

SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Implantable Pacemaker System

System Trade Name: Revo MRI™ SureScan™ Pacing System

Applicant's Name and Address: Medtronic, Inc.
Cardiac Rhythm Disease Management
8200 Coral Sea Street
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Date of Panel Recommendation: March 19, 2010

Premarket Approval Application (PMA) Number: P090013

Date of FDA notice of approval: February 8, 2011

Expedited: Granted expedited review status on August 28, 2008 because: 1) pacemakers deliver therapy to treat a condition that is life threatening or irreversibly debilitating, 2) The Revo MRI SureScan Pacing System may offer patients a clinically meaningful advantage by allowing patients to undergo MRI procedures under certain conditions, and, 3) no legally marketed MR Conditional pacemaker is available.

II. INDICATIONS FOR USE

A. RevoMRI™ SureScan™ Model RVDR01 IPG

The Medtronic RevoMRI™ SureScan™ Model RVDR01 IPG is indicated for use as a system consisting of a Revo MRI SureScan IPG implanted with two CapSure Fix MRI™ SureScan™ 5086MRI leads. A complete system is required for use in the MRI environment.

The Medtronic RevoMRI™ SureScan™ Model RVDR01 IPG 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-degree 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 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.

B. CapSureFix MRI™ SureScan™ 5086MRI Lead

The Medtronic CapSureFix™ MRI™ SureScan™ 5086MRI lead is indicated for use as a system consisting of a Medtronic RevoMRI™ SureScan™ Model RVDR01 IPG implanted with two SureScan leads. A complete system is required for use in the MRI environment. This lead has application where implantable dual chamber MR Conditional pacing systems are indicated.

III. CONTRAINDICATIONS

Revo MRI IPG RVDR01 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.

5086MRI Lead 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.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Revo MRI SureScan Pacing System labeling.

V. MR Conditions of Use

A complete SureScan pacing system including a Revo MRI SureScan IPG and two SureScan leads is required for use in the MRI environment. Any other combination may result in a hazard to the patient during an MRI scan. The SureScan feature must be programmed to “On” prior to scanning a patient according to the specified conditions for use.

Cardiology requirements:

- 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 as confirmed by lead impedance history
 - 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 volts (V) at a pulse width of 0.4 milliseconds (ms)
 - a lead impedance value of ≥ 200 ohms (Ω) and $\leq 1500 \Omega$
 - 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.

Radiology requirements:

- Horizontal 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 Tesla per meter per second (T/m/s) must be used.
- The scanner must be operated in Normal Operating Mode:
 - The whole body averaged specific absorption rate (SAR) must be ≤ 2.0 watts per kilogram (W/kg).
 - The head SAR must be < 3.2 W/kg.

- 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.
- Proper patient monitoring must be provided during the MRI scan. The methods include visual and verbal contact with the patient, electrocardiography, and pulse oximetry (plethysmography).

Training requirements:

- A health professional who has completed cardiology SureScan training must be present during the programming of the SureScan feature.
- A health professional who has completed radiology SureScan training must be present during the MRI scan.

VI. DEVICE DESCRIPTION

A. System Description

The Revo MRI™ SureScan™ Pacing System consists of the Medtronic Revo MRI Model RVDR01 Implantable Pulse Generator (IPG), Model SW018 Application Software, and the Model 5086MRI lead. The Revo MRI System is MR Conditional and, as such, is designed to allow implanted patients the ability to undergo MRI exams under the specified MR Conditions of Use. In order to ensure pacemaker patient safety in an MRI environment, a complete system consisting of an active implantable pulse generator and both an atrial and a ventricular pace/sense lead are required.

B. Revo MRI™ SureScan™ Pacemaker Model RVDR01

The Medtronic Revo MRI SureScan RVDR01 IPG is a multi-programmable, bipolar implantable dual chamber pacemaker that monitors, detects, and treats atrial tachyarrhythmia episodes. It also provides bradycardia pacing and monitoring of ventricular tachycardia (VT) episodes. The device senses the electrical activity of the patient's heart using the sensing electrodes of the implanted leads. It then analyzes the heart rhythm based on selectable sensing and detection parameters. If the device detects an atrial tachyarrhythmia, it delivers programmed atrial ATP therapy to the patient's heart. If the device identifies a bradyarrhythmia, it delivers bradycardia pacing therapy to the patient's heart.

If an MRI scan is required for a patient, the MRI SureScan feature allows the patient to be safely scanned while the device continues to provide appropriate pacing. When programmed "ON," MRI SureScan feature operation disables arrhythmia detection, magnet mode, and all user-defined diagnostics.

C. Revo MRI™ Application Software Model SW018

The Medtronic Revo MRI Model RVDR01 utilizes application software Model SW018. The Medtronic programmer and Revo MRI SureScan application software allow you to perform the following tasks:

- Configure the detection, therapy, and bradycardia features for your patient
- Perform electrophysiological studies and system tests

- Monitor, display, or print patient cardiac activity information
- View patient and device diagnostic data
- Program the device into MRI SureScan mode

The Revo MRI SureScan device and application software are compatible with the Medtronic CareLink Model 2090 Programmer with a Model 2067 or 2067L programming head.

D. CapSureFix MRI™ SureScan™ Model 5086MRI Lead

The Medtronic CapSureFix MRI Model 5086MRI lead is based upon the commercially available Medtronic Lead Models 5076 (P930039/S009) and 4076 (P930039/S017). It is designed to be used within the MRI environment when used in combination with the Revo MRI IPG. The CapSureFix MRI 5086MRI is a bipolar, silicone, steroid eluting, screw-in extendible/retractable pacing lead. The steroid is dexamethasone acetate and is identical to the steroid used in lead models 5076 and 4076. The nominal amount of steroid on the lead is 692 µg. The lead body features a radiopaque anchoring sleeve for suturing down the lead. The lead Model 5086MRI is designed for use in either the right atrium or the ventricle. As with the Model 5076 and Model 4076 leads, the lead Model 5086MRI has application where implantable atrial or ventricular, single or dual-chamber pacing systems are indicated.

E. Overview of Features

Functionally, the Revo MRI SureScan pacing system is comparable to the commercially available EnRhythm pacing system. The Revo MRI SureScan pacing system contains the following features and therapies:

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.

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.

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.

Additional operations

MRI SureScan feature – This feature allows patients with an implanted SureScan pacing system to have a safe MRI scan. When programmed “ON,” MRI SureScan feature operation disables arrhythmia detection, magnet mode, and all user-defined diagnostics.

Other Features

By means of the commercially available Model 2696 InCheck Patient Assistant, the patient can use the Model 2696 InCheck AT 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.

VII. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for rate adaptive pacing and chronic cardiac pacing. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

While other pacemaker systems are commercially available, at this time of approval of the Revo MRI™ SureScan™ Pacing System, there are no other MR Conditional pacing systems commercially available in the US. The Revo MRI SureScan pacing system is an MR Conditional system and, as such, enables pacemaker patients implanted with this system to undergo MRI scans under specified conditions.

VIII. MARKETING HISTORY

Marketing approval in Europe (CE Mark) for the EnRhythm MRI system was obtained in September 2008. 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). The system has not been withdrawn from the market in any country for any reason related to the safety or effectiveness of the device.

IX. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below are lists of the potential adverse events (e.g., complications) that may occur with the use of pacing systems and transvenous leads as well as those potential adverse events that may occur when typical pacemaker systems are used in the MRI environment. These adverse events are listed in alphabetical order and include, but are not limited to the following.

A. Potential Adverse Events with Pacemaker Systems and Transvenous Leads

- Acceleration of tachyarrhythmias (caused by device)
- Bleeding
- Cardiac dissection
- Cardiac tamponade
- Death
- Erosion
- Excessive fibrotic tissue growth
- Fibrillation or other arrhythmias
- Formation of hematomas or cysts
- Heart wall or vein wall rupture
- Infection
- Lead abrasion and discontinuity
- Muscle stimulation, nerve stimulation, or both
- Myocardial irritability
- Pericardial effusion
- Pneumothorax
- Threshold elevation
- Thrombolytic and air embolism
- Transvenous lead-related thrombosis
- Venous occlusion
- Air embolism
- Body rejection phenomena including local tissue reaction
- Cardiac perforation
- Chronic nerve damage
- Endocarditis
- Erosion through the skin
- Extrusion
- Fluid accumulation
- Heart block
- Hematoma/seroma
- Keloid formation
- Lead migration/dislodgment
- Myocardial damage
- Myopotential sensing
- Pericardial rub
- Rejection phenomena (local tissue reaction, fibrotic tissue formation, device migration)
- Thromboemboli
- Thrombosis
- Valve damage (particularly in fragile hearts)
- Venous or cardiac perforation

B. Pacemaker systems in the MRI Environment

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

- 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 resulting in dislodgement
- Competitive pacing and potential for VT/VF induction due to ambulatory asynchronous pacing in MRI SureScan mode

For the specific adverse events that occurred in the clinical study, please see Section X below.

X. SUMMARY OF PRECLINICAL STUDIES

Extensive preclinical MRI testing was necessary in order to characterize the potential patient hazards at environmental conditions (e.g., radiofrequency fields, gradient fields, and MRI exposure durations) beyond those that can be obtained using currently available MRI scanners. In addition, the pre-clinical testing assessed the safety and effectiveness for a wide range of system implant and patient anatomy configurations, at the limit and beyond limits usually encountered in clinical practice.

Preclinical 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.

A. MRI Environment Testing

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. 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).

MRI-Induced Lead Heating

MRI-Induced Lead Heating	
Field interaction	Radiofrequency
Mechanism and source of hazard	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.
Clinical impact	Tissue heating near the tip electrode may result in thermal damage to the tissue, changes in pacing capture threshold, and, in extreme cases, loss of pacing therapy.
Evaluation method	Medtronic CRDM used pacing capture threshold to evaluate the patient risks associated with RF-induced lead heating. Medtronic CRDM developed a 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, and CapSureFix MRI 5086MRI leads. The simulations of the RF body coils and human body models were performed using a widely-used 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: 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 canine study.
Results & Conclusions	The Revo MRI SureScan pacing system modeling and in vivo evaluation indicate that the probability of a clinically significant change in pacing capture threshold is low. The testing and modeling support the safety and effectiveness of the Revo MRI SureScan pacing system in relation to the lead heating hazard.

MRI-Induced Unintended Cardiac Stimulation (UCS)

MRI-Induced Unintended Cardiac Stimulation		
Field interaction	Gradient and radiofrequency	
Mechanism and source of hazard	Gradient: The time-varying gradient magnetic fields will induce a time-varying voltage along the pacing leads.	Radiofrequency: The pacemaker circuitry connected to pacing leads may rectify the radiofrequency pulses.
Clinical impact	If the MRI-induced voltage pulses are large enough, they may directly stimulate the heart.	
Evaluation method	Gradient: 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.	Radiofrequency: The minimum stimulation threshold for rectified pulses was determined in a canine study and compared to worst-case induced pulses.
Results & Conclusions	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 appears to be low and has been mitigated to an acceptable level.	

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.

MRI-Induced Device Interactions	
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 (which included vibration testing, bench testing, and clinical scanner testing) at worst-case exposure settings and positions.
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 & Conclusions	The Revo MRI SureScan Pacemaker in vitro evaluation confirmed that the system meets the requirements for the device interactions hazard. Analysis and testing indicates 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.

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.
Evaluation method	Case heating was evaluated in vitro at the worst-case conditions for RF and gradient magnetic field exposure allowed by the MR Conditions of Use specified in the labeling.
Results & Conclusions	The testing confirmed that at worst-case test conditions, there is minimal heating of the pacemaker case.

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.
Evaluation method	Force and torque were measured at worst-case conditions for: • pacemakers alone, • pacemakers with leads attached, • leads alone.

MRI-Induced Force and Torque		
	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."	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".
Results & Conclusions	The in vitro testing demonstrated that there is minimal MRI-induced force and torque on the device. This testing supports the safety of the Revo MRI SureScan Pacemaker and CapSureFix MRI 5086MRI leads with regard to MRI-induced force and torque hazards.	

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.
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 worst-case conditions for static and gradient magnetic field exposure allowed by the MR Conditions of Use specified in the labeling Vibration testing was conducted at vibration stress levels above what a device would reasonably be exposed to during its lifetime.
Results & Conclusions	The in vitro evaluation showed no missing pacing pulses during the testing, as well as proper operation following testing. No device resets or battery replacement indications were observed. These results support the safety and effectiveness of the Revo MRI SureScan Pacing System with regard to MRI-induced vibration.

Effects of Multiple Scans

Medtronic CRDM conducted a canine study to evaluate the effect of multiple MRI scans on change in pacing capture threshold. The leads were exposed to RF energy every two (2) weeks (five (5) RF exposures per lead). RF power was applied at two levels intended to represent clinically reasonable worst case and beyond clinically reasonable worst case conditions.

At the lower power level, there was no observable effect on capture thresholds due to the first or the subsequent RF exposures. At the higher power level (higher power than what is expected to occur clinically), average capture thresholds increased following the first RF exposure, but without any additional changes following the subsequent RF exposures. Overall, no cumulative effect due to multiple RF exposures was observed.

In addition, fourteen (14) clinical study patients, and one emergency use patient received multiple MRI scans, as shown below:

Total MRI Scans	Number of Patients
2	10
3	2
4	2
7	1

In all of the above cases, no pacing capture threshold increases greater than 0.5 V were observed, and no MRI-related complications were reported.

B. Standard Testing (outside of the MRI Environment)

Revo MRI IPG RVDR01 Testing

Biocompatibility

The materials used in the Revo MRI IPG that are directly exposed to body tissue and/or fluids are titanium, polyurethane, silicone adhesive, and silicone rubber. These materials have all been used in Medtronic IPGs (P980035/S038) for several years and have been previously tested and approved for their biocompatibility. No new materials or processes were introduced with the Revo MRI IPG that would introduce new issues of biocompatibility.

Package Testing

The shelf box, label stock adhesive, and sterile package used for the Revo MRI IPG have been used in other commercially available Medtronic IPGs. The package qualification per ASTM D4169 passed, demonstrating that the model meets standard performance requirements.

Sterilization Qualification

The Revo MRI IPG uses a 100% ethylene oxide (EtO) sterilization process. The 100% EtO sterilization process used to sterilize Revo MRI IPG Model RVDR01 is the same

process that was previously reviewed and approved by the FDA for the commercially available EnRhythm IPG (P980035/S038). This process is considered an overkill sterilization cycle with twelve (12) logs of reduction. This method is accepted by all major guidelines including: AAMI, ANSI, and ISO/CEN.

Hardware Testing

Qualification activities were carried out at the component level for the Model RVDR01 IPG. These qualification activities were conducted on the connector module, electronic module assembly, antenna assembly, activity sensor, filtered feed through, integrated circuits and battery. Several of the Model RVDR01's components are equivalent to those of the previously approved EnRhythm IPG therefore qualification and qualification by similarity activities were performed according to specification. All components used in the Revo MRI IPG were determined to have acceptable quality and reliability.

Mechanical and Electrical Testing

The Revo MRI Model RVDR01 IPG uses the same mechanical platform and design as the commercially available EnRhythm IPG. The only mechanical differences for the Model RVDR01 are the addition of a radiopaque symbol (which identifies the device as being an MR Conditional device) and a modification to the connector to fit the new radiopaque symbol. Therefore, the standard testing performed on the currently marketed EnRhythm IPG applies to the Model RVDR01. Qualification or qualifying by similarity evaluations were performed to the extent of its mechanical performance outside of the MRI environment using EMC testing (pre-MRI), EMI Testing (Post MRI), Electrical Design Verification Testing, and Mechanical Design Verification Testing. All evaluations were successfully completed demonstrating the electrical and mechanical testing meets its requirements.

Firmware Testing

Firmware verification activities were carried out in accordance with a firmware development plan which was created to ensure that the firmware meets its requirements as defined in the device requirements specification. These verification activities were carried out and the results demonstrated that the firmware implements the product features and firmware requirements as specified.

Software Testing

Verification testing of all software requirements was conducted in accordance with a software verification plan developed to ensure that the Revo MRI IPG Model RVDR01 software was tested to its specified requirements. The Model SW018 software verification testing was successfully completed demonstrating that the SW018 software application meets its requirements.

5086MRI Lead Testing

Biocompatibility

The materials used in the CapSureFix 5086 MRI pacing lead that are directly exposed to body tissue and/or fluids are platinum/iridium, titanium nitride, polyurethane, silicone rubber and silicone/polyurethane adhesive. These materials have all been used in

Medtronic Lead Models 4076 and 5076 for several years and have been previously tested and approved for their biocompatibility. No new materials or processes were introduced with the CapSureFix 5086 MRI pacing lead that would introduce new issues of biocompatibility.

Package Testing

The Model 5086MRI Lead passed package qualification testing completed per ASTM D4169 demonstrating that the packaging meets standard performance requirements.

Sterilization Qualification

The lead Model 5086MRI uses a 100% ethylene oxide (EtO) sterilization process. The 100% EtO sterilization process used to sterilize all bradycardia pacing leads was approved October 31, 1995. This process is considered an overkill sterilization cycle with twelve (12) logs of reduction. This method is accepted by all major guidelines, including: AAMI, ANSI, DHSS and ISO/CEN.

Mechanical and Electrical Verification

Two (2) separate verification activities occurred on the 5086 MRI lead. Both series of verification activities included environmental pre-conditioning which consisted of four (4) cycles of ethylene oxide (EtO) sterilization and five (5) cycles of thermal shock (-45°C to 70°C) prior to undergoing mechanical and electrical testing.

The first series of design verification tests were conducted on 5086 MRI lead samples without a radiopaque marker band. This standard series of lead design verification tests consisted of:

• Helix Electrode Extension and Retraction	• Connector Mating (Insertion and Withdrawal) Test
• Tip Pressure / Stiffness Test	• Lead Body Fluid Leak Test
• Helix Seal Leak Test	• Composite Torsional Test
• Composite Tensile Integrity Test	• Lead Composite Pull Test
• Pin to Sleeve Pull Strength	• Conductor Joint Test
• Anchor Sleeve Suture Test	• Lead Body Flex Test
• Connector Flex Test	• Composite Distal Lead Fatigue Test
• Lead Percutaneous Lead Introducer (PLI) Compatibility	• Stylet Insertion and Withdrawal Test
• Stylet Mismatch Test	• Stylet Perforation Test

The standard electrical testing consisted of:

- DC Resistance, IS-1 Connector AC Leakage Impedance
- Electrical Intermittency
- Dielectric Withstand

All of the standard mechanical and electrical testing conducted on the 5086MRI lead met established requirements. Therefore, the verification activities conducted on the Model

5086 MRI lead indicate that the Model 5086MRI lead performs according to its specifications and has appropriate characteristics for safety and effectiveness.

The second series of tests were conducted in order verify lead functionality after the incorporation of the radiopaque marker band element. Verification testing was performed. This second series of testing consisted of:

- Helix Electrode Extension and Retraction
- Connector Mating (Insertion and Withdrawal) Test
- Connector Flex Test
- Composite Tensile Test
- Lead Composite Pull Test

All of the standard mechanical and electrical testing conducted on the 5086MRI lead met requirements. Therefore, the verification activities conducted on the Model 5086 MRI lead indicate that the Model 5086 lead performs according to its specifications and has appropriate characteristics for safety and effectiveness.

Steroid Qualification

The steroid used on the 5086MRI lead is dexamethasone acetate and is identical to the steroid used in the Model 4076 and 5076 leads. This drug component is qualified by similarity to that of an approved predecessor lead, the Model 4076. Equivalence of these two (2) leads drug components was demonstrated by the following:

- Design information demonstrating that both leads have the exact same steroid and distal tip components
- Manufacturing information illustrating that both leads have similar manufacturing processes
- Elution and related substances testing which demonstrates that the Model 5086 lead's drug component, regardless of whether it is in or out of the MRI environment, has equivalent performance to that of the predecessor lead, Model 4076 lead.

The drug component of the Model 5086MRI lead is qualified as safe and effective by similarity to that of the approved legacy lead, Model 4076.

System Validation Testing

System validation testing was successfully completed and included the following:

- Installing the software application onto the market approved Model 2090 Programmer
- Review of the applicable manuals that are provided with the system
- Testing the operation of the new software features
- Evaluation of the software's basic functions
- System compatibility with accessory devices

- Anomaly Inducement Testing which simulated actual use of the product in a stress scenario in an attempt to uncover anomalous behavior. No issues were discovered.
- Release/Protocol Testing which simulated actual uses of the product in the field to assure the system performs reliably. No issues were discovered.

The system validation testing demonstrates that the software and firmware of the Model RVDR01 pacemaker meet their requirements, are validated for human use, and have appropriate characteristics for safety and effectiveness.

XI. SUMMARY OF PRIMARY CLINICAL STUDY

Due to the similarities of Revo MRI to the commercially available EnRhythm pacing system, prior clinical studies were also used to support the feature functionality of the Revo MRI SureScan pacing system. These studies are comprised of the following:

- ASPECT (Atrial Septal Pacing Efficacy Clinical Trial) clinical study: This clinical study, provides support for the atrial intervention pacing therapies.
- ATTEST (Atrial Therapy Efficacy and Safety Trial) clinical study: This clinical study provides support for atrial intervention pacing therapies.
- Kappa 700 Implant Study provides support for the Right Ventricular Capture Management feature and other bradycardia pacing features
- Gem III DR Model 7275 MVP (Managed Ventricular Pacing) Study: This study provides support for the MVP pacing mode.
- Marquis MVP Download Study: This study provides support for the MVP pacing mode.
- EnRhythm Clinical Study: This study provides support for the MVP pacing mode and the Reactive Antitachycardia Pacing (ATP) therapy.

The Revo MRI SureScan pacing system clinical study evaluated the safety and effectiveness of the Revo MRI SureScan Pacing System in the clinical MRI environment. The Revo MRI SureScan Pacing System was originally named the EnRhythm MRI SureScan Pacing System and the clinical study is also referred to as the EnRhythm MRI SureScan pacing system clinical study. The Revo MRI SureScan pacing system clinical study will be the primary focus of the clinical studies summarized in this document.

A. Study Purpose

The study purpose was to confirm the results of earlier pre-clinical bench and animal testing and to assess whether the Revo MRI SureScan pacing system is safe and effective for human use in the MRI environment under the specified MR Conditions of Use.

B. Study Scope, Design and Methods

The clinical study was designed as a prospective, randomized, controlled, unblinded, global multi-center study of typical Class I or II indicated pacemaker patients comparing outcomes between those with and without exposure to a single investigational protocol MR scan.

Pacemaker function and adverse events were assessed at implant, two-months post-implant, before and after MRI at 9-12 weeks post-implant (control group patients had a waiting period), at 3, 4 and 6 months post-implant (one week, one month and 3 months after MRI) and every 6 months thereafter. Data from the 9-12 week visit and the visit occurring one month later were used for the primary endpoints.

Up to 470 patients at 75 centers were planned for implant and follow-up.

C. Patient Inclusion and Exclusion Criteria

Patients who met all inclusion and no exclusion criteria were eligible.

Inclusion Criteria

- Patients who have a Class I or II indication for implantation of a dual chamber pacemaker according to the ACC/AHA/NASPE guidelines¹.
- Patients must be able to undergo a pectoral implant.
- Patients who are able and willing to undergo elective MRI scanning without sedation.
- Patients who are geographically stable and available for follow-up at the study center for the length of the study.

Exclusion Criteria

- Patients who require a legally authorized representative to obtain consent.
- Patients with a mechanical tricuspid heart valve.
- Patients with a history of tricuspid valvular disease.
- Patients for whom a single dose of 1.0 mg dexamethasone acetate may be contraindicated.
- Patients who have a previously implanted pacemaker or implantable cardioverter defibrillator (ICD) (abandoned pacemaker and/or defibrillator leads not permitted; however, patients with complete system explants are not excluded).
- Patients who are immediate candidates for an ICD.
- Patients 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.
- Patients with previously implanted active medical devices.
- Patients 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).
- Patients with medical conditions that preclude the testing required by the protocol or limit study participation.

¹ Gregoratos G, Abrams J, Epstein AE, Freedman RA, Hayes DL, Hlatky MA, Kerber RE, Naccarelli GV, Schoenfeld NH, Silka MJ, Winters SL. ACC/AHA/NASPE 2002 Guideline Update for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/NASPE Committee on Pacemaker Implantation). 2002. Available at: www.acc.org/clinical/guidelines/pacemaker/Pacemakerclean.pdf.

- Patients who are enrolled or intend to participate in another clinical trial (of an investigational drug or device, new indication for an approved drug or device, or requirement of additional testing beyond standard clinical practice) during this clinical study.
- Pregnant women, or women of child bearing potential and who are not on a reliable form of birth control.
- Patients with exclusion criteria required by local law (e.g. age, breastfeeding).

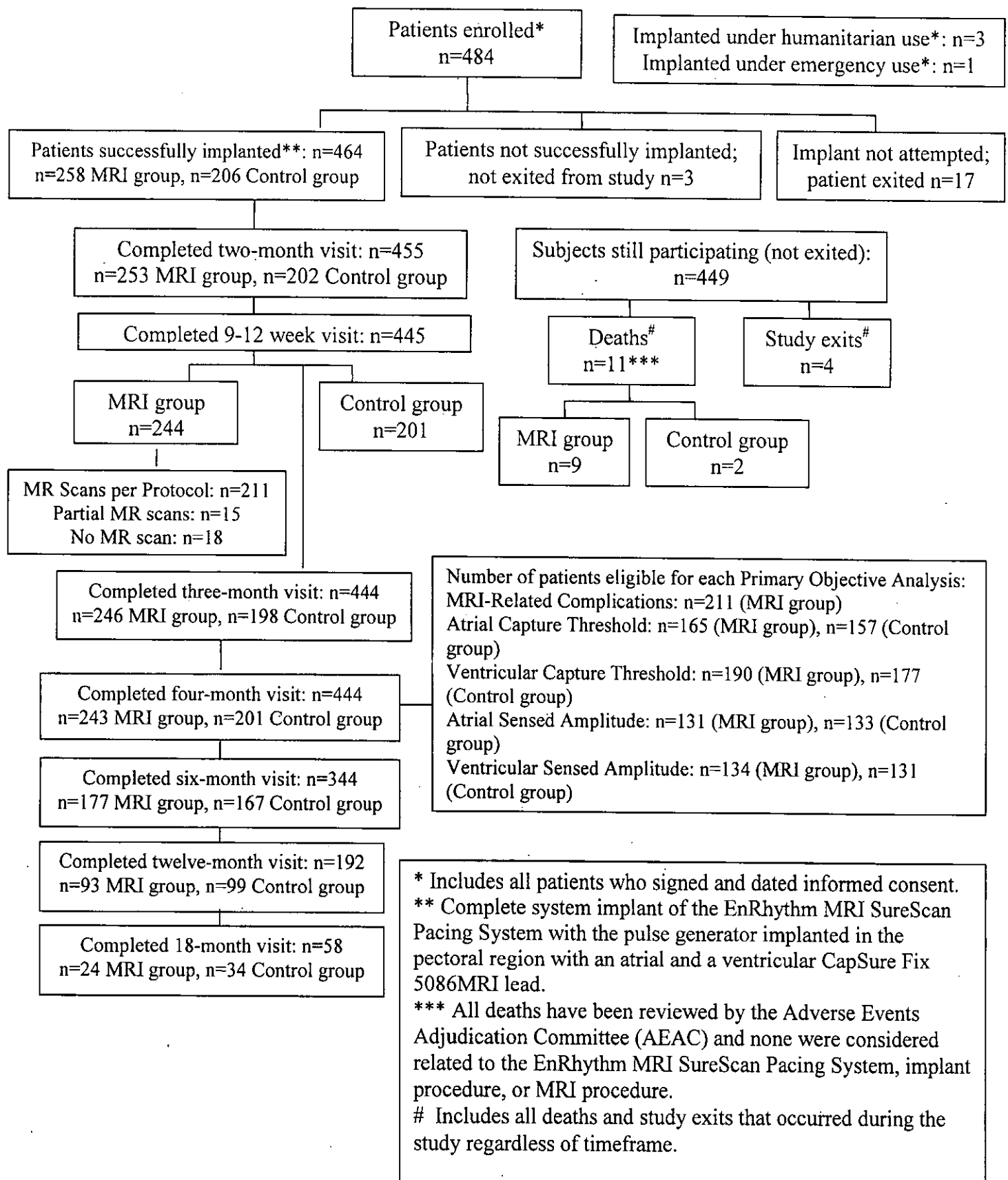
D. Results

The first enrollment occurred 5 February 2007. Enrollment was between February 2007 and July 2008. Follow up continued through November 2008 for an average duration of 11.2 months. These results include any visit or event that occurred on or before 21 November 2008 and received by December 18, 2008 (all data) or by September 14, 2009 (adverse event updates).

Patient Accountability

A total of 484 patients were enrolled at 42 centers, including 113 (23%) enrollments at 13 centers in the US and 371 (77%) 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 patients, 464 patients were successfully implanted with the EnRhythm MRI pacing system and randomized. Among these, 99 (21%) patients were from the US and 365 (79%) patients were from the outside of the US. Figure 1 shows a study flow chart which accounts for patient withdrawal due to death or exits and denotes missing follow-up visit data. (Note: although a patient can miss a follow-up visit, they can contribute to data at a subsequent follow-up visit).

Figure 1: Patient Distribution



Patient Demographics

Table 1 and Table 2 summarize baseline clinical characteristics, including patient demographics and the primary indication for successfully implanted patients.

Table 1: Baseline Clinical Characteristics

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

Table 2: 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%)
Cardiac 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).

Summary of Missing Data

The number of patients analyzed for each primary endpoint was substantially lower than the number of patients randomized (n=464) in the study. Table 3 summarizes the missing data for each primary objective.

Table 3: Summary of Missing/Excluded Data in Primary Objectives

	Missing data n (%)	
	MRI Group (n = 258)	Control (n=206)
MRI-Complications	47(18.2%)	N/A
Pacing Capture Threshold		
• Atrial	93 (36%)	49 (24%)
• Ventricular	68 (26%)	29 (14%)
Sensed Amplitudes		
• Atrial	127 (49%)	73 (35%)
• Ventricular	124 (48%)	75 (36%)

Patients were missing or excluded from the primary objective analyses for the following reasons:

- Follow-up visits missed or outside of follow-up window (30)
- PCT increase exceeding 0.5 V from 2 months to 9-12 weeks (6)
- Atrial arrhythmia at follow up and therefore no threshold obtained (45)
- Incomplete sensing test at 9-12 weeks or 4-month visit (26 atrial, 51 ventricular)
- Sensing values less than 1.5 mV (atrial) or 5.0 mV (ventricular) at 9-12 weeks (38 atrial, 53 ventricular)
- MRI scan not conducted (18), for reasons including:
 - High PCT (3)
 - Unknown PCT (2)
 - Non-MRI compatible stent (1)
 - Pacemaker stimulation of the diaphragm (2)
 - Presence of an MRI-incompatible lead (1)
 - Pregnancy (1)
 - Patient refusal (8)
- MRI scan not conducted according to protocol (15), with deviations including
 - SAR exceeded 2 W/kg (8)
 - Patient discomfort (4)
 - MRI system malfunction (1)
 - Ventricular threshold exceeded 2V at pre-MRI check (scan completed) (1)
 - Inability to fit the patient into the scanner (head sequences completed) (1)

For each reason for missing or excluding data (other than MRI scans not done), the proportions of excluded data between the MRI and Control groups were comparable. Statistical analyses were also performed to assess the likelihood that missing/excluded data could affect the conclusions from the study. The results from these analyses are consistent with the primary analyses.

Primary Objectives

There were three (3) primary endpoints. Analyses for each primary objective were performed per-protocol which included patients who met the following criteria:

- Successfully implanted with pacing system and randomized
- Have 9-12 week visit data (pre-MRI/waiting period)
- Met the MR Conditions of Use
- Received an MR scan (if in the MRI group)
- Have 4-month visit data

MRI-Related Complications Primary Objective: To assess the MRI-related complication-free rate in the month following MRI. The hypothesis is that the MRI-related complication free-rate between the MRI procedure and 1-month post-MRI is greater than 90%, tested with one-sided type I error, alpha level of 0.025. The result is shown in Table 4.

Table 4: Results of MRI-Related Complications Primary Objective

Success Criteria	Patients	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

Pacing Capture Threshold Primary 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 hypotheses are that the proportion of patients who experience an increase greater than 0.5V in atrial and ventricular voltage thresholds are non-inferior across treatment and control, with margin = 10%. The result is shown in Table 5.

Table 5: Results of Capture Threshold Primary Objective

Success Criteria	Comparison	Group	Success/ n	Success Rates	P-value	Conclusion
The proportions of patients who experienced an increase less than or equal to 0.5 V are non-inferior, defined as within 10%.	Atrial	MRI	165 / 165	100%	Not Applicable*	Objective Met
		Control	157 / 157	100%		
	Ventricular	MRI	190 / 190	100%	Not Applicable*	Objective Met
		Control	177 / 177	100%		

* P-values cannot be calculated since the success rates were 100% for both the MRI and the Control groups.

Sensed Amplitude Primary Objective: To compare the changes in 1) atrial and 2) ventricular sensed amplitudes before and after MRI between the MRI and control groups. The hypotheses are that the proportion of patients who experienced a sensed amplitude decrease not exceeding 50%, and a 1-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 non-inferior, defined as within 10%. The result is shown in Table 6.

Table 6: Results of Sensed Amplitude Primary Objective

Success Criteria	Comparison		Success/ n	Success Rates	P-value	Conclusion
The proportion of patients who experienced a sensed amplitude decrease not exceeding 50%, and a 1-month post-MRI/waiting period	Atrial	MRI	124 / 131	94.7%	$p = 0.01$	Objective Met
		Control	123 / 133	92.5%		
	Ventricular	MRI	130 / 134	97.0%	$p = 0.003$	Objective Met
		Control	125 / 131	95.4%		

Success Criteria	Comparison		Success/ n	Success Rates	P-value	Conclusion
sensed amplitude not less than 1.5 mV for atrial measurements and not less than 5.0 mV for ventricular measurements, are non-inferior, defined as within 10%.						

Secondary Objectives

Note that prespecified Secondary Objectives #1, #7 and # 6 were prespecified by study protocol to include statistical considerations necessary to allow testing for significance in this order (provided that all primary objectives were met).

Secondary Objective #1 - Characterize all system-related complications. The result is shown in Table 7, and a listing of these events is shown in Table 8.

Table 7: Results of System-Related Complications Secondary Objective

Success Criteria	Patients	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

Table 8: 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

Adverse Event	Observations (MRI / Control)	Complications (MRI / Control)	Total AEs (MRI / Control)
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 - Confirm that labeling instructions for completing the MRI scans were followed to ensure patient safety. The result is shown in Table 9. There were no defined success criteria for this endpoint.

Table 9: Results of Labeling Instructions Secondary Objective

Success Criteria	Patients	Patients with a System-Related Adverse Device Effect that occurred due to Insufficiencies or Incorrect Following of MRI Labeling Instructions
None Defined	211	0

Secondary Objective #3 - Characterize occurrence of sustained ventricular arrhythmias and asystole seen during MR scans. The result is shown in Table 10. There were no defined success criteria for this endpoint. As shown, no arrhythmias were reported during MRI scanning.

Table 10: Results of Occurrence of Arrhythmias Secondary Objective

Success Criteria	Patients (MRI Group)	Patients with Sustained Ventricular Arrhythmias and Asystole Attributed to MR Scan
None Defined	211	0

Secondary Objective #4 - Characterize all implant procedure, pacing system- and MRI-procedure-related adverse events. The result is shown in Table 11. There were no defined success criteria for this endpoint.

Table 11: Results of Adverse Events Secondary Objective

Success Criteria	Patients	System- and Procedure-Related Adverse Event-Free Rate
None Defined	452	78.5%

Secondary Objective #5 - Characterize atrial and ventricular lead impedance through four (4) months post-implant. The result is shown in Table 12. There were no defined success criteria for this endpoint. The findings indicate that lead impedance was stable through the period of MRI exposure.

Table 12: Results of Lead Impedance Secondary Objective

Success Criteria	Comparison	Group	n	Mean $\pm$ SD Impedance (Ω)		
				Pre-MRI/Control	One-month post-MRI/Control	changes from pre-MRI to one-month post-MRI
None Defined	Atrial	MRI	201	516.0 $\pm$ 81.4	515.5 $\pm$ 78.1	-0.6 $\pm$ 61.8
		Control	197	523.6 $\pm$ 92.8	530.9 $\pm$ 97.7	7.3 $\pm$ 50.4
	Ventricular	MRI	201	570.3 $\pm$ 109.2	561.3 $\pm$ 104.8	-9.0 $\pm$ 48.5
		Control	196	571.6 $\pm$ 103.0	565.9 $\pm$ 105.4	-5.7 $\pm$ 51.8

Secondary Objective #6 - Characterize the lead handling of the CapSureFix MRI lead Model 5086MRI in relation to the commercially available lead Model 5076.

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 was for PMA supplement approval of the Medtronic Model 5076 lead (P930039/S009). 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 result is shown in Table 13.

Table 13: Results of Lead Handling Secondary Objective

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

Secondary Objective #7 - Characterize 4-month pacing thresholds and sense amplitudes of the MRI group and control group in relation to the commercially available lead Model 5076.

This objective compared the 1-month post-MRI/control visit (4-months post-implant) pacing thresholds and sensed amplitudes of the CapSureFix MRI 5086MRI leads in both the MRI and control groups to the 3-month post-implant follow-up data from the commercially available Medtronic Model 5076 lead study. The result is shown in Table 14.

Table 14: Results of Lead Performance Secondary Objective

Pacing Capture Thresholds				
Success Criteria	Comparison	Model 5086MRI Mean $\pm$ SD (V)	p-Value for equivalence between MRI or control and 5076	Conclusion
Pacing thresholds are non-inferior (Delta=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 non-inferior (Delta=0.9 mV for atrial sensed amplitudes, 2.5 mV for ventricular sensed amplitudes)	Lead Implant Site	Model 5086MRI Mean $\pm$ 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

Additional Analyses

Additional Analysis #1 - Demonstrate that the EnRhythm MRI SureScan Pacing System (both IPG 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). The result is shown in Table 15.

Table 15: Results of Identification of Radiopaque Additional Analysis

Radiopaque	Questionnaire	Results (Median Scores)
Pacemaker	Cardiology Staff	1 (Slightly above expectations)
	Radiologists	2 (Moderately above expectations)
Lead	Cardiology Staff	2 (Moderately above expectations)
	Radiologists	2 (Moderately above expectations)

Additional Analysis #2 - Summarize ease of use scores by cardiology users of the SureScan feature, including assessment for any aberrant or undesirable behavior. 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 result is shown in Table 16.

Table 16: Results of SureScan Feature Performance Additional Analysis

Question	Median Score
Ease of locating the SureScan feature	6 (Easy)
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 - Summarize ease of safely coordinating and assuring appropriate MRI-related care including whether safeguards and procedures were followed at the time of the MR 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 Table 17.

Table 17: Results of Analysis of Procedure Additional Analysis

Question	Results (Median Scores)
Cardiology staff's ease of scheduling the appointment with radiology	6 (Easy)*
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

E. Adverse Events Summary

Of the 484 enrolled patients, there were 283 patients who experienced a total of 600 adverse events. Sixty percent (60%) of all of the adverse events were clinical observations which required no invasive action. Seventy-eight percent (78%) 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 pacing system-related and procedure-related adverse events are summarized in secondary objective #4.

While there were no MRI-related complications in the EnRhythm MRI clinical study, the adverse events committee classified four (4) events as MRI-procedure related observations: paraesthesia (n=3) and palpitations (n=1). In all cases, the center investigator and 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.

Additionally, there were four (4) observations of unknown relatedness to the MRI procedure: chest discomfort (1), dyspnea (1), atrial flutter (1), and atrial fibrillation (1). Two (2) of these four (4) events were atrial arrhythmias which were classified by the center investigator and the Adverse Events Committee as unknown relatedness to the MRI procedure. The patient with atrial flutter had a baseline history of atrial arrhythmias and persistent atrial fibrillation. The patient with atrial fibrillation had a baseline history of paroxysmal atrial fibrillation. In both cases, the arrhythmia resolved the same day as the MRI procedure. Table 18 provides a full listing of all adverse events reported in the clinical study listed by incidence rate, including both observations and complications.

Table 18: All Adverse Events

Adverse Event Key Term	Observations	Complications	Total AEs	Number (%) of Patients (n = 484)
Atrial fibrillation	32	25	57	49 (10.1%)
Chest pain	13	10	23	23 (4.8%)
Lead dislodgement	1	18	19	19 (3.9%)
Pneumothorax	8	9	17	17 (3.5%)
Dizziness	16	1	17	17 (3.5%)
Palpitations	12	1	13	12 (2.5%)
Elevated pacing threshold	3	9	12	10 (2.1%)
Syncope	7	4	11	10 (2.1%)
Pneumonia	4	6	10	10 (2.1%)
Myocardial infarction	1	7	8	8 (1.7%)
Anaemia	2	6	8	7 (1.4%)
Implant site infection	5	3	8	7 (1.4%)
Urinary tract infection	6	2	8	8 (1.7%)
Atrial flutter	8	0	8	7 (1.4%)
Dyspnea	8	0	8	8 (1.7%)
Cardiac failure	1	6	7	6 (1.2%)
Pleural effusion	1	5	6	4 (0.8%)
Bronchitis	4	2	6	6 (1.2%)
Hypotension	5	1	6	6 (1.2%)
Presyncope	5	1	6	6 (1.2%)
Fatigue	6	0	6	6 (1.2%)
Implant site hematoma	6	0	6	6 (1.2%)
Cataract	0	5	5	4 (0.8%)
Pericardial effusion	1	4	5	5 (1.0%)
Angina pectoris	2	3	5	5 (1.0%)
Atrial tachycardia	3	2	5	5 (1.0%)
Dyspnea exertional	3	2	5	5 (1.0%)
Paraesthesia	5	0	5	5 (1.0%)
Ventricular extrasystoles	5	0	5	5 (1.0%)
Cardiac failure congestive	0	4	4	4 (0.8%)
Coronary artery disease	1	3	4	4 (0.8%)
Failure to capture	1	3	4	4 (0.8%)
Thrombosis	2	2	4	3 (0.6%)
Fall	4	0	4	4 (0.8%)
Insomnia	4	0	4	4 (0.8%)
Diverticulitis	1	2	3	2 (0.4%)
Supraventricular tachycardia	1	2	3	3 (0.6%)
Back pain	2	1	3	3 (0.6%)
Cerebrovascular accident	2	1	3	3 (0.6%)
Chest discomfort	2	1	3	3 (0.6%)
Constipation	2	1	3	3 (0.6%)

Adverse Event Key Term	Observations	Complications	Total AEs	Number (%) of Patients (n = 484)
Inappropriate device stimulation of tissue	2	1	3	3 (0.6%)
Liver disorder	2	1	3	3 (0.6%)
Pain	2	1	3	3 (0.6%)
Ventricular tachycardia	2	1	3	3 (0.6%)
Chronic obstructive pulmonary disease	3	0	3	3 (0.6%)
Depression	3	0	3	3 (0.6%)
Hypertension	3	0	3	3 (0.6%)
Implant site pain	3	0	3	3 (0.6%)
Influenza	3	0	3	3 (0.6%)
Musculoskeletal pain	3	0	3	3 (0.6%)
Vertigo	3	0	3	3 (0.6%)
Benign prostatic hyperplasia	0	2	2	2 (0.4%)
Cardiac perforation	0	2	2	2 (0.4%)
Endocarditis	0	2	2	2 (0.4%)
Hip fracture	0	2	2	2 (0.4%)
Inguinal hernia	0	2	2	2 (0.4%)
Laceration	0	2	2	2 (0.4%)
Mesenteric artery stenosis	0	2	2	1 (0.2%)
Pulmonary edema	0	2	2	1 (0.2%)
Renal failure chronic	0	2	2	2 (0.4%)
Spinal column stenosis	0	2	2	2 (0.4%)
Urethral stenosis	0	2	2	2 (0.4%)
Acute coronary syndrome	1	1	2	2 (0.4%)
Aortic stenosis	1	1	2	2 (0.4%)
Carpal tunnel syndrome	1	1	2	2 (0.4%)
Headache	1	1	2	2 (0.4%)
Pain in extremity	1	1	2	2 (0.4%)
Pneumonia bacterial	1	1	2	1 (0.2%)
Pulmonary embolism	1	1	2	2 (0.4%)
Pyrexia	1	1	2	2 (0.4%)
Transient ischemic attack	1	1	2	2 (0.4%)
Venous thrombosis	1	1	2	2 (0.4%)
Anxiety	2	0	2	2 (0.4%)
Atrioventricular block second degree	2	0	2	1 (0.2%)
Cough	2	0	2	2 (0.4%)
Electric shock	2	0	2	2 (0.4%)
Hematuria	2	0	2	2 (0.4%)
Heart rate increased	2	0	2	2 (0.4%)
Hypertensive crisis	2	0	2	1 (0.2%)
Hypothyroidism	2	0	2	2 (0.4%)

Adverse Event Key Term	Observations	Complications	Total AEs	Number (%) of Patients (n = 484)
Infection	2	0	2	2 (0.4%)
Oedema peripheral	2	0	2	2 (0.4%)
Sinusitis	2	0	2	2 (0.4%)
Syncope vasovagal	2	0	2	2 (0.4%)
Undersensing	2	0	2	2 (0.4%)
Venous insufficiency	2	0	2	2 (0.4%)
Abscess soft tissue	0	1	1	1 (0.2%)
Acute myocardial infarction	0	1	1	1 (0.2%)
Adenocarcinoma	0	1	1	1 (0.2%)
Angina unstable	0	1	1	1 (0.2%)
Aortic aneurysm	0	1	1	1 (0.2%)
Arteriosclerotic retinopathy	0	1	1	1 (0.2%)
Atrial septal defect	0	1	1	1 (0.2%)
Bacterial pyelonephritis	0	1	1	1 (0.2%)
Basal cell carcinoma	0	1	1	1 (0.2%)
Blood creatinine increased	0	1	1	1 (0.2%)
Bronchial carcinoma	0	1	1	1 (0.2%)
Bronchopneumonia	0	1	1	1 (0.2%)
Bursitis	0	1	1	1 (0.2%)
Cachexia	0	1	1	1 (0.2%)
Cardiac pacemaker revision	0	1	1	1 (0.2%)
Cholecystitis	0	1	1	1 (0.2%)
Cholelithiasis	0	1	1	1 (0.2%)
Colon adenoma	0	1	1	1 (0.2%)
Endometrial disorder	0	1	1	1 (0.2%)
Fecaloma	0	1	1	1 (0.2%)
Fibroadenoma	0	1	1	1 (0.2%)
Fistula	0	1	1	1 (0.2%)
Gastritis erosive	0	1	1	1 (0.2%)
Glioblastoma	0	1	1	1 (0.2%)
Hemangioma	0	1	1	1 (0.2%)
Hematoma	0	1	1	1 (0.2%)
Hemorrhoids	0	1	1	1 (0.2%)
Hypoglycemia	0	1	1	1 (0.2%)
Incontinence	0	1	1	1 (0.2%)
Intestinal perforation	0	1	1	1 (0.2%)
Intracranial aneurysm	0	1	1	1 (0.2%)
Ischemic stroke	0	1	1	1 (0.2%)
Knee arthroplasty	0	1	1	1 (0.2%)
Limb injury	0	1	1	1 (0.2%)
Lumbar spinal stenosis	0	1	1	1 (0.2%)
Lung infection	0	1	1	1 (0.2%)
Medical device complication	0	1	1	1 (0.2%)

Adverse Event Key Term	Observations	Complications	Total AEs	Number (%) of Patients (n = 484)
Micturition disorder	0	1	1	1 (0.2%)
Multiple myeloma	0	1	1	1 (0.2%)
Osteoarthritis	0	1	1	1 (0.2%)
Peptic ulcer	0	1	1	1 (0.2%)
Postoperative thoracic procedure complication	0	1	1	1 (0.2%)
Postoperative wound infection	0	1	1	1 (0.2%)
Renal cell carcinoma stage unspecified	0	1	1	1 (0.2%)
Renal failure acute	0	1	1	1 (0.2%)
Renal neoplasm	0	1	1	1 (0.2%)
Respiratory failure	0	1	1	1 (0.2%)
Sciatica	0	1	1	1 (0.2%)
Sepsis	0	1	1	1 (0.2%)
Spondylolisthesis	0	1	1	1 (0.2%)
Subclavian vein thrombosis	0	1	1	1 (0.2%)
Urinary retention	0	1	1	1 (0.2%)
Vomiting	0	1	1	1 (0.2%)
Abdominal pain upper	1	0	1	1 (0.2%)
Acute vestibular syndrome	1	0	1	1 (0.2%)
Aneurysm	1	0	1	1 (0.2%)
Arterial occlusive disease	1	0	1	1 (0.2%)
Arthralgia	1	0	1	1 (0.2%)
Asthenia	1	0	1	1 (0.2%)
Atelectasis	1	0	1	1 (0.2%)
Atrial thrombosis	1	0	1	1 (0.2%)
Blood glucose increased	1	0	1	1 (0.2%)
Bradycardia	1	0	1	1 (0.2%)
Brain neoplasm	1	0	1	1 (0.2%)
Brain stem infarction	1	0	1	1 (0.2%)
Calcinosis	1	0	1	1 (0.2%)
Cardiac arrest	1	0	1	1 (0.2%)
Carotid artery stenosis	1	0	1	1 (0.2%)
Cellulitis	1	0	1	1 (0.2%)
Cervicobrachial syndrome	1	0	1	1 (0.2%)
Cholinergic syndrome	1	0	1	1 (0.2%)
Chronic myelomonocytic leukemia	1	0	1	1 (0.2%)
Clavicle fracture	1	0	1	1 (0.2%)
Clostridium difficile colitis	1	0	1	1 (0.2%)
Confusional state	1	0	1	1 (0.2%)
Contusion	1	0	1	1 (0.2%)

Adverse Event Key Term	Observations	Complications	Total AEs	Number (%) of Patients (n = 484)
Convulsion	1	0	1	1 (0.2%)
Cystitis	1	0	1	1 (0.2%)
Device psychogenic complication	1	0	1	1 (0.2%)
Diarrhea	1	0	1	1 (0.2%)
Diastolic dysfunction	1	0	1	1 (0.2%)
Dyspepsia	1	0	1	1 (0.2%)
Dysphonia	1	0	1	1 (0.2%)
Ear pain	1	0	1	1 (0.2%)
Ejection fraction decreased	1	0	1	1 (0.2%)
Epistaxis	1	0	1	1 (0.2%)
Erythema migrans	1	0	1	1 (0.2%)
Eye hemorrhage	1	0	1	1 (0.2%)
Gastroenteritis	1	0	1	1 (0.2%)
Gout	1	0	1	1 (0.2%)
Gouty arthritis	1	0	1	1 (0.2%)
Grand mal convulsion	1	0	1	1 (0.2%)
Groin infection	1	0	1	1 (0.2%)
Head injury	1	0	1	1 (0.2%)
Heat exhaustion	1	0	1	1 (0.2%)
Hypercholesterolemia	1	0	1	1 (0.2%)
Hyperhidrosis	1	0	1	1 (0.2%)
Hyponatremia	1	0	1	1 (0.2%)
Impaired healing	1	0	1	1 (0.2%)
Implant site discharge	1	0	1	1 (0.2%)
Implant site swelling	1	0	1	1 (0.2%)
Inappropriate device therapy	1	0	1	1 (0.2%)
Incision site complication	1	0	1	1 (0.2%)
Incision site erythema	1	0	1	1 (0.2%)
Incision site hemorrhage	1	0	1	1 (0.2%)
Influenza like illness	1	0	1	1 (0.2%)
Loss of consciousness	1	0	1	1 (0.2%)
Lower respiratory tract infection	1	0	1	1 (0.2%)
Lumbar vertebral fracture	1	0	1	1 (0.2%)
Mental status changes	1	0	1	1 (0.2%)
Mouth ulceration	1	0	1	1 (0.2%)
Muscle spasms	1	0	1	1 (0.2%)
Muscle strain	1	0	1	1 (0.2%)
Nasopharyngitis	1	0	1	1 (0.2%)
Neuralgia	1	0	1	1 (0.2%)
Nodal rhythm	1	0	1	1 (0.2%)
Non-cardiac chest pain	1	0	1	1 (0.2%)

Adverse Event Key Term	Observations	Complications	Total AEs	Number (%) of Patients (n = 484)
Orthostatic hypotension	1	0	1	1 (0.2%)
Panic attack	1	0	1	1 (0.2%)
Parkinson's disease	1	0	1	1 (0.2%)
Pericarditis	1	0	1	1 (0.2%)
Peripheral vascular disorder	1	0	1	1 (0.2%)
Petit mal epilepsy	1	0	1	1 (0.2%)
Plantar fasciitis	1	0	1	1 (0.2%)
Pleuritic pain	1	0	1	1 (0.2%)
Polymyalgia rheumatica	1	0	1	1 (0.2%)
Prostate cancer	1	0	1	1 (0.2%)
Renal failure	1	0	1	1 (0.2%)
Renal tubular acidosis	1	0	1	1 (0.2%)
Respiratory tract infection	1	0	1	1 (0.2%)
Restlessness	1	0	1	1 (0.2%)
Rib fracture	1	0	1	1 (0.2%)
Salivary gland calculus	1	0	1	1 (0.2%)
Sarcoidosis	1	0	1	1 (0.2%)
Sinus arrhythmia	1	0	1	1 (0.2%)
Skin laceration	1	0	1	1 (0.2%)
Stomatitis	1	0	1	1 (0.2%)
Subclavian artery stenosis	1	0	1	1 (0.2%)
Supraventricular extrasystoles	1	0	1	1 (0.2%)
Swelling	1	0	1	1 (0.2%)
Tendonitis	1	0	1	1 (0.2%)
Thrombophlebitis	1	0	1	1 (0.2%)
Thyroid disorder	1	0	1	1 (0.2%)
Traumatic hematoma	1	0	1	1 (0.2%)
Upper respiratory tract infection	1	0	1	1 (0.2%)
Ventricular dysfunction	1	0	1	1 (0.2%)
Viral infection	1	0	1	1 (0.2%)
Vision blurred	1	0	1	1 (0.2%)
Weight decreased	1	0	1	1 (0.2%)
Whiplash injury	1	0	1	1 (0.2%)
Total	359	241	600	283 (58.5%)

F. Death Summary

The Adverse Event Adjudication Committee (AEAC) determined that the 11 patient 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.

Table 19: Study Deaths

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

* Non-cardiac deaths are not classified as sudden or non-sudden.

G. Clinical Study Conclusion

The Revo MRI SureScan pacing system clinical study demonstrated that the Revo MRI SureScan pacing system is safe and effective for use in the MRI environment when used in accordance with its labeling as determined by the following:

- The MRI-related complication-free rate primary objective was met and there were no occurrences of sustained ventricular arrhythmias or asystole.
- The proportions of patients in the MRI-treated group who experienced an increase of 0.5V or less in atrial and ventricular voltage pacing capture thresholds were non-inferior to the control group patients (those patients who did not undergo a MRI scan).
- The proportions of patients in the MRI-treated group who experienced atrial and ventricular sensed amplitude decreases < 50% and whose atrial and ventricular sense amplitudes remained above an acceptable minimum at 1-month post MRI/waiting period were non-inferior to the control group patients.

In summary, all primary objectives were met. All secondary objectives were met where performance criteria were predefined. Overall, there were no differences noted in performance between the MRI and the control groups. In the MRI environment studied, the EnRhythm MRI pacing system performance was commensurate with MR-Conditional labeling requirements.

XII. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

A. Panel meeting recommendation

At an advisory meeting held on March 19, 2010, the Circulatory System Devices Advisory Panel recommended that Medtronic's PMA be conditionally approved. The panel meeting transcript can be found at:

<http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/CirculatorySystemDevicesPanel/ucm204585.htm>.

The panel recommended three (3) conditions of approval:

1. A post approval study should be conducted as discussed in the deliberations. See panel transcript for details.
2. Radiologist/MR technicians/clinical sites should receive a training/certification prior to scanning patients who have the Revo MRI SureScan pacing system.
3. The labeling includes a bold statement stating that the Revo IPG should be used in conjunction with the 5086MRI lead to support MR Conditional use.

B. FDA's Post-Panel Action

FDA has implemented all of the Panel's recommended conditions of approval. A post-approval study design was developed which addresses the issues raised during the Panel deliberations. Specifically, the post-approval study will evaluate additional questions regarding the safety and effectiveness of the device for patients who receive multiple MR exams and will also evaluate the long-term reliability and performance of the 5086MRI pacing lead. A training program has been implemented and clinician requirements for completion of the program are specified in the MR Conditions of Use. The labeling now includes a bold statement stating that the Revo IPG should be used in conjunction with the 5086MRI lead to support MR Conditional use.

XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Safety Conclusions

The adverse effects of the device are based on data collected in a clinical study conducted to support PMA approval as described above. The preclinical and clinical results demonstrate a reasonable assurance of safety for the Revo MRI SureScan Pacing System both inside and outside of the MRI environment. The MRI-related complication-free rate primary objective was met and there were no occurrences of sustained ventricular arrhythmias or asystole. The system-related complications secondary objective was also met. FDA's review concluded that the adverse events observed and the rates of adverse events were acceptable and supportive of the primary objective results. This conclusion is consistent with the feedback provided to FDA by the Panel.

B. Effectiveness Conclusions

The preclinical and clinical results demonstrate a reasonable assurance of effectiveness for the Revo MRI SureScan Pacing System both inside and outside of the MRI environment. Basic effectiveness of the device was demonstrated through preclinical testing. The Revo MRI SureScan clinical study demonstrated that the system continues to function appropriately and without adverse consequences for patients when exposed to the MR environment under the specified MR Conditions of Use.

C. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. The Revo MRI SureScan Pacing System was developed to enable patients to undergo MR scans under specified MR Conditions of Use. Pre-clinical laboratory testing was conducted to evaluate the device inside and outside of the MRI environment. All test results were found to be acceptable. The Revo MRI SureScan pacing system clinical study further evaluated this system and confirmed the results of the pre-clinical investigations. The results of the pre-clinical and the clinical investigation provide a reasonable assurance of safety and effectiveness for the Medtronic Revo MRI SureScan Pacing System. FDA's Advisory Panel recommended that the PMA be approved, patient to several conditions. FDA implemented all of these conditions following the Panel meeting. The system performs according to its design intent and is suitable for market release.

XIV. CDRH Decision

CDRH issued an approval order on February 8, 2011. The final conditions of approval cited in the approval order are described below.

As a condition of approval, the applicant agreed to conduct the following post-approval study of Chronic Lead Performance and Multiple MRI Scans for the REVO SureScan Pacing System.

The study is global, non-randomized, multi-center cohort study of patients undergoing implantation of the SureScan Pacing System. The study will include two arms: 1) the Chronic Lead Performance Arm and 2) the Multiple MRI Scan Arm.

1. The Chronic Lead Performance Arm will consist of

- a. a prospective study design to characterize chronic lead performance following device implant, as well as a robust process to retrospectively collect implant data for each study subject;
- b. a post-approval study duration of at least 5 years;
- c. a sample size of 1,810, accounting for estimated attrition, which will be derived from subjects enrolled pre-implant and post-implant with a minimum of 50% of the total enrollment originating from the pre-implant cohort, results in a 2-sided 95% upper confidence bound of no more than 1.0% for individual adverse event rates, assuming an expected rate of 0.4%, using the exact binomial;
- d. enrollment plan which attempts to fully enroll the study within 30 months;
- e. a primary safety endpoint as Model 5086MRI leads that are placed in the right ventricle complication-free rate greater than 92.5% at 5 years, with any clinical

- adverse events omitted from the primary endpoint collected and reported as secondary data;
- f. a primary safety endpoint as Model 5086MRI leads that are placed in the right atrium complication-free rate greater than 92.5% at 5 years, with any clinical adverse events omitted from the primary endpoint collected and reported as secondary data;
 - g. a rigorous process to monitor the status of all study subjects, to actively follow-up missed visits, and to document the reason for all subject dropouts;
 - h. inclusion of a trend analysis process in the protocol to provide a robust early warning mechanism to identify, characterize, and report adverse events, failure modes, and failure rates;
 - i. post-approval study status reporting at least every 6 months and a mechanism for providing non-scheduled trend analysis reports for new information;
 - j. inclusion of a full list of complications, failure modes, and definition of terms within the study protocol; and
 - k. collection of secondary data including implant data, demographic information, all reported adverse device effects, electrical performance, returned product analyses, extraction experience, and other parameters of interest.

2. Multiple MRI Scans Arm will consist of:

- a. enrollment of patients with a REVO SureScan system when they are indicated for a MRI scan, allowing for the enrollment of patients greater than 30 days post implant and the inclusion of EnRhythm MRI IDE subjects;
- b. a design which tests whether the MRI-related complication rate (as an Individual Failure Mode) will be less than 2%, i.e. the one-sided confidence interval upper bound is lower than 2% as a primary endpoint, where 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;
- c. the characterization of the cumulative change in pacing capture thresholds (PCT) for subjects with multiple (2 or more) MRI scans.

The applicant is required to submit PAS Progress Reports every six months.

The applicant's manufacturing facilities were inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XV. Approval Specifications

Directions for Use: See product labeling.

Hazards to Health from use of Device: See Indications, Contraindications, Warnings and Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.