear)***	

* Numerical range was 1 to 7, extremely difficult to extremely easy

** Numerical range was 1 to 7, extremely uncomfortable to extremely comfortable
*** Numerical range was 1 to 7, extremely unclear to extremely clear

Supplementary Analysis: Control Group Subjects Who Would Have Failed the Clinical Investigational Plan Pre-MRI Scan Clearance Checks (If Randomized to MRI group)

This supplementary analysis was requested by the FDA, and was not pre-specified in the clinical investigational plan or statistical plan.

Per the clinical investigational plan as a safety measure, MRI group subjects at the 9-12 week follow-up visit were required to complete pre-MRI scan clearance checks by both cardiology and radiology prior to allowing the MRI scan procedure. Those that didn't pass the checklist did not get an MRI scan. The statistical plan did not pre-specify to exclude control group subjects who failed the pre-MRI scan clearance checks. The FDA requested a list of control group subjects who would have failed the pre-MRI scan clearance checks to evaluate any potential bias. Specifically to identify control group subjects who were not eligible for an MRI, if randomized to the MRI group.

A total of ten control group subjects who would have failed the clearance checks were identified. Results for the 4 primary effectiveness endpoints excluding these 10 control subjects are shown in the two tables below. Note that some subjects had already been excluded from the analysis for other reasons, so the control group denominators drop by less than 10.

The primary safety endpoint does not include control group subjects therefore those results remain unchanged.

Table 4-9. Results of Capture Threshold Primary Objective

Success Criteria	Comparison	Group	Success/ n	Success Rates	P-value	Conclusion
The proportions of subjects who experienced an increase less than or equal to 0.5 V are clinically equivalent, defined as within 10%.	Atrial	MRI Control	165 / 165 157 / 157	100% 100%	NA*	Objective Met
	Ventricular	MRI Control	190 / 190 177 / 177	100% 100%	NA*	Objective Met

* Since the success rates were both 100%, the one-sided 97.5% confidence boundary and p-value could not be calculated.

Table 4-13. Results of Sensed Amplitude Primary Objective

Success Criteria	Comparison		Success/ n	Success Rates	P-value	Conclusion
The proportion of subjects who experienced a sensed amplitude decrease not exceeding 50%, and a one-month post-MRI/waiting period sensed amplitude not less than 1.5 mV for atrial measurements and not less than 5.0 mV for ventricular measurements, are clinically equivalent, defined as within 10%.	Atrial	MRI Control	124 / 131 123 / 133	94.7% 92.5%	p = 0.01	Objective Met
	Ventricular	MRI Control	130 / 134 125 / 131	97.0% 95.4%	p = 0.003	Objective Met

All four objectives were met in both the primary analysis and this additional analysis which excluded control group subjects who failed the pre-MRI scan clearance checks and who would not have been eligible to undergo an MRI if randomized to the MRI group. The potential biases introduced by the MRI screening checklist categories were deemed to be minimal because none of the factors assessed would influence a change in pacing capture thresholds or sensed amplitudes, which is why these control subjects are included in the primary analysis.

4.4.4. Adverse Events

Table 4-29 includes all adverse events in the clinical study, classified as observation or complication, randomization assignment, by incidence rate. A complication was defined as an adverse event that resulted in invasive intervention or the termination of significant device function regardless of other treatments. Intravenous and intramuscular drug therapies were considered invasive treatment. An observation was defined as an adverse event that was not a complication.

There were 484 subjects in the clinical study. Of those, 258 were randomized to the MRI group. The remaining 206 randomize to control, 3 implanted with a partial system, and 17 not attempting implant are included in the table as control subjects. There were 260 subjects who experienced a total of 527 adverse events in this study. Fifty-nine percent of all of the adverse events were clinical observations which required no invasive action. Seventy-seven percent of the adverse events were not related to the pacing system or to the study procedures, the implant procedure or the MRI procedure. All adverse events were reviewed and classified by the adverse events committee.

Note that these adverse events include the implant-procedure and system-related adverse events from secondary objective #4.

As noted in **Table 4-29**, the highest incidence rates were reported as atrial fibrillation, chest pain and lead dislodgement adverse events. Forty-two subjects reported 47 adverse events of atrial fibrillation (25 MRI group subjects and 17 control group subjects). Recall in **Table 4-5** the large number of subjects with a history of atrial tachyarrhythmias (MRI group 50.4% and control group 39.8%). Subjects had primary indication for pacemaker and were indicated for atrial therapies. Atrial fibrillation results highlight natural disease progression, with timing often coincidental in both MRI and control groups. Nineteen subjects reported 19 adverse events of lead dislodgements (12 MRI group subjects and 7 control group subjects). All lead dislodgement events occurring in MRI group subjects had occurred prior to the MRI procedure.

Total adverse event rates are similar in comparison to the Medtronic EnRhythm clinical study results as reported in the EnRhythm clinical study P980035/S038 approved by FDA.

Table 4-29. Listing of All Adverse Events

Adverse Event Key Term	Observations (MRI / Control)	Complications (MRI / Control)	Total AEs (MRI / Control)	Number (%) of Subjects (MRI / Control) (N = 258 / N = 226)
Atrial fibrillation	16 / 12	12 / 7	28 / 19	25 (9.7%) / 17 (7.5%)
Chest pain	5 / 4	4 / 6	9 / 10	9 (3.5%) / 10 (4.4%)
Lead dislodgement	0 / 1	12 / 6	12 / 7	12 (4.7%) / 7 (3.1%)
Dizziness	9 / 6	1 / 0	10 / 6	10 (3.9%) / 6 (2.7%)
Pneumothorax	4 / 1	4 / 5	8 / 6	8 (3.1%) / 6 (2.7%)
Elevated pacing threshold	2 / 1	6 / 3	8 / 4	7 (2.7%) / 3 (1.3%)

Adverse Event Key Term	Observations (MRI / Control)	Complications (MRI / Control)	Total AEs (MRI / Control)	Number (%) of Subjects (MRI / Control) (N = 258 / N = 226)
Palpitations	6 / 5	1 / 0	7 / 5	6 (2.3%) / 5 (2.2%)
Anaemia	2 / 0	3 / 3	5 / 3	5 (1.9%) / 2 (0.9%)
Atrial flutter	4 / 4	0 / 0	4 / 4	4 (1.6%) / 3 (1.3%)
Implant site infection	2 / 3	2 / 1	4 / 4	3 (1.2%) / 4 (1.8%)
Pneumonia	2 / 1	3 / 2	5 / 3	5 (1.9%) / 3 (1.3%)
Syncope	6 / 0	2 / 0	8 / 0	8 (3.1%) / 0
Myocardial infarction	1 / 0	4 / 2	5 / 2	5 (1.9%) / 2 (0.9%)
Cardiac failure	1 / 0	5 / 0	6 / 0	5 (1.9%) / 0
Dyspnoea	5 / 1	0 / 0	5 / 1	5 (1.9%) / 1 (0.4%)
Hypotension	3 / 2	1 / 0	4 / 2	4 (1.6%) / 2 (0.9%)
Implant site haematoma	2 / 4	0 / 0	2 / 4	2 (0.8%) / 4 (1.8%)
Pleural effusion	1 / 0	2 / 3	3 / 3	2 (0.8%) / 2 (0.9%)
Presyncope	4 / 1	1 / 0	5 / 1	5 (1.9%) / 1 (0.4%)
Urinary tract infection	3 / 1	2 / 0	5 / 1	5 (1.9%) / 1 (0.4%)
Bronchitis	3 / 1	1 / 0	4 / 1	4 (1.6%) / 1 (0.4%)
Paraesthesia	4 / 1	0 / 0	4 / 1	4 (1.6%) / 1 (0.4%)
Ventricular extrasystoles	4 / 1	0 / 0	4 / 1	4 (1.6%) / 1 (0.4%)
Angina pectoris	1 / 0	1 / 2	2 / 2	2 (0.8%) / 2 (0.9%)
Atrial tachycardia	2 / 0	2 / 0	4 / 0	4 (1.6%) / 0
Cardiac failure congestive	0 / 0	2 / 2	2 / 2	2 (0.8%) / 2 (0.9%)
Cataract	0 / 1	3 / 0	3 / 1	2 (0.8%) / 1 (0.4%)
Coronary artery disease	0 / 1	1 / 2	1 / 3	1 (0.4%) / 3 (1.3%)
Dyspnoea exertional	2 / 1	1 / 0	3 / 1	3 (1.2%) / 1 (0.4%)
Failure to capture	0 / 1	0 / 3	0 / 4	0 / 4 (1.8%)
Fatigue	2 / 2	0 / 0	2 / 2	2 (0.8%) / 2 (0.9%)
Pericardial effusion	0 / 0	3 / 1	3 / 1	3 (1.2%) / 1 (0.4%)
Thrombosis	1 / 1	0 / 2	1 / 3	1 (0.4%) / 2 (0.9%)
Back pain	2 / 0	1 / 0	3 / 0	3 (1.2%) / 0
Cerebrovascular accident	1 / 1	1 / 0	2 / 1	2 (0.8%) / 1 (0.4%)

Adverse Event Key Term	Observations (MRI / Control)	Complications (MRI / Control)	Total AEs (MRI / Control)	Number (%) of Subjects (MRI / Control) (N = 258 / N = 226)
Chest discomfort	2 / 0	1 / 0	3 / 0	3 (1.2%) / 0
Chronic obstructive pulmonary disease	3 / 0	0 / 0	3 / 0	3 (1.2%) / 0
Constipation	0 / 2	1 / 0	1 / 2	1 (0.4%) / 2 (0.9%)
Depression	3 / 0	0 / 0	3 / 0	3 (1.2%) / 0
Diverticulitis	1 / 0	0 / 2	1 / 2	1 (0.4%) / 1 (0.4%)
Hypertension	3 / 0	0 / 0	3 / 0	3 (1.2%) / 0
Inappropriate device stimulation of tissue	1 / 1	1 / 0	2 / 1	2 (0.8%) / 1 (0.4%)
Influenza	1 / 2	0 / 0	1 / 2	1 (0.4%) / 2 (0.9%)
Insomnia	3 / 0	0 / 0	3 / 0	3 (1.2%) / 0
Musculoskeletal pain	1 / 2	0 / 0	1 / 2	1 (0.4%) / 2 (0.9%)
Pain	0 / 2	0 / 1	0 / 3	0 / 3 (1.3%)
Supraventricular tachycardia	0 / 1	1 / 1	1 / 2	1 (0.4%) / 2 (0.9%)
Vertigo	1 / 2	0 / 0	1 / 2	1 (0.4%) / 2 (0.9%)
Anxiety	2 / 0	0 / 0	2 / 0	2 (0.8%) / 0
Atrioventricular block second degree	2 / 0	0 / 0	2 / 0	1 (0.4%) / 0
Benign prostatic hyperplasia	0 / 0	2 / 0	2 / 0	2 (0.8%) / 0
Cardiac perforation	0 / 0	2 / 0	2 / 0	2 (0.8%) / 0
Carpal tunnel syndrome	1 / 0	0 / 1	1 / 1	1 (0.4%) / 1 (0.4%)
Cough	1 / 1	0 / 0	1 / 1	1 (0.4%) / 1 (0.4%)
Electric shock	1 / 1	0 / 0	1 / 1	1 (0.4%) / 1 (0.4%)
Endocarditis	0 / 0	2 / 0	2 / 0	2 (0.8%) / 0
Fall	0 / 2	0 / 0	0 / 2	0 / 2 (0.9%)
Haematuria	2 / 0	0 / 0	2 / 0	2 (0.8%) / 0
Headache	1 / 0	1 / 0	2 / 0	2 (0.8%) / 0
Heart rate increased	2 / 0	0 / 0	2 / 0	2 (0.8%) / 0
Hip fracture	0 / 0	2 / 0	2 / 0	2 (0.8%) / 0

Adverse Event Key Term	Observations (MRI / Control)	Complications (MRI / Control)	Total AEs (MRI / Control)	Number (%) of Subjects (MRI / Control) (N = 258 / N = 226)
Hypertensive crisis	2 / 0	0 / 0	2 / 0	1 (0.4%) / 0
Laceration	0 / 0	2 / 0	2 / 0	2 (0.8%) / 0
Liver disorder	0 / 1	1 / 0	1 / 1	1 (0.4%) / 1 (0.4%)
Mesenteric artery stenosis	0 / 0	2 / 0	2 / 0	1 (0.4%) / 0
Oedema peripheral	0 / 2	0 / 0	0 / 2	0 / 2 (0.9%)
Pain in extremity	1 / 0	0 / 1	1 / 1	1 (0.4%) / 1 (0.4%)
Pulmonary embolism	0 / 1	1 / 0	1 / 1	1 (0.4%) / 1 (0.4%)
Pulmonary oedema	0 / 0	2 / 0	2 / 0	1 (0.4%) / 0
Pyrexia	1 / 0	0 / 1	1 / 1	1 (0.4%) / 1 (0.4%)
Renal failure chronic	0 / 0	1 / 1	1 / 1	1 (0.4%) / 1 (0.4%)
Sinusitis	1 / 1	0 / 0	1 / 1	1 (0.4%) / 1 (0.4%)
Syncope vasovagal	1 / 1	0 / 0	1 / 1	1 (0.4%) / 1 (0.4%)
Transient ischaemic attack	0 / 1	0 / 1	0 / 2	0 / 2 (0.9%)
Undersensing	1 / 1	0 / 0	1 / 1	1 (0.4%) / 1 (0.4%)
Urethral stenosis	0 / 0	2 / 0	2 / 0	2 (0.8%) / 0
Venous insufficiency	0 / 2	0 / 0	0 / 2	0 / 2 (0.9%)
Venous thrombosis	1 / 0	0 / 1	1 / 1	1 (0.4%) / 1 (0.4%)
Ventricular tachycardia	1 / 0	0 / 1	1 / 1	1 (0.4%) / 1 (0.4%)
Abdominal pain upper	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)
Abscess soft tissue	0 / 0	1 / 0	1 / 0	1 (0.4%) / 0
Acute coronary syndrome	0 / 0	0 / 1	0 / 1	0 / 1 (0.4%)
Acute myocardial infarction	0 / 0	1 / 0	1 / 0	1 (0.4%) / 0
Adenocarcinoma	0 / 0	1 / 0	1 / 0	1 (0.4%) / 0
Aneurysm	1 / 0	0 / 0	1 / 0	1 (0.4%) / 0
Angina unstable	0 / 0	0 / 1	0 / 1	0 / 1 (0.4%)
Aortic aneurysm	0 / 0	1 / 0	1 / 0	1 (0.4%) / 0
Aortic stenosis	0 / 0	1 / 0	1 / 0	1 (0.4%) / 0
Arterial occlusive disease	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)

Adverse Event Key Term	Observations (MRI / Control)	Complications (MRI / Control)	Total AEs (MRI / Control)	Number (%) of Subjects (MRI / Control) (N = 258 / N = 226)
Arteriosclerotic retinopathy	0 / 0	1 / 0	1 / 0	1 (0.4%) / 0
Arthralgia	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)
Asthenia	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)
Atelectasis	1 / 0	0 / 0	1 / 0	1 (0.4%) / 0
Atrial thrombosis	1 / 0	0 / 0	1 / 0	1 (0.4%) / 0
Bacterial pyelonephritis	0 / 0	0 / 1	0 / 1	0 / 1 (0.4%)
Basal cell carcinoma	0 / 0	1 / 0	1 / 0	1 (0.4%) / 0
Blood creatinine increased	0 / 0	1 / 0	1 / 0	1 (0.4%) / 0
Blood glucose increased	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)
Bradycardia	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)
Brain neoplasm	1 / 0	0 / 0	1 / 0	1 (0.4%) / 0
Brain stem infarction	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)
Bronchial carcinoma	0 / 0	0 / 1	0 / 1	0 / 1 (0.4%)
Bursitis	0 / 0	1 / 0	1 / 0	1 (0.4%) / 0
Cachexia	0 / 0	0 / 1	0 / 1	0 / 1 (0.4%)
Calcinosis	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)
Cardiac arrest	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)
Cardiac pacemaker revision	0 / 0	1 / 0	1 / 0	1 (0.4%) / 0
Carotid artery stenosis	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)
Cellulitis	1 / 0	0 / 0	1 / 0	1 (0.4%) / 0
Cervicobrachial syndrome	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)
Cholecystitis	0 / 0	1 / 0	1 / 0	1 (0.4%) / 0
Cholelithiasis	0 / 0	0 / 1	0 / 1	0 / 1 (0.4%)
Cholinergic syndrome	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)
Chronic myelomonocytic leukaemia	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)
Clavicle fracture	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)
Clostridium difficile colitis	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)
Colon adenoma	0 / 0	1 / 0	1 / 0	1 (0.4%) / 0

Adverse Event Key Term	Observations (MRI / Control)	Complications (MRI / Control)	Total AEs (MRI / Control)	Number (%) of Subjects (MRI / Control) (N = 258 / N = 226)
Confusional state	1 / 0	0 / 0	1 / 0	1 (0.4%) / 0
Contusion	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)
Convulsion	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)
Cystitis	1 / 0	0 / 0	1 / 0	1 (0.4%) / 0
Device psychogenic complication	1 / 0	0 / 0	1 / 0	1 (0.4%) / 0
Diastolic dysfunction	1 / 0	0 / 0	1 / 0	1 (0.4%) / 0
Dyspepsia	1 / 0	0 / 0	1 / 0	1 (0.4%) / 0
Dysphonia	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)
Ear pain	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)
Ejection fraction decreased	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)
Endometrial disorder	0 / 0	0 / 1	0 / 1	0 / 1 (0.4%)
Epistaxis	1 / 0	0 / 0	1 / 0	1 (0.4%) / 0
Erythema migrans	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)
Eye haemorrhage	1 / 0	0 / 0	1 / 0	1 (0.4%) / 0
Faecaloma	0 / 0	0 / 1	0 / 1	0 / 1 (0.4%)
Gastritis erosive	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)
Gastroenteritis	1 / 0	0 / 0	1 / 0	1 (0.4%) / 0
Glioblastoma	0 / 0	0 / 1	0 / 1	0 / 1 (0.4%)
Gouty arthritis	1 / 0	0 / 0	1 / 0	1 (0.4%) / 0
Grand mal convulsion	1 / 0	0 / 0	1 / 0	1 (0.4%) / 0
Groin infection	1 / 0	0 / 0	1 / 0	1 (0.4%) / 0
Haematoma	0 / 0	1 / 0	1 / 0	1 (0.4%) / 0
Head injury	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)
Heat exhaustion	1 / 0	0 / 0	1 / 0	1 (0.4%) / 0
Hypercholesterolaemia	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)
Hyperhidrosis	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)
Hyponatraemia	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)
Hypothyroidism	1 / 0	0 / 0	1 / 0	1 (0.4%) / 0

Adverse Event Key Term	Observations (MRI / Control)	Complications (MRI / Control)	Total AEs (MRI / Control)	Number (%) of Subjects (MRI / Control) (N = 258 / N = 226)
Implant site discharge	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)
Implant site pain	1 / 0	0 / 0	1 / 0	1 (0.4%) / 0
Implant site swelling	1 / 0	0 / 0	1 / 0	1 (0.4%) / 0
Inappropriate device therapy	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)
Incision site erythema	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)
Incontinence	0 / 0	0 / 1	0 / 1	0 / 1 (0.4%)
Infection	1 / 0	0 / 0	1 / 0	1 (0.4%) / 0
Influenza like illness	1 / 0	0 / 0	1 / 0	1 (0.4%) / 0
Inguinal hernia	0 / 0	1 / 0	1 / 0	1 (0.4%) / 0
Intestinal perforation	0 / 0	1 / 0	1 / 0	1 (0.4%) / 0
Intracranial aneurysm	0 / 0	1 / 0	1 / 0	1 (0.4%) / 0
Ischaemic stroke	0 / 0	1 / 0	1 / 0	1 (0.4%) / 0
Knee arthroplasty	0 / 0	0 / 1	0 / 1	0 / 1 (0.4%)
Limb injury	0 / 0	1 / 0	1 / 0	1 (0.4%) / 0
Loss of consciousness	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)
Lumbar spinal stenosis	0 / 0	1 / 0	1 / 0	1 (0.4%) / 0
Lumbar vertebral fracture	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)
Lung infection	0 / 0	0 / 1	0 / 1	0 / 1 (0.4%)
Medical device complication	0 / 0	1 / 0	1 / 0	1 (0.4%) / 0
Mental status changes	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)
Micturition disorder	0 / 0	1 / 0	1 / 0	1 (0.4%) / 0
Multiple myeloma	0 / 0	1 / 0	1 / 0	1 (0.4%) / 0
Muscle spasms	1 / 0	0 / 0	1 / 0	1 (0.4%) / 0
Muscle strain	1 / 0	0 / 0	1 / 0	1 (0.4%) / 0
Nasopharyngitis	1 / 0	0 / 0	1 / 0	1 (0.4%) / 0
Neuralgia	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)
Nodal rhythm	1 / 0	0 / 0	1 / 0	1 (0.4%) / 0
Non-cardiac chest pain	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)

Adverse Event Key Term	Observations (MRI / Control)	Complications (MRI / Control)	Total AEs (MRI / Control)	Number (%) of Subjects (MRI / Control) (N = 258 / N = 226)
Orthostatic hypotension	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)
Osteoarthritis	0 / 0	0 / 1	0 / 1	0 / 1 (0.4%)
Panic attack	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)
Peptic ulcer	0 / 0	0 / 1	0 / 1	0 / 1 (0.4%)
Pericarditis	1 / 0	0 / 0	1 / 0	1 (0.4%) / 0
Peripheral vascular disorder	1 / 0	0 / 0	1 / 0	1 (0.4%) / 0
Petit mal epilepsy	1 / 0	0 / 0	1 / 0	1 (0.4%) / 0
Plantar fasciitis	1 / 0	0 / 0	1 / 0	1 (0.4%) / 0
Pleuritic pain	1 / 0	0 / 0	1 / 0	1 (0.4%) / 0
Pneumonia bacterial	0 / 0	1 / 0	1 / 0	1 (0.4%) / 0
Polymyalgia rheumatica	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)
Postoperative thoracic procedure complication	0 / 0	0 / 1	0 / 1	0 / 1 (0.4%)
Postoperative wound infection	0 / 0	1 / 0	1 / 0	1 (0.4%) / 0
Prostate cancer	1 / 0	0 / 0	1 / 0	1 (0.4%) / 0
Renal cell carcinoma stage unspecified	0 / 0	1 / 0	1 / 0	1 (0.4%) / 0
Renal failure	1 / 0	0 / 0	1 / 0	1 (0.4%) / 0
Renal failure acute	0 / 0	1 / 0	1 / 0	1 (0.4%) / 0
Renal tubular acidosis	1 / 0	0 / 0	1 / 0	1 (0.4%) / 0
Respiratory failure	0 / 0	0 / 1	0 / 1	0 / 1 (0.4%)
Respiratory tract infection	1 / 0	0 / 0	1 / 0	1 (0.4%) / 0
Restlessness	1 / 0	0 / 0	1 / 0	1 (0.4%) / 0
Rib fracture	1 / 0	0 / 0	1 / 0	1 (0.4%) / 0
Salivary gland calculus	1 / 0	0 / 0	1 / 0	1 (0.4%) / 0
Sarcoidosis	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)
Sciatica	0 / 0	1 / 0	1 / 0	1 (0.4%) / 0
Sepsis	0 / 0	1 / 0	1 / 0	1 (0.4%) / 0

Adverse Event Key Term	Observations (MRI / Control)	Complications (MRI / Control)	Total AEs (MRI / Control)	Number (%) of Subjects (MRI / Control) (N = 258 / N = 226)
Spinal column stenosis	0 / 0	1 / 0	1 / 0	1 (0.4%) / 0
Spondylolisthesis	0 / 0	1 / 0	1 / 0	1 (0.4%) / 0
Stomatitis	1 / 0	0 / 0	1 / 0	1 (0.4%) / 0
Subclavian vein thrombosis	0 / 0	0 / 1	0 / 1	0 / 1 (0.4%)
Supraventricular extrasystoles	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)
Swelling	1 / 0	0 / 0	1 / 0	1 (0.4%) / 0
Tendonitis	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)
Thrombophlebitis	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)
Traumatic haematoma	1 / 0	0 / 0	1 / 0	1 (0.4%) / 0
Upper respiratory tract infection	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)
Urinary retention	0 / 0	1 / 0	1 / 0	1 (0.4%) / 0
Ventricular dysfunction	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)
Viral infection	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)
Vision blurred	0 / 1	0 / 0	0 / 1	0 / 1 (0.4%)
Vomiting	0 / 0	1 / 0	1 / 0	1 (0.4%) / 0
Weight decreased	1 / 0	0 / 0	1 / 0	1 (0.4%) / 0
Whiplash injury	1 / 0	0 / 0	1 / 0	1 (0.4%) / 0
Total	**183 / 129**	**137 / 78**	**320 / 207**	**152 (58.9%) / 108 (47.8%)**

Table 4-30 summarizes the 215 complications' relatedness. One-hundred and forty-nine (149) of the 215 complications (69%) were *not* related to the implant, system, or MRI procedure. Secondary objective #4 details the related adverse events that occurred prior to the one-month post-MRI/control visit. In many instances, adverse events were adjudicated by the AEAC to be related to more than one system or procedure component (e.g. implant and RV lead, or IPG and RA lead). Because of this, while there were 36 (=137-101) MRI group complications related to the system or a procedure, the 1 IPG, 10 RA lead, 19 RV lead, and 30 implant-related add up to more than 36.

Table 4-30. Adverse Event Complications by Relatedness

Relatedness		MRI Group		Control Group	
		Complications	Subjects (n=258)	Complications	Subjects (n = 226)*
System	Pacemaker (IPG)	1	1 (0.4%)	2	2 (0.9%)
	RA lead	10	10 (3.9%)	9	9 (4.0%)
	RV lead	19	16 (6.2%)	12	10 (4.4%)
	Programmer	0	0	0	0
	Software	0	0	0	0
	MRI SureScan	0	0	0	0
Procedure	Implant	30	27 (10.5%)	26	20 (8.8%)
	MRI	0	0	0	0
Non-system and non-procedure related		101	72 (27.9%)	48	32 (14.2%)
Total**		137	93 (36.0%)	78	54 (23.9%)

* Twenty (20) enrolled non-randomized subjects included in the control group.

** Some complications were attributed to more than one system component or procedure, so the total row is less than the sum of the other rows.

4.4.5. Study Deviations

Table 4-31 summarizes all study deviations. Study deviation event rates are similar in comparison other Medtronic clinical studies results as reported in the EnRhythm, EnPulse, and Adapta clinical studies P980035/S038, P980035/S030, P980038/S043 approved by FDA.

Table 4-31. Study Deviations

Deviation Description	Number of Deviations	Number (%) of Subjects (n = 484)
Additional diagnostic/non-protocol MRI scan performed on subject	7	7 (1.4%)
Body measurements	4	4 (0.8%)
Chest X-ray not collected / not performed per protocol	22	22 (4.5%)
Co-investigator participated in study before being activated	2	2 (0.4%)
Collection of MRI scan data	24	23 (4.8%)
Current IRB/MEC approved consent version not used	2	2 (0.4%)
Device interrogation not done per protocol (not performed at all)	2	2 (0.4%)
Device interrogation not performed per protocol (performed, but not compliant)	1	1 (0.2%)
Device strips not collected / not performed per protocol	1	1 (0.2%)
Enrolled (or intend to) in concurrent study	2	2 (0.4%)
Impedance (device interrogation not performed at all)	50	35 (7.2%)
Impedance (device interrogation performed, but not compliant)	4	4 (0.8%)
Incomplete visit / multiple data collection / testing not collected / not performed per protocol	8	8 (1.7%)
Initiated/changed medication post-enrollment in violation of protocol	1	1 (0.2%)
MRI SureScan printout not saved/ forwarded to Medtronic (device strips)	1	1 (0.2%)
Monitoring of a subject	5	5 (1.0%)
Multiple (device interrogation not performed at all)	17	17 (3.5%)
Multiple (device interrogation performed, but not compliant)	7	7 (1.4%)
Multiple (device strips)	7	7 (1.4%)
Non-authorized site personnel completing or signing CRF/QC	18	18 (3.7%)
Non-MRI compatible device or material implant	1	1 (0.2%)
Not able/willing to have elective MRIscanning without sedation	1	1 (0.2%)
Pre-MRI system checks by cardiology staff	2	2 (0.4%)
Pacing outputs not programmed to 5 V at 1.0 ms pre-MRI	9	9 (1.9%)
Pacing outputs not programmed to 5 V at 1.0 ms until 3-month visit	6	6 (1.2%)
Pre-MRI screening by radiology staff	1	1 (0.2%)

Deviation Description	Number of Deviations	Number (%) of Subjects (n = 484)
Pre-MRI system checks by cardiology staff	1	1 (0.2%)
Pregnancy or without reliable birth control	1	1 (0.2%)
Previously implanted pacemaker or defibrillator	1	1 (0.2%)
Required source documentation permanently missing	3	3 (0.6%)
Sensing (device interrogation not performed at all)	27	27 (5.6%)
Sensing (device interrogation performed, but not compliant)	5	4 (0.8%)
Sensing (test strips)	59	42 (8.7%)
Study visit early	19	18 (3.7%)
Study visit late	82	72 (14.9%)
Study visit missed	57	40 (8.3%)
Subject not randomized within study timeframe	2	2 (0.4%)
Subject received wrong randomization scheme (e.g., out of order)	2	2 (0.4%)
System not implanted per protocol	5	5 (1.0%)
Thresholds (device strips)	116	89 (18.4%)
Trained personnel did not attend visit	1	1 (0.2%)
Unable to determine capture threshold value (device strips)	3	3 (0.6%)
Unauthorized or untrained study personnel obtained consent	2	2 (0.4%)
Waiting period instructions not followed	4	4 (0.8%)
Written consent not signed and dated by subject or legal representative*	1	1 (0.2%)
Total	596	284 (58.7%)

* Power of Attorney dated for patient. At a later date, patient re-acknowledged consent process and confirmed original consent date to be accurate.

4.4.6. Subject Accountability

4.4.6.1. Study Exits

Twenty-one subjects were exited from the study. Seventeen of these subjects did not attempt the implant procedure. Of the remaining four:

- One MRI subject had a complete system explant due to diaphragmatic stimulation 93 days post-implant.
- One MRI subject had a complete system explant due to infection 401 days post-implant and 332 days post-MRI.
- One control subject had a complete system explant due to infection 55 days due to thoracic pain.
- One control subject was lost to follow-up after 118 days post-implant.

4.4.6.2. Subjects Not Successfully Implanted

Three subjects were not successfully implanted but remained in the study to be analyzed for system safety:

- One subject received the investigational ventricular CapSureFix MRI 5086MRI lead with other commercially available implanted system components (Medtronic Adapta IPG and Medtronic Model 5076 atrial lead). According to the implanting physician, three atrial CapSureFix MRI 5086MRI leads were attempted but required excessive turns to deploy the helix and could not be verified radiographically. The atrial leads were returned to Medtronic for analysis, and no anomalies were found.
- One subject received the investigational atrial CapSureFix MRI 5086MRI lead with other commercially available system components (Biotronik Philos IPG and Medtronic Model 4076 ventricular lead). According to the implanting physician, the threshold and sensing values for the ventricular lead were unacceptable during several attempts. The ventricular lead was returned to Medtronic for analysis, and no anomalies were found.
- One subject received the investigational ventricular CapSureFix MRI 5086MRI lead with the EnRhythm MRI pacemaker with no other commercially available atrial component. According to the implanting physician, the atrial lead was too long to achieve good fixation and a stable position. The atrial lead was returned to Medtronic for analysis, and no anomalies were found.

4.4.6.3. MRI Scan Exclusions

Thirty-three subjects were randomized to the MRI group, but did not undergo an MRI per protocol. The reasons for these are listed in **Table 4-32**.

Table 4-32. MRI Group MRI Scan Deviations

Reason			Subjects (n)
Did not undergo an MRI scan (n=18)	Scan sequences were not completed due to subject non-compliance (subjects refused)		8
	Scan sequences were not completed due to pre-scan pacing capture thresholds being greater than 2.0 V at 0.5 ms	Atrial	1
		Ventricular	2
	Scan sequences were not completed due to inability to verify pre-scan capture thresholds	Atrial	2
		Ventricular	0
	Scan sequences were not completed due to subject having diaphragmatic stimulation at a ventricular pacing output of 5.0 V at a pulse width of 1.0 ms		2
	Scan sequences were not completed due to non-MRI compatible stent		1
	Scan sequences were not completed due to replacement of CapSureFix MRI 5086MRI lead with non-5086 MRI lead		1
	Scan sequences were not completed due to subject pregnancy		1
Underwent a partial scan (n=6)	Several sequences were not completed due to subject discomfort while in supine position		4
	Lumbar scan sequences were not completed due to MRI machine malfunction		1
	Lumbar scan sequences were not completed because subject did not fit in the scanner		1
Did not undergo an MRI scan per protocol (n=9)	SAR exceeded 2.0 W/kg for one scan sequence		7
	SAR exceeded 2.0 W/kg for three scan sequences		1
	Ventricular capture threshold exceeded 2.0 V at pre-MRI check		1
Total			33

Results from subjects who underwent a partial scan or did not undergo an MRI scan per protocol are included in the sensitivity analyses of the primary objectives.

Of these 33 subjects, one did not complete the one-month post-MRI/control visit and therefore is not included in the primary objective missing data tables, which report 32 missing.

In addition, one control group subject mistakenly underwent an MRI scan. A study deviation form was completed and the subject continued to be followed in the control group. The subject is included in secondary analyses of objectives related to MRI-related complications, labeling instructions, and occurrence of arrhythmias.

4.4.7. Subject Deaths

Eleven subject deaths were reported, including nine in the MRI group and two in the control group. Of the nine that occurred in the MRI group, three occurred before the MRI and six occurred after the MRI. Of the six that occurred after the MRI, the closest in time to the MRI procedure was a pulmonary edema ten days post MRI. Other events occurred no earlier than six months post MRI and further out to one year. The adverse event advisory committee (AEAC) adjudicated that the 11 subject deaths were not related to the pacing system (pacemaker, leads, programmer/software components), not related to the implant procedure, and not-related to the MRI procedure. The Data Monitoring Committee (DMC) concurred with the AEAC in stating they did not believe that the higher number of deaths observed in the MRI group, in comparison to the control group, was of clinical concern upon review of the causes, classifications, and timing relative to the MRI scan. **Table 4-33** summarizes each subject death.

Table 4-33. Study Deaths

Subject ID	Group	Days Post-Implant	Days Post-MRI/control Visit	Cause of Death	Cardiac or Non-Cardiac*	Sudden or Non-Sudden
	Control	226	153	Glioblastoma	Non-Cardiac	Not Applicable
	Control	378	308	Myocardial infarction	Cardiac	Sudden
	MRI	3	Pre-MRI	Decompensation cardiac	Cardiac	Non-Sudden
	MRI	21	Pre-MRI	Pneumonia	Non-Cardiac	Not Applicable
	MRI	28	Pre-MRI	Adenocarcinoma	Non-Cardiac	Not Applicable
	MRI	79	10	Pulmonary edema	Cardiac	Non-Sudden
	MRI	135	51	Sepsis	Non-Cardiac	Not Applicable
	MRI	267	183	Myocardial infarction	Cardiac	Sudden
	MRI	404	340	Stroke	Non-Cardiac	Not Applicable
	MRI	481	403	Acute ischemic stroke	Non-Cardiac	Not Applicable
	MRI	544	461	Terminal cardiac failure	Cardiac	Non-Sudden

deaths are not classified as sudden or non-sudden.

4.5. Conclusion

The EnRhythm MRI clinical study evaluated and confirmed the following:

- The EnRhythm MRI system is safe for use in the MRI environment when used in accordance with its labeling as determined by the MRI-related complication-free rate and no occurrences of sustained ventricular arrhythmias or asystole.
- The EnRhythm MRI system is effective for use in the MRI environment when used in accordance with its labeling as determined by:
    - The clinical equivalence of the atrial and ventricular pacing capture threshold results between the MRI group and the control group.
    - The clinical equivalence of the atrial and ventricular sensed amplitude results between the MRI group and the control group.

In summary, all five primary safety and effectiveness objectives were met. All secondary objectives were met when performance criteria was predefined. Overall, there was no difference in performance between the MRI group and the control group. In the MRI environment under specific guidelines at 1.5 T field strength, the EnRhythm MRI pacing system performance was commensurate with MR-Conditional labeling requirements. As noted previously, the total adverse event and deviation rates are similar in comparison to other Medtronic clinical investigations of pacemakers and leads.

The Data Monitoring Committee chair wrote on behalf of the board, “We concur that the study met its objectives”. The study has confirmed the safety and effectiveness of the EnRhythm MRI SureScan Pacing System in the clinical MRI environment.

4.6. Clinical Study Application to MRI Hazards

The clinical study was designed to examine the effect of lead heating by comparing pacing capture threshold changes between the MRI and non-MRI groups, the data generated from the clinical study substantiated the pre-clinical data results for all the hazards as summarized in **Table 4-34.** No MRI-induced adverse event complications related to case heating, force, torque, vibration, or device interactions were observed in the clinical study, which is consistent with expectations from the pre-clinical results. Similarly, no subjects experienced MRI-induced arrhythmias, and pacing capture threshold changes were comparable between the MRI and control groups.

Table 4-34. Summary of Clinical Study Application to MRI Hazards

Hazard	Clinical Evaluation	Clinical Result
Lead Heating	Primary effectiveness objective: To compare the changes in atrial and ventricular pacing capture thresholds before and after MRI between the MRI and control groups.	The proportion of subjects who experienced an increase in atrial or ventricular pacing capture thresholds ≥0.5 V are clinically equivalent, defined as within 10% (p<0.001).
Unintended Cardiac Stimulation	Primary safety objective: To assess the MRI-related complication-free rate in the month following MRI.	The MRI-related complication-free rate between the MRI procedure and one-month post-MRI is greater than 90% (p<0.001)*
Device Interactions	System-related adverse events and technical observations related to MRI Dislodgements related to MRI	No patients with system-related complication adverse events (associated with discomfort or tissue damage) or technical observations, related to MRI** No patients with dislodgements related to MRI
Pacemaker Case Heating		
Force and Torque		
Vibration		

* The independent Adverse Event Committee classified two events in two patients as observations of atrial flutter and atrial fibrillation with unknown relatedness to MRI and unknown relatedness to the pacing system. Patient 317620506 reported atrial flutter during the MRI procedure. Baseline history indicated the following atrial arrhythmias: persistent atrial fibrillation, atrial tachycardia, sinus arrest, and sinus bradycardia. Patient 451320012 reported atrial fibrillation during the MRI procedure. Baseline history indicated the following atrial arrhythmias: paroxysmal atrial fibrillation, atrial tachycardia, premature atrial contraction, and sinus bradycardia.
** One observation of chest discomfort with unknown relatedness to MRI.

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Appendix 5 - List of Acronymns

Appendix 5 - Acronyms and Definitions

Abbreviation or Acronym	Term	Definition
ACR	American College of Radiology	The principal organization of radiologists, radiation oncologists, and clinical medical physicists in the United States, with more than 30,000 members.
AEAC	Adverse Event Advisory Committee	A committee of physicians appointed to review Adverse Events occurring during clinical studies.
AIMD	Active implantable medical device	Examples of AIMD's include implantable pacemakers and defibrillators, cochlear implants, and implantable nerve stimulators.
AF	Atrial fibrillation	An atrial arrhythmia marked by rapid randomized contractions of small areas of the atrial myocardium, causing a totally irregular and often rapid, ventricular rate.
AT	Atrial tachycardia	A rapid heart rate that originates in the atrium.
ATP	Antitachycardia pacing	Therapies that deliver rapid sequences of pacing pulses to terminate tachyarrhythmias.
AV	Atrioventricular	Of or relating to the relationship of the atrium and the ventricle.
---	Body coil, coil, RF coil	Radiofrequency coil used in magnetic resonance imaging systems.
CEM	Cumulative Equivalent Minutes	Thermal dose metric.
CIP	Clinical Investigational Plan	A document that states the rationale, objectives, design and proposed analysis, methodology, monitoring, conduct and record-keeping of the clinical study. It provides complete documentation necessary for an Investigator to conduct a clinical study and for the potential review and approval of a clinical study by the Medical Ethics Committee (MEC)/Institutional Review Board (IRB).
CT	Computed tomography	Medical imaging method used to generate a three-dimensional image of a section of a body from a large series of two-dimensional X-ray images taken around a single axis of rotation.

Abbreviation or Acronym	Term	Definition
dB/dt	Magnetic Field Time Rate of Change	Time rate of change of magnetic field flux density. In the general case, this is a vector entity having the same vector direction as the magnetic field B. The symbol dB/dt is used very generally in gradient field discussions, with any more specific meaning defined by the context in which it is used. The symbol dB/dt is often used to denote the scalar magnitude only of the time rate of change of magnetic field flux density.
---	Dissipated power at the tip-tissue interface, dissipated power, tip dissipated power	Refers to the RF power dissipated at the tip-to-tissue interface.
---	Distal lead end	The end of an implantable pacing lead that contains the pacing electrodes (tip and ring) and is fixated to cardiac tissue.
DUT	Device under test	Device (e.g., pacemaker or lead) that is being tested.
EM	Electromagnetic	Refers to the electromagnetic field present in the MRI environment.
EMC	Electromagnetic Compatibility	Unintentional generation, propagation and reception of electromagnetic energy with reference to the unwanted effects.
EMI	Electromagnetic Interference	Disturbance that affects an electrical circuit due to either electromagnetic conduction or electromagnetic radiation emitted from an external source.
FFT	Filtered feed through	Capacitors used at the lead to pacemaker interface to protect the internal circuitry from electromagnetic interference.
ICD	Implantable cardioverter defibrillator	Active implantable device to treat tachycardia.
IDE	Investigational Device Exemption	An IDE allows the investigational device to be used in a clinical study in order to collect safety and effectiveness data required to support a Pre-market Approval (PMA) application or a Pre-market Notification [510(k)] submission to FDA. See PMA below.
IEC	International Electrotechnical Commission	International standards and conformity assessment body for all fields of electrotechnology.

Abbreviation or Acronym	Term	Definition
IPG	Implantable pulse generator	Active implantable device to treat bradycardia (pacemaker).
----	In vitro	Refers to experiments performed outside of a living subject.
----	In vivo	Refers to experiments performed on a living subject.
IRB	Institutional Review Board	Any board, committee, or other group formally designated by an institution to review, to approve the initiation of, and to conduct periodic review of, biomedical research involving human subjects. The primary purpose of the rights and welfare of the human subjects.
ISO	International Organization for Standardization	ISO is the world's largest developer and publisher of international standards.
----	Isocenter, iso-center	The 3-dimensional geometric center in the bore of a magnetic resonance imaging scanner.
----	Lead path	Lead routing in the body, body model, or body phantom.
----	Lead heating, lead tip heating	Heating at the tip electrode due to RF energy being coupled to the lead during an MRI scan.
MEC	Medical Ethics Committee	An independent and properly constituted competent body whose responsibility is to ensure that the safety, well-being and human rights of the subjects participating in a clinical investigation are protected.
MHz	Megahertz	Number of million cycles per second.
MR	Magnetic resonance	Absorption of energy exhibited by particles in a static magnetic field when the particles are exposed to electromagnetic radiation of certain frequencies.
MRI	Magnetic resonance imaging	Diagnostic technique that relies on magnetic fields to produce images of the body based on the magnetic resonance of nuclei (see above).
mV	milliVolt	Unit of electric potential, one thousandth of one Volt (see Volt below).
mW	milliWatt	Unit of power, one thousandth of one Watt (see Watt below).

Abbreviation or Acronym	Term	Definition
----	Normal Operating Mode	Mode of operation of MRI scanners, which limits the patient SAR averaged over six minutes as follows (as defined in IEC 60601-2-33): Whole body SAR: 2 W/kg; head SAR: 3.2 W/kg. In addition, the SAR limits over any 10 second period shall not exceed three times the stated values.
N	Newton	SI unit of force, is equal to approximately 0.225 pounds of force.
N-m	Newton-meter	SI unit of torque.
Pa	Pascal	Unit of pressure, equal to 1 Newton/m^2 ($1.45 \cdot 10^{-4}$ pounds/in^2). See Newton above.
PAS	Post Approval Study	FDA has the authority to require sponsors to perform a post-approval study (or studies) at the time of approval of a PMA to help assure continued safety and effectiveness of the approved device.
PMA	Pre-market approval	Pre-market approval by FDA is the required process of scientific review to ensure the safety and effectiveness of Class III devices.
PCT	Pacing capture threshold	Minimum electrical stimulus needed to consistently elicit cardiac depolarization. As used in this document, assumes a 0.5 ms pulse width.
PNS	Peripheral nerve stimulation	---
---	Proximal lead end	The end of an implantable pacing lead which connects to an IPG or ICD.
RA	Right atrium	Chamber of the patient's heart where the distal end of the pacing lead is implanted.
RF	Radio frequency	Refers to the frequency of operation of an MRI birdcage coil (for 1.5 static magnet, the frequency is 64 MHz).
RV	Right ventricle	Chamber of the patient's heart where the distal end of the pacing lead is implanted.
SAC	Scan Advisory Committee	A committee that developed the manufacturer specific scan sequences for the EMRI study.
SAR	Specific absorption rate	Amount of RF power absorbed per unit mass, defined in terms of Watts/kilogram (W/kg).
---	Slew rate (Gradient slew rate)	Rate at which the fields can change when adjusting from one amplitude to another. Usually refers to gradient fields.

Abbreviation or Acronym	Term	Definition
T	Tesla	MKS unit for magnetic flux density. 1 Tesla = 10,000 Gauss.
---	Tip-to-tissue interface, tip-tissue interface	Small volume of tissue directly in contact with the lead helix. This is the volume where RF energy is dissipated.
t	Effective pulse width	The effective width of a gradient-induced voltage pulse appearing on the pacing electrode is defined as the product of the pacemaker capacitance and the tip-to-tissue resistance.
$T_{s,eff}$	Effective stimulus duration	The time that the gradient magnetic field is changing.
UCS	Unintended cardiac stimulation	Cardiac stimulation in pacemaker patients caused by signals induced on pacing lead(s) by MRI RF and / or gradient magnetic fields.
VT	Ventricular tachyarrhythmia	Ventricular arrhythmia originating in the bifurcation of the His bundle or lower, i.e., bundle branches, Purkinje network or ventricles.
VF	Ventricular fibrillation	Ventricular arrhythmia where small areas of ventricular myocardium depolarize randomly without any coordination possibly many reentry circuits.
V	Volt	Unit of electric potential.
W	Watt	Unit of power, equal to 1 Joule per second.

Appendix 6 - Summary of Literature

Appendix 6 - Summary of Literature

1. Abdel-Aty H, et al. Diagnostic performance of cardiovascular magnetic resonance in patients with suspected acute myocarditis: comparison of different approaches. *J Am Coll Cardiol.* 45(11): 1815-1822.

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Appendix 7 - Proposed Labeling

Appendix 7 - Proposed Labeling

This section includes the relevant product manuals.

7.1 – Revo MRI™ SURESCAN™ RVDR01 Technical Manual

7.2 – Revo MRI™ SURESCAN™ RVDR01 Implant Manual

7.3 – CAPSUREFIX MRI™ SURESCAN 5086MRI Technical Manual

Slipsheet

Medtronic

REVO MRI™ SURESCAN™ RVDR01

SureScan

MR

MRI procedural information for Revo MRI™ SureScan™ RVDR01, CapSureFix MRI™ SureScan™ 5086MRI

Technical Manual

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

The following are trademarks of Medtronic:

CapSureFix, CapSureFix MRI, Checklist, Medtronic, Medtronic CareLink, Quick Look, Revo MRI, SureScan

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4

1 Introduction

It is important to read the information in this manual before conducting an MRI scan on a patient with an implanted SureScan pacing system. Contact a Medtronic representative if you have any questions about the information in this manual.

Refer to the appropriate Medtronic device reference manual or lead technical manual for non-MRI related instructions for use.
The Medtronic SureScan pacing system includes a Medtronic SureScan device connected to Medtronic SureScan leads. The labeling for SureScan pacing system components displays the SureScan symbol and the MR Conditional symbol.

SureScan symbol

MR Conditional symbol. The SureScan pacing system is safe for use in the MRI environment when used according to the instructions in this SureScan technical manual.

The MRI SureScan feature permits a mode of operation that allows a patient with a SureScan device to be safely scanned by an MRI machine when used according to the instructions in this SureScan technical manual.

2 MRI conditions for use

Clinical and non-clinical testing has demonstrated that the SureScan pacing system is safe for use in the MRI environment when used according to the instructions in this manual.

The SureScan pacing system can be scanned in patients under these conditions:

- Cylindrical bore magnet, clinical MRI systems with a static magnetic field of 1.5 tesla (T) must be used.
- Gradient systems with maximum gradient slew rate performance per axis of ≤ 200 T/m/s must be used.
- Whole body averaged specific absorption rate (SAR) as reported by the MRI equipment must be ≤ 2.0 W/kg. The head SAR as reported by the MRI equipment must be < 3.2 W/kg.
- Patients and their implanted systems must be screened to meet the following requirements:
  - No previously implanted (active or abandoned) medical devices, leads, lead extenders, or lead adaptors
  - No broken or intermittent leads
  - A SureScan pacing system that has been implanted for a minimum of 6 weeks
  - A SureScan pacing system implanted in the left or right pectoral region
  - Pacing capture thresholds of ≤ 2.0 V at a pulse width of 0.4 ms
  - A lead impedance value of ≥ 200 Ω or ≤ 1500 Ω
  - No diaphragmatic stimulation at a pacing output of 5.0 V and at a pulse width of 1.0 ms in patients whose device will be programmed to an asynchronous pacing mode when MRI SureScan is on
- The patient must be positioned within the bore such that the isocenter (center of the MRI bore) is superior to the C1 vertebra or inferior to the T12 vertebra.
- There are no restrictions on the placement of any receive-only coils.
- There are no restrictions on the use of local transmit or local transmit/receive coils for imaging of the head or of the extremities.

- Proper patient monitoring must be provided during the MRI scan. This includes continuous monitoring of the patient's hemodynamic function. Since the MR environment may interfere with the patient monitoring system, it is recommended that more than one of the following systems be used:
  - Electrocardiography
  - Pulse oximetry
  - Non-invasive blood pressure measurements
- The implanted system must consist solely of a Medtronic Revo MRI SureScan Model RVDR01 device and 2 CapSureFix MRI SureScan Model 5086MRI leads.

3 MR conditional contraindications

Patients with broken or intermittent leads are contraindicated for an MRI scan.

Patients with a SureScan pacing system implanted in sites other than the left and right pectoral region are contraindicated for an MRI scan.

Patients who do not have a complete SureScan pacing system, which includes a SureScan device and both atrial and ventricular SureScan leads, are contraindicated for an MRI scan.

Patients with a lead impedance value of < 200 Ω or > 1500 Ω are contraindicated for an MRI scan.

4 Warnings and precautions

4.1 MRI warnings and precautions

Cautions:

- Do not scan patients with a SAR level exceeding 2.0 W/kg. A scan above 2.0 W/kg may increase the risk of myocardial tissue damage due to lead tip heating, resulting in an increase in the pacing capture threshold.
- Do not scan patients with pacing capture threshold values of > 2.0 V at a pulse width of 0.4 ms. The higher pacing capture threshold indicates there may be an issue with the implanted lead.
- Do not scan patients with previously implanted (active or abandoned) medical devices, leads, lead extenders, or lead adaptors as it may increase the risk of myocardial tissue damage due to lead tip heating and other MR RF field-related hazards. The interaction with other implantable devices has not been evaluated by Medtronic.
- Do not scan patients whose device will be programmed to an asynchronous pacing mode when MRI SureScan is on, and who have diaphragmatic stimulation at a pacing output of 5.0 V and at a pulse width of 1.0 ms. It may be difficult for the patient to remain still in order to obtain a quality image.
- Do not scan the patient positioned such that the isocenter (center of the MRI bore) is inferior to the C1 vertebra and superior to the T12 vertebra as it may cause mycocardial damage due to lead tip heating, resulting in an increase in pacing capture threshold. This has not been studied clinically by Medtronic.

5 Radiology-specific requirements

5.1 MRI equipment requirements

The MRI equipment requirements listed in this section must be satisfied during all MRI scans performed on patients with a SureScan pacing system. If you are unsure of the capabilities of your MRI machine, contact the MRI manufacturer.

Compatible MRI equipment operating characteristics – The safety and reliability of the SureScan pacing system has been evaluated for scanning patients using MRI equipment that has the following operating characteristics:

- hydrogen proton magnetic resonance imaging equipment with a static magnetic field of 1.5 T
- RF excitation frequency that is approximately 64 MHz in a 1.5 T static magnetic field
- cylindrical bore magnet, clinical MRI systems
- gradient systems with a maximum gradient slew rate performance per axis of 200 T/m/s or less

5.2 MRI scan requirements

MRI radio frequency (RF) power – The whole body SAR as reported by the MRI equipment must be ≤ 2.0 W/kg. The head SAR as reported by the MRI equipment must be < 3.2 W/kg.

Use of transmit/receive, transmit-only, and receive-only coils – If a local, volume, interventional, or surface coil is needed, position the patient such that the isocenter (center of the MRI bore) is superior to the C1 vertebra or inferior to the T12 vertebra as described in Section 8.

5.3 Patient safety during the MRI scan

Preparation for patient rescue – Keep an external defibrillator available during the MRI scan.

Patient monitoring – Proper patient monitoring must be provided during the MRI scan. This includes continuous monitoring of the patient's hemodynamic function. Since the MR environment may interfere with the patient monitoring system, it is recommended that more than one of the following systems be used:

- electrocardiography
- pulse oximetry
- noninvasive blood pressure measurements

Note: If the patient's hemodynamic function is compromised during the MRI scan, discontinue the MRI scan and take the proper measures to restore the patient's hemodynamic function.

5.4 Image quality

If the SureScan device or leads are within or near the imaging area of interest, then MRI image quality may be compromised.

6 Cardiology-specific requirements

6.1 Cardiac equipment requirements

Configuration restrictions – Patient safety during MRI scans requires that the implanted system consists solely of a SureScan device and both atrial and ventricular SureScan leads. Any other combination may result in a hazard to the patient during MRI scans.

Competitive pacing – If an asynchronous MRI SureScan pacing mode is selected, be aware that some patients may be susceptible to cardiac arrhythmia induced by competitive pacing. For these patients, it is important to first select an MRI SureScan pacing rate that avoids competitive pacing and then minimize the duration of the asynchronous pacing operation. For more information, contact a Medtronic representative.

6.2 Patient communications

System information and records – All pertinent information about the components of the implanted SureScan pacing system, such as model names, model numbers, and serial numbers, should be recorded in the patient record and on the Patient Information Screen on the programmer.

Patient ID card requirements – Reference materials, such as an ID card, should be provided to all patients with an implanted SureScan pacing system. These reference materials should indicate that the patient has a SureScan pacing system.

7 Potential adverse events

The SureScan pacing system has been designed to minimize the potential adverse events that may cause patient harm. The following potential adverse events may occur in the MRI environment:

- lead electrode heating and tissue damage resulting in loss of sensing or capture or both
- device heating resulting in tissue damage in the implant pocket or patient discomfort or both
- induced currents on leads resulting in continuous capture, VT/VF, hemodynamic collapse, or all three
- damage to the device or leads causing the system to fail to detect or treat irregular heartbeats or causing the system to treat the patient's condition incorrectly
- damage to the functionality or mechanical integrity of the device resulting in the inability of the device to communicate with the programmer
- movement or vibration of the device or leads
- lead dislodgment
- competitive pacing and potential for VT/VF induction due to ambulatory asynchronous pacing in MRI SureScan mode

8 Patient positioning restrictions within the MRI bore

Cautions:

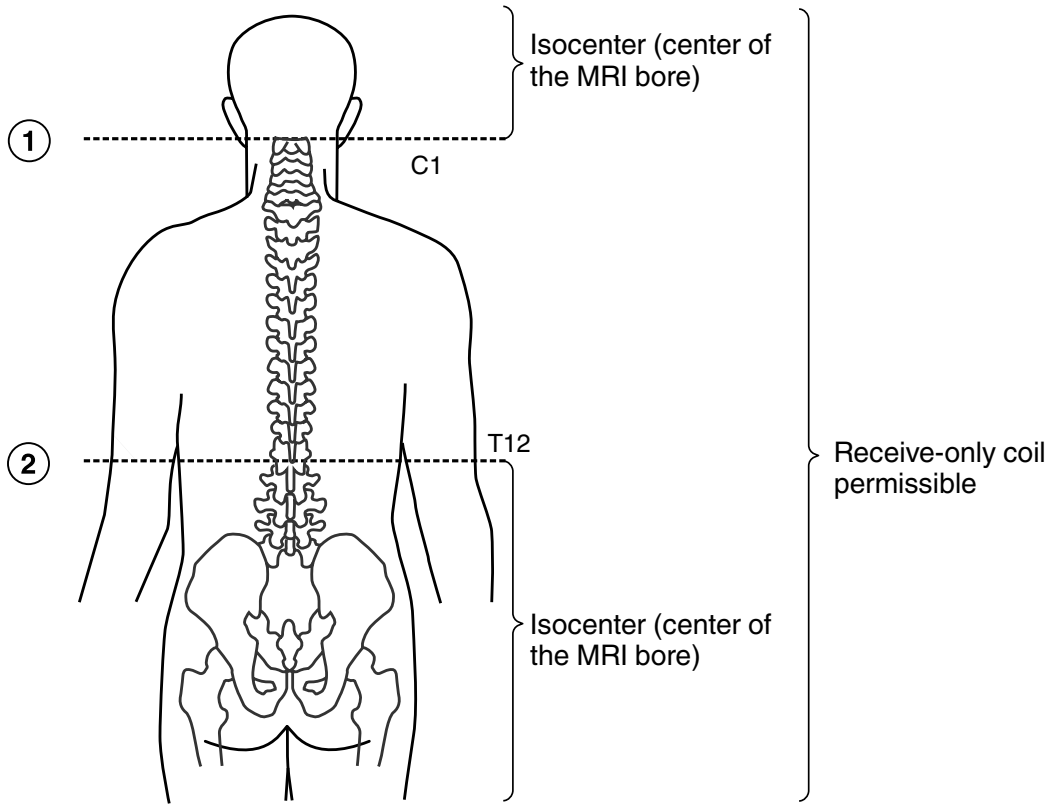
- The SureScan pacing system is compatible only with certain MRI scan procedures. Safely imaging a patient with an implanted SureScan pacing system is dependent upon compliance to the MR conditional criteria described in this section. Before starting the imaging procedure, confirm the patient's position as described here.
- Do not scan the patient positioned such that the isocenter (center of the MRI bore) is inferior to the C1 vertebra and superior to the T12 vertebra as it may cause mycocardial damage due to lead heating, resulting in an increase in pacing capture threshold. This has not been evaluated clinically by Medtronic.

Note: The C1-T12 positioning criteria do not depict restrictions on allowed scan anatomies.

8.1 Use of radio-frequency (RF) transmit/receive, transmit-only, and receive-only coils

- Position the patient so the isocenter (center of the MRI bore) of any transmit/receive or transmit-only coil is superior to the C1 vertebra or inferior to the T12 vertebra (see Figure 1).
- There are no restrictions on the placement of the receive-only coil.

Figure 1. Patient positioning criteria



1 The dashed line labeled “C1” depicts a transverse plane adjacent to the superior surface of the C1 vertebra.

2 The dashed line labeled “T12” depicts a transverse plane adjacent to the inferior surface of the T12 vertebra.

8.2 Allowed scan types

Localizer scans – All position localizer scans are allowed. These scans may be used to confirm compliance with the patient positioning criteria as described in Section 8 during diagnostic scans. If the localizer scan image indicates that the patient is positioned such that the isocenter (center of the MRI bore) is between C1 and T12, reposition the patient and confirm that the new relationship complies with the patient positioning criteria as described.

Diagnostic scans – All standard diagnostic scans of anatomies may be performed if the patient positioning criteria are followed. Achieving diagnostic-quality imaging of the desired anatomies may require manipulation of the scan parameters used during normal practice, for example: Field of View.

Note: The C1-T12 positioning criteria do not depict restrictions on allowed scan anatomies.

9 Pre-MRI scan operations

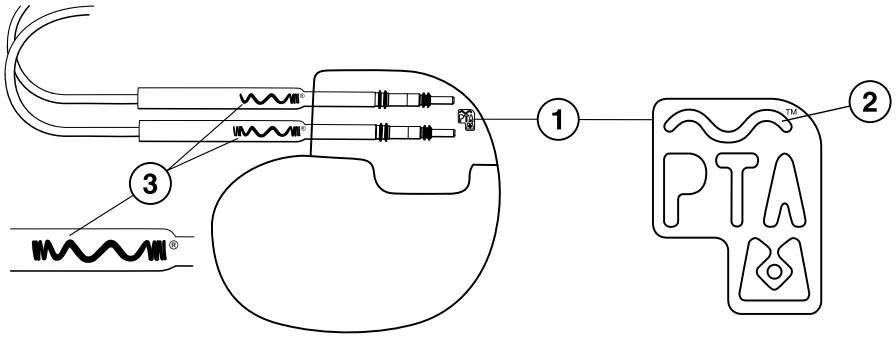
Required patient care – The following steps are required before performing an MRI scan:

- Verify that the pacing capture threshold values are ≤ 2.0 V at a pulse width of 0.4 ms.
  Note: Patients experiencing atrial fibrillation may be scanned if all other pre-MRI scan requirements are satisfied.

Identification of SureScan pacing system components – There are 3 ways to verify that a patient has SureScan pacing system components:

- **Radiopaque MRI symbols:** A radiopaque MRI symbol is present on all implanted SureScan pacing system components. By taking an x-ray of the implanted system, the clinician can verify whether the components have SureScan technology. An x-ray also indicates whether the patient has any additional active implantable devices.
  The device radiopaque MRI symbol is located in the header of the can. The radiopaque MRI symbol is a wavy line located in the upper portion of the full device radiopaque. A similar wavy line is visible on the lead, adjacent to the can and lead interface. See Figure 2 for the device and lead radiopaque MRI symbols and their locations.

  Figure 2. Radiopaque MRI symbols and their locations



1 Location of the device radiopaque symbol
2 Device radiopaque MRI symbol
3 Lead radiopaque MRI symbol

- **Patient records or patient ID card (if applicable):** The patient records or patient ID card, if applicable, must be complete and accurate if they are to be used to verify that the patient has a SureScan pacing system and to determine whether the patient has any additional active implantable devices.
- **Patient information on the programmer:** The patient information must be complete and accurate on the programmer if this feature is to be used to determine whether the patient has a SureScan pacing system and to determine whether the patient has any additional active implantable devices.

Preparing a SureScan device for an MRI scan – The following tasks must be completed before performing an MRI scan on a patient with a SureScan pacing system:

- **Check that the SureScan pacing system has been implanted for more than 6 weeks:** The 6-week post-implant waiting period allows the device and lead to become fixated in the patient. Maturation of the lead and tissue interface increases the stability of the pacing capture threshold.
- **Check that the device was implanted in the pectoral region:** A device that is implanted in the pectoral region limits the lead loop area. This device implant location helps to prevent lead electrode heating due to RF energy and unintended cardiac capture due to the gradient magnetic fields.
- **Check that no additional implantable devices are present:** Interactions with all other implantable devices, active or abandoned, have not been studied by Medtronic. Patients can be considered safe for an MRI scan only if no other implantable devices are present.
- **Check that the leads are labeled as SureScan leads:** Leads other than SureScan leads have not been tested by Medtronic. Patients can be considered safe for an MRI scan only if the implanted system consists of a SureScan device connected to SureScan leads.
- **Check that the leads are electrically intact:** Lead fractures or other damage to the leads may cause changes in the electrical properties of the SureScan pacing system that will make the system unsafe for an MRI scan. Patients with damaged leads may be harmed if an MRI scan is performed.

- **Check that abandoned or additional leads are not present:** Abandoned or additional leads have not been tested by Medtronic. Patients can be considered safe for an MRI scan only if no other implanted leads are present.
- **Check that no lead extenders or adaptors are present:** Lead extenders or adaptors are not considered part of the SureScan pacing system, and they have not been designed for MRI use. Use of lead extenders or adaptors with the SureScan pacing system components may change important parameters that are designed to prevent lead tip heating due to RF energy and unintended cardiac capture due to the gradient magnetic fields.

Maximum pacing capture threshold – The patient's atrial and ventricular pacing capture thresholds must be evaluated before performing an MRI scan. If either the atrial or ventricular capture threshold exceeds 2.0 V at a pulse width of 0.4 ms, there may be an issue with the implanted lead.

Pacing therapy during MRI scans – Each patient must be evaluated to determine whether or not pacing support is needed during the MRI scan. For patients that require pacing support, the MRI SureScan pacing mode must be set to DOO, AOO, or VOO while MRI SureScan is programmed to On. For patients that do not require pacing support, the MRI SureScan pacing mode should be set to ODO while MRI SureScan is programmed to On.

Pacing rate – The appropriate pacing rate for patients who require pacing support must be determined before performing the MRI scan. The pacing rate must be selected to avoid competitive pacing during MRI SureScan operation.

10 Initiating the MRI SureScan feature

Caution: Do not bring the Medtronic CareLink Model 2090 programmer into Zone 4 (magnet room), as defined by the American College of Radiology. It is MRI Unsafe.

To safely perform an MRI scan on a patient with the SureScan pacing system, MRI SureScan must be programmed to On using the 2090 programmer. To program MRI SureScan, the user must select parameters that are appropriate for the patient when the MRI scan is performed.

Note: Pacing mode and rate (if applicable) are to be programmed per the physician's discretion. Based on whether the patient needs pacing support or not, an asynchronous pacing mode (DOO, AOO, or VOO) or sensing only mode (ODO) can be programmed. Sensed events will be ignored by the device when MRI SureScan is programmed to On, regardless of the programmed mode.

The device maintains the selected parameters until MRI SureScan is programmed to Off after the MRI scan is done. After MRI SureScan is programmed to Off, the permanent device parameters are restored.

10.1 SureScan pacing system integrity verification

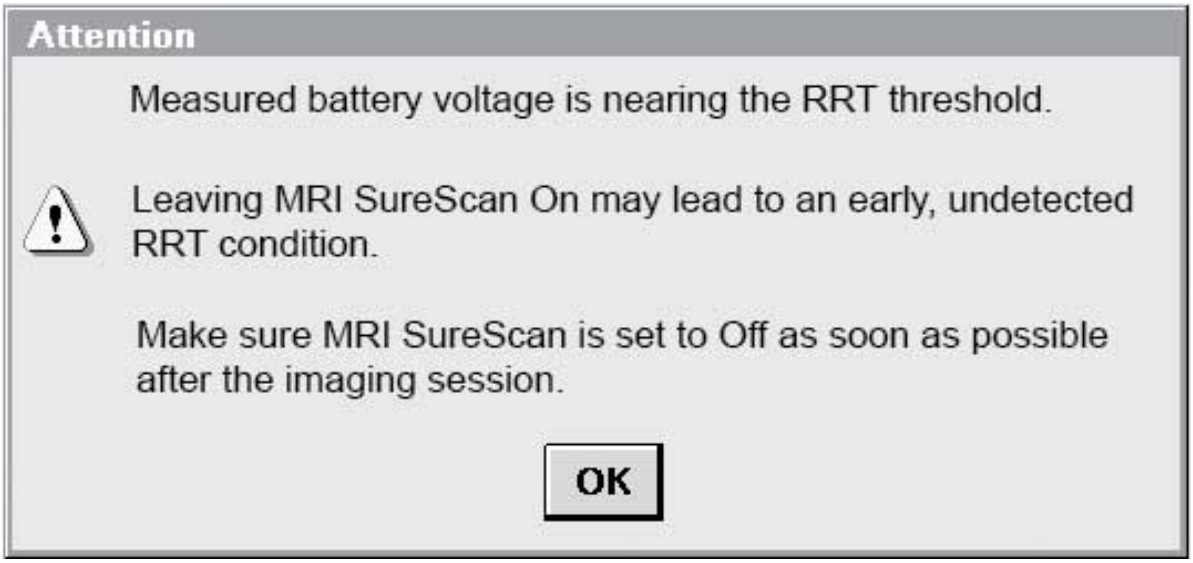
The SureScan pacing system provides automatic verification that no device or lead issues that may compromise patient safety during an MRI scan are detected. Before allowing the user to initiate the MRI SureScan feature, the SureScan device application software checks for the following 2 situations:

Lead impedance is out of range – If either of the bipolar lead impedance measurements is greater than 1500 Ω, is less than 200 Ω, or is unavailable, the software prevents the MRI SureScan feature from being initiated.

Insufficient battery longevity – If the device is at Recommended Replacement Time (RRT) or End of Service (EOS), the software prevents the MRI SureScan feature from being initiated.

Note: If the battery voltage is at or below 2.85 V, the user is notified that the device is nearing the RRT threshold. (See Figure 3). The MRI SureScan feature may be programmed to On; however, prolonged use of the MRI SureScan feature may lead to an early, undetected RRT.

Figure 3. Programmer display: Device is nearing the RRT threshold

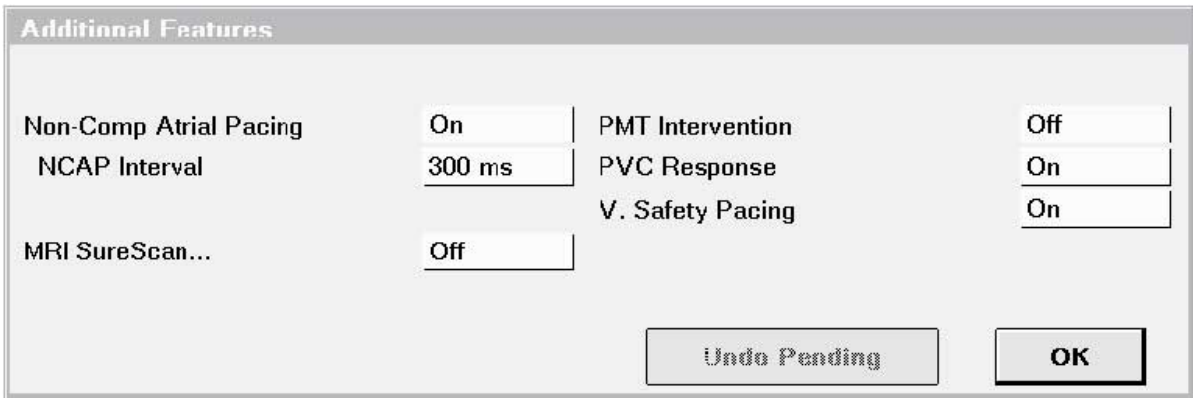


10.2 Programming MRI SureScan to On

Use the following steps to program MRI SureScan to On:

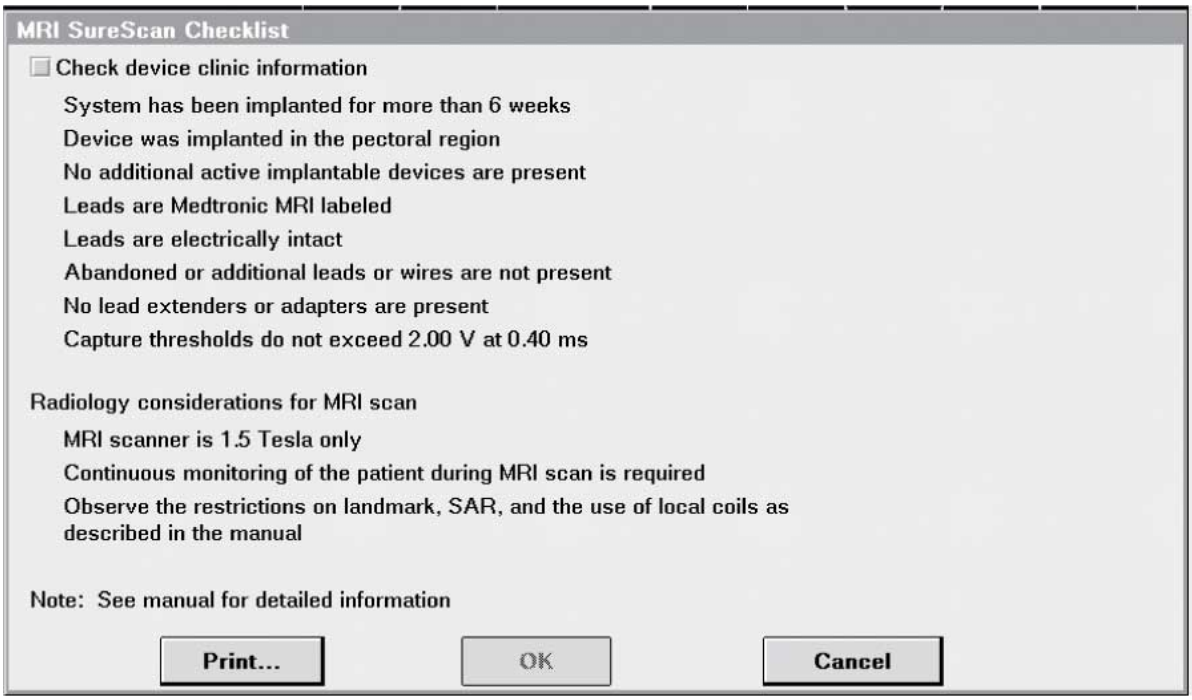
1. Select the Params icon from the tool palette.
2. Select Additional Features… on the Parameters screen.
3. Select the MRI SureScan… field (see Figure 4). The MRI SureScan Checklist appears.

Figure 4. Selecting the MRI SureScan… field



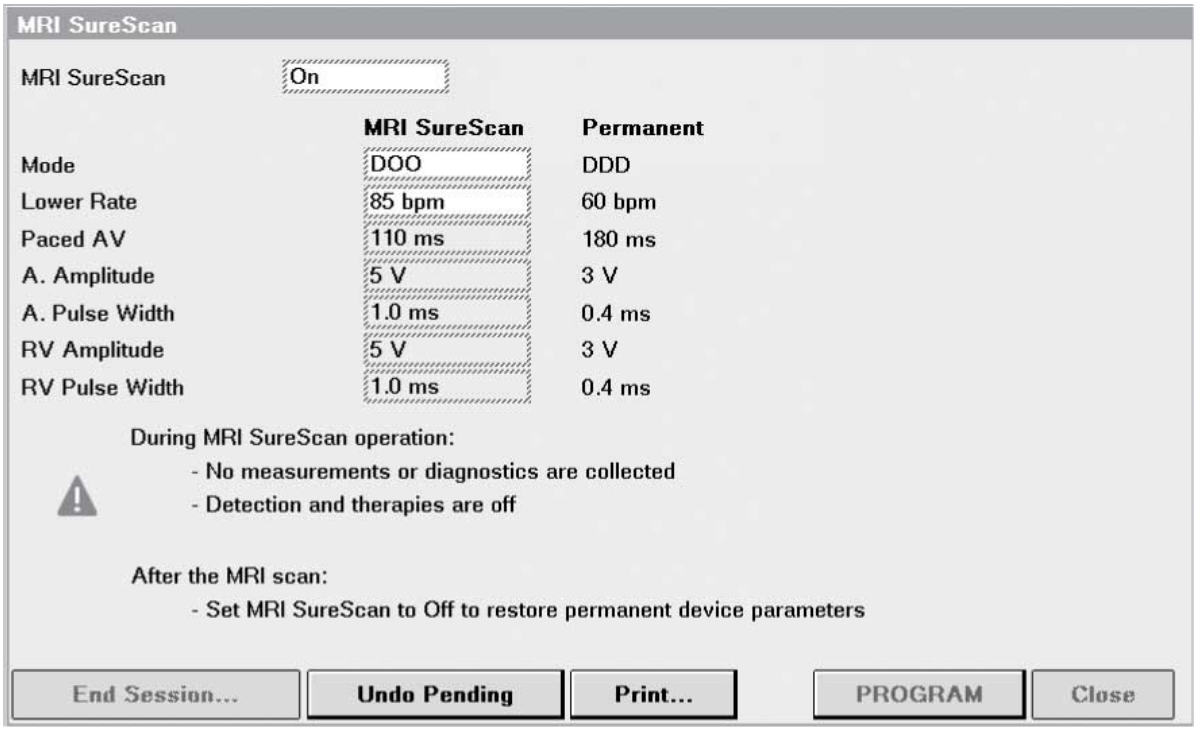
4. Select the check box in the upper-left corner if all items on the MRI SureScan Checklist are satisfied for the patient (see Figure 5).
   Note: Print the MRI SureScan Checklist if desired.

Figure 5. MRI SureScan Checklist



5. Select [OK]. The MRI SureScan window appears.
6. Program MRI SureScan to On.
7. Select an appropriate MRI SureScan pacing mode and MRI SureScan pacing rate (see Figure 6).
   - For patients who require pacing support, program the device to an asynchronous pacing mode (DOO, AOO, VOO).
     Note: An MRI SureScan pacing rate must be selected for these pacing modes to avoid competitive pacing during the operation of MRI SureScan.
   - For patients who do not require pacing support, program the device to the non-pacing mode (ODO).
     Note: An MRI SureScan pacing rate is not necessary for patients whose device is programmed to ODO.

Figure 6. Selecting MRI SureScan settings



8. Select [PROGRAM].
   Note: After the device has been programmed for an MRI scan, available options are [Print…], [End Session…], and [Emergency]. MRI SureScan can also be programmed to Off.
   Note: The status of MRI SureScan and the programmed parameters may be confirmed by printing the MRI SureScan parameter screen.

The device is now ready for the MRI scan.

11 During MRI SureScan operation

11.1 Device considerations

Suspension of diagnostics and counters – When MRI SureScan is programmed to On, the following device diagnostics and counters are suspended:

- Daily Automatic EGM Amplitude Measurements
- Daily Automatic Battery Measurement
- Daily Automatic Lead Impedance Measurements
- Daily Atrial Lead Position Check
- Short Interval Counter
- Bradycardia Event Counters

Suspension of Magnet Mode – When MRI SureScan is programmed to On, the device does not initiate asynchronous, fixed-rate bradycardia pacing in the presence of a magnet.

Suspension of tachyarrhythmia and PVC detection – When MRI SureScan is programmed to On, the device does not detect atrial or ventricular tachyarrhythmias or PVCs.

Suspension of tachyarrhythmia therapies – When MRI SureScan is programmed to On, the device does not deliver tachyarrhythmia therapies. However, bradyarrhythmia pacing therapy is provided when an asynchronous pacing mode is selected for MRI SureScan operation.

Automatic PAV selection for MRI DOO mode – If DOO mode is selected when MRI SureScan is programmed to On, the device automatically sets the PAV to either the permanently programmed PAV interval or 110 ms, whichever is less. However, if the permanently programmed PAV is less than 50 ms, the device automatically sets the PAV to 50 ms when MRI SureScan is programmed to On.

Automatic amplitude and pulse width selection for MRI SureScan pacing modes – When MRI SureScan is programmed to On and the pacing mode is DOO, VOO, or AOO, the device may automatically reset the amplitude and pulse width values. If the permanently RA. Amplitude or RV Amplitude is less than 5.0 V, the amplitude is reset to 5.0 V. If the permanently programmed RA Pulse Width or RV Pulse Width is less than 1.0 ms, the pulse width is reset to 1.0 ms.

Increased current drain – When MRI SureScan is programmed to On, the current drain from the battery is increased. Therefore, the feature should be programmed off following the MRI scan to prevent significant reduction in battery longevity.

No RRT indication – When MRI SureScan is programmed to On, if the battery voltage falls below 2.81 V, the normal RRT indication may not be displayed.[1] If the feature is left on indefinitely, the patient will have no indication that the device has reached RRT.

11.2 Radiology considerations during the MRI scan

Image artifact and distortion – SureScan leads have demonstrated minimal image distortion for areas surrounding the implanted leads when the device is out of the field of view. Significant image distortion can result from the presence of the device within the field of view. Image artifacts and distortion resulting from the presence of the device and the leads within the field of view must be considered when selecting the field of view and imaging parameters. These factors must also be considered when interpreting the MRI images.

Patient monitoring – Proper patient monitoring must be provided during the MRI procedure. This includes continuous monitoring of the patient's hemodynamic function. Since the MRI environment may interfere with the patient monitoring system, it is recommended that more than one of the following systems be used:

- electrocardiography
- pulse oximetry
- noninvasive blood pressure measurements

Preparation for patient rescue – Keep an external defibrillator available during MRI scans.

Note: If the patient's hemodynamic function is compromised during the MRI scan, discontinue the MRI scan and take the proper measures to restore the patient's hemodynamic function.

12 Following the MRI scan

Required patient care – The following steps are required after performing an MRI scan:

- Program MRI SureScan to Off.
- Check the pacing capture threshold to ensure that there is a proper safety margin.

IPG capture output resolution – The Medtronic Revo MRI RVDR01 IPG measures pacing capture threshold in 0.5 V increments. The actual pacing capture threshold change associated with a 0.5 V change is between 0.0 V and 1.0 V. For example, actual thresholds of 1.49 V and 1.51 V correspond to measured thresholds of 1.5 V and 2.0 V respectively. In this case, an actual change of 0.02 V results in a measured change of 0.5 V. Similarly, actual

[1] RRT indication consists of the following indicators: automatic mode programming to VVI; automatic Lower Rate programming to 65 bpm; atrial ATP automatically disabled; response to application of magnet = VOO, 65 bpm; upon interrogation, an RRT warning message is displayed to the user.

thresholds of 1.01 V and 2.00 V correspond to measured thresholds of 1.5 V and 2.0 V. In this situation, an actual change of 0.99 V results in a measured change of 0.5 V.

12.1 Returning the device to the pre-MRI configuration

Note: The device maintains the parameters that were set while initiating the SureScan feature until the MRI SureScan parameter is programmed to Off after the MRI scan.

After the MRI scan is complete, MRI SureScan must be programmed to Off using the 2090 programmer. This restores the device parameter values to the pre-MRI SureScan configuration.

Perform the following steps to program MRI SureScan to Off:

1. Program the MRI SureScan parameter to Off.
2. Select [PROGRAM].
3. Select [Close] to return to the Additional Features window. Select [OK] to return to the Parameters screen.

The device parameter values are now restored to the pre-MRI SureScan configuration.

Note: During each interrogation, the device is monitored for possible electrical reset conditions and disabled therapies. If a condition is detected that requires attention, the programmer displays a Device Status Indicator warning in a pop-up window and on the Quick Look screen.

13 General information on MRI procedures

13.1 Types of electromagnetic fields generated by MRI systems

An MRI system produces 3 types of electromagnetic fields that may interact with implanted device systems. All of these fields are necessary to produce an MRI image. The fields are defined as follows:

Static magnetic field – This is a steady state non-varying magnetic field that is normally always present around an MRI machine, even when no scan is underway.

Gradient magnetic fields – These low-frequency pulsed magnetic fields are present only during a scan. MRI equipment uses 3 orthogonal gradient magnetic fields to form the image.

RF field – This is a pulsed radio frequency (RF) field that is present only during a scan. The RF field can be produced by a variety of transmission RF coils, such as a whole body transmit coil or an extremity coil (for example, a transmit head coil).

13.2 Potential interactions for implanted SureScan pacing systems in the MRI environment

The SureScan pacing system has been designed to minimize the potential interactions described in this section.

Magnetic field interactions – The magnetic material of an implanted system may exert force, vibration, and torque effects due to the static magnetic field and gradient magnetic fields produced by an MRI scanner. The SureScan pacing system has been designed to reduce these effects so that the mechanical stress on the implanted system and tissue interface is minimized. Patients may feel a mild tugging or vibration sensation at the site of the device implant while in or near the MRI scanner.

Induced stimulation – The gradient magnetic and RF fields produced by an MRI scanner induce energies onto an implanted lead system that could potentially cause unintended stimulation of the heart. The SureScan pacing system has been designed to limit the voltages and pulse widths induced on the leads so that the potential for capturing the heart is minimized.

Lead electrode heating – The RF fields generated by an MRI scanner induce voltages onto an implanted lead system that may cause heating at the lead electrodes. This heating could damage the tissue surrounding the

electrodes and compromise pacing and sensing thresholds at that site. SureScan leads have been designed to limit heating at the electrodes to minimize thermal damage of the surrounding cardiac tissue.

The patient must be positioned such that the isocenter (center of the MRI bore) is superior to the C1 vertebra or inferior to the T12 vertebra, as described in Section 8.

Image artifacts and distortion – SureScan leads have demonstrated minimal image distortion for areas surrounding the implanted leads when the device is out of the field of view. Significant image distortion can result from the presence of the device within the field of view. Image artifacts and distortion resulting from the presence of the device and the leads within the field of view must be considered when selecting the field of view and imaging parameters.

14 Medtronic warranty information

Please see the literature enclosed with the products for information regarding the product warranty or disclaimer of warranty as applicable.

15 Service

Medtronic employs highly trained representatives and engineers located throughout the world to serve you and, upon request, to provide training to qualified hospital personnel in the use of Medtronic products. Medtronic also maintains a professional staff to provide technical consultation to product users. For more information, contact your local Medtronic representative, or call or write Medtronic at the appropriate telephone number or address listed on the back cover.

World Headquarters
Medtronic, Inc.
710 Medtronic Parkway
Minneapolis, MN 55432-5604
USA
Internet: www.medtronic.com
Tel. +1-763-514-4000
Fax +1-763-514-4879

Medtronic USA, Inc.
Toll-free in the USA (24-hour technical consultation for physicians and medical professionals)
Bradycardia: 1-800-505-4636
Tachycardia: 1-800-723-4636

Europe/Africa/Middle East Headquarters
Medtronic International Trading Sàrl
Route du Molliau 31
Case Postale 84
CH-1131 Tolochenaz
Switzerland
Internet: www.medtronic.com
Tel. +41-21-802-7000
Fax +41-21-802-7900

Medtronic E.C. Authorized Representative/Distributed by
Medtronic B.V.
Earl Bakkenstraat 10
6422 PJ Heerlen
The Netherlands
Tel. +31-45-566-8000
Fax +31-45-566-8668

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Slipsheet

Medtronic

REVO MRI™ SURESCAN™ RVDR01

Dual Chamber Pacemaker with SureScan™ Technology (OAE-DDDR)

MR

MR Conditional with MVP® Mode, AT/AF Suite Diagnostics and Therapies, and Cardiac Compass® Trends

Implant Manual

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

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4

1 Description

The Medtronic Revo MRI SureScan Model RVDR01 implantable pulse generator (IPG) is a multiprogrammable, implantable cardiac device that monitors and regulates the patient's heart rate by providing single or dual chamber rate-responsive bradycardia pacing and atrial antitachycardia pacing (atrial ATP) therapy.

The Revo MRI SureScan device, along with the SureScan leads, constitutes the implantable portion of the SureScan pacing system.

The Medtronic SureScan pacing system includes a Medtronic SureScan device connected to Medtronic SureScan leads. Labeling for SureScan pacing system components displays the SureScan symbol and the MR Conditional symbol.

SureScan symbol

MR Conditional symbol. The SureScan pacing system is safe for use in the MRI environment when used according to the instructions in the SureScan technical manual.

The MRI SureScan feature permits a mode of operation that allows a patient with a SureScan device to be safely scanned by an MRI machine. **Before performing an MRI scan, refer to the SureScan pacing system technical manual provided with the SureScan device for important information about procedures and MRI-specific contraindications, warnings, and precautions.**

Contents of sterile package – The package contains 1 implantable pulse generator and 1 torque wrench.

Programmer and software – Use the appropriate Medtronic programmer and software to program this device. Programmers from other manufacturers are not compatible with Medtronic devices but will not damage Medtronic devices.

Network connectivity and data exchange – The SureScan pacing system supports network connectivity and the exchange of data between the Medtronic Carelink 2090 programmer and the Medtronic Paceart data management system using the SessionSync feature, if available.

The SureScan pacing system supports the use of the Medtronic 2290 Analyzer, which allows you to have a device session and an analyzer session running at the same time, quickly switch from one to the other without having to end or restart sessions, and export data from the analyzer to the device software application.

Medtronic Model 2696 InCheck Patient Assistant – The patient can use the Model 2696 InCheck Patient Assistant to verify whether the implanted device has detected a suspected atrial arrhythmia, and can initiate recording of cardiac event data in the device memory.

About this manual – This document is primarily an implant manual. Regular patient follow-up sessions should be scheduled after implant. Follow-up procedures such as monitoring battery measurements and confirming therapy parameters are described in the product documentation that is included with the software that supports this device. To obtain additional copies of product documentation, contact a Medtronic representative.

Before performing an MRI scan, refer to the SureScan pacing system technical manual for important information about MRI-specific contraindications, warnings, and procedures.

Explanation of IPG code acronyms used on the device package label – The following list of acronyms applies to various IPG products. Refer to the package label for acronyms that apply to this product.

S	Single chamber IPG
D	Dual chamber IPG
SR	Single chamber rate responsive IPG
DR	Dual chamber rate responsive IPG
TR	Triple chamber rate responsive IPG

2 Indications

The device is indicated for the following:

- Rate adaptive pacing in patients who may benefit from increased pacing rates concurrent with increases in activity
- Accepted patient conditions warranting chronic cardiac pacing include:
  - Symptomatic paroxysmal or permanent second- or third-degree AV block
  - Symptomatic bilateral bundle branch block
  - Symptomatic paroxysmal or transient sinus node dysfunctions with or without associated AV conduction disorders
  - Bradycardia-tachycardia syndrome to prevent symptomatic bradycardia or some forms of symptomatic tachyarrhythmias

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

- Various degrees of AV block to maintain the atrial contribution to cardiac output
- VVI intolerance (for example, pacemaker syndrome) in the presence of persistent sinus rhythm

Antitachycardia pacing (ATP) is indicated for termination of atrial tachyarrhythmias in bradycardia patients with one or more of the above pacing indications.

Atrial rhythm management features such as Atrial Rate Stabilization (ARS), Atrial Preference Pacing (APP), and Post Mode Switch Overdrive Pacing (PMOP) are indicated for the suppression of atrial tachyarrhythmias in bradycardia patients with atrial septal lead placement and one or more of the above pacing indications.

The Revo MRI SureScan IPG has been designed for use in the MRI environment when used according to the conditions for use.

3 MRI conditions for use

Clinical and non-clinical testing has demonstrated that the SureScan pacing system is safe for use in the MRI environment when used according to the instructions in the SureScan pacing system technical manual.

The SureScan pacing system can be scanned in patients under these conditions:

- Cylindrical bore magnet, clinical MRI systems with a static magnetic field of 1.5 tesla (T) must be used.
- Gradient systems with maximum gradient slew rate performance per axis of ≤ 200 T/m/s must be used.
- Whole body averaged specific absorption rate (SAR) as reported by the MRI equipment must be ≤ 2.0 W/kg. The head SAR as reported by the MRI equipment must be < 3.2 W/kg.
- Patients and their implanted systems must be screened to meet the following requirements:
  - No previously implanted (active or abandoned) medical devices, leads, lead extenders, or lead adaptors
  - No broken or intermittent leads
  - A SureScan pacing system that has been implanted for a minimum of 6 weeks

  - A SureScan pacing system implanted in the left or right pectoral region
  - Pacing capture thresholds of ≤ 2.0 V at a pulse width of 0.4 ms
  - A lead impedance value of ≥ 200 Ω or ≤ 1500 Ω
  - No diaphragmatic stimulation at a pacing output of 5.0 V and at a pulse width of 1.0 ms in patients whose device will be programmed to an asynchronous pacing mode when MRI SureScan is on
- The patient must be positioned within the bore such that the isocenter (center of the MRI bore) is superior to the C1 vertebra or inferior to the T12 vertebra.
- There are no restrictions on the placement of any receive-only coils.
- There are no restrictions on the use of local transmit or local transmit/receive coils for imaging of the head or of the extremities.
- Proper patient monitoring must be provided during the MRI scan. This includes continuous monitoring of the patient's hemodynamic function. Since the MR environment may interfere with the patient monitoring system, it is recommended that more than one of the following systems be used:
  - Electrocardiography
  - Pulse oximetry
  - Noninvasive blood pressure measurements
- The implanted system must consist solely of a Medtronic Revo MRI SureScan Model RVDR01 device and 2 CapSureFix MRI SureScan Model 5086MRI leads.

4 Contraindications

Before performing an MRI scan, refer to the SureScan pacing system technical manual for MRI-specific contraindications.
The device is contraindicated for the following conditions:

- implant with unipolar pacing leads
- concomitant implant with another bradycardia device
- concomitant implant with an implantable cardioverter defibrillator

There are no known contraindications for the use of pacing as a therapeutic modality to control heart rate. The patient's age and medical condition, however, may dictate the particular pacing system, mode of operation, and implant procedure used by the physician.

- Rate responsive modes may be contraindicated in those patients who cannot tolerate pacing rates above the programmed Lower Rate.
- Dual chamber sequential pacing is contraindicated in patients with chronic or persistent supraventricular tachycardias, including atrial fibrillation or flutter.
- Single chamber atrial pacing is contraindicated in patients with an AV conduction disturbance.
- ATP therapy is contraindicated in patients with an accessory antegrade pathway.

5 Warnings and precautions

Before performing an MRI scan, refer to the SureScan pacing system technical manual for MRI-specific warnings and precautions.

5.1 General

Electrical isolation during implant – Do not allow the patient to have contact with grounded equipment that might produce electrical current leakage during implant. Electrical current leakage may induce arrhythmias that may result in the patient's death.

External defibrillation equipment – Keep external defibrillation equipment nearby for immediate use whenever arrhythmias are possible or intentionally induced during device testing, implant procedures, or post-implant testing.

5.2 Handling and storage instructions

Follow these guidelines when handling or storing the device.

Device temperature – Allow the device to reach room temperature before it is programmed or implanted. Device temperature above or below room temperature may affect initial device function.

Dropped device – Do not implant the device if it has been dropped on a hard surface from a height of 30 cm (12 in) or more after it is removed from its packaging.

Sterilization – Medtronic has sterilized the package contents with ethylene oxide before shipment. This device is for single use only and is not intended to be resterilized.

Explant and disposal – Consider the following information related to device explant and disposal:

- Explant the implantable device postmortem. In some countries, explanting battery-operated implantable devices is mandatory because of environmental concerns; please check the local regulations. In addition, if subjected to incineration or cremation temperatures, the device may explode.
- Medtronic implantable devices are intended for single use only. Do not resterilize and reimplant explanted devices.
- Please use the Removed Product Information Report to return explanted devices to Medtronic for analysis and disposal.

Inspecting the sterile package – Carefully inspect the package before opening it:

- If the seal or package is damaged, contact a Medtronic representative.
- Do not use the product after the “Use by” date on the package label.
- For instructions on opening the sterile package, see the diagram inside the lid of the shelf box.

Temperature limits – Store and transport the package between –18 °C and +55 °C (0 °F and 131 °F). Electrical reset may occur at temperatures below –18 °C (0 °F). Device longevity may decrease and performance may be affected at temperatures above +55 °C (131 °F).

Use by date – Do not implant the device after the “Use by” date on the package label. Battery longevity may be reduced.

5.3 Lead evaluation and lead connection

Atrial lead maturation – Do not enable AT/AF detection or automatic atrial ATP therapies until the atrial lead has matured (approximately 1 month after implant).

Hex wrench – Use only the torque wrench supplied with the device. The torque wrench is designed to prevent damage to the device from overtightening a setscrew. Other torque wrenches, (for example a blue-handled or right-angled hex wrench) have torque capabilities greater than the lead connector can tolerate.

Lead compatibility – Do not use another manufacturer’s leads without demonstrated compatibility with Medtronic devices. If a lead is not compatible with a Medtronic device, the result may be undersensing of cardiac activity, failure to deliver necessary therapy, or a leaking or intermittent electrical connection.

A SureScan pacing system includes a SureScan device connected to SureScan leads. **Before performing an MRI scan, refer to the SureScan pacing system technical manual for additional information.**

5.4 Device operation

Anti-coagulation – Use of the device should not change the application of established anti-coagulation protocols.

Crosstalk – Crosstalk may cause the device to self-inhibit, which results in no pacing. Program Ventricular Safety Pacing to On to prevent inhibition due to crosstalk.

Electrical reset – Electrical reset can be caused by exposure to temperatures below –18 °C (0 °F) or strong electromagnetic fields. Advise patients to avoid strong electromagnetic fields. Observe temperature storage limits to avoid exposure of the device to cold temperatures. If a partial reset occurs, pacing resumes in the programmed mode with many of the programmed settings retained. If a full reset occurs, the device operates in VVI mode at

65 bpm. Electrical reset is indicated by a programmer warning message that is displayed immediately upon interrogation. To restore the device to its previous operation, it must be reprogrammed. Inform a Medtronic representative if your patient's device has reset.

End of Service (EOS) indicator – Replace the device immediately if the programmer displays an EOS indicator. The device may not perform adequately after the EOS indicator appears.

Fixed bipolar operation – Use of unipolar leads will result in loss of pacing output and sensing.

Magnets – Placing a magnet over the device suspends tachyarrhythmia detection and initiates asynchronous, fixed-rate bradycardia pacing. The programming head contains a magnet that can cause magnet operation to occur. However, magnet operation does not occur if telemetry between the device and programmer is established.

Pacing and sensing safety margins – Consider lead maturation when selecting pacing amplitudes, pacing pulse widths, and sensing levels. Loss of capture may occur if lead maturation is not considered when selecting settings.

Rate control – Decisions regarding rate controls should not be based on the ability of the device to prevent atrial arrhythmias.

Rate-responsive modes – Do not program rate-responsive modes for patients who cannot tolerate rates above the programmed Lower Rate. Rate-responsive modes may cause discomfort for those patients.

Shipping values – Do not use shipping values or nominal values for pacing amplitude and sensitivity without verifying that the values provide adequate safety margins for the patient.

Single chamber atrial modes – Do not program single chamber atrial modes for patients with impaired AV nodal conduction. Ventricular pacing does not occur in these modes.

Slow retrograde conduction – Slow retrograde conduction may induce pacemaker-mediated tachycardia (PMT) when the VA conduction time is greater than 400 ms. Programming PMT intervention may help prevent PMT when the VA conduction time is less than 400 ms.

Telemetry – Exposure to EMI may briefly interrupt programming and/or telemetry operations. Successful interrogation or programming of the device verifies that reliable communication between the device and the programmer has occurred.

Testing for cross-stimulation – At implant and when atrial ATP therapy is enabled, conduct regular testing at the programmed ATP output settings to ensure that ventricular capture does not occur. This is particularly important when the lead is placed in the inferior atrium.

5.5 Pacemaker-dependent patients

Pacemaker-dependent patients – Always program Ventricular Safety Pacing to On for pacemaker-dependent patients. Ventricular Safety Pacing prevents ventricular asystole due to inappropriate inhibition of ventricular pacing caused by oversensing.

ODO pacing mode – Do not program the ODO mode for pacemaker-dependent patients. Instead, use the Underlying Rhythm Test for brief interruption of outputs.

Underlying Rhythm Test – Use caution when using the Underlying Rhythm Test to inhibit pacing. The patient is without pacing support when pacing is inhibited.

5.6 Medical therapy hazards

Computed tomographic x-ray (CT scan) – If the patient undergoes a CT scan procedure and the device is not directly in the CT scan beam, the device is not affected.

If the device is directly in the CT scan beam, oversensing may occur for the duration of time the device is in the beam. If the device will be in the beam for more than 4 s, take the following precautions to minimize complications:

- Suspend tachyarrhythmia detection using a magnet, or disable tachyarrhythmia detection using the programmer. After the CT scan is complete, remove the magnet or use the programmer to enable tachyarrhythmia detection.
- If appropriate for the patient, program the pacing mode to minimize the effects of oversensing on pacing (for example, false inhibition). For pacemaker-dependent patients, program the device to an asynchronous pacing mode. After the CT scan is complete, program the pacing mode to its original setting.

Diathermy – People with metal implants such as pacemakers, implantable cardioverter defibrillators (ICDs), and accompanying leads should not receive diathermy treatment. The interaction between the implant and diathermy can cause tissue damage, fibrillation, or damage to the device components, which could result in serious injury, loss of therapy, and/or the need to reprogram or replace the device.

Electrosurgical cautery – Electrosurgical cautery may induce ventricular arrhythmias and fibrillation or may cause device malfunction or damage. If electrosurgical cautery cannot be avoided, observe the following precautions to minimize complications:

- Keep temporary pacing and defibrillation equipment available.
- Program the device to an asynchronous pacing mode for pacemaker-dependent patients.
- Suspend tachyarrhythmia detection using a magnet, or disable detection using the programmer. Do not enable tachyarrhythmia detection until the electrosurgical cautery procedure is complete.
- Use a bipolar electrocautery system if possible. If unipolar cautery is used, position the ground plate so the current pathway does not pass through or near the device and lead system. The current pathway should be a minimum of 15 cm (6 in) away from the device and lead system.
- Avoid direct contact of the cautery equipment with the implanted device or leads.
- Use short, intermittent, and irregular bursts at the lowest clinically appropriate energy levels.

External defibrillation – External defibrillation may damage the implanted device. External defibrillation may also temporarily or permanently elevate pacing thresholds or temporarily or permanently damage the myocardium at the electrode tissue interface. Current flow through the device and lead may be minimized by taking the following precautions:

- Use the lowest clinically appropriate defibrillation energy.
- Position the defibrillation patches or paddles a minimum of 15 cm (6 in) away from the device.
- Position the defibrillation patches or paddles perpendicular to the device and lead system.

If an external defibrillation is delivered within 15 cm (6 in) of the device, contact a Medtronic representative.

High-energy radiation – Do not direct high-energy radiation sources such as cobalt 60 or gamma radiation at the device. High-energy radiation may damage the device, however, the damage may not be immediately detectable. If a patient requires radiation therapy near the device, radiation exposure to the device should not exceed 500 rads.

Lithotripsy – Lithotripsy may permanently damage the device if the device is at the focal point of the lithotripter beam. If lithotripsy must be performed, take the following precautions:

- Keep the focal point of the lithotripter beam a minimum of 2.5 cm (1 in) away from the implanted device.
- For pacemaker-dependent patients, program the implanted device to an asynchronous pacing mode or to a single chamber mode without rate response before treatment.

Magnetic resonance imaging (MRI) – Patients with a SureScan pacing system are able to undergo an MRI scan if the requirements provided in the SureScan pacing system technical manual are followed. **Refer to the SureScan pacing system technical manual for additional information.**

Radio frequency (RF) ablation – An RF ablation procedure may cause device malfunction or damage to the device. Radio frequency ablation risks may be minimized by taking the following precautions:

- Keep temporary pacing and defibrillation equipment available.
- Avoid direct contact between the ablation catheter and the implanted system.

- Position the ground plate so the current pathway does not pass through or near the device and lead system. The current pathway should be a minimum of 15 cm (6 in) away from the device and lead system.
- Suspend atrial tachyarrhythmia detection using a magnet, or program atrial detection to Monitor using the programmer. Do not program atrial detection to On until the RF procedure is complete.
- Program the device to an asynchronous pacing mode for pacemaker-dependent patients.

Therapeutic ultrasound – Do not expose the device to therapeutic ultrasound. Therapeutic ultrasound may permanently damage the device.

Susceptibility to radiotherapy – Exposing the device to direct or scattered neutrons may cause reset of the device, errors in diagnostic data, or loss of diagnostic data. To help prevent device reset due to neutron exposure, deliver radiotherapy treatment using photon beam energies less than or equal to 10 MV. Electron beam treatments are not a problem. Using a lead shield during radiotherapy does not protect the device from the effects of the neutrons. Immediately after radiotherapy treatment, Medtronic suggests interrogating the device. In some devices, an alarm in the device sounds when a reset occurs. A device reset requires device parameters to be reprogrammed.

5.7 Home and occupational environments

Cellular phones – This device contains a filter that prevents most cellular telephone transmissions from interacting with device operation. To further minimize the possibility of interaction, take the following precautions:

- Maintain a minimum separation of 15 cm (6 in) between the device and the cellular telephone, even if the cellular telephone is not on.
- Maintain a minimum separation of 30 cm (12 in) between the device and any antenna transmitting above 3 W.
- Hold the cellular telephone to the ear farthest from the device.

This device has been tested using the ANSI/AAMI PC-69 standard to ensure compatibility with cellular telephones and other hand-held transmitters with similar power. These transmission technologies represent the majority of cellular telephones used worldwide. The circuitry of this device, when operating under nominal conditions, has been designed to eliminate any significant effects from cellular telephones.

Electromagnetic interference (EMI) – Instruct patients to avoid devices that generate strong EMI. Electromagnetic interference may result in delivery of unneeded therapy. Electromagnetic interference may also cause device malfunction or damage. The patient should move away from the EMI source or turn off the source because this usually allows the device to return to its normal mode of operation. EMI may be emitted from the following sources:

- high-voltage power lines
- communication equipment such as microwave transmitters, linear power amplifiers, or high-powered amateur transmitters
- commercial electrical equipment such as arc welders, induction furnaces, or resistance welders

Home appliances that are in good working order and properly grounded do not usually produce enough EMI to interfere with device operation. There are reports of temporary disturbances caused by electric hand tools or electric razors used directly over the implant site.

Carefully evaluate the possibility of increased susceptibility to EMI and oversensing before changing the sensitivity to its minimum (most sensitive) setting of 0.15 mV.

Static magnetic fields – Patients should avoid equipment or situations where they would be exposed to static magnetic fields greater than 10 gauss or 1 mT. Static magnetic fields may suspend arrhythmia detection. Sources of static magnetic fields include, but are not limited to, stereo speakers, bingo wands, extractor wands, magnetic badges, or magnetic therapy products.

Note: The SureScan pacing system has been designed to mitigate the effects of magnetic fields present in 1.5 T MRI machines. **Refer to the SureScan pacing system technical manual for additional information.**

Electronic article surveillance (EAS) – Electronic article surveillance equipment, such as retail theft prevention systems, may interact with devices and result in inappropriate therapy delivery. Advise patients to walk directly through an EAS system and not remain near an EAS system longer than necessary.

6 Potential adverse events

Before performing an MRI scan, refer to the SureScan technical manual for MRI-specific potential adverse events.
Potential adverse events associated with the use of transvenous leads and pacing systems include, but are not limited to, the following events (listed in alphabetical order):

- acceleration of tachyarrhythmias (caused by device)
- air embolism
- bleeding
- body rejection phenomena including local tissue reaction
- cardiac dissection
- cardiac perforation
- cardiac tamponade
- chronic nerve damage
- death
- endocarditis
- erosion
- erosion through the skin
- excessive fibrotic tissue growth
- extrusion
- fibrillation or other arrhythmias
- fluid accumulation
- formation of hematomas or cysts
- heart block
- heart wall or vein wall rupture
- hematoma/seroma
- infection
- keloid formation
- lead abrasion and discontinuity
- lead migration/dislodgment
- muscle stimulation, nerve stimulation, or both
- myocardial damage
- myocardial irritability
- myopotential sensing
- pericardial effusion
- pericardial rub
- pneumothorax
- rejection phenomena (local tissue reaction, fibrotic tissue formation, device migration)
- threshold elevation
- thromboemboli
- thrombolytic and air embolism
- thrombosis
- transvenous lead-related thrombosis
- valve damage (particularly in fragile hearts)
- venous occlusion
- venous or cardiac perforation

7 Adverse events and clinical trial data

Information regarding clinical studies and adverse events related to this device is available at www.medtronic.com/manuals. To view, download, print, or order the following clinical studies from the Medtronic website, perform the following steps:

1. Navigate your web browser to http://www.medtronic.com/manuals.
2. Select the hyperlink that corresponds to your location.

3. Select the Search field on the left side of the screen and type “RVDR01”.
4. Click [Search]. All technical literature for this device is listed.

The following clinical studies are related to this device:

Atrial Septal Pacing Efficacy Trial (ASPECT) – This clinical study, which evaluated the safety and efficacy of the Medtronic AT500 DDDRP Pacing System devices, provides support for the atrial intervention pacing therapies.

Atrial Therapy Efficacy and Safety Trial (ATTEST) – This clinical study, which evaluated the safety and efficacy of the Medtronic AT500 DDDRP Pacing System devices, provides support for the Revo MRI SureScan Model RVDR01 devices.

EnRhythm clinical study – This clinical study, which evaluated the safety and efficacy of the EnRhythm Model P1501DR devices, provides support for MVP mode pacing and the Reactive ATP feature in the Revo MRI SureScan Model RVDR01 devices.

EnRhythm MRI SureScan clinical study – This clinical study, which evaluated the safety and efficacy of the EnRhythm MRI SureScan pacing system in the clinical magnetic resonance imaging (MRI) environment, provides support for the MRI SureScan feature in the Revo MRI SureScan device.

GEM III DR Model 7275 MVP study – This clinical study, which evaluated the performance of MVP mode pacing in the GEM III DR Model 7275 devices, provides support for MVP mode in the Revo MRI SureScan Model RVDR01 devices.

Kappa 700 clinical study – This study, which evaluated the safety and clinical performance of the Kappa 700 pacemakers, provides support for the Right Ventricular Capture Management feature and other bradycardia pacing features.

Marquis MVP download study – This clinical study, which evaluated the performance of MVP mode pacing in the Marquis DR Model 7274 devices, provides support for MVP mode in the Revo MRI SureScan Model RVDR01 devices.

8 Physician and patient information

In addition to this Implant Manual, documentation for the Medtronic Revo MRI SureScan Model RVDR01 device includes the following:

- *Revo MRI SureScan RVDR01 Reference Manual*
  Comprehensive reference on system design, operations, programming and clinical use (shipped with software)
- *Revo MRI SureScan Pacemaker Patient Manual*
  Information for the patient, patient’s family, and other interested people (shipped with device).
- *Revo MRI SureScan Technical Manual*
  Information for cardiologists and radiologists on how to perform a safe MRI scan on patients implanted with a SureScan pacing system.

To obtain additional copies of these documents, contact your Medtronic representative.

8.1 Device registration

Verify device operating characteristics at the time of implant and record them in the patient file. Complete the Device Registration Form and return it to Medtronic as it provides necessary information for warranty purposes and patient tracking.

8.2 Patient counseling

Physicians should consider the following points in counseling the patient about this implanted device:

- Encourage the patient to use the identification card(s) issued by Medtronic and/or the identification bracelets documenting the implanted device system.
- Discuss information in the patient manual so that the patient is fully familiar with the operation of the implanted device.
- Advise the patient how to obtain additional copies of the patient manual.

9 Implant procedure

Proper surgical procedures and sterile techniques are the responsibility of the physician. The following procedures are provided for information only. Each physician must apply the information in these procedures according to professional medical training and experience.

The implant procedure includes the following steps:

- Program the device before implant.
- Verify lead and connector compatibility.
- Position the leads.
- Test the lead system.
- Connect the leads to the device.
- Position and secure the device.
- Program the device.

For information about replacing a previously implanted device, see Section 9.8, “Replacing a device”, page 19.

9.1 Programming the device before implant

Caution: Do not implant the device after the “Use by” date. Battery longevity may be reduced.

9.1.1 How to program the device for implant

Before opening the sterile package, prepare the device for implant by performing the following steps.

1. Interrogate the device. Print an initial interrogation report.
   Note: If the programmer reports that an electrical reset occurred, do not implant the device. Contact a Medtronic representative.
2. Check the initial interrogation report or the Quick Look screen to confirm that the battery voltage is at least 2.85 V at room temperature.
   If the device has been exposed to low temperatures, the battery voltage will be temporarily lower. Allow the device to warm to room temperature for at least 48 hours and check the battery voltage again. If an acceptable battery voltage cannot be obtained, contact a Medtronic representative.
   Note: The device measures the battery voltage daily at 2:15 AM based on the device clock. The most recent automatic daily battery voltage measurement is displayed on the Battery and Lead Measurements screen.
3. Set the internal clock of the device.
4. Program the therapy and pacing parameters to values appropriate for the patient. Ensure that tachyarrhythmia detection is disabled.
   Note: Do not enable the Atrial Preference Pacing feature or a rate responsive pacing mode before implanting the device. Doing so may result in a pacing rate that is faster than expected.

9.2 Verifying lead and connector compatibility

Warning: Verify lead and connector compatibility before using a lead with this device. Using an incompatible lead may damage the connector, result in electrical current leakage, or result in an intermittent electrical connection.

Note: The SureScan pacing system includes a SureScan device connected to SureScan leads. **Before performing an MRI scan, refer to the SureScan pacing system technical manual for additional information.**

Lead adaptors compromise the ability to safely scan the SureScan pacing system. **Refer to the SureScan pacing system technical manual for additional information.**

Select a compatible lead. Refer to the following table.

Table 1. Lead and connector compatibility[a]

Port	Primary Lead	Lead Adaptor
A, V	IS-1[b] bipolar	5866-24M for 5 mm bifurcated 5866-40M for Medtronic 3.2 mm low-profile

[a] Lead adaptors have not been tested for MRI safety.
[b] IS-1 refers to the International Connector Standard (see Document No. ISO 5841-3) whereby pulse generators and leads so designated are assured of meeting the electrical and mechanical parameters specified in the IS-1 International Standard.

9.3 Positioning the leads

Warning: When implanting a SureScan pacing system, consider the risks associated with removing previously implanted leads before doing so. Abandoned leads or previously implanted non-SureScan labeled leads compromise the ability to safely scan the SureScan pacing system during MRI scans.

Warning: Proceed with extreme caution if a lead must be removed or repositioned. Chronic repositioning or removal of transvenous leads may be difficult because of fibrotic tissue development on the lead. In most clinical situations, it is preferable to abandon unused leads in place. Return all removed leads, unused leads, or lead sections to Medtronic for analysis.

Note: For active fixation leads, if the helix does not disengage from the endocardium by rotating the connector pin, rotating the lead body counterclockwise may withdraw the helix and decrease the possibility of damage to cardiovascular structures during removal.

- Lead removal may result in avulsion of the endocardium, valve, or vein.
- Lead junctions may separate, leaving the lead tip and bare wire in the heart or vein.
- Chronic repositioning of a lead may adversely affect a steroid lead's low-threshold performance.
- An abandoned lead should be capped so that the lead does not transmit electrical signals.
- Severed leads should have the remaining lead end sealed and the lead body sutured to adjacent tissue.

Warning: Implant transvenous leads according to the supplied instructions unless suitable chronic leads are already in place. Do not use any lead with this device without first verifying connector compatibility. A bipolar atrial lead with closely spaced pacing and sensing electrodes is recommended. Closely spaced bipolar epicardial leads can be used if warranted by the patient's age or medical condition.

If using a subclavian approach, position the lead using a more lateral approach to avoid pinching the lead body between the clavicle and the first rib.

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

Note: Only bipolar leads can be used with this device.

9.4 Testing the lead system

For lead testing procedures, refer to the technical manual supplied with the implant support instrument.

Table 2. Acceptable implant values

Measurements required	Acute transvenous leads	Chronic leads[bc]
R-wave amplitude	≥ 5 mV	≥ 3 mV
P-wave amplitude	≥ 2 mV	≥ 1 mV
Slew rate	≥ 0.5 V/s (atrial)	≥ 0.3 V/s (atrial)
	≥ 0.75 V/s (ventricular)	≥ 0.5 V/s (ventricular)
Capture threshold (0.5 ms pulse width)	≤ 1.5 V (atrial)	≤ 3.0 V (atrial)
	≤ 1.0 V (ventricular)	≤ 3.0 V (ventricular)
Typical pacing lead impedance[a]	250 – 1000 Ω	250 – 1000 Ω

[a] The measured pacing lead impedance is a reflection of measuring equipment and lead technology. Refer to the lead technical manual for acceptable impedance values.
[b] Chronic leads are leads implanted for 30 days or more.
[c] During an MRI scan, the MRI conditions for use information in the SureScan pacing system technical manual will supersede these values.

9.4.1 Cross-stimulation testing

Caution: Perform testing at the programmed atrial ATP output settings to ensure that ventricular capture does not occur. This is particularly important when the lead is placed in the inferior atrium.

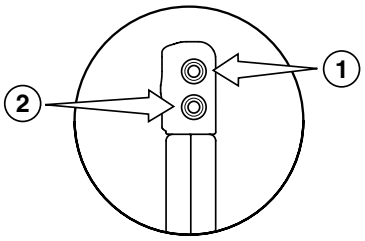
9.5 Connecting the leads to the device

Warning: Verify that the lead connections are secure. Loose lead connections may result in inappropriate sensing and failure to deliver arrhythmia therapy.

Caution: Use only the wrench supplied with the device. The wrench is designed to prevent damage to the device from overtightening a setscrew.

See Figure 1 for information about lead connections.

Figure 1. Lead connections

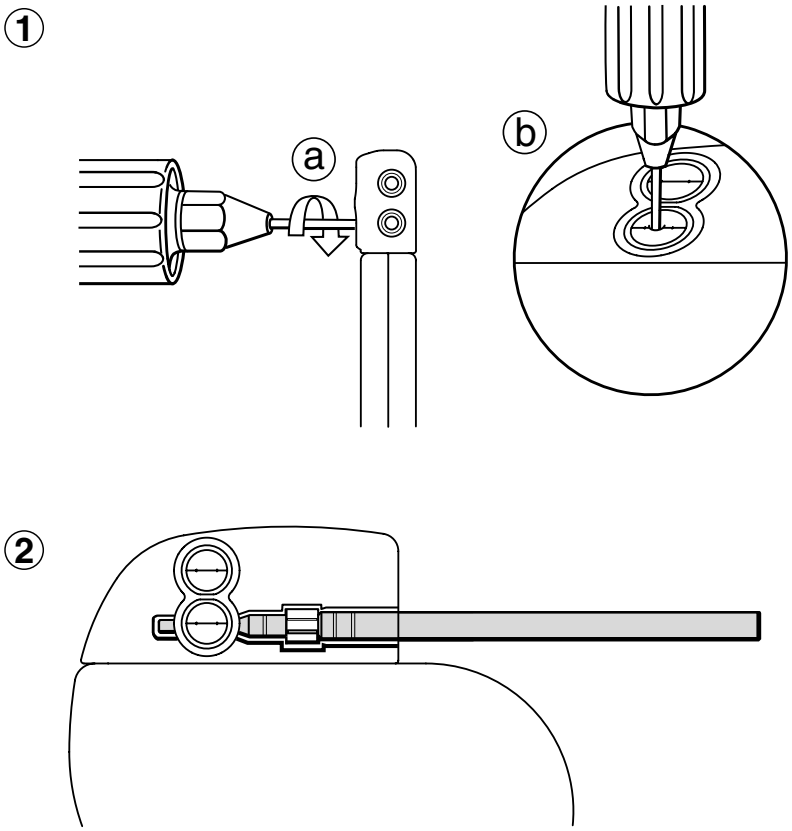


1 IS-1 connector port, A
2 IS-1 connector port, V

9.5.1 How to connect a lead to the device

1. Insert the wrench into a grommet on the connector port.
   a. Check that the setscrew is retracted from the connector port. If the connector port is obstructed, retract the setscrew to clear it. Do not disengage the setscrew from the connector block.
   b. Leave the wrench in the grommet until the lead is secure. This allows a pathway for venting trapped air when the lead is inserted.

   Figure 2. Preparing the connector port setscrew



2. Push the lead connector pin into the connector port until the connector pin is visible in the lead viewing area. Sterile water may be used as a lubricant. Sealant is not required.
3. Tighten the setscrew by turning the wrench clockwise until the wrench clicks.

4. Repeat these steps for each lead.
5. Gently pull on the lead to confirm the connection.

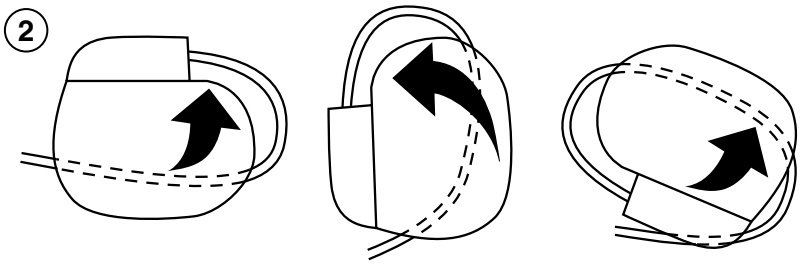
9.6 Positioning and securing the device

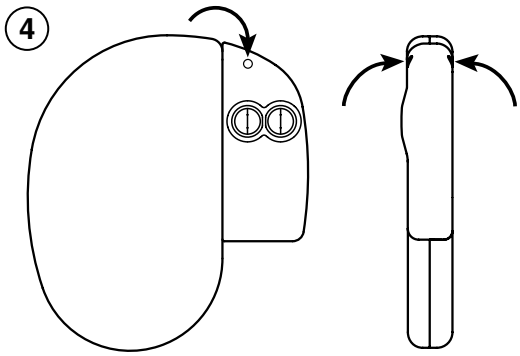
Caution: Ensure that AT/AF detection is programmed to Monitor before closing the pocket to avoid inappropriate therapy delivery while closing the pocket.

Note: Implant the device within 5 cm (2 in) of the surface of the skin to optimize post-implant ambulatory monitoring.

9.6.1 How to position and secure the device

1. Verify that each lead connector pin or plug is fully inserted into the connector port and that all setscrews are tight.
2. To prevent twisting of the lead body, rotate the device to loosely wrap the excess lead length. Do not kink the lead body.
3. Place the device and leads into the surgical pocket.
4. Suture the device securely within the pocket. Use non-absorbable sutures. Secure the device to minimize post-implant rotation and migration. Use a surgical needle to penetrate the suture hole on the device.





5. Suture the pocket incision closed.

9.7 Programming the device

Caution: Do not program AT/AF detection to On or enable automatic atrial ATP therapies until the atrial lead has matured (approximately 1 month after implant).

9.7.1 How to complete programming the device

1. Program the pacing parameters to values appropriate for the patient.
2. Monitor the patient after the implant, and take x-rays as soon as possible to document and assess the location of the leads.
3. Program patient information.

4. Set up data collection parameters.
5. Initialize data to begin diagnostic data collection.

9.7.2 How to assess the performance of the device and leads

1. Interrogate the device to check for spontaneous episodes to evaluate detection settings.
2. Recheck pacing and sensing values, and adjust if necessary.
3. Interrogate the device and print a Final Report to document the post-operative programmed device status.

9.8 Replacing a device

To retain the ability to safely scan the SureScan pacing system, refer to the SureScan pacing system technical manual for additional information.

Warning: When implanting a SureScan pacing system, consider the risks associated with removing previously implanted leads before doing so. Abandoned leads or previously implanted non-SureScan labeled leads compromise the ability to safely scan the SureScan pacing system during MRI scans.

Warning: Keep external pacing equipment nearby for immediate use. The patient does not receive pacing therapy from the device when the lead is disconnected.

Caution: Disable tachyarrythmia detection to avoid inappropriate therapy delivery while explanting the device.

Note: To meet the implant requirements, you may need to reposition or replace the chronic leads. Any unused leads that remain implanted must be capped with a lead pin cap to avoid transmitting electrical signals. Contact your Medtronic representative for information about lead pin caps. For more information, see Section 9.3, “Positioning the leads”, page 15.

Note: Only bipolar leads can be used with this device. Chronic unipolar leads cannot be used with this device.

9.8.1 How to explant and replace a device

1. Program the device to a mode that is not rate responsive to avoid potential rate increases while handling the device.
2. Dissect the leads and the device free from the surgical pocket. Do not nick or breach the lead insulation.
3. Use a torque wrench to loosen the setscrews in the connector port.
4. Gently pull the leads out of the connector ports.
5. Evaluate the condition of each lead (see Section 9.4, “Testing the lead system”, page 16). Replace a lead if the electrical integrity is not acceptable or if the lead connector pin is pitted or corroded.
6. Connect the leads to the replacement device (see Section 9.5, “Connecting the leads to the device”, page 16).
   Note: Lead adaptors may be needed to connect the leads to the replacement device. However, lead adaptors compromise the ability to safely scan the SureScan pacing system. Refer to the SureScan pacing system technical manual or contact your Medtronic representative for questions about lead adaptor compatibility with the SureScan pacing system.
7. Use the replacement device to evaluate stimulation thresholds and sensing potentials.
8. After confirming acceptable electrical measurements, position and secure the device in the surgical pocket and suture the pocket incision closed (see Section 9.6, “Positioning and securing the device”, page 18).
9. Return the explanted device and any explanted leads to Medtronic for analysis and disposal.

10 Feature summary

See the “Shipped” column of the tables in Section 11.5 for a list of which features are enabled at shipping.

10.1 Tachyarrhythmia operations

Antitachycardia pacing (ATP) therapy – This therapy delivers rapid pacing pulses to overdrive and terminate the detected arrhythmia.

Auto-adjusting sensitivity – This feature automatically adjusts the sensitivity thresholds following certain paced and sensed events to reduce the incidence of oversensing.

Reactive ATP – This feature allows the device to repeat programmed atrial ATP therapies during long AT/AF episodes. Therapies are repeated after a programmed time interval or when the atrial rhythm changes in regularity or cycle length.

10.2 Pacing operations

Atrial Preference Pacing – This atrial rhythm management feature adapts the pacing rate to slightly higher than the intrinsic sinus rate.

Atrial Rate Stabilization – This feature adjusts the pacing rate dynamically to eliminate the long pause that typically follows a premature atrial contraction (PAC).

Mode Switch – This feature prevents tracking of paroxysmal atrial tachycardias by switching from a tracking mode to a non-tracking mode.

MVP (Managed Ventricular Pacing) – This feature promotes intrinsic conduction by reducing unnecessary right ventricular pacing. MVP operates when the programmed mode is either AAIR<=>DDDR or AAI<=>DDD.

Non-Competitive Atrial Pacing (NCAP) – This feature delays an atrial pace from falling within the atrium’s relative refractory period.

Pacemaker-Mediated Tachycardia (PMT) Intervention – This feature provides automatic detection and interruption of device-defined PMTs.

Post Mode Switch Overdrive Pacing (PMOP) – This feature applies an elevated DDIR rate for a programmable period following AT/AF reversion.

Premature Ventricular Contraction (PVC) response – This feature extends the atrial refractory period following a PVC to promote dual chamber synchrony.

Rate Adaptive AV (RAAV) – This feature varies the Paced AV (PAV) and Sensed AV (SAV) intervals as the heart rate increases or decreases during dual chamber operation.

Rate Responsive Pacing – This feature varies the pacing rate in response to the patient’s physical motion as detected by the activity sensor of the device.

Ventricular Rate Stabilization – This feature adjusts the pacing rate dynamically to eliminate the long pause that typically follows a premature ventricular contraction (PVC).

Ventricular Safety Pacing – This feature prevents inappropriate inhibition of ventricular pacing caused by crosstalk or ventricular oversensing.

10.3 Monitoring operations

Cardiac Compass trends – This report plots long-term trends in heart rhythm and device status for up to 14 months.

Episode data and EGM storage – The device records diagnostic quality electrogram during every detected arrhythmia episode.

Flashback memory – This diagnostic stores interval data for several minutes prior to recent detected arrhythmia episodes, and prior to interrogation.

Heart Rate Histograms – This report shows heart rate range distributions from the most recent follow-up period and previous follow-up period.

Holter telemetry – This function allows the implanted device to continuously transmit an EGM with marker telemetry, with or without applying the programming head, for up to 46 hours.

10.4 Additional operations

MRI SureScan feature – This feature allows patients with an implanted SureScan pacing system to have a safe MRI scan. **Refer to the SureScan pacing system technical manual for additional information.**

11 Product specifications

Note: Functional parameters and electrical characteristics are measured at 37 °C (98.6 °F) with a 500 Ω load on the pacing terminals.

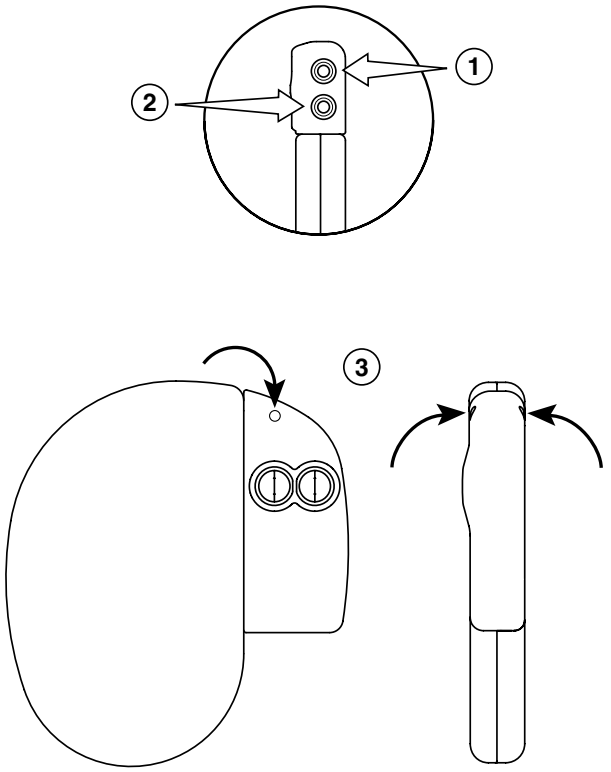
11.1 Physical characteristics

Table 3. Device physical characteristics (nominal)

Volume[a]	12.7 cm^3
Mass	21.5 g
H x W x D[b]	45 mm x 51 mm x 8 mm
Radiopaque IDs	PTA and MRI symbol[c]
Materials in contact with human tissue[d]	Titanium, polyurethane, silicone rubber
Battery	Lithium silver vanadium oxide hybrid

[a] Volume with connector bores unplugged.
[b] Grommets may protrude slightly beyond the can surface.
[c] Refer to the SureScan pacing system technical manual for a description and drawing of the 2 radiopaque symbols.
[d] These materials have been successfully tested for the ability to avoid biological incompatibility. The device does not produce an injurious temperature in the surrounding tissue during normal operation.

Figure 3. Connector and suture holes



1 IS-1 connector port, A
2 IS-1 connector port, V
3 Suture hole

11.2 Replacement indicators

Battery voltage and messages about replacement status appear on the programmer display and on printed reports. The Recommended Replacement Time (RRT) and the End of Service (EOS) conditions are listed in Table 4.

Table 4. Replacement indicators

Recommended Replacement Time (RRT)	≤ 2.81 V on 3 consecutive daily automatic measurements
End of Service (EOS)	3 months after RRT

RRT date – The Quick Look and Battery and Lead Measurements screens display the date when the battery reached RRT.

Replace at EOS – If the programmer indicates that the device is at EOS, replace the device immediately.

RRT operation – When the device reaches RRT, it automatically changes the value of several parameters as shown in Table 5.

Table 5. Parameter settings after RRT

Pacing Mode	VVI
Lower Rate	65 bpm
RV Amplitude	as programmed
RV Pulse Width	as programmed
Rate Hysteresis	Off
V. Rate Stabilization	Off
AT/AF Detection	Monitor (fixed)[a]
Pre-arrhythmia EGM	Off (fixed)

[a] When AT/AF Detection is set to Monitor, AT/AF therapies are not available.

Prolonged service period – The prolonged service period is the time between the RRT and EOS. This 3 month period between RRT and EOS assumes 100% pacing at these settings, with RV Amplitude set to 3.5 V and RV Pulse Width set to 0.4 ms, and a pacing load of 500 Ω. Reprogramming the pacing parameters may reduce the duration of the RRT to EOS period.

11.3 Projected service life

The following service life estimates are based on accelerated battery discharge data and device modeling, as specified.

11.3.1 Considerations

Pacing outputs – If the patient's pacing threshold allows for an appropriate safety margin (at least a factor of 2 after the acute implant period), consider decreasing the pacing outputs. Always consider the patient's access to regular follow-up care in selecting a safety margin for chronic pacing.

Pacing mode – If the patient's intrinsic rhythm allows for appropriate rate support, you can decrease the pacing burden by programming the Mode, Rate Response, and AV Interval parameters to promote intrinsic activation or conduction.

Pre-arrhythmia EGM storage – When Pre-arrhythmia EGM storage is enabled, the device collects up to 10 s of EGM information before the onset or detection of VT Monitor or SVT episodes.

Note: The Pre-arrhythmia EGM feature does not apply to AT/AF episodes. The device stores up to 5 s of EGM prior to AT/AF detection, regardless of the Pre-arrhythmia EGM setting.

Using Pre-arrhythmia EGM storage reduces longevity by approximately 34% or by 4 months per year.[1] In a patient who uniformly repeats the same onset mechanisms, the greatest clinical benefit of Pre-arrhythmia EGM storage is achieved after a few episodes are captured.

To maximize the effectiveness of the Pre-arrhythmia EGM feature and optimize device longevity, consider these programming options:

- Enable Pre-arrhythmia EGM to capture possible changes in the onset mechanism following significant clinical adjustments, for example, device implant, medication changes, and surgical procedures.
- Disable Pre-arrhythmia EGM once you have successfully captured the information of interest.

[1] Based on device modeling with 50% atrial pacing and 5% ventricular pacing.

Note: When Pre-arrhythmia EGM is disabled, the device starts storing EGM information for VT Monitor and SVT episodes after the third tachyarrhythmia event occurs. However, the device still records up to 20 s of information before the onset or detection of the episode, including interval measurements and Marker Channel annotations. In addition, the most recent tachyarrhythmia episodes also provide Flashback interval data.

11.3.2 Projected service life

Delivery of atrial antitachycardia pacing therapy does not appreciably alter the service life of the device, when considered with the inhibition of atrial pacing during the AT/AF episode.

Table 6. Projected service life in years with 0.4 ms pulse width and 60 bpm pacing rate[a]

Pacing	Pre-arrhythmia EGM storage[b]	500 Ω pacing impedance		600 Ω pacing impedance		1000 Ω pacing impedance	
		2.5 V	3.0 V	2.5 V	3.0 V	2.5 V	3.0 V
DDD, 0%	Off	12.6	12.6	12.6	12.6	12.6	12.6
	On	12.4	12.4	12.4	12.4	12.4	12.4
DDD, 15%	Off	12.0	11.8	12.1	12.0	12.4	12.2
	On	11.8	11.6	11.9	11.7	12.1	12.0
DDD, 50%	Off	10.8	10.3	11.1	10.6	11.8	11.4
	On	10.6	10.1	10.9	10.4	11.5	11.2
AAI<=>DDD, 50% atrial, 5% ventricular	Off	11.4	11.1	11.6	11.3	12.0	11.8
	On	11.2	10.9	11.4	11.1	11.7	11.5
DDD, 100%	Off	9.4	8.7	9.9	9.2	11.0	10.4
	On	9.3	8.5	9.7	9.0	10.7	10.2

[a] The service life projections in this table assume less than 75 hours of total MRI SureScan feature use throughout the device lifetime.

[b] The data provided for programming Pre-arrhythmia EGM On assumes that it is enabled for a period of 6 months following the implant of the device. Additional use of Pre-arrhythmia EGM reduces projected service life by approximately 34% or 4 months per year.

11.4 Magnet application

When a magnet is placed near the device, the device responds as shown in Table 7. When the magnet is removed, the device returns to its programmed operations.

Table 7. Effects of magnet application on the device[a]

Pacing mode	The device changes to an asynchronous pacing mode. The specific mode depends on the programmed pacing mode: • DOO if the programmed mode is AAIR<=>DDDR, AAI<=>DDD, DDDR, DDD, DDIR, DDI, or DOO • VOO if the programmed mode is VVIR, VVI, or VOO • AOO if the programmed mode is AAIR, AAI, or AOO
Pacing rate and interval	The device applies a fixed pacing rate. The specific rate depends on the status of the device. • 85 bpm (700 ms) if device conditions are normal • 65 bpm (920 ms) if RRT or an electrical reset occurred
Tachyarrhythmia detection	The device suspends detection.

[a] Tachyarrhythmia detection and the programmed pacing mode and rate resume if telemetry between the device and the programmer is established and the application software is running.

11.5 Functional parameters

Programmable parameters are determined by the software used in the programmer. If the programmer displays a message that an electrical reset has occurred, contact your Medtronic representative.

The ⊕ symbol in parameter tables indicates the Medtronic nominal value for that parameter.

11.5.1 Emergency settings

Table 8. Emergency VVI settings

Parameter	Selectable values
Pacing Mode	VVI
Lower Rate	70 bpm
RV Amplitude[a]	6 V
RV Pulse Width	1.5 ms
V. Blank Post VP	240 ms
Rate Hysteresis	Off
V. Rate Stabilization	Off
MRI SureScan	Off

[a] Peak pacing amplitude. When tested per CENELEC standard EN 45502-2-1:2003, the tolerance is applied not to the programmed setting, but to the calculated amplitude A, which depends upon the programmed amplitude A_p and programmed pulse width W_p: $A = A_p \times [0.9 - (W_p \times 0.145\ ms^{-1})]$.

11.5.2 Tachyarrhythmia detection parameters

Table 9. Tachyarrhythmia detection parameters

Parameter	Programmable values	Shipped	Reset
AT/AF Detection	On; Monitor⊕	Monitor	Monitor
Zones	1⊕; 2	1	1
AT/AF Interval[a]	150; 160 … 350⊕ … 450 ms	350 ms	350 ms

Table 9. Tachyarrhythmia detection parameters (continued)

Parameter	Programmable values	Shipped	Reset
Fast AT/AF Interval[a]	150; 160 … 200◈ … 250 ms	200 ms	200 ms
VT Monitor	Monitor◈; Off	Monitor	Off
VT Monitor Interval[a]	280; 290 … 400◈ … 500 ms	400 ms	400 ms
RV Sensitivity[b,c]	0.45; 0.6; 0.9◈; 1.2; 1.5; 2.1 mV	0.9 mV	0.9 mV
Atrial Sensitivity[c,d]	0.15 mV; 0.3◈; 0.45; 0.6; 0.9; 1.2; 1.5; 2.1 mV	0.3 mV	0.3 mV

[a] The measured intervals are truncated to a 10 ms multiple (for example, 457 ms becomes 450 ms). The device uses this truncated interval value when applying the programmed criteria and calculating interval averages.
[b] With a 40 ms sine^2 waveform. When using the CENELEC waveform, the sensing threshold value will be 1.5 times the rated sine^2 sensing threshold.
[c] This setting applies to all sensing in this chamber for both tachyarrhythmia detection and bradycardia pacing operations.
[d] With a 20 ms sine^2 waveform. When using the CENELEC waveform, the sensing threshold value will be 1.4 times the rated sine^2 sensing threshold.

11.5.3 Atrial tachyarrhythmia therapy parameters

Table 10. Atrial tachyarrhythmia therapy parameters

Parameter	Programmable values	Shipped	Reset
AT/AF Rx Status	On; Off◈	Off	Off
Therapy Type	Ramp; Burst+ Rx1: Ramp◈ Rx2: Burst+◈ Rx3: Ramp◈	—	—
Fast AT/AF Rx Status	On; Off◈	Off	Off
Therapy Type	Ramp; Burst+ Rx1: Ramp◈ Rx2: Burst+◈ Rx3: Ramp◈	—	—
Burst+ parameters			
Initial # S1 Pulses	1; 2 … 15◈; 20; 25	—	—
A-S1 Interval (%AA)	28; 31; 34; 38; 41 … 59; 63; 66 … 84; 88; 91◈; 94; 97%	—	—
S1-S2 (%AA)	Off; 28; 31; 34; 38; 41 … 59; 63; 66; 69 … 84◈; 88; 91; 94; 97%	—	—
S2-S3 Decrement	Off; 0; 10◈; 20 … 80 ms	—	—
Interval Decrement	0; 10◈; 20; 30; 40 ms	—	—
# Sequences	1; 2 … 6◈ … 10	—	—

Table 10. Atrial tachyarrhythmia therapy parameters (continued)

Parameter	Programmable values	Shipped	Reset
Ramp parameters			
Initial # S1 Pulses	1; 2 … 6◈ … 15; 20; 25	—	—
A-S1 Interval (% AA)	28; 31; 34; 38; 41 … 59; 63; 66 … 84; 88; 91◈; 94; 97%	—	—
Interval Decrement	0; 10◈ … 40 ms	—	—
# Sequences	1; 2 … 8◈; 9; 10	—	—
Shared atrial therapy parameters			
Duration to Stop	12; 24; 48◈; 72 hr; None	48 hr	48 hr
Disable all atrial therapies if atrial lead position is suspect?	Yes◈; No	No	No
Disable Atrial ATP if it accelerates V. rate?	Yes◈; No	Yes	Yes
Episode Duration Before ATP	0; 1◈; 2; 3; 4; 5; 7; 10; 15; 20; 25; 30; 40; 50 min; 1; 2; 3; 4; 5; 6; 12; 24 hr	1 min	1 min
Reactive ATP Rhythm Change	On◈; Off	On	On
Reactive ATP Time Interval	Off; 2; 4; 7◈; 12; 24; 36; 48 hr	Off	Off
A-A Minimum ATP Interval[b]	100; 110; 120; 130◈ … 400 ms	150 ms	150 ms
A. Pacing Amplitude[a]	1; 2 … 6◈; 8 V	6 V	6 V
A. Pacing Pulse Width	0.1; 0.2 … 1.5◈ ms	1.5 ms	1.5 ms
VVI Backup Pacing	Off; On (Always); On (Auto-Enable)◈	On (Auto- Enable)	On (Auto- Enable)
VVI Backup Pacing Rate	60; 70◈ … 120 bpm	70 bpm	70 bpm

[a] Peak pacing amplitude. When tested per CENELEC standard EN 45502-2-1:2003, the tolerance is applied not to the programmed setting, but to the calculated amplitude A, which depends upon the programmed amplitude A_p and programmed pulse width W_p: $A = A_p \times [0.9 - (W_p \times 0.145\ ms^{-1})]$.

[b] The measured intervals are truncated to a 10 ms multiple (for example, 457 ms becomes 450 ms). The device uses this truncated interval value when applying the programmed criteria and calculating interval averages.

11.5.4 Bradycardia pacing parameters

Table 11. Bradycardia pacing parameters

Parameter	Programmable values	Shipped	Reset
Mode	DDDR; DDD; AAIR<=>DDDR◆; AAI<=>DDD; DDIR; DDI; AAIR; AAI; VVIR; VVI; DOO; AOO; VOO; ODO	AAI<=>DDD	VVI
Mode Switch	On◆; Off	On	Off
Lower Rate[a]	30; 35 … 60◆; 70; 75 … 150 bpm	60 bpm	65 bpm
Upper Tracking Rate	80; 85 … 130◆ … 150 bpm	130 bpm	120 bpm
Upper Sensor Rate	80; 85 … 130◆ … 150 bpm	130 bpm	120 bpm
Paced AV	30; 40 … 180◆ … 350 ms	180 ms	180 ms
Sensed AV	30; 40 … 150◆ … 350 ms	150 ms	150 ms
PVARP	Varied; 150; 160 … 310◆ … 500 ms	310 ms	310 ms
A. Refractory Period	150; 160 … 310◆ … 500 ms	310 ms	310 ms
RV Amplitude[b]	0.5; 1 … 3◆; 3.5; 4; 5; 6 V	3 V	6 V
RV Pulse Width	0.03; 0.06; 0.1; 0.2; 0.3; 0.4◆ … 1.5 ms	0.4 ms	1.5 ms
RV Sensitivity[c,d]	0.45; 0.6; 0.9◆; 1.2; 1.5; 2.1 mV	0.9 mV	0.9 mV
Atrial Amplitude[b]	0.5; 1 … 3◆; 3.5; 4; 5; 6 V	3 V	4 V
Atrial Pulse Width	0.03; 0.06; 0.1; 0.2; 0.3; 0.4◆ … 1.5 ms	0.4 ms	0.4 ms
Atrial Sensitivity[d,e]	0.15 mV; 0.3◆; 0.45; 0.6; 0.9; 1.2; 1.5; 2.1 mV	0.3 mV	0.3 mV
PVAB Interval	10; 20 … 150◆ … 300 ms	150 ms	150 ms
PVAB Method	Partial◆; Partial+; Absolute	Partial	Partial
A. Blank Post AP	150; 160 … 200◆ … 250 ms	200 ms	240 ms
A. Blank Post AS	100◆; 110 … 170 ms	100 ms	100 ms
V. Blank Post VP	150; 160 … 200◆ … 320 ms	200 ms	240 ms
V. Blank Post VS	120◆; 130 … 170; 200; 220; 250; 280; 300; 320 ms	120 ms	120 ms
Rate Response Pacing parameters			
Rate Response	1; 2 … 7◆ … 10	7	7
Activity Threshold	Low; Medium Low◆; Medium High; High	Medium Low	Medium Low
Activity Acceleration	15; 30◆; 60 s	30 s	30 s
Activity Deceleration	Exercise◆; 2.5; 5; 10 min	5 min	5 min
Rate Adaptive AV parameters			
Rate Adaptive AV	On; Off◆	Off	On
Start Rate	50; 55 … 80◆ … 145 bpm	80 bpm	60 bpm
Stop Rate	55; 60 … 130◆ … 150 bpm	130 bpm	120 bpm

Table 11. Bradycardia pacing parameters (continued)

Parameter	Programmable values	Shipped	Reset
Minimum Paced AV	30; 40 … 140◈ … 200 ms	140 ms	140 ms
Minimum Sensed AV	30; 40 … 110◈ … 200 ms	110 ms	110 ms
Arrhythmia intervention parameters			
A. Rate Stabilization	On; Off◈	Off	Off
Maximum Rate	80; 85 … 100◈ … 150 bpm	100 bpm	100 bpm
Interval Percentage Increment	12.5; 25◈; 50%	25%	25%
A. Preference Pacing	On; Off◈	Off	Off
Maximum Rate	80; 85 … 100◈ … 150 bpm	100 bpm	100 bpm
Interval Decrement	30; 40; 50◈ … 100; 150 ms	50 ms	50 ms
Search Beats	5; 10◈ … 25; 50	10	5
Post Mode Switch	On; Off◈	Off	Off
Overdrive Rate	70; 75; 80◈ … 120 bpm	80 bpm	65 bpm
Overdrive Duration	0.5; 1; 2; 3; 5; 10◈; 20; 30; 60; 90; 120 min	10 min	10 min
V. Rate Stabilization	On; Off◈	Off	Off
Maximum Rate	80; 85 … 120◈ bpm	120 bpm	120 bpm
Interval Increment	50; 60 … 150◈ … 400 ms	150 ms	150 ms
Additional pacing features			
Non-Comp Atrial Pacing	On◈; Off	On	On
NCAP Interval	200; 250; 300◈; 350; 400 ms	300 ms	300 ms
Rate Hysteresis	Off◈; 30; 40 … 80 bpm	Off	Off
PMT Intervention	On; Off◈	Off	Off
PVC Response	On◈; Off	On	On
V. Safety Pacing	On◈; Off	On	On
MRI SureScan	Off◈; On	Off	Off
MRI Pacing Mode	DOO; AOO; VOO; ODO	—	—
MRI Pacing Rate	30; 35 … 60; 70; 75 … 120 bpm	—	—

[a] The corresponding Lower Rate Interval can be calculated as follows: Lower Rate Interval (ms) = 60,000/Lower Rate. The tolerance for Lower Rate Interval is (+30; –2 ms).

[b] Peak pacing amplitude. When tested per CENELEC standard EN 45502-2-1:2003, the tolerance is applied not to the programmed setting, but to the calculated amplitude A, which depends upon the programmed amplitude A_p and programmed pulse width W_p: $A = A_p \times [0.9 - (W_p \times 0.145\ ms^{-1})]$.

[c] With a 40 ms $sine^2$ waveform. When using the CENELEC waveform, the sensing threshold value will be 1.5 times the rated $sine^2$ sensing threshold.

[d] This setting applies to all sensing in this chamber for both tachyarrhythmia detection and bradycardia pacing operations.

[e] With a 20 ms $sine^2$ waveform. When using the CENELEC waveform, the sensing threshold value will be 1.4 times the rated $sine^2$ sensing threshold.

11.5.5 Data collection parameters

Table 12. Data collection parameters

Parameter	Programmable values	Shipped	Reset
EGM 1 Source	Vtip to Vring; Atip to Aring◈; Atip to Vring; Aring to Vring	Atip to Aring	Atip to Aring
EGM 1 Range	±2; ±4; ±8◈; ±16 mV	±8 mV	±8 mV
EGM 2 Source	Vtip to Vring (fixed)	Vtip to Vring	Vtip to Vring
EGM 2 Range	±2; ±4; ±8◈; ±16 mV	±8 mV	±8 mV
Pre-arrhythmia EGM	Off◈; On – 1 month; On – 3 months; On Continuous	Off	Off
Device Date/Time[a]	(enter time and date)	—	—
Holter Telemetry	Off◈; 0.5; 1; 2; 4; 8; 16; 24; 36; 46 hr	Off	Off

[a] The times and dates stored in episode records and other data are determined by the Device Date/Time clock.

11.5.6 System test parameters

Table 13. System test parameters

Parameter	Selectable values
Pacing Threshold Test parameters	
Test Type	Amplitude; Pulse Width
Chamber	RV; Atrium
Decrement after	2; 3 … 15 pulses
Mode[a] (RV test)	VVI; VOO; DDI; DDD; DOO
Mode[a] (Atrium test)	AAI; AOO; DDI; DDD; DOO
Lower Rate	30; 35 … 60; 70; 75 … 150[b] bpm
RV Amplitude[c]	0.5; 1 … 4; 5; 6; 8 V
RV Pulse Width	0.03; 0.06; 0.1; 0.2 … 1.5 ms
A. Amplitude[c]	0.5; 1 … 4; 5; 6; 8 V
A. Pulse Width	0.03; 0.06; 0.1; 0.2 … 1.5 ms
AV Delay	30; 40 … 350 ms
RV Pace Blanking	150; 160 … 320 ms
A. Pace Blanking	150; 160 … 250 ms
PVARP	150; 160 … 500 ms

Table 13. System test parameters (continued)

Parameter	Selectable values
Sensing Test parameters	
Mode[a]	AAI; DDD; DDI; VVI; ODO
AV Delay	30; 40 … 350 ms
Lower Rate	30; 35 … 60; 70; 75 … 120 bpm

[a] The selectable values for this parameter depend on the programmed pacing mode.
[b] The maximum Lower Rate value is 145 bpm if you perform the test in DDD mode.
[c] Peak pacing amplitude. When tested per CENELEC standard EN 45502-2-1:2003, the tolerance is applied not to the programmed setting, but to the calculated amplitude A, which depends upon the programmed amplitude A_p and programmed pulse width W_p: $A = A_p \times [0.9 - (W_p \times 0.145\ ms^{-1})]$.

11.5.7 EP study parameters

Table 14. EP Study parameters

Parameter	Selectable values
Fixed Burst induction parameters	
Resume at Burst	Enabled◈; Disabled
Chamber	RV; Atrium
Interval	100; 110 … 600◈ ms
Amplitude[a]	0.5; 1 … 4◈; 5; 6; 8 V
Pulse Width	0.1; 0.2 … 0.5◈ … 1.5 ms
VVI Backup (for atrial Fixed Burst)[c]	On; Off◈
Pacing Rate	60; 70◈ … 120 bpm
RV Amplitude[a,b]	0.5; 1 … 4; 5; 6; 8 V
RV Pulse Width[b]	0.1; 0.2 … 1.5 ms
PES induction parameters	
Resume at Deliver	Enabled◈; Disabled
Chamber	RV; Atrium
#S1	1; 2 … 8◈ … 15
S1S1	100; 110 … 600◈ … 2000 ms
S1S2	Off; 100; 110 … 400◈ … 600 ms
S2S3	Off◈; 100; 110 … 600 ms
S3S4	Off◈; 100; 110 … 600 ms
Amplitude[a]	0.5; 1 … 4◈; 5; 6; 8 V
Pulse Width	0.1; 0.2 … 0.5◈ … 1.5 ms
VVI Backup (for atrial PES)[c]	On; Off◈
Pacing Rate	60; 70◈ … 120 bpm
RV Amplitude[a,b]	0.5; 1 … 4; 5; 6; 8 V
RV Pulse Width[b]	0.1; 0.2 … 1.5 ms

Table 14. EP Study parameters (continued)

Parameter	Selectable values
General manual ATP therapy parameters	
Minimum Interval (atrial ATP)	100; 110; 120; 130⊕ … 400 ms
Minimum Interval (ventricular ATP)	150; 160 … 200⊕ … 400 ms
Amplitude[a]	0.5; 1 … 4; 5; 6⊕; 8 V
Pulse Width	0.1; 0.2 … 1.5⊕ ms
VVI Backup (for atrial ATP therapy)[c]	On; Off⊕
Pacing Rate	60; 70⊕ … 120 bpm
RV Amplitude[a,b]	0.5; 1 … 4; 5; 6; 8 V
RV Pulse Width[b]	0.1; 0.2 … 1.5 ms
Manual Ramp therapy parameters	
Chamber	RV; Atrium
RV Ramp therapy parameters	
# Pulses	1; 2 … 6⊕ … 15
%RR Interval	50; 53; 56; 59; 63; 66 … 84; 88; 91; 94; 97⊕%
Dec/Pulse	0; 10⊕; 20; 30; 40 ms
Atrial Ramp therapy parameters	
# Pulses	1; 2 … 6⊕ … 15; 20; 30 … 100
%AA Interval	28; 31; 34; 38; 41 … 59; 63; 66 … 84; 88; 91; 94; 97⊕%
Dec/Pulse	0; 10⊕; 20; 30; 40 ms
Manual Burst therapy parameters	
# Pulses	1; 2 … 8⊕ … 15
%RR Interval	50; 53; 56; 59; 63; 66 … 84; 88⊕; 91; 94; 97%
Manual Ramp+ therapy parameters	
# Pulses	1; 2; 3⊕ … 15
R-S1 (%RR)	50; 53; 56; 59; 63; 66 … 75⊕ … 84; 88; 91; 94; 97%
S1-S2 (%RR)	50; 53; 56; 59; 63; 66; 69⊕ … 84; 88; 91; 94; 97%
S2-SN (%RR)	50; 53; 56; 59; 63; 66⊕ … 84; 88; 91; 94; 97%
Manual Burst+ therapy parameters	
# S1 Pulses	1; 2 … 6⊕ … 15; 20; 30 … 100
%AA Interval	28; 31; 34; 38; 41 … 59; 63; 66 … 84; 88; 91⊕; 94; 97%

Table 14. EP Study parameters (continued)

Parameter	Selectable values
S1S2	Off; 28; 31; 34; 38; 41 … 59; 63; 66 … 84◈; 88; 91; 94; 97%
S2S3 Dec	Off; 0; 10; 20◈ … 80 ms

[a] Peak pacing amplitude. When tested per CENELEC standard EN 45502-2-1:2003, the tolerance is applied not to the programmed setting, but to the calculated amplitude A, which depends upon the programmed amplitude A_p and programmed pulse width W_p: $A = A_p \times [0.9 - (W_p \times 0.145\ ms^{-1})]$.
[b] The default value for this parameter is set according to the permanently programmed settings for bradycardia pacing.
[c] Crosstalk may occur when atrial pacing amplitude is greater than 6 V.

11.5.8 Nonprogrammable parameters

Table 15. Nonprogrammable parameters

Parameter	Value
Premature threshold	69%
Fixed blanking periods	
Atrial blanking after a paced ventricular event	30 ms
Ventricular blanking after a paced atrial event	30 ms
Fixed bradycardia pacing parameters	
Ventricular Safety Pacing intervals	110 ms 70 ms[a]
PVC Response (PVARP extension)[b]	Extended to 400 ms
PVC Response (NCAP extension)[c]	Extended to 400 ms
PMT Intervention (PVARP extension)[b]	Extended to 400 ms
PMT Intervention (NCAP extension)[c]	Extended to 400 ms
Fixed tachyarrhythmia detection parameters	
Ventricular events to detect AT/AF	32
VT Monitor initial beats to detect	16
Stability criterion interval	90 ms
AF/Afl criterion	On
Sinus Tach criterion	On
Fixed automatic atrial ATP therapy parameters	
VVI Backup Pacing amplitude[d]	6 V
VVI Backup Pacing pulse width	1.5 ms

Table 15. Nonprogrammable parameters (continued)

Parameter	Value
Hardware parameters	
Atrial rate limit[e] (protective feature)	171 bpm
Ventricular rate limit[e] (protective feature)	171 bpm
Input impedance	150 kΩ minimum

[a] The shorter VSP interval takes effect when the pacing rate exceeds the results of the following formula: 60,000/2 x (Ventricular Pace Blanking + 110) per minute.

[b] PVARP is extended to 400 ms only if the current PVARP (either the programmed PVARP value or the current Varied PVARP value) is less than 400 ms.

[c] The NCAP extension applies only if NCAP is enabled.

[d] Peak pacing amplitude. When tested per CENELEC standard EN 45502-2-1:2003, the tolerance is applied not to the programmed setting, but to the calculated amplitude A, which depends upon the programmed amplitude A_p and programmed pulse width W_p: $A = A_p \times [0.9 - (W_p \times 0.145\ ms^{-1})]$.

[e] Does not apply during therapies, programmed high rates, or ventricular safety pacing.

World Headquarters
Medtronic, Inc.
710 Medtronic Parkway
Minneapolis, MN 55432-5604
USA
Internet: www.medtronic.com
Tel. +1-763-514-4000
Fax +1-763-514-4879

Medtronic USA, Inc.
Toll-free in the USA (24-hour technical consultation for physicians and medical professionals)
Bradycardia: 1-800-505-4636
Tachycardia: 1-800-723-4636

Europe/Africa/Middle East Headquarters
Medtronic International Trading Sàrl
Route du Molliau 31
Case Postale 84
CH-1131 Tolochenaz
Switzerland
Internet: www.medtronic.com
Tel. +41-21-802-7000
Fax +41-21-802-7900

Medtronic E.C. Authorized Representative/Distributed by
Medtronic B.V.
Earl Bakkenstraat 10
6422 PJ Heerlen
The Netherlands
Tel. +31-45-566-8000
Fax +31-45-566-8668

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Slipsheet

Medtronic

CAPSUREFIX MRI™ SURESCAN™ 5086MRI

MR

MR Conditional, steroid-eluting, bipolar, implantable, screw-in, ventricular/atrial, transvenous lead

Technical Manual

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

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1 Description

The Medtronic CapSureFix MRI SureScan Model 5086MRI steroid-eluting, bipolar, implantable, screw-in, ventricular/atrial, transvenous lead is designed for pacing and sensing applications in either the atrium or ventricle. The lead has also been designed for use in the MRI environment that is specified in the SureScan pacing system technical manual. The platinum alloy tip and ring electrodes feature a high-active surface area of titanium nitride microstructure. This electrode configuration contributes to low polarization.

The lead has a helical tip electrode made of platinum alloy that can be actively fixed in the endocardium. The helix electrode can be extended or retracted by rotating the lead connector pin with either the Quick Twist tool attached to the lead or with the white fixation tool. An active fixation lead is particularly beneficial for patients who have smooth or hypertrophic hearts where lead dislodgement may be a potential problem. The lead also has a second, larger electrode proximal to the helical tip electrode and an IS-1 Bipolar (BI) connector[1] with one terminal pin. It features MP35N nickel alloy conductors and silicone rubber insulation. The outer insulation of the lead has been treated to facilitate ease of implant.

The distal tip contains a nominal dosage of 692 µg of dexamethasone acetate. Upon exposure to body fluids, the steroid elutes from the lead tip. The steroid is known to suppress the inflammatory response that is believed to cause threshold rises typically associated with implanted pacing electrodes.

The Medtronic SureScan pacing system includes a Medtronic SureScan device connected to Medtronic SureScan leads. Labeling for SureScan pacing system components displays the SureScan symbol and the MR Conditional symbol.

SureScan symbol

MR Conditional symbol. The SureScan pacing system is safe for use in the MRI environment when used according to the instructions in the SureScan technical manual.

The MRI SureScan feature permits a mode of operation that allows a patient with a SureScan device to be safely scanned by an MRI machine. **Before performing an MRI scan, refer to the SureScan pacing system technical manual provided with the SureScan device for important information about procedures and MRI-specific contraindications, warnings, and precautions.**

1.1 Package contents

Leads and accessories are supplied sterile. Each package contains the following items:

- 1 lead with radiopaque anchoring sleeve, stylet, and Quick Twist tool
- 1 white fixation tool
- 1 vein lifter
- extra stylets
- product literature

1.2 Accessory descriptions

Anchoring sleeve – An anchoring sleeve secures the lead to prevent it from moving and protects the lead insulation and conductors from damage caused by tight sutures.

White fixation tool – The white fixation tool facilitates connector pin rotation.

Quick Twist tool – The Quick Twist tool facilitates both connector pin rotation and stylet insertion into the lead. This tool comes attached to the lead.

Stylet – A stylet provides additional stiffness and controlled flexibility for maneuvering the lead into position. Each stylet knob is labeled with the stylet diameter and length.

Vein lifter – A vein lifter facilitates lead insertion into a vein.

2 Indications

The Medtronic CapSureFix MRI SureScan Model 5086MRI steroid-eluting, bipolar, implantable, screw-in, ventricular/atrial, transvenous lead is designed to be used with a pulse generator as part of a cardiac pacing system. It has been designed for use in the MRI environment, but only when used with a Medtronic SureScan IPG. The lead has application where implantable atrial or ventricular, single chamber or dual chamber pacing systems are indicated.

[1] IS-1 BI refers to an International Connector Standard (ISO 5841-3) whereby pulse generators and leads so designated are assured of a basic mechanical fit.

3 Contraindications

Before performing an MRI scan, refer to the SureScan pacing system technical manual for MRI-specific contraindications.

- Use of ventricular transvenous leads is contraindicated in patients with tricuspid valvular disease.
- Use of ventricular transvenous leads is contraindicated in patients with mechanical tricuspid heart valves.
- Use of steroid-eluting transvenous leads is contraindicated in patients for whom a single dose of 1.0 mg dexamethasone acetate may be contraindicated.

4 Warnings and precautions

Before performing an MRI scan, refer to the SureScan pacing system technical manual for MRI-specific warnings and precautions.

Line-powered and battery-powered equipment – An implanted lead forms a direct current path to the myocardium. During lead implant and testing, use only battery-powered equipment or line-powered equipment specifically designed for this purpose to protect against fibrillation that may be caused by alternating currents. Line-powered equipment used in the vicinity of the patient must be properly grounded. Lead connector pins must be insulated from any leakage currents that may arise from line-powered equipment.

Diathermy – People with metal implants such as pacemakers, implantable cardioverter defibrillators (ICDs), and accompanying leads should not receive diathermy treatment. The interaction between the implant and diathermy can cause tissue damage, fibrillation, or damage to the device components, which could result in serious injury, loss of therapy, and/or the need to reprogram or replace the device.

Vessel and tissue damage – Use care when positioning the lead. Avoid known infarcted or thin ventricular wall areas to minimize the occurrence of perforation and dissection.

Single use – The lead is for single use only.

Inspecting the sterile package – Inspect the sterile package with care before opening it.

- Contact a Medtronic representative if the seal or package is damaged.
- Do not store this product above 40 °C (104 °F).
- Do not use the product after its expiration date.

Sterilization – Medtronic has sterilized the package contents with ethylene oxide before shipment. This lead is for single use only and is not intended to be resterilized.

Steroid use – It has not been determined whether the warnings, precautions, or complications usually associated with injectable dexamethasone acetate apply to the use of this highly localized, controlled-release lead. For a list of potential adverse effects, refer to the *Physicians' Desk Reference*.

Handling the steroid tip – Avoid reducing the amount of steroid available before implanting the lead. Reducing the available amount of steroid may adversely affect low-threshold performance.

- Do not allow the electrode surface to come in contact with surface contaminants.
- Do not wipe or immerse the electrode in fluid, except blood, at the time of implant.

Handling a screw-in lead – Handle the lead with care at all times.

- Do not implant the lead if it is damaged. Return the lead to a Medtronic representative.
- Protect the lead from materials that shed small particles such as lint and dust. Lead insulators attract these particles.
- Handle the lead with sterile surgical gloves that have been rinsed in sterile water or a comparable substance.
- Do not severely bend, kink, or stretch the lead.
- Do not immerse the lead in mineral oil, silicone oil, or any other liquid, except blood, at the time of implant.
- Do not use surgical instruments to grasp the lead or connector pin.
- Do not force the lead if resistance is encountered during lead passage.
- Exercise the helix electrode before implanting the lead. On initial extension, more rotations may be required to extend and retract the helix electrode, or the helix electrode may extend suddenly when torque is built up.
  Note: The estimated number of rotations (using the fixation tool) needed to initially extend or retract the helix electrode is stated in Section 7, "Specifications (nominal)", page 11.
- Ensure helix is retracted prior to implant.
- Identify helix electrode extension and retraction using fluoroscopy during implant (Figure 7). Overrotation of the connector pin may result in fracture or distortion of the inner conductor or retraction of the helix electrode out of its channel.

Handling the stylet – Handle the stylet with care at all times.

- Curve the stylet before inserting it into the lead to achieve a curvature at the lead's distal end. Do not use a sharp object to impart a curve to the distal end of the stylet.
- Do not use excessive force or surgical instruments when inserting the stylet into the lead.
- Avoid overbending or kinking the stylet.
- Use a new stylet when blood or other fluids accumulate on the stylet. Accumulated blood or other fluids may damage the lead or cause difficulty in passing the stylet into the lead.

Necessary hospital equipment – Keep external defibrillation equipment nearby for immediate use during acute lead system testing, the implant procedure, or whenever arrhythmias are possible or intentionally induced during post-implant testing.

Concurrent devices – Output pulses, especially from unipolar devices, may adversely affect device sensing capabilities. If a patient requires a separate stimulation device, either permanent or temporary, allow enough space between the leads of the separate systems to avoid interference in the sensing capabilities

of the devices. Previously implanted pulse generators and implantable cardioverter defibrillators should generally be explanted.

Chronic lead removal and the SureScan pacing system – When implanting a SureScan pacing system, consider the risks associated with removing previously implanted leads before doing so. Abandoned leads or previously implanted non-SureScan labeled leads compromise the ability to safely scan the SureScan pacing system during MRI scans.

Chronic repositioning or removal of a screw-in lead – Proceed with extreme caution if a lead must be removed or repositioned. Chronic repositioning or removal of screw-in transvenous leads may not be possible because of blood or fibrotic tissue development into the helix mechanism on the lead. In most clinical situations, it is preferable to abandon unused leads in place. Return all removed leads, unused leads, or lead sections to Medtronic for analysis.

Note: If a helix electrode does not disengage from the endocardium by rotating the connector pin, rotating the lead body counterclockwise may withdraw the helix electrode and decrease the possibility of damage to cardiovascular structures during removal.

- Lead removal may result in avulsion of the endocardium, valve, or vein.
- Lead junctions may separate, leaving the lead tip and bare wire in the heart or vein.
- Chronic repositioning of a lead may adversely affect the low-threshold performance of a steroid lead.
- An abandoned lead should be capped so that the lead does not transmit electrical signals.
- Severed leads should have the remaining lead end sealed and the lead body sutured to adjacent tissue.

5 Potential adverse events

The potential complications (listed in alphabetical order) related to the use of transvenous leads include, but are not limited to, the following patient-related conditions that can occur when the lead is being inserted or repositioned:

- cardiac perforation
- cardiac tamponade
- fibrillation and other arrhythmias
- heart wall rupture
- infection
- muscle or nerve stimulation
- myocardial irritability
- pericardial rub
- pericarditis
- pneumothorax
- thrombotic and air embolism
- thrombosis
- valve damage (particularly in fragile hearts)

Other potential complications related to the screw-in lead and the programmed parameters include, but are not limited to, the complications listed in the following table. Symptoms of the following potential complications include loss of capture or intermittent or continuous loss of capture or sensing:[2]

Complication	Corrective action to be considered
Lead dislodgement	Reposition the lead.
Lead conductor or helix electrode fracture or insulation failure	Replace the lead. In some cases with a bipolar lead, the implantable device may be programmed to a unipolar configuration or the lead may be unipolarized.
Threshold elevation or exit block[a]	Adjust the implantable device output. Replace or reposition the lead.

[a] Evidence indicates that there is a higher frequency of exit block in the ventricle when using a screw-in lead. This should be considered when selecting a screw-in lead for use in the ventricle.

Potential acute or chronic complications associated with screw-in lead placement that may require lead replacement to correct include, but are not limited to, the following:

Implant technique	Potential complication
Forcing the lead through the introducer	Screw electrode damage, insulation damage
Use of too medial of an approach with venous introducer resulting in clavicle and first rib binding	Conductor coil fracture, insulation damage, helix engagement issues
Puncturing the periosteum and/or tendon when using subclavian introducer approach	Conductor coil fracture, insulation damage
Advancing the lead into the venous insertion site and/or through the veins without the stylet fully inserted	Tip distortion, insulation perforation
Bending the lead or manually pinching the lead body during extension or retraction of the helix electrode	Delayed torque transfer

In addition, prolonged implant procedures or repositioning the lead multiple times may allow blood or body fluids to build up on the helix mechanism. This may result in an increased number of rotations needed to extend or retract the helix electrode, which may damage the lead.

[2] Transient loss of capture or sensing may occur for a short time following implant until lead stabilization takes place. If stabilization does not occur, lead dislodgement may be suspected.

6 Implant procedure

Warning: When implanting a SureScan pacing system, consider the risks associated with removing previously implanted leads before doing so. Abandoned leads or previously implanted non-SureScan labeled leads compromise the ability to safely scan the SureScan pacing system during MRI scans.

Proper surgical procedures and sterile techniques are the responsibility of the medical professional. Some implant techniques vary according to physician preference and the patient's anatomy or physical condition.

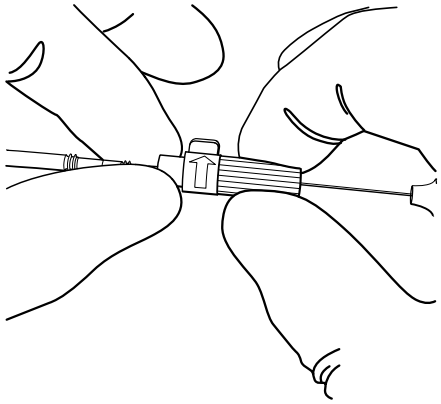
6.1 Verifying the mechanical functioning of the helix electrode

Note: The package includes 2 tools, the Quick Twist tool attached to the lead and the white fixation tool. Either tool may be used to verify the mechanical functioning of the helix electrode. The choice of tool is left to the discretion of the physician.

Before implant, verify the mechanical functioning of the helix electrode using the following steps:

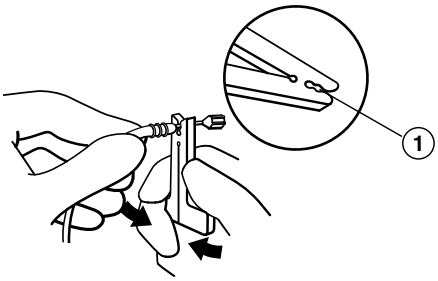
1. Attach either the Quick Twist tool or the white fixation tool to the lead. Ensure that the stylet is inserted into the lead and proceed as indicated, according to the tool being used.
   a. **Quick Twist tool:** Push the Quick Twist tool onto the connector pin (Figure 1).

Figure 1.



   b. **White fixation tool:** Press both legs of the white fixation tool together and place the most distal hole on the connector pin (Figure 2).

Figure 2.



1 The most distal hole of the white fixation tool.

2. Keep the lead body and the IS-1 connector sleeve as straight as possible (Figure 2). Ensure that the stylet is fully inserted, then rotate the selected fixation tool clockwise until the helix electrode is fully extended (Figure 3 or Figure 4). When the helix electrode is fully extended, approximately 1.5 to 2 helix coils are exposed.

Figure 3.

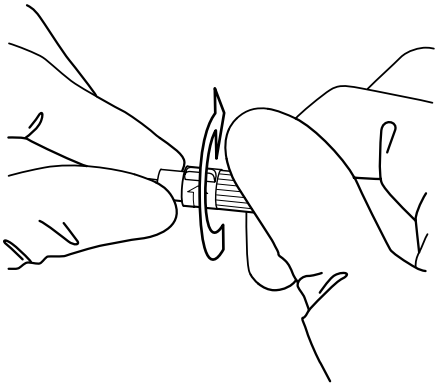
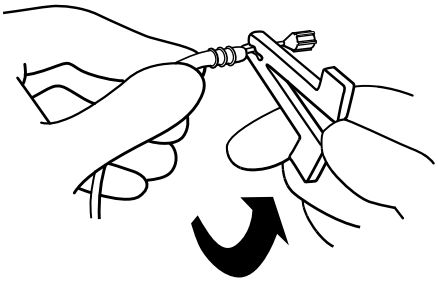


Figure 4.



Caution: Do not severely bend the IS–1 connector sleeve or the lead body while extending the helix electrode.
Caution: Overrotating the connector pin after the helix electrode is fully extended may damage the lead.

The number of rotations required to extend the helix electrode increases proportionately with the length of the lead. Additional curvatures made to the stylet may increase the number of rotations needed to extend or retract the helix electrode. Refer to Table 3, page 12 for the estimated number of rotations required to extend or retract the helix electrode.
Note: The number of rotations required to extend the helix electrode is variable depending on the lead path.
During the initial helix electrode extension, the helix electrode may extend suddenly due to accumulated torque in the lead, or the helix electrode may require additional rotations for extension.

3. Disconnect the selected fixation tool from the connector pin and release the proximal end of the lead body. Allow several seconds for relief of the residual torque in the lead.
4. After allowing for relief of the residual torque, reattach the selected fixation tool and rotate it counterclockwise until the helix electrode tip is retracted into the sheath.

6.2 Inserting the lead

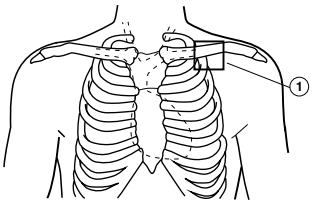
Caution: Use care when handling the lead during insertion.

- Do not severely bend, kink, or stretch the lead.
- Do not use surgical instruments to grasp the lead or connector pins.

Insert the lead using the following techniques:

1. Select a site for lead insertion. The lead may be inserted by venotomy through several different venous routes, including the right or left cephalic vein or the external or internal jugular vein. Use the cephalic vein whenever possible to avoid lead damage in the first rib or clavicular (thoracic inlet) space.
   Cautions:
   - Certain anatomical abnormalities, such as thoracic outlet syndrome, may also precipitate pinching and subsequent fracture of the lead.
   - When using a subclavian approach, avoid techniques that may damage the lead.
   - Place the insertion site as far lateral as possible to avoid clamping the lead body between the clavicle and the first rib (Figure 5).

Figure 5.



1 Suggested entry site

   - Do not force the lead if significant resistance is encountered during lead passage.
   - Do not use techniques such as adjusting the patient's posture to facilitate lead passage. If resistance is encountered, it is recommended that an alternate venous entry site be used.
2. Insert the tapered end of a vein lifter into the incised vein and gently push the lead tip underneath and into the vein (Figure 6).
   Note: A percutaneous lead introducer (PLI) kit may be used to facilitate insertion. If a slittable introducer is used, it should be at least 2.6 mm (8 French). Refer to the technical manual packaged with an appropriate percutaneous lead introducer for further instructions.

Figure 6.

3. Advance the lead into the right atrium using a straight stylet to facilitate movement through the veins.

6.3 Positioning a screw-in ventricular lead

Caution: Use care when handling the lead during positioning:

- Do not severely bend, kink, or stretch the lead.
- Do not use surgical instruments to grasp the lead or connector pin.

1. Insert the tapered end of a vein lifter into the incised vein and gently push the lead tip underneath and into the vein. A vein lifter facilitates lead insertion.
2. Advance the lead into the right atrium using a straight stylet to facilitate movement through the veins.
3. Advance the lead through the tricuspid valve. Replacing the straight stylet with a gently curved stylet may add control in maneuvering the lead through the tricuspid valve. Then, advance the lead directly through the tricuspid valve, or project the lead tip against the lateral atrial wall and retract the curved portion of the lead body through the tricuspid valve until the lead tip enters the ventricle.
4. Position the lead in the ventricle using the following techniques. Accurate positioning of the helix electrode is essential for stable pacing.
   Caution: If there is reason to believe the patient has an unusually thin wall at the apex of the right ventricle, you may want to consider another site for placement of the lead.
   Caution: If placing the lead in or near the right ventricular apex, use caution if passing the distal end of the lead directly from the valve to the apex. This technique may result in excessive tip pressure.
   Caution: If an awake patient feels a twinge of pain, this may be an early sign of perforation.

Using one of the following techniques may help minimize transmission of pressure directly toward the tip of the lead:

- Partially withdraw the stylet so that the stylet tip is proximal to the electrode ring while positioning the lead, to minimize tip stiffness. The stylet can then be gently advanced to the tip of the lead before securing the electrode in the endocardium.
- A curved stylet may be used during positioning to minimize direct pressure on the apex.
- Using a curved stylet, or partially withdrawing the stylet to allow the lead to be carried by blood flow, the lead may be curved up toward the outflow tract and then allowed to fall gently into position near the apex by pulling back on the lead body.

Use fluoroscopy (lateral position) to ensure that the tip is not in a retrograde position or is not lodged in the coronary sinus.

5. After placing the lead in a satisfactory position, extend the helix electrode by following the procedure in Section 6.5, “Securing the helix electrode into the endocardium”, page 8.

6.4 Positioning a screw-in atrial lead

Caution: Use care when handling the lead during positioning:

- Do not severely bend, kink, or stretch the lead.
- Do not use surgical instruments to grasp the lead or connector pin.

The following procedure is suggested for atrial placement of the lead:

1. Insert the tapered end of a vein lifter into the incised vein and gently push the lead tip underneath and into the vein. A vein lifter facilitates lead insertion.
2. Advance the lead into the right atrium using a straight stylet to facilitate movement through the veins. After the lead tip is passed into the atrium, replace the straight stylet with a gently curved stylet or one of the J-shaped stylets supplied with the lead.
3. Direct the lead tip into an appropriate position. Accurate positioning of the helix electrode is essential for stable pacing and sensing.
   Generally, a satisfactory position has the lead tip situated against the atrial endocardium in or near the apex of the appendage. As viewed on the fluoroscope (A-P view), the lead tip points medially and forward toward the left atrium. A successful position is usually achieved with an anterior, medial, or lateral tip location.

Caution: If an awake patient feels a twinge of pain, this may be an early sign of perforation.

After placing the lead tip in a satisfactory position, extend the helix electrode by following the procedure in Section 6.5, “Securing the helix electrode into the endocardium”, page 8.

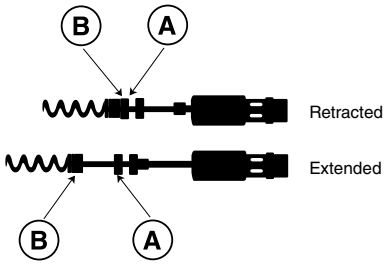
6.5 Securing the helix electrode into the endocardium

Note: The package includes 2 tools, the Quick Twist tool attached to the lead and the white fixation tool. Either tool may be used to secure the helix electrode into the endocardium. The choice of tool is left to the discretion of the physician.

Secure the helix electrode using the following techniques:

1. Attach either the Quick Twist tool or the white fixation tool to the lead. Ensure that the stylet is inserted into the lead and proceed as indicated, according to the tool being used.
   a. **Quick Twist tool:** Push the Quick Twist tool onto the connector pin (Figure 1, page 6).
   b. **White fixation tool:** Press both legs of the white fixation tool together and place the most distal hole on the connector pin (Figure 2, page 6).
2. Press the lead tip against the endocardium using the appropriate technique:
   a. **Ventricular placement:** Press the lead tip against the endocardium by gently pushing the stylet and lead at the vein entry site.
   b. **Atrial placement:** With the lead tip advanced into the atrium and a J-shaped or gently curved stylet in the lead, press the lead tip against the endocardium by gently pulling the stylet and the lead at the vein entry site.
3. Rotate the selected fixation tool clockwise until the helix electrode is fully extended.
   Caution: Do not severely bend the IS-1 connector sleeve or the lead body while extending the helix electrode.
4. Use fluoroscopy to verify helix electrode extension. This is the only reliable method to confirm extension. Extension of the space between the indicator ring (A) and the drive mechanism (B) implies complete exposure of the helix electrode (Figure 7). The top view illustrates no gap between the indicator ring and the drive mechanism (retracted) and the bottom view illustrates a gap (extended).
   Cautions:
   - The estimated number of rotations required to fully extend or retract the helix electrode is variable. Refer to Table 3, page 12, for the estimated number of rotations.
   - Prolonged implant procedures or repositioning the lead multiple times may allow blood or body fluids to build up on the helix mechanism. This may result in an increased number of rotations required to extend or retract the helix electrode, which may damage the lead.

Figure 7.



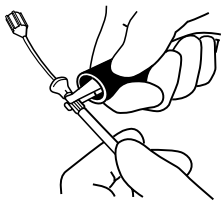
5. Remove the selected fixation tool from the IS-1 connector pin and release the proximal end of the lead body. Allow several seconds for relief of the residual torque in the lead.
6. Partially withdraw the stylet.
7. Verify that the lead is affixed.
   a. **For a lead placed in the ventricle:** Gently pull back on the lead and check for resistance to verify affixation. A properly affixed helix electrode will remain in position. If the helix electrode is not properly affixed, the lead tip may become loose in the right ventricle.
   b. **For a lead placed in the atrial appendage:** After the lead tip is fixed, allow lead slack to build up in the atrium. Lead slack helps prevent tip dislodgement. Enough slack is assumed present if, under fluoroscopy, the lead assumes an "L" shape during deep inspiration. Avoid excessive slack buildup that may cause the loop of the lead to drop near the tricuspid valve.
8. If repositioning is required, reattach the selected fixation tool and rotate counterclockwise until the helix electrode is retracted. Use fluoroscopy to verify withdrawal of the helix electrode before attempting to reposition (Figure 7).
   Caution: Do not rotate the selected fixation tool more than the number of rotations required to fully retract the helix electrode.
9. After final positioning, remove the stylet and the Quick Twist tool completely. When removing the Quick Twist tool, grip the lead firmly just below the connector pin to help prevent lead dislodgement.
10. Obtain final electrical measurements.

6.6 Taking electrical measurements

Take electrical measurements:

1. Attach the clip of a surgical cable to the notch on the stylet guide (Figure 8).

Figure 8.



   Note: A unipolar lead requires the use of an indifferent electrode.
2. Use an implant support instrument to obtain electrical measurements. Medtronic recommends using a pacing system analyzer. For information on the use of the implant support instrument, see the product literature for that device. Satisfactory lead placement is indicated by low stimulation thresholds and adequate sensing of intracardiac signal amplitudes. Refer to Table 1 for recommended stimulation threshold and sensing amplitude measurements at implant.
   - A low stimulation threshold provides for a desirable safety margin, allowing for a possible rise in thresholds that may occur within 2 months following implant.
   - Adequate sensing amplitudes ensure that the lead is properly sensing intrinsic cardiac signals. Minimum signal requirements depend on the device's sensitivity capabilities. Acceptable acute signal amplitudes for the lead must be greater than the minimum device sensing capabilities, including an adequate safety margin to account for lead maturity.

Table 1. Recommended measurements at implant

	Ventricle	Atrium
Recommended maximum acute stimulation thresholds[a]	1.0 V 3.0 mA	1.5 V 4.5 mA
Minimum acute sensing amplitudes	5.0 mV	2.0 mV

[a] At pulse duration setting of 0.5 ms.

3. If electrical measurements do not stabilize to acceptable levels, repositioning the lead and repeating the testing procedure may be necessary.
   Note: Initial electrical measurements may deviate from the recommendations because of acute cellular trauma. If such a deviation occurs, wait 5 to 15 min and repeat the testing procedure. Values may vary depending upon lead type, device settings, cardiac tissue condition, and drug interactions.

6.6.1 Checking diaphragmatic stimulation for screw-in leads

Diaphragmatic stimulation should also be checked by pacing at 10 V and observing on fluoroscopy whether the diaphragm contracts with each paced stimulus. If diaphragmatic stimulation occurs, reposition the lead.

6.6.2 Taking pacing impedance (or resistance) measurements

Pacing impedance (or resistance) is used to assess device function and lead integrity during routine device patient follow-up sessions and to assist in troubleshooting suspected lead failures. Additional troubleshooting procedures include ECG analysis, visual inspection, measurement of thresholds, and electrogram characteristics.

Pacing impedance values are affected by many factors including lead position, electrode size, conductor design and integrity, insulation integrity, and the patient's electrolyte balance. Apparent pacing impedance is also significantly affected by the measurement technique. Comparison of pacing impedance should be done using consistent methods of measurements and equipment.

An impedance higher or lower than the typical values is not necessarily a conclusive indication of a lead failure. Other causes must be considered as well. Before reaching a conclusive diagnosis, the full clinical picture must be considered. The full clinical picture includes pacing artifact size and morphology changes in 12-lead analog ECGs, muscle stimulation with bipolar leads, sensing and/or capture problems, patient symptoms, and device characteristics.

Recommendations for clinically monitoring and evaluating leads in terms of impedance characteristics are listed below.

Consider the following recommendations for devices with telemetry readout of impedance:

- Routinely monitor and record impedance values at implant and follow-up sessions using consistent output settings. **Note:** Impedance values may be different at different programmable output settings (for example, pulse width or pulse amplitude) of the device or pacing system analyzer.
- Establish a baseline chronic impedance value once the impedance has stabilized, generally within 6 to 12 months after implant.
- Monitor for significant impedance changes and abnormal values.
- Where impedance abnormalities occur, closely monitor the patient for indications of pacing and sensing problems. The output settings used for measuring impedance should be the same as those used for the original measurements.
- For patients at high risk, such as implantable device-dependent patients, you may want to consider further action such as increased frequency of monitoring, provocative maneuvers, and ambulatory ECG monitoring.

Consider the following recommendations for devices without telemetry:

- Record the impedance value at implant. Also record the measurement device, its output settings, and the procedure used.
- At the time of device replacement, if pacing system analyzer-measured impedance is abnormal, carefully evaluate lead integrity (including thresholds and physical appearance) and patient condition before electing to reuse the lead.
- Impedances below 250 Ω may result in excessive battery current drain, which may seriously compromise device longevity, regardless of lead integrity.

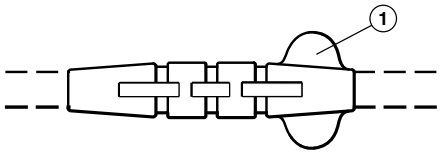
For more information on obtaining electrical measurements, consult the product literature supplied with the testing device.

6.7 Anchoring the lead

Cautions:

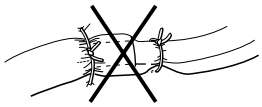
- Use care when anchoring the lead.
- Use an anchoring sleeve with all leads.
- Do not use absorbable sutures to anchor the lead.
- Do not secure the sutures so tightly that they damage the vein, lead, or anchoring sleeve.
- Do not use the anchoring sleeve tabs for suturing (Figure 9).
- Do not tie a suture directly to the lead body (Figure 10).
- Do not dislodge the lead tip.
- Do not attempt to remove or cut the anchoring sleeve.
- Do not remove the tabs on anchoring sleeves. Tabs are provided to minimize the possibility of the sleeve entering the vein.
- If a large diameter percutaneous lead introducer (PLI) sheath is used, take extreme care to prevent passage of the anchoring sleeve into the PLI lumen or the venous system.

Figure 9.



1 Anchoring sleeve tab

Figure 10.



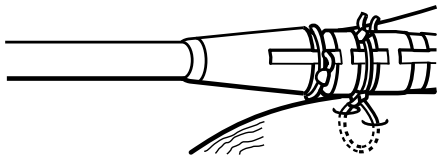
With a triple groove anchoring sleeve, generally 2 or 3 of the grooves may be used with the following procedure.

Note: The anchoring sleeves contain a radiopaque substance, which allows visualization of the anchoring sleeve on a standard x-ray and may aid in follow-up examinations.

Anchor the lead:

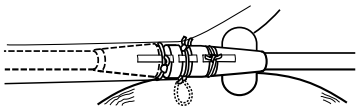
1. Position the anchoring sleeve close to the lead's connector pin to prevent inadvertent passage of the sleeve into the vein.
2. Insert the anchoring sleeve partially into the vein.
3. Use the most distal suture groove to secure the anchoring sleeve to the vein.
4. Use the middle groove to secure the anchoring sleeve to the fascia and lead (Figure 11):
   a. Create a base by looping a suture through the fascia underneath the middle groove and tying a knot.
   b. Firmly wrap the suture around the middle groove and tie a second knot.

Figure 11.



5. If anchoring with all 3 grooves, use the third and most proximal groove to secure the anchoring sleeve to the lead body (Figure 12).

Figure 12.



6.8 Connecting the lead

Caution: Always remove the stylet and stylet guide before connecting the lead to the device. Failure to remove the stylet and stylet guide may result in lead failure.

Connect the lead to the device according to the instructions in the product literature supplied with the device.

Connect the lead to the device:

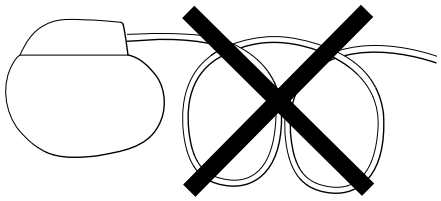
1. Carefully and completely remove the stylet and stylet guide. **Note:** When removing the stylet and stylet guide, firmly grip the lead just below the connector pin to help prevent possible lead dislodgement.
2. Obtain final electrical measurements.
3. Insert the lead connector into the connector block on the device. For instructions on proper lead connections, see the product literature supplied with the device.

6.9 Placing the device and lead into the pocket

Cautions:

- Use care when placing the device and lead into the pocket.
- Ensure that the lead does not leave the device at an acute angle.
- Do not grip the lead or device with surgical instruments.
- Do not coil the lead (Figure 13). Coiling the lead can twist the lead body and may result in lead dislodgement.

Figure 13.

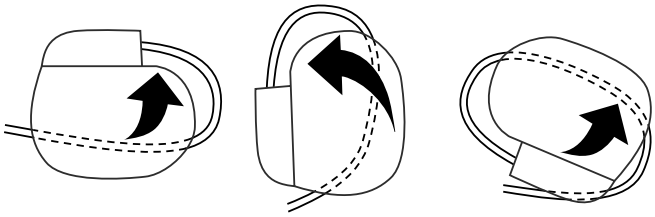


Caution: To prevent undesirable twisting of the lead body, wrap the excess lead length loosely under the device and place both the device and the lead into the subcutaneous pocket.

Place the device and lead into the pocket:

1. Rotate the device to loosely wrap the excess lead length under the device (Figure 14).

Figure 14.



2. Insert the device and lead into the pocket.
3. Suture the pocket closed.
4. Monitor the patient's electrocardiogram until the patient is discharged. If a lead dislodges, it usually occurs during the immediate postoperative period.

7 Specifications (nominal)

Table 2. Specifications (nominal)

Parameter		Model 5086MRI
Type		Bipolar
Chamber		Atrium/Ventricle
Fixation		Screw-in
Lengths		45, 52, 58 cm
Connector		IS-1 BI
Materials	Conductor:	MP35N nickel alloy
	Insulation:	Treated silicone rubber
	Connector pin:	Stainless steel
	Connector ring:	Stainless steel
Electrode materials	Helix electrode:	Titanium nitride coated platinum alloy
	Ring electrode:	Titanium nitride coated platinum alloy
Electrode surface area	Helix:	4.2 mm^2
	Ring:	22 mm^2
Tip to ring spacing		10 mm
Diameter	Lead body:	2.3 mm
Lead introducer (recommended size)		
	without guide wire:	2.7 mm (8 French)
	with guide wire:	3.7 mm (11 French)

Table 2. Specifications (nominal) (continued)

Parameter		Model 5086MRI
Helix length (fully extended)		1.8 mm
Resistance	Unipolar:	70.0 Ω (58 cm)
	Bipolar:	105.0 Ω (58 cm)
Steroid	Type:	Dexamethasone acetate
Nominal dosage of steroid		692 µg
Steroid binder		Silicone

Table 3. Estimated number of rotations required to extend or retract the helix electrode for initial placement[a]

Lead length	Straight stylet	J-shaped stylet
45 cm	12	18
52 cm	13	20
58 cm	14	21

[a] The number of rotations required to extend the helix electrode is variable depending on the lead path.

8 Medtronic disclaimer of warranty

For complete disclaimer of warranty information, see the accompanying disclaimer of warranty document.

9 Service

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World Headquarters
Medtronic, Inc.
710 Medtronic Parkway
Minneapolis, MN 55432-5604
USA
Internet: www.medtronic.com
Tel. +1-763-514-4000
Fax +1-763-514-4879

Medtronic USA, Inc.
Toll-free in the USA (24-hour technical consultation for physicians and medical professionals)
Bradycardia: 1-800-505-4636
Tachycardia: 1-800-723-4636

Europe/Africa/Middle East Headquarters
Medtronic International Trading Sàrl
Route du Molliau 31
Case Postale 84
CH-1131 Tolochenaz
Switzerland
Internet: www.medtronic.com
Tel. +41-21-802-7000
Fax +41-21-802-7900

Medtronic E.C. Authorized Representative/Distributed by
Medtronic B.V.
Earl Bakkenstraat 10
6422 PJ Heerlen
The Netherlands
Tel. +31-45-566-8000
Fax +31-45-566-8668

Technical manuals:
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Appendix 8 -
Proposed SS&ED

Appendix 8 - Proposed Summary of Safety and Effectiveness Data (SS&ED)

This section includes the proposed SS&ED for the Revo™ MRI SureScan™ Pacing System.

Slipsheet

Pages 295 through 341 redacted for the following reasons:
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