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Medtronic

Clinical Investigation Plan

Clinical Investigation Plan/Study Title	Imaging Study of Lead Implant for His Bundle Pacing (IMAGE-HBP)
Clinical Investigation Plan Identifier	MDT17005
Sponsor/Local Sponsor	Medtronic, PLC. Cardiac Rhythm and Heart Failure Clinical Research 8200 Coral Sea Street NE Mounds View, MN 55112 USA 1-800-328-2518
Document Version	V4 19 Mar 2018
Lead Principal Investigator	Pugazhendhi Vijayaraman, MD Director, Cardiac Electrophysiology Geisinger Wyoming Valley Medical Center 1000 E Mountain Blvd Wilkes Barre, PA 18711 (570) 808-5995 Pvijayaraman1@geisinger.edu

1. Investigator Statement

The Investigator Statement will be provided as a separate document.

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Sponsor Contact Information

Medtronic contact information is provided below. This information is subject to change during the course of the clinical study. Periodic updates to study contact information will be sent to the sites as needed.

Study sponsors and contacts
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Monitoring contacts
US monitoring leader Taryn Randall, Clinical Monitoring Manager Direct Phone: 763-250-0785 Taryn.randall@medtronic.com

CROs and Core Labs

No core labs will be used in this study. At the time of finalization of this clinical investigation plan, there is only one CRO currently planned:

Contact Information	Duties Performed
Cognizant Technology Solutions 500 Frank W Burr Blvd Teaneck, NJ 07666 Direct Phone: 201-801-0233 Direct Fax: 201-801-0243	• Development of study electronic case report forms, edit checks, and study management reports • Review of electronic case report forms, and management of discrepancies

2. Glossary

Below is a list of terms and definitions and/or acronyms used within this document.

Term	Definition
AE	Adverse Event
AVN	Atrioventricular Node
BBB	Bundle Branch Block
CIP	Clinical Investigation Plan
CRF	Case Report Form
CTA	Clinical Trial Agreement
CV	Curriculum Vitae
DD	Device Deficiency
e.g.	For example
eCRF	Electronic Case Report Form
EGM	Electrogram
EKG	Electrocardiogram
EP	Electrophysiology
GCP	Good Clinical Practice
HB	Bundle of His / His Bundle
HBP	His bundle pacing
HIPAA	Health Insurance Portability and Accountability Act
HV	His-Ventricular
IC	Informed Consent
ICF	Informed Consent Form
IPG	Implantable Pulse Generator

Term	Definition
IRB	Institutional Review Board
LAO	Left Anterior Oblique (fluoroscopy view angle)
LV	Left Ventricle
MA	Medical Advisor
MedDRA	Medical Dictionary for Regulatory Activities
PCT	Pacing Capture Threshold
RA	Right Atrial
RAO	Right Anterior Oblique (fluoroscopy view angle)
RV	Right Ventricle
S-QRS	Stimulus to QRS
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
US	United States
V	Ventricle or Ventricular

3. Synopsis

Title	Imaging Study of Lead Implant for His Bundle Pacing (IMAGE-HBP)
Product Name	Medtronic SelectSecure™ MRI SureScan™ Model 3830 pacing lead
Sponsor	Medtronic, PLC Cardiac Rhythm and Heart Failure Clinical Research 8200 Coral Sea Street NE Mounds View, MN 55112 USA 1-800-328-2518
Investigation Purpose	The purpose of this research study is to assess the implant success proportion of the Medtronic SelectSecure™ MRI SureScan™ Model 3830 pacing lead at the bundle of His for His bundle pacing, evaluate implant lead electrical measurements and changes over time, estimate the correlation between lead location and selective vs. non-selective HBP, and estimate the correlation between long-term lead performance and implant characteristics. Data from the study may be used to standardize the implant workflow to help improve the ease and predictability of His bundle pacing implants.
Product Status	The IMAGE-HBP Study will be conducted using market released products. The implanted system will comprise of any market approved Medtronic implantable pacemaker, market approved Medtronic pacing lead for the right atrium (if applicable) and the Medtronic SelectSecure™ MRI SureScan™ Model 3830 pacing lead for His bundle pacing. The Medtronic SelectSecure™ MRI SureScan™ Model 3830 pacing lead is market approved for pacing and sensing in the atrium or ventricle.
Primary Objective(s)	Assess the implant success proportion of the Medtronic SelectSecure™ MRI SureScan™ Model 3830 pacing lead at the bundle of His for His bundle pacing. • Implant success will be defined as the presence of a H wave on the implanted lead electrogram and a His bundle pacing capture threshold equal to or less than 2.5V at 1.0ms.
Secondary Objective(s)	The secondary objectives are descriptive in nature and are intended to provide additional information about His bundle pacing with the Medtronic SelectSecure™ MRI SureScan™ Model 3830 lead. There will be no established performance requirements for these secondary objectives.

	• Estimate the correlation between lead position and selective vs. non-selective His bundle pacing occurrence at implant • Assess changes in lead electrical measurements over time • Assess changes in QRS duration over time • Estimate the correlation between implant characteristics and long-term lead electrical performance at 12 months • Characterize the occurrence of complications related to the procedure or lead for His bundle pacing up to 12 months
Study Design	This is a prospective, non-randomized, multi-site, clinical research study. All subjects included in the study will be implanted with a Medtronic market released de novo Implantable Pacemaker, Medtronic SelectSecure™ MRI SureScan™ Model 3830 lead at the bundle of His for His bundle pacing, and compatible market released Medtronic Right Atrial lead (if applicable). The subjects with an implant of the Medtronic SelectSecure™ MRI SureScan™ Model 3830 lead for His bundle pacing will undergo a Cardiac CT Scan and be followed up to twelve months post implant for electrical testing. Subjects that do not receive an implanted SelectSecure™ MRI SureScan™ Model 3830 pacing lead for His bundle pacing will be exited from the study at the time of the unsuccessful implant or after any reportable Adverse Events are resolved.
Sample Size	Up to 70 patients will be enrolled to ensure approximately 62 patients undergo an implant procedure. • A sample size of 62 patients (who undergo an implant procedure) will produce a two-sided 95% confidence interval with a width equal to 0.15 for the implant success proportion when the observed implant success proportion is 0.9.
Inclusion/Exclusion Criteria	The following is a list of inclusion/exclusion criteria: **Inclusion criteria** • Subject has a Class I or II indication for implantation of an implantable pacemaker • Subject (or legally authorized representative) has signed and dated the study-specific Consent Form • Subject is 18 years of age or older, or is of legal age to give informed consent per local and national law • Subject is expected to remain available for follow-up visits **Exclusion criteria**

	• Subject is contraindicated for Cardiac CT • Subject has an existing or prior pacemaker, ICD or CRT device implant • Subject is intended to receive an implant of a Left Ventricle lead or CRT device • Subject life expectancy is less than 1 year • Pregnant women or breastfeeding women, or women of child bearing potential and who are not on a reliable form of birth regulation method or abstinence • Subjects with exclusion criteria required by local law (e.g. age or other) • Subject with a medical condition that precludes the patient from participation in the opinion of the investigator • Subject is enrolled in a concurrent study that may confound the results of this study. Co-enrollment in any concurrent clinical study (including registries) requires approval of the study manager or designee.
Study Procedures and Assessments	**Enrollment/Baseline** • Eligibility Verification • Informed Consent • Demographics • Primary Indication for implant • Medical History **Implant** • Implant tools used • His mapping testing • Implant procedure times • Final lead electrical testing • Final system configuration • EKG measurements • Fluoroscopy Cine images • Physician Questionnaire **Pre-hospital discharge** • Electrical lead testing • EKG rhythm strips and measurements **Cardiac CT Scan** • Cardiac CT Scan images **1 week, 3 month, 6 month, 12 month Follow-up**

	• Electrical lead testing • Electrical lead testing with strength duration (3 month only) • DR220 Holter monitor (1 week and 3 or 6 month) • EKG rhythm strips and measurements **Adverse Events/Device Deficiency** • Description • Diagnostic tests and procedures • Actions taken • Relatedness and Classifications • Outcome **System Modification** • Reason for modification • Final device information • Final lead electrical testing • EKG printouts and measurements **Protocol Deviation** • Description • Reason **Study Exit** • Reason for exit • Lost to follow-up
Safety Assessments	Device Deficiencies and Adverse Events related to the procedure or Medtronic SelectSecure™ MRI SureScan™ Model 3830 pacing lead for His bundle pacing will be collected. In addition, all SAEs that result in death will be collected.
Statistics	The estimated implant success proportion will be calculated as the proportion of all subjects who undergo an implant attempt that is successful. A 95% confidence interval for the proportion of successful implants will be constructed using the Wilson method.

4. Introduction

4.1. Background

The human cardiac conduction system is admirably suited to deliver coordinated electrical impulses that result in synchronous and mechanically efficient ventricular myocardial contraction. Pacing stimulation at the bundle of His (HB), which conducts through the Purkinje system is fundamentally different than a myocardial stimulation elsewhere in the right ventricle (RV) which results in abnormal physiology. Indeed, chronic right ventricular apical pacing may be associated with increased risk of death[1,2], heart failure, hospitalization[3], and the development of persistent atrial fibrillation[4,5].

The bundle of His, or common atrioventricular (AV) bundle, consists of specialized myocardial cells located distal to the atrioventricular node (AVN). The HB acts as a conduit between the atrium and the ventricles, transmitting depolarization from the AVN through the fibrous skeleton to the right and left bundle branches and ultimately the Purkinje system[6].

Permanent pacing of the HB to restore the native intrinsic AV conduction system continues to gain popularity with implanters.[7] Over the last two decades several investigators reported experience with permanent His bundle pacing (HBP) resulting in paced QRS morphology similar to an intrinsically conducted beat.[8-13] These clinical data showed HBP was feasible and associated with improvement in left ventricular dimensions, functional status, cardiothoracic ratio, and ejection fraction. Reaching the targeted implant area for HBP remains technically challenging because of the lack of anatomical and electrical markers used to facilitate traditional lead implant. Paced QRS morphology is not sufficient to confirm successful HBP location and the fluoroscopic image may mislead the implanter to an undesirable pacing site. AV nodal, HB, AV septal and proximal bundle branch pacing may result in the same QRS morphology but completely different electrical performance (**Figure 1**).[14]

Definitions for Selective HBP and Non-Selective HBP are separated based on the patient's intrinsic QRS morphology and determined by electrocardiogram (EKG) identifiers and pacing capture thresholds (PCT). **Table 1**[15] provides the definitions for Selective and Non-Selective HBP for patients with initial normal QRS and patients with a bundle branch block (BBB).

Table 1: Definitions for His Bundle Pacing

	Normal QRS	Bundle Branch Block#	
		With correction*	Without correction
Selective HBP	• S-QRS = HV with isoelectric interval • Discrete local V electrogram in HBP lead with S-V=H-V • Paced QRS = native QRS • Single capture thresholds (His bundle)	• S-QRS ≤ H-QRS with isoelectric interval • Discrete local V electrogram in HBP lead • Paced QRS < native QRS • 2 distinct capture thresholds (HBP with BBB correction, HBP without BBB correction)	• S-QRS ≤ or > H-QRS with isoelectric interval • Discrete local V electrogram in HBP • Paced QRS = native QRS • Single capture threshold (HBP with BBB)

Non-Selective HBP	• S-QRS < H-QRS (usually 0, $S\text{-}QRS_{end}$ = $H\text{-}QRS_{end}$) with or without isoelectric interval (Pseudodelta wave +/-) • Direct capture of local V electrogram in HBP lead by stimulus artifact (local myocardial capture) • Paced QRS > native QRS with normalization of precordial and limb lead axes with respect to rapid dV/dt components of the QRS • 2 distinct capture thresholds (HBP capture, RV capture)	• S-QRS < H-QRS (usually 0, $S\text{-}QRS_{end}$ < $H\text{-}QRS_{end}$) with or without isoelectric interval (Pseudodelta wave +/-) • Direct capture of local V electrogram in HBP lead by stimulus artifact • Paced QRS ≤ native QRS • 3 distinct capture thresholds (HBP with BBB correction, HBP without BBB correction, RV capture)	• S-QRS < H-QRS (usually 0) with or without isoelectric interval (Pseudodelta wave +/-) • Direct capture of local V electrogram in HBP lead by stimulus artifact • Paced QRS > native QRS • 2 distinct capture thresholds (HBP with BBB, RV capture)

including infra-nodal AV block; * Narrowing of QRS

S-QRS stimulus to QRS; V ventricular; BBB bundle branch block; RV right ventricle; HBP His bundle pacing

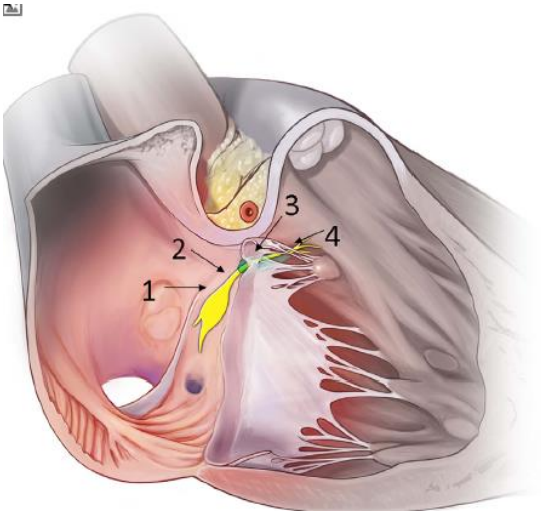


Figure 1: His Bundle Anatomy

Compact AV node (1) converges into a transitional zone (2) before continuing as the His bundle (3) at the apex of triangle of Koch. The His bundle penetrates the membranous septum and continues as bundle branches (4) on the summit of muscular septum.

To address the clinical challenges, the IMAGE-HBP study will seek to evaluate and understand the correlation between implant electrical performance, lead implant location and chronic HBP lead electrical performance.

Additionally, the IMAGE-HBP study will look to identify a correlation between anatomical landmarks and the electrical signature of HBP, which may allow investigators to refine an implant flowchart and lead to a better understanding of use conditions of both implant tools and leads during an implant for HBP.

Therefore, the IMAGE-HBP study will collect data to help improve the ease and predictability of the implant and improve electrical performance of HBP.

4.2. Purpose

The IMAGE-HBP Study is a prospective, non-randomized, multi-site, clinical research study.

The purpose of this research study is to assess the implant success proportion of the Medtronic SelectSecure™ MRI SureScan™ Model 3830 pacing lead at the bundle of His for His bundle pacing, evaluate implant lead electrical measurements and changes over time, evaluate changes in QRS duration over time, estimate the correlation between lead location and selective vs. non-selective HBP, and estimate the correlation between long-term lead performance and implant characteristics. Data from the study may be used to standardize the implant workflow to help improve the ease and predictability of His bundle pacing implants.

5. Objectives and Endpoints

5.1. Objectives

5.1.1. Primary Objective

The primary objective is to assess the implant success proportion of the Medtronic SelectSecure™ MRI SureScan™ Model 3830 pacing lead at the bundle of His for His bundle pacing. Implant success will be defined as the presence of a H wave on the implanted lead EGM and a HB pacing capture threshold equal to or less than 2.5V at 1.0ms.

5.1.2. Secondary Objectives

The secondary objectives are descriptive in nature and are intended to provide additional information about HBP with the SelectSecure™ MRI SureScan™ Model 3830 pacing lead. There will be no established performance requirements for these secondary objectives.

- Estimate the correlation between the lead position and selective vs. non-selective HBP occurrence at implant
- Assess changes in lead electrical measurements over time
- Assess changes in QRS duration over time
- Estimate the correlation between implant characteristics and long-term lead electrical performance at 12 months
- Characterize the occurrence of complications related to the procedure or lead for His bundle pacing up to 12 months

5.1.3. Ancillary Objectives

Additional analyses may be done on data and images collected during the study as outlined below. These analyses are descriptive in nature and are intended to provide additional information about His bundle pacing with the Medtronic SelectSecure™ MRI SureScan™ Model 3830 lead.

- To characterize performance of existing delivery tools and Medtronic SelectSecure™ MRI SureScan™ Model 3830 lead for HBP
- To summarize implant procedure information
- To characterize the survival for subjects up to 12 months post-implant.

6. Study Design

The Imaging Study of Lead Implant for His Bundle Pacing (IMAGE-HBP) is a prospective, non-randomized, multi-site, clinical research study. The purpose of this research study is to assess the implant success proportion of the Medtronic SelectSecure™ MRI SureScan™ Model 3830 pacing lead at the bundle of His for His bundle pacing, evaluate implant lead electrical measurements and changes over time, evaluate changes in QRS duration over time, estimate the correlation between lead location and selective vs. non-selective HBP, and estimate the correlation between long-term lead performance and implant characteristics. Data from the study may be used to standardize the implant workflow to help improve the ease and predictability of His bundle pacing implants.

All subjects included in the study will be implanted with a Medtronic market released de novo implantable pacemaker, Medtronic SelectSecure™ MRI SureScan™ Model 3830 lead for HBP, and compatible market released Medtronic Right Atrial lead (if applicable). The subjects with an implant of the Medtronic SelectSecure™ MRI SureScan™ Model 3830 lead for HBP will undergo a Cardiac CT Scan and be followed up to twelve months post implant for electrical testing. Subjects that do not receive an implanted SelectSecure™ MRI SureScan™ Model 3830 pacing lead for HBP will be exited from the study at the time of the unsuccessful implant or after any reportable AEs are resolved.

An unsuccessful implant is not considered an adverse event; however any adverse events occurring during an unsuccessful implant attempt (e.g. perforation) must be evaluated for reporting.

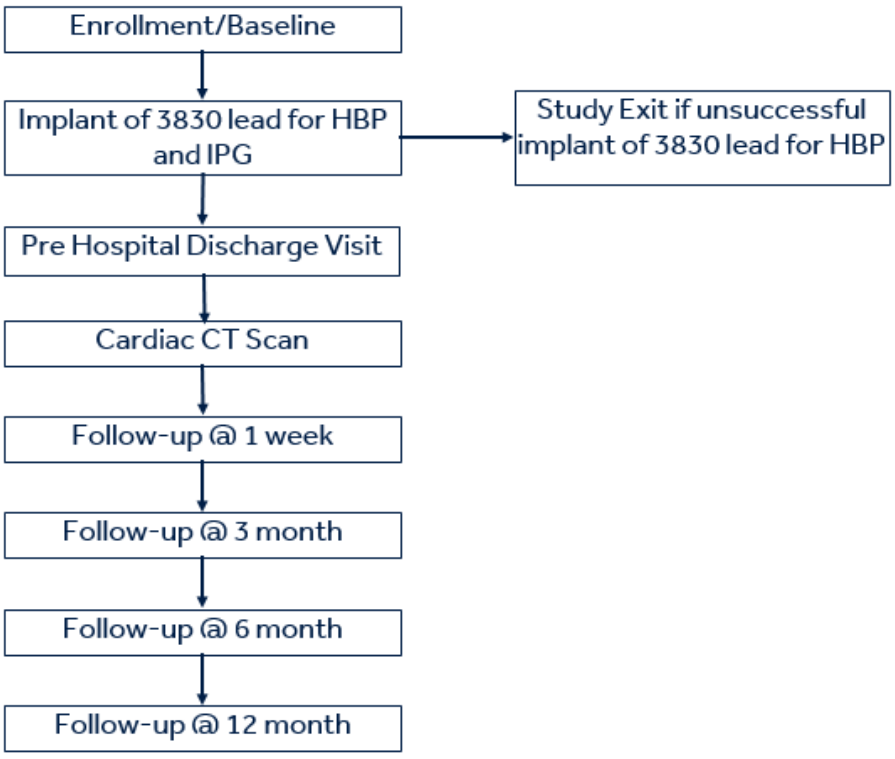
The SelectSecure™ MRI SureScan™ Model 3830 pacing lead implant for HBP procedure data collection will occur during the standard implant procedure and is expected to add approximately 20 minutes to the procedure. This time includes:

- Collection of electrical measurements during lead placement and fixation
- Two fluoroscopy cine image views of final lead system implant

The study will enroll up to 70 subjects in order to achieveapproximately 62 subjects who will undergo an intended Medtronic SelectSecure™ MRI SureScan™ Model 3830 lead implant procedure attempt for HBP. The study is expected to be conducted at up to 5 sites in the United States (US).

See **Figure 2** and Section 9 for further detail on study procedures and data collection as well as time points for data collection.

Figure 2: Study Visits



6.1. Duration

The study duration is expected to be approximately 28 months from first center activation until closure. This represents 10 months for subject enrollments, 12 months for subject follow-up and 6 months for study closure. Subjects are anticipated to be in the study for 12 months. Subjects will complete visits at enrollment/baseline, implant, pre-hospital discharge, 1 week, 3 months, 6 months and 12 months.

6.2. Rationale

Over the last two decades several investigators reported experience with permanent HBP resulting in paced QRS morphology similar to an intrinsically conducted beat.[8-13] These clinical data showed HBP was feasible and associated with improvement in left ventricular dimensions, functional status, cardiothoracic ratio, and ejection fraction. Reaching the targeted implant area for HBP remains technically challenging[14]. To address the clinical challenges, the IMAGE-HBP study will seek to evaluate and understand the correlation between lead location implant electrical performance using electro-anatomical images and chronic HBP lead electrical performance. The study will collect data to help improve the ease and predictability of the implant and better electrical performance of HBP.

See section 4 for further background on the study design. See section 13 for further background information and evaluation of clinical data.

7. Product Description

7.1. General

The study will be conducted using the components described in section 7.5. All components are market released and will be used according to approved indications. Instructions for use of the devices used in this study are provided in their respective manuals.

7.2. Manufacturer

The SelectSecure™ MRI SureScan™ Model 3830 pacing lead is manufactured by Medtronic, PLC. In addition, all other study equipment is manufactured by Medtronic, unless otherwise noted.

7.3. Packaging

Packaging and labeling for all market approved system components can be found with each package insert. Manuals can be found on *http://manuals.medtronic.com*

7.4. Intended Population

All subjects in this study will receive a Medtronic single or dual chamber pacemaker for approved indications.

7.5. Equipment

All of the components are being used according to approved labeling.

Medtronic SelectSecure™ MRI SureScan™ Model 3830 Lead or Medtronic SelectSecure Model 3830 Lead

The Medtronic SelectSecure™ MRI SureScan™ Model 3830 steroid eluting, bipolar, implantable, nonretractable screw-in, atrial/ventricular, catheter delivered, transvenous lead is designed for pacing and sensing in the atrium or ventricle. The Medtronic SelectSecure™ MRI SureScan™ Model 3830 may also be labeled and referred to as the Medtronic SelectSecure Model 3830.

Medtronic Leads and Pacemaker device

The Medtronic lead is a commercially available bipolar pace/sense lead labeled for implantation in the right atrium or right ventricle. The leads are connected to a commercially available Medtronic implantable pacemaker.

Medtronic Delivery Catheter

The Medtronic delivery catheters are commercially available and indicated for the introduction of various types of pacing or defibrillator leads and catheters within the chambers.

Medtronic CareLink (2090) Programmer

The Medtronic approved IPG devices will be programmed and interrogated using a Medtronic CareLink (2090) programmer or Medtronic CareLink Encore programmer. Medtronic may incorporate additional programmers as they receive regulatory approval.

Medtronic Pacing System Analyzer

Medtronic's commercially available Model 2090 Analyzer must be available at each center during the implant procedure to determine acceptable electrical parameters. Medtronic may incorporate additional analyzers as they receive regulatory approval.

Medtronic Model 5833SL Cable

The Medtronic Model 5833SL surgical cables will provide connectivity from the lead connector pins to the Temporary Extension Cable.

Temporary Extension Cables

The temporary extension cables connect the Medtronic Model 5833SL Cable to the EP Data recording system. The cable features a patented 2 mm protected pin quick connection allowing for a safe and fast connection between an electrode/lead from a patient or another cable to a diagnostic machine or an external pacemaker. (e.g. Cardiotronic Osypka Medical XI.MDT)

Disposable Pacing Cable

Disposable Pacing Cable used for transvenous and temporary pacing. The cable is designed to provide a safe connection between 2 mm shrouded pin pacing catheters and Medtronic temporary pacemaker or Medtronic Pacing System Analyzer. (e.g. Remington Medical Adap-2000-12)

EP Data recording system

The EP recording system used in this procedure must be able to record and export data in a digital format and provide standard 2 mm female touch protected sockets for connectivity. The EP recording system will record signals originating from the electrodes in the Medtronic SelectSecure™ MRI SureScan™ Model 3830 lead or market released EP catheter and save them in an electronic format for subsequent analysis.

DR220 Holter Monitor

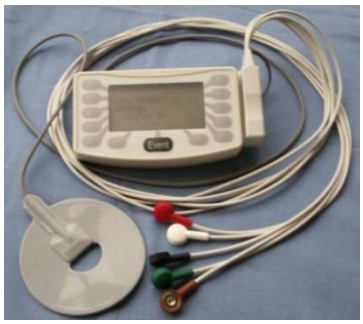
The DR220 Digital Recorder (NorthEast Monitoring, Inc, MA, USA) is a Holter monitor that is designed to facilitate the ambulatory cardiac monitoring of those subjects who may benefit from such monitoring on order of a physician, including but not limited to those with complaints of palpitations, syncope, chest pains, shortness of breath, or those who need to be monitored to judge their current cardiac function, such as subjects who have recently received pacemakers. The DR220 Digital Recorder is intended for use with Medtronic System-B compatible implantable pulse generators, implantable cardiac defibrillators, and cardiac resynchronization therapy devices and implantable cardiac monitors. A Holter monitor is an external box used to record electrical heart signals from electrode patches attached to the skin (ECG) as well as from the cardiac device (EGM). There are no contraindications for the use of a DR220 Holter monitor. The Holter monitor will be used in accordance with its labeling. Only trained study personnel should apply the monitors.

The data obtained by monitoring is not analyzed at the time of the recording. After the recording is complete, the data must later be returned and analyzed at Medtronic. No personal information will be entered and collected by DR220 recorder.

The DR220 Holter Recorder used in this study is a portable ECG device able to collect telemetry signals and marker channel information from a Medtronic device for up to 48 hours. For the purposes of this study, the holter will be used during the in-office visit and will be removed at the conclusion of the visit. Each patient will have 2 DR220 Holter monitors collected during the study. The first during the 1 week

visit and second at the 3 month visit (the second can be collected at the 6 month visit if missed at the 3 month visit). The Holter Recorder has application for any subject with a Medtronic IPG. For the purposes of this study, the intended use of the Holter Recorder is to acutely uplink continuous EGM signals that will be collected by the IPG in Holter mode.

Figure 3: DR220 Holter



8. Selection of Subjects

8.1. Study Population

Subjects of both genders that are 18 years of age and older (or of legal age to give informed consent per local and national law) that are indicated for a de novo pacemaker implant and lead for His bundle pacing who meet all inclusion and no exclusion criteria are eligible for the study. There will be no control group for this study.

8.2. Subject Enrollment

Subjects who meet all the inclusion and none of exclusion criteria (see sections 8.3 and 8.4) are eligible to be enrolled in the study. Upon signing and dating the Informed Consent Form (ICF), the patient is considered enrolled in the study.

8.3. Inclusion Criteria

- Subject has a Class I or II indication for implantation of an implantable pacemaker
- Subject (or legally authorized representative) has signed and dated the study-specific Consent Form
- Subject is 18 years of age or older, or is of legal age to give informed consent per local and national law
- Subject is expected to remain available for follow-up visits

8.4. Exclusion Criteria

- Subject is contraindicated for Cardiac CT
- Subject has an existing or prior pacemaker, ICD or CRT device implant
- Subject is intended to receive an implant of a LV lead or CRT device
- Subject life expectancy is less than 1 year
- Pregnant women or breastfeeding women, or women of child bearing potential and who are not on a reliable form of birth regulation method or abstinence
- Subjects with exclusion criteria required by local law (e.g. age or other)
- Subject with a medical condition that precludes the patient from participation in the opinion of the investigator
- Subject is enrolled in a concurrent study that may confound the results of this study. Co-enrollment in any concurrent clinical study (including registries) requires approval of the study manager or designee.

8.5. Minimization of Bias

Potential sources of bias in this study may result from selection of subjects, treatment of subjects, and evaluation of study data. Methods incorporated in the study design to minimize potential bias include but are not limited to:

- To ensure widespread distribution of data between sites, the maximum number of subjects allowed per site is half of the final study implant attempt enrollments.
- Patients will be screened to confirm eligibility for enrollment with defined inclusion/exclusion criteria prior to enrollment (Section 8.3 and 8.4)
- Subject demographics will be collected at baseline to investigate possible differences that may affect study endpoints
- Data collection requirements and study procedures will be standardized across all centers
- All study center personnel and Medtronic personnel will be trained on their respective roles in the study using standardized training materials. All study clinicians will be trained on and required to follow the CIP.
- All implanters in the study will have at least 1 year of experience in the implantation of the Medtronic SelectSecure™ MRI SureScan™ Model 3830 pacing lead for His bundle pacing and has performed at least 20 procedures

In summary, potential sources of bias that may be encountered in this clinical investigation have been considered and minimized by careful study design.

9. Study Procedures

9.1. Schedule of Events

Table 2: Data collection and study procedure requirements

Study Procedure	Enrollment /Baseline	Implant	Cardiac CT Scan	Pre-Hospital Discharge, 1 week, 6 month, 12 month	3 month	Study exit
Patient informed consent	X					
Inclusion/Exclusion Assessment	X					
Demographics	X					
Medical History	X					
Implant procedure times		X				
Physician questionnaire		X				
Pacing Capture Thresholds at 0.5ms and 1.0ms		X		X	X	
Pacing Capture Thresholds for strength duration curve		X			X	
12 Lead EKG rhythm strips and measurements		X		X	X	
Device interrogation / Save-to-media		X		X	X	X
Cine images RAO 30 / LAO 60		X				
EP recordings		X				
Cardiac CT Scan			X			
Holter (DR220)				X* (1 week visit)	X*	
Exit subject						X
Study deviations		As they occur				
System modifications						
Adverse Events / Deaths						
Device Deficiencies						

*2 Holters will be collected per patient. First at 1 week and the second at the 3 month visit (the second can be collected at the 6 month visit if missed at the 3 month visit).

9.2. Subject Screening

Screening will be performed as patients are scheduled for initial pacemaker implants with intended lead placement for His bundle pacing.

9.3. Subject Consent

The patient is considered enrolled in the study upon signing and dating the informed consent form. Informed Consent is defined as a legally effective documented confirmation of a subject's (or their legally authorized representative) voluntary agreement to participate in a particular clinical study after information has been given to the subject on all aspects of the clinical study that are relevant to the subject's decision to participate. This process includes obtaining an Informed Consent Form (ICF) and an Authorization to Use and Disclose Personal Health Information/Research Authorization/and other privacy language as required by law that has been approved by the study site's Ethics Committee/Institutional Review Board (IRB) and signed and dated by the subject (or their legally authorized representative). A subject may only consent after information has been given to the subject on all aspects of the clinical investigation that are relevant to the subject's decision to participate. Informed consent may be given by the legally authorized representative only if a subject is unable to make the decision to participate in a clinical investigation and the site/IRB agrees to allow this. In such cases, the subject shall also be informed about the clinical investigation within his/her ability to understand.

Investigators shall consider all subjects who meet eligibility requirements for study participation to avoid any bias in the subject population. Prior to enrolling subjects, each site's Ethics Committee/IRB will be required to approve the CIP, ICF, the Authorization to Use and Disclose Personal Health Information/Research Authorization/other privacy language, and any other written study information to be provided to the subjects. The document(s) must be controlled (i.e. versioned and/or dated) to ensure it is clear which version(s) were approved by the Ethics Committee/IRB. Any adaptation of the sample ICF must be reviewed and approved by Medtronic and the Ethics Committee/IRB reviewing the application prior to enrolling subjects.

Refer to Appendix B for the sample Informed Consent Form.

The investigator must notify the subject (or their legally authorized representative) of any significant new findings about the study that become available during the course of the study which are pertinent to the safety and well-being of the subject, as this could impact a subject's willingness to participate in the study. If relevant, approval may be requested from subjects to confirm their continued participation.

Prior to initiation of any study-specific procedures, patient informed consent must be obtained from the subject (or their legally authorized representative). Likewise, privacy or health information protection regulation may require subjects to sign additional forms to authorize sites to submit subject information

to the study sponsor. The informed consent process must be conducted by the principal investigator or an authorized designee, and the ICF and Authorization to Use and Disclose Personal Health Information/ Research Authorization/other privacy language as required by law must be given to the subject (or their legally authorized representative) in a language he/she is able to read and understand. The process of patient informed consent must be conducted without using coercion, undue improper influence on or inducement of the subject to participate by the investigator or other site personnel. The informed consent process shall not waive or appear to waive the subject's legal rights. The language used shall be as non-technical as possible and must be understandable to the subject and the impartial witness, where applicable.

The subject must have ample time and opportunity to read and understand the ICF, to inquire about details of the study, and to decide whether to participate in the clinical study. All questions about the study should be answered to the satisfaction of the subject.

When the subject decides to participate in the clinical study, the ICF and the Authorization to Use and Disclose Personal Health Information/research Authorization/other privacy language must be signed and personally dated by the subject and investigator or authorized designee, as required by local law. If applicable, a witness shall also sign and personally date the ICF to attest that the information in the ICF was accurately explained and clearly understood by the subject, and that informed consent was freely given.

A copy of the ICF and the Authorization to Use and Disclose Personal Health Information/research Authorization/other privacy language, signed and dated as required by law, must be provided to the subject.

If the ICF is obtained the same day the subject begins participating in study-related procedures, it must be documented in the subject's case history that consent was obtained prior to participation in any study-related procedures. It is best practice for the informed consent process to be documented in the subject's case history, regardless of circumstance.

In the event the subject cannot read and/or write, a witnessed (impartial third party) IC will be allowed, provided detailed documentation of the process is recorded in the subject's case history and the witness signs and dates the ICF. The subject should "make his/her mark" (sign, or otherwise physically mark, the document so as to indicate consent) on the ICF as well. The ICF should document the method used for communication with the prospective subject and the specific means by which the prospective subject communicated agreement to participate in the study.

The original of the signed ICF and the Authorization to Use and Disclose Personal Health Information/Research Authorization/other privacy language as required by law must be filed in the hospital/clinical chart or with the subject's study documents. The ICF and Authorization to Use and Disclose Personal Health Information/Research Authorization/other privacy language as required by law must be available for monitoring and auditing. Any Medtronic personnel who support the study

procedure must be able to review the subject's signed and dated ICF and verify its completeness prior to proceeding with the procedure. In the event that Medtronic personnel identify patient informed consent as being incomplete, the study procedures will not be allowed to occur until the consent of the subject can be adequately and appropriately obtained.

9.4. Enrollment

The point of enrollment is defined as the time at which a patient has signed and dated the ICF. The date the subject signed (or legally authorized representative) the ICF and data protection authorization, as required by law, must be documented in the subject's medical records. At that point, the patient is considered a subject in the study, a study subject ID number will be assigned, and the subject must be followed through their 12 month post-implant clinic visit unless the subject exits the study prior to study closure. Once informed consent is obtained, report AEs/deaths, study deviations and subject exits as they occur.

9.5. Enrollment Data Collection

An Enrollment Form will be completed for all study subjects, which will collect at a minimum the following information:

- Standard demographics
- Medical History
- Adherence to inclusion/exclusion criteria

9.6. Implant

For this study a successful implant of a lead for His bundle pacing is defined as His bundle pacing capture threshold of less than or equal to 2.5V at 1.0ms.

9.7. Implant Data Collection

The implant CRF will be used to collect data at implant.

The implanted system must include a Medtronic commercially released IPG device, SelectSecure™ MRI SureScan™ 3830 lead for His bundle pacing and a second market approved lead (if applicable).

Set-up and Implantation

The following steps outline the suggested setup procedure for the study. The specific order is a guideline, not a requirement:

- Assemble the HBP recording system according to the IMAGE-HBP Study Procedure Workbook
- Prep subject for standard IPG implant and HB mapping
- Use SelectSecure delivery system of choice to place a SelectSecure™ MRI SureScan™ Model 3830 lead to the desired HB location.
- Implant SelectSecure™ MRI SureScan™ model 3830 lead for HBP
- Perform lead sensing, impedance and pacing capture threshold tests. Print threshold test strips at final implant location at 0.5ms and 1.0ms
- Remove delivery system
- Collect RAO 30/LAO 60 cine images of final lead location after delivery system removal
- Implant second lead (if applicable) and permanent pacemaker as standard procedure

Electrical Mapping and 12 lead EKG recording

- Print an initial 12 lead through EP recording system of patient intrinsic rhythm
- Pacing capture threshold for each lead location
- Record HV interval, Stimulus-V interval, QRS duration, P wave amplitude and R wave amplitude for each testing location

Pacing Capture Thresholds (PCT) / Sensing / Impedance at final lead location

- Perform a manual HB and RV PCT through the analyzer and device at 0.5ms and 1.0ms and print threshold test strips
- For Selective HB patients perform a manual HB PCT at 0.1 (or 0.12) ms; 0.2 (or 0.21) ms; 0.76 (or 0.8) ms ; and 1.5 ms and print test results
- Print a screen of pacing at HB PCT, RV PCT at 0.5ms and 1.0ms from EP recording system
- Document R wave and impedance results

Physician Questionnaire

Other Data Collection

- Final device interrogation/Save to Media
- Adverse Events
- Study deviations
- Device Deficiencies

9.8. Scheduled Follow-up Visits

After the index implant of a Medtronic SelectSecure™ MRI SureScan™ Model 3830 pacing lead for His bundle pacing is reported in the study database, the database will calculate the target dates and windows for each follow-up visit to the site. Should a subject miss a visit or the visit fall outside the pre-

specified window, a study deviation must be reported and the original follow-up schedule maintained for subsequent visits.

Data analyses include follow-up visits, regardless of whether the visit occurs within the window. Therefore, a late visit is preferred over a missed visit but must be accompanied by a deviation. Follow-up visit windows are listed in **Table 3** and are based on days post-index procedure.

Subject compliance to the follow-up windows will be monitored through protocol deviation reporting.

Table 3: Follow-up Visit Windows

Occurrence/Visit	Window (Calculated days post-procedure)	
	Window Start (# of days)	Window End (# of days)
Pre-hospital discharge	0	5
Cardiac CT Scan	0	17
1 week office	5	17
3 month office	60	106
6 month office	153	213
12 month office	335	395

9.8.1. Pre-Hospital Discharge

The following electrical testing will be performed using the implanted IPG and the device programmer:

Pacing Capture Thresholds (PCT) / Sensing / Impedance measurements

- Perform a manual HB and RV PCT at 0.5ms and 1.0ms and print threshold test strips
- Document R wave and impedance results

12 Lead EKG rhythm strip

- Print 12 lead EKG rhythm strip capturing presenting rhythm, intrinsic rhythm, PCTs at 0.5ms, PCTs at 1.0ms and while pacing at final device programmed outputs and document QRS duration for each

Other Data Collection

- Final device interrogate ALL and Save to Media
- Adverse Events
- Study deviations
- Device Deficiencies

9.8.2. Cardiac CT Scan

The following data will be collected during the Cardiac CT Scan.

- Cardiac CT Scan with contrast focusing on RA and RV chambers

9.8.3. 1 week, 6 month and 12 month visit

The following electrical testing will be performed using the implanted IPG and the device programmer. In addition, a DR220 Holter monitor will be used at the 1 week visit. The DR220 Holter monitor will also be used at the 6 month visit if missed at the 3 month visit.

Pacing Capture Thresholds (PCT) / Sensing / Impedance measurements

- Perform a manual HB and RV PCT at 0.5ms and 1.0ms and print threshold test strips
- Document R wave and impedance results

12 Lead EKG rhythm strip

- Print 12 lead EKG rhythm strip capturing presenting rhythm, intrinsic rhythm, PCTs at 0.5ms, PCTs at 1.0ms and while pacing at final device programmed outputs and document QRS duration for each

Other Data Collection

- Final device interrogate ALL and Save to Media
- Adverse Events
- Study deviations
- Device Deficiencies

9.8.4. 3 month visit

The following electrical testing will be performed using the implanted IPG and the device programmer. In addition, a second DR220 Holter monitor will be used at the 3 month visit (if not able to collect at this visit, collect at the 6 month visit).

Pacing Capture Thresholds (PCT) / Sensing / Impedance measurements

- Selective HBP patients
  - Perform a manual HB PCT at 0.1 (or 0.12) ms; 0.2 (or 0.21) ms; 0.5 (or 0.52) ms; 0.76 (or 0.8) ms ; 1.0 ms; and 1.5 ms and print test results
  - Perform a manual RV PCT at 0.5ms and 1.0ms and print threshold test strips
  - Document R wave and impedance results

- Non-Selective HBP patients
  - Perform a manual HB and RV PCT at 0.5ms and 1.0ms and print threshold test strips
  - Document R wave and impedance results

12 Lead EKG rhythm strip

- Print 12 lead EKG rhythm strip capturing presenting rhythm, intrinsic rhythm, at all PCTs and while pacing at final device programmed outputs and document QRS duration for each

Other Data Collection

- Final device interrogate ALL and Save to Media
- Adverse Events
- Study deviations
- Device Deficiencies

9.9. Device Interrogation / Save-to-Media

For the implant and follow-up visits, a final "Interrogate ALL" device interrogation file (.pdd) must be obtained and saved in a digital format (Save-to-Media). Store one copy of the save-to-media at the site and send a copy to Medtronic. Do not clear device data.

A device interrogation (final "Interrogate ALL") and Save-to-Media should also be completed at the time of study exit, system modification and in the case of a death (where possible).

9.10. System Modification

A system modification CRF will be completed in the event the device and/or lead(s) require invasive modification (e.g. generator or lead explant, generator or lead replacement, lead repositioning). In the event of a system modification, regardless of outcome of the modification, the follow-up visit schedule for the subject will remain unchanged. For a system modification, the following information/activities are required to be collected:

- Modification or replace/explant date
- Reason for modification
- Information on device or lead modified
- Information on any replacement device or lead(s)
- SelectSecure™ MRI SureScan™ Model 3830 Pacing Capture Thresholds at 0.5ms and 1.0ms
- Final System Configuration
- Initial and Final device interrogate ALL and save-to-media
- Adverse Events
- Study deviations
- Device Deficiencies

It is recommended that all explanted Medtronic products (device, leads, etc.) are returned to Medtronic for analysis per local process and when permissible by local laws and regulations.

In the event that a subject has a re-attempt after a previous unsuccessful system modification, the subsequent attempt(s) must be reported via CRF as separate system modifications.

9.11. Subject Withdrawal or Discontinuation

Study exit is defined as the moment when a subject officially stops participating in the study. From that moment onward no data will be collected from the subject. The date and the reason for exiting the subject must be reported to Medtronic at the earliest opportunity.

Subjects will be exited from the study for any of the following situations:

- Study completed
- Subject does not have an implant of a SelectSecure™ MRI SureScan™ 3830 lead for His bundle pacing
- Subject death
- Subject lost to follow-up
- Subject did not meet eligibility criteria
- Subject chooses to exit
- Investigator withdraws subject

If possible, the following procedures should be performed / data collected at the exit visit:

- Report the reason for exit
- Final interrogate ALL and save-to-media file for exits occurring prior to the 12 month visit
- Adverse Events
- Study deviations
- Device Deficiencies

Following exit, subjects will continue to receive standard medical care. There will be no further required study-related follow-up visits for these subjects. All data through the time of the subject's exit will be available for data analyses.

9.11.1. Lost to Follow-up

In the case that the subject is determined to be lost to follow-up, details of a minimum of two attempts and the method of attempt (e.g., one letter and one phone record or two letters) to contact the subject must be recorded. In addition, follow the regulations set forth by the governing IRB.

9.11.2. Subject chooses to exit (i.e. revokes informed consent)

A subject can withdraw from the study at any time. If the subject wishes to exit from the study (i.e. the subject revokes informed consent), the site is required to document the reason for exit on the Study Exit eCRF. In addition, study sites shall follow the regulations set forth by the governing IRB. If possible, the following data should be collected prior to subject withdrawal:

- Report the reason for the subject withdrawal
- Final device interrogation/save-to-media
- Adverse Events
- Study deviations
- Device deficiencies

9.11.3. Investigator Withdraws Subject

No subjects should be withdrawn by investigators unless compelling medical justification is present. It is recommended investigators discuss any withdrawals with the study sponsor prior to exiting subjects. If an Investigator withdrawal is necessary, the following data should be collected prior to subject withdrawal if possible:

- Report the reason for subject withdrawal
- Final device interrogation/save-to-media
- Adverse Events
- Study deviations
- Device deficiencies

9.12. Assessment of Safety

Device Deficiencies and Adverse Events related to the procedure or Medtronic SelectSecure™ MRI SureScan™ Model 3830 pacing lead for His bundle pacing will be collected. In addition, all SAEs that result in death will be collected. Further information on the collection and assessment of Adverse Events is discussed in Section 11.

9.13. Recording Data

The study will collect data using Oracle Clinical, an electronic data management system for clinical studies. Sites will enter data onto electronic case report forms (eCRFs) within the Oracle Clinical database.

Data reported on the eCRFs shall be derived from source documents, which may include worksheets, patient medical records, EP Recording system printouts, 12 lead EKG, Device interrogation files, fluoroscopy image files, and programmer threshold test printouts. These source documents must be created and maintained by the clinical research study site team. Further detail on data management is provided in Section 15.2.

9.14. Deviation Handling

A deviation is defined as an event in which the investigator or site personnel did not conduct the study according to the Clinical Investigational Plan (CIP) or applicable laws and regulations. Every attempt must be made to avoid deviations.

In the event the investigator deviates from the CIP to protect the life or physical well-being of a subject in an emergency, the investigator shall notify the sponsor and reviewing IRB within 5 working days after the emergency occurred.

Except in such an emergency, prior approval by the sponsor is required for changes in or deviations from the CIP. Prior approval is not expected in situations where unforeseen circumstance is beyond the investigator's control.

Medtronic will be responsible for documenting and analyzing deviations, assessing their significance, and identifying any necessary corrective and/or preventive action. All deviations will be recorded on the Protocol Deviation Case Report Form. Medtronic will provide site-specific reports to investigators summarizing information on deviations that occurred at the investigational site on a periodic basis.

10. Risks and Benefits

10.1. Potential Risks

Medtronic 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.

All devices used in the IMAGE-HBP study will be commercially released and used in accordance with their approved labeling. The safety and clinical performance of these devices have been demonstrated through previous-pre-clinical testing and previous clinical studies.

Subjects who are pregnant may be at increased risk (e.g. radiation exposure and other unforeseen risk to the fetus), and are excluded from participation in the study. If a subject becomes pregnant during the study, she must notify the physician immediately. The subject will remain in the study for analysis, but the investigator will avoid any procedures that may be determined harmful.

Incremental risks for participating in this study may include the following risks associated with the additional procedures listed below:

- Risk associated with Fluoroscopy exposure
  - During the implant procedure, additional cine recordings will be collected at the final lead fixation location. The duration of the extra radiation exposure is expected to be less than 5 minutes of incremental time beyond what would be experienced during a standard implant procedure.
- Risk associated with Cardiac CT Scans
  - Exposure to radiation from one test is similar to the amount of radiation you are naturally exposed to over one to five years.
  - The Cardiac CT Scan may detect an incidental finding, which is something that doesn't cause symptoms now but may require more tests after being found.
  - Allergic reaction to contrast used during the Cardiac CT Scan

10.2. Potential Benefits

There may be no direct benefit to the subject from participating in this study. The benefits of receiving a lead implant for His bundle pacing are the same if the patient participates in the study or not.

The Cardiac CT Scan performed in this study is not for diagnostic purposes. However, any potential abnormalities that are identified by the site investigator will be relayed to the subject with instruction for medical follow up.

10.3. Risk-Benefit Rationale

All identified risks as described in the previous sections have been successfully mitigated. Any potential risks associated with this study are further minimized by selecting qualified investigators and training study personnel on the CIP. While there may be no benefit of participation in the study there is the potential to aid in collecting information that may lead to new His bundle implant techniques for pacing.

Overall residual risk of participating in the IMAGE-HBP study is considered acceptable.

11. Adverse Events and Device Deficiencies

Timely, accurate, and complete reporting and analysis of safety information for clinical studies are crucial for the protection of subjects. Medtronic has established procedures to ensure appropriate reporting of safety information.

11.1. Adverse Events

Adverse Event (AE) definitions are provided in **Table 4**. The following AEs will be collected throughout the study duration:

- All AEs related to the Medtronic SelectSecure™ MRI SureScan™ model 3830 lead for His bundle pacing
- Procedure related AEs related to the Medtronic SelectSecure™ MRI SureScan™ model 3830 lead for His bundle pacing
- SAEs resulting in subject death

Events should be reported for the procedure or the lead for His bundle pacing that are considered to be possibly related, probably related or have a causal relationship.

Reporting of these events to Medtronic will occur on an AE eCRF, including date of AE, treatment, resolution, assessment of both the seriousness of the AE and the relatedness to the product. Each AE must be recorded on a separate AE eCRF. Documented pre-existing conditions are not considered AEs unless the nature or severity of the condition has worsened.

For AEs that require immediate reporting (see **Table 6**), initial reporting may be done by phone, email or on the eCRF completing as much information as possible. The original completed AE eCRF must be submitted to Medtronic as soon as possible.

Any medication, whether cardiovascular or not, associated with the treatment of an AE must be reported. Medication changes that are not related to adverse events will not be collected.

Subject deaths are also required to be reported. Refer to Section 11.6 for Subject Death collection and reporting requirements.

11.2. Device Deficiencies

Device Deficiency (DD) information will be collected throughout the study and reported to Medtronic. Note that DDs that result in an Adverse Device Effect (ADE) to the subject should be captured on the AE eCRF only. Device Deficiencies that did not lead to an AE but could have led to a Serious Adverse Device Effect (SADE) (i.e. if suitable action had not been taken, if intervention had not been made, or if the circumstances had been less fortunate) require immediate reporting (see **Table 6**). For DDs that require immediate reporting, initial reporting may be done by contacting the study sponsor per the sponsor contact information.

11.3. Processing Updates and Resolution

For any changes in status of a previously reported AE (i.e. change in actions taken, change in outcome, change in relatedness), information needs to be updated on, or added to the original AE eCRF. All AEs must be followed until the AE has been resolved, the subject dies or exits the study, or until study closure, whichever occurs first.

At the time of the study exit, all collected AEs with an outcome of "not recovered/not resolved", "recovering/resolving" or "unknown" must be reviewed and updates provided as applicable.

11.4. Definitions/Classifications

Where the definition indicates "device", it refers to the SelectSecure™ MRI SureScan™ Model 3830 pacing lead for His bundle pacing used in the study.

Table 4: Adverse Event and Device Deficiency Definitions

General	
Adverse Event (AE) (ISO 14155:2011, 3.2)	Any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other person, whether or not related to the investigational medical device NOTE 1: This definition includes events related to the investigational medical device or the comparator. NOTE 2: This definition includes events related to the procedures involved. NOTE 3: For users or other persons, this definition is restricted to events related to investigational medical devices.
Adverse Device Effect (ADE) (ISO 14155:2011, 3.1)	Adverse event related to the use of an investigational medical device NOTE 1: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device. NOTE 2: This definition includes any event resulting from an error use or from intentional misuse of the investigational medical device.
Device Deficiency (DD) (ISO 14155:2011, 3.15)	Inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance. NOTE: Device deficiencies include malfunctions, use errors and inadequate labeling.
Relatedness	

Lead for His bundle pacing Related	An adverse event that results from the presence or performance (intended or otherwise) of the lead for HBP
Procedure Related	An Adverse Event that is **directly** related to the implantation or surgical modification of the lead for His bundle pacing. NOTE: In general, this excludes events that are inherent to any surgical procedure (e.g. anesthesia complications) as well as indirect subsequent consequences of the procedure (e.g. reaction to pain medication).
Not Related	Relationship to the device or procedures can be excluded when: • The event is not a known side effect of the product category the device belongs to or of similar devices and procedures; • The event has no temporal relationship with the use of the investigational device or the procedures; • The serious event does not follow a known response pattern to the medical device (if the response pattern is previously known) and is biologically implausible; • The discontinuation of medical device application or the reduction of the level of activation/exposure – when clinically feasible – and reintroduction of its use (or increase of the level of activation/exposure), do not impact on the serious event; • The event involves a body-site or an organ not expected to be affected by the device or procedure; • The serious event can be attributed to another cause (e.g. an underlying or concurrent illness/clinical condition, an effect of another device, drug, treatment or other risk factors); • The event does not depend on a false result given by the investigational device used for diagnosis, when applicable; • Harms to the subject are not clearly due to use error; • In order to establish the non-relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the serious event. *The study will not be collecting AEs that are not related to the lead for His bundle pacing

Unlikely	The relationship with the use of the device seems not relevant and/or the event can be reasonably explained by another cause, but additional information may be obtained. *The study will not be collecting AEs that are unlikely related to the lead for His bundle pacing
Possible	The relationship with the use of the investigational device is weak but cannot be ruled out completely. Alternative causes are also possible (e.g. an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or treatment). Cases were relatedness cannot be assessed or no information has been obtained should also be classified as possible.
Probably	The relationship with the use of the investigational device seems relevant and/or the event cannot reasonably be explained by another cause, but additional information may be obtained
Causal Relationship	The event is associated with the device or study procedures beyond reasonable doubt when: • The event is a known side effect of the product category the device belongs to or of similar devices and procedures; • The event has a temporal relationship with device use/application or procedures; • The event involves a body-site or organ that the device or procedures are applied to or the device or procedures have an effect on; • The serious event follows a known response pattern to the medical device (if the response pattern is previously known); • The discontinuation of medical device application (or reduction of the level of activation/exposure) and reintroduction of its use (or increase of the level of activation/exposure) impact on the serious event (when clinically feasible); • Other possible causes (e.g., an underlying or concurrent illness/clinical condition or/and an effect of another device, drug, or treatment) have been adequately ruled out; • Harm to the subject is due to error in use; • The event depends on a false result given by the device used for diagnosis (when applicable);

	• In order to establish the relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the serious event.
Seriousness	
Serious Adverse Event (SAE) (ISO 14155:2011, 3.37)	Adverse event that a) led to death, b) led to serious deterioration in the health of the subject, that either resulted in 1) a life-threatening illness or injury, or 2) a permanent impairment of a body structure or a body function, or 3) in-patient or prolonged hospitalization, or 4) medical or surgical intervention to prevent life threatening illness or injury or permanent impairment to a body structure or a body function. c) led to fetal distress, fetal death or a congenital abnormality or birth defect NOTE 1: Planned hospitalization for a pre-existing condition, or a procedure required by the CIP, without serious deterioration in health, is not considered a serious adverse event * The study will be collecting only SAEs that led to a death
Serious Adverse Device Effect (ISO 14155:2011, 3.36)	Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.
Complication	An Adverse event that includes the following is considered a complication: a) Results in death, b) Involves any termination of significant device function, or c) Requires an invasive intervention Non-invasive (FDA, CFR 21; 812.3 (k)): when applied to a diagnostic device or procedure, means one that does not by design or intention: Penetrate or pierce the skin or mucous membranes of the body, the ocular cavity, or the urethra, or enter the ear beyond the external auditory canal, the nose beyond the nares, the mouth beyond the pharynx, the anal canal beyond the rectum, or the vagina beyond the cervical os
Observation	Any adverse event that is not a complication

11.5. Reporting of Adverse Events

11.5.1. Adverse Event and Device Deficiency Classification

All reported AEs and DDs will be reviewed by a Medtronic representative. AEs will be classified according to the definitions provided.

In this study, Device Deficiencies and Adverse Events classified as **possibly related, probably related or has causal relationship** with the procedure or Medtronic SelectSecure™ MRI SureScan™ Model 3830 pacing lead for His bundle pacing will be collected. In addition, all SAEs that result in death will be collected.

Upon receipt of AEs at Medtronic, a Medtronic representative will review the AE/DD for completeness and accuracy and when necessary will request clarification and/or additional information from the Investigator. Medtronic will utilize MedDRA, The Medical Dictionary for Regulatory Activities (MedDRA), to assign a MedDRA term for each adverse event based on the information provided by the investigator.

Regulatory reporting of AEs and DDs will be completed according to local regulatory requirements. Refer to **Table 6** for a list of required investigator and Medtronic reporting requirements and timeframes. It is the responsibility of the investigator to abide by any additional AE reporting requirements stipulated by the IRB responsible for oversight of the study.

For emergency contact regarding a SADE, contact an IMAGE-HBP Study representative immediately (refer to the study contact list provided in the site's study documents binder/investigator site file or refer to the Sponsor Contact Information section provided in the CIP).

Adverse Events and Deaths will be classified according to the standard definitions as outlined below:

Table 5: Adverse Event Classification Responsibilities

What is classified?	Who classifies?	Classification Parameters
Relatedness	Investigator	Lead for His bundle pacing, procedure
	Sponsor	Lead for His bundle pacing, procedure
Seriousness	Investigator	SAE
	Sponsor	SAE
Complication/Observation	Sponsor	Complication, Observation
Diagnosis	Investigator	Based on presenting signs and symptoms and other supporting data
	Sponsor	MedDRA term assigned based on the data provided by Investigator

11.5.2. Adverse Event and Device Deficiency Reporting Requirements

Regulatory reporting of AEs and DDs will be completed according to local regulatory requirements. It is the responsibility of the Investigator to abide by the adverse event reporting requirements stipulated by local law and the site's IRB.

Table 6: Reporting Requirements

Adverse Device Effects (ADEs)	
Investigator submit to:	
Medtronic	Submit in a timely manner after the investigator first learns of the effect.
Regulatory authorities	Submit to regulatory authority per local reporting requirement.
Institutional Review Board	Submit to Institutional Review Board per local reporting requirement.
Sponsor submit to	
Regulatory authorities	Submit to regulatory authority per local reporting requirement.
Institutional Review Board	Submit to Institutional Review Board per local reporting requirement.
Serious Adverse Device Effects (SADEs)	
Investigator submit to	
Medtronic	Submit to Medtronic as soon as possible
Regulatory authorities	Submit to regulatory authority per local reporting requirement.
Institutional Review Board	Submit to Institutional Review Board per local reporting requirement.
Sponsor submit to	
Regulatory authorities	Submit to regulatory authority per local reporting requirement
Institutional Review Board	Submit to Institutional Review Board per local reporting requirement.
Investigators	Submit per local reporting requirement.
All other reportable Adverse Events	
Investigator submit to	
Medtronic	Submit in a timely manner after the investigator first learns of the effect.
Regulatory authorities	Submit to regulatory authority per local reporting requirement.
Institutional Review Board	Submit to Institutional Review Board per local reporting requirement.
Device Deficiencies with SADE potential	

Investigator submit to	
Medtronic	Submit as required per local reporting requirements.
Regulatory authorities	Submit to regulatory authority per local reporting requirement.
Institutional Review Board	Submit to Institutional Review Board per local reporting requirement.
Sponsor submit to	
Regulatory authorities	Submit to regulatory authority per local reporting requirement
Institutional Review Board	Submit to Institutional Review Board per local reporting requirement.
All other Device Deficiencies	
Medtronic	Submit in a timely manner after the investigator first learns of the deficiency.
Regulatory authorities	Submit to regulatory authority per local reporting requirement.
Institutional Review Board	Submit to Institutional Review Board per local reporting requirement.

11.6. Subject Death

11.6.1. Death Data Collection

All subject deaths must be reported by the investigator to Medtronic on an AE eCRF (AE with outcome of death) as soon as possible after the investigator first learns of the death.

In the event of a subject's death, it is recommended that the implanted system be explanted and returned to Medtronic for analysis whenever possible per local process. Local laws and procedures must be followed where applicable.

System Interrogation Data Recommendations:

- After the subject has died but prior to explant, it is strongly recommended that the system be interrogated and a full summary interrogation (Interrogate All) performed when possible, and saved in a digital format. Store one copy of the save-to-media at the site and send a copy to Medtronic.
- Make the device interrogation/save-to-media file before any programming to prevent overwriting information in the device's memory and/or distinguishing between events detected during versus before the explant procedure.

If any system component is returned to Medtronic, internal return product reporting systems may be used to gather additional information about the returned device/component.

A copy of the death certificate, if available and allowed by state/local law, should be sent to the Medtronic IMAGE-HBP Study team. When a death occurs in a hospital, a copy of the death summary report and all relevant hospital records should be sent to the Medtronic IMAGE-HBP Study team, if available. If an autopsy is conducted, the autopsy report should also be sent to the Medtronic IMAGE-HBP Study team if available and allowed by state/local laws. When the death occurs at a remote site, it is the investigative site's responsibility to attempt retrieval of information about the death. In summary, the following data will be collected:

- Date of death
- Detailed description of death
- Cause of death
- Relatedness to system and/or procedure
- Device interrogation and Save-to-Media (if available)
- Death summary/hospital records (if available and allowed by state/local law)
- Autopsy report (if available and allowed by state/local law)
- Death certificate (if available and allowed by state/local law)

11.6.2. Death Classification and Reporting

Sufficient information will be required to properly classify the subject's death. The Investigator shall classify each subject death per the following definitions:

- Cardiac Death: A death directly related to the electrical or mechanical dysfunction of the heart.
- Sudden Cardiac Death (SCD): Natural death due to cardiac causes, indicated by abrupt loss of consciousness within one hour of the onset of acute symptoms; preexisting heart disease may have been known to be present, but the time and mode of death are unexpected. If time of onset cannot be determined, SCD will alternatively be defined as any unexpected cardiac death occurring out of the hospital or in the emergency room as dead on arrival.
- Non-sudden Cardiac Death: All cardiac deaths that are not classified as sudden deaths, including all cardiac deaths of hospitalized subjects on inotropic support.
- Non-cardiac Death: A death not classified as a cardiac death.
- Unknown Classification: Unknown death classification is intended for use only when there is insufficient or inadequate information to classify the death.

Table 7: Subject Death Classification Responsibilities

What is classified?	Who classifies?	Classification Parameters
Death Classification	Investigator	Cardiac, Sudden Cardiac, Non-sudden Cardiac, Non-cardiac, Unknown

12. Data Review Committees

This study will not be using a Data Management Committee or Clinical Events Committee.

13. Statistical Design and Methods

13.1. Primary Objective

13.1.1. Objective

The primary objective is to assess the implant success proportion of the Medtronic SelectSecure™ MRI SureScan™ Model 3830 pacing lead at the bundle of His for His Bundle Pacing.

13.1.2. Endpoint Definition

Implant success will be defined as the presence of a H wave on the implanted lead EGM and a HB pacing capture threshold equal to or less than 2.5V at 1.0ms.

Implant success proportion is defined as the proportion of all subjects who undergo an implant attempt that is successful.

13.1.3. Sample Size Determination

A sample size of 62 subjects with an implant attempt will produce a two-sided 95% confidence interval with a width equal to 0.15 (using the Wilson method) for the implant success proportion when the observed implant success proportion is 0.9. **Table 8** below shows various scenarios for the precision of the implant success proportion estimate depending on the actual observed data.

Table 8: Estimation Precision for Implant Success Proportion

Observed implant success proportion (N=62 subjects attempting implant)	Width of the two-sided 95% confidence interval
0.95	0.116
0.92	0.14
0.90	0.15
0.87	0.168
0.82	0.188

13.1.4. Analysis Methods

The observed implant success proportion will be calculated as follows:

$$\text{Implant Success Proportion} = \frac{\#\text{ Subjects with implant success}}{\#\text{ Subjects with implant attempt}}$$

A 95% confidence interval for the implant success proportion will be constructed using the Wilson method.

13.2. Secondary Objectives

The secondary objectives are descriptive in nature and are intended to provide additional information about His bundle pacing with the SelectSecure™ MRI SureScan™ Model 3830 pacing lead. There will be no established performance requirements for these secondary objectives.

13.2.1. Secondary Objective #1

13.2.1.1. Objective

This secondary objective is to estimate the correlation between the lead position and selective vs. non-selective HBP occurrence at implant.

13.2.1.2. Endpoint Definition

The lead position is identified as anterior septum, mid septum or posterior septum. Location is determined by the implanting physician during implant and verified by Medtronic through evaluation of cardiac CT scan images. The location determined from CT scan will be used in the analysis.

The HBP at implant is classified as either selective or non-selective by the implanting physician based on the definitions specified in section 4.1, Table 1: Definitions for His Bundle Pacing.

13.2.1.3. Analysis Methods

The relationship between lead position (anterior septum, mid septum, posterior septum) and HBP selectivity (selective vs. non-selective) will be assessed using a logistic regression. Additionally, HV intervals will be compared between the three groups of lead positions using linear regression.

13.2.2. Secondary Objective #2

13.2.2.1. Objective

This secondary objective is to assess changes in lead electrical measurements over time (HB PCT, R waves and impedance).

13.2.2.2. Endpoint Definition

The lead electrical measurements that will be evaluated include HB pacing capture threshold (PCT) (in Volts) at 0.5ms, impedance (in Ohms), and R-wave amplitude (in mV) measured at the final lead location during the implant procedure, and then at the 3-month, 6-month, and 12-month follow-up visits.

13.2.2.3. Analysis Methods

The lead electrical measurements from each visit will be summarized using descriptive statistics (mean, median, standard deviation, minimum, maximum, etc.) and graphical displays. Longitudinal analysis will be conducted to estimate differences in electrical measurements from implant to subsequent follow-up visits.

13.2.3. Secondary Objective #3

13.2.3.1. Objective

This secondary objective is to assess changes in QRS duration over time.

13.2.3.2. Endpoint Definition

Intrinsic QRS duration will be measured prior to the implant procedure, and then at the 3-month, 6-month, and 12-month follow-up visits.

13.2.3.3. Analysis Methods

The QRS durations from each visit will be summarized using descriptive statistics (mean, median, standard deviation, minimum, maximum, etc.) and graphical displays. Longitudinal analysis will be conducted to estimate differences in QRS duration from implant to subsequent follow-up visits.

13.2.4. Secondary Objective #4

13.2.4.1. Objective

This secondary objective is to estimate the correlation between implant characteristics and long-term lead electrical performance at 12 months post-implant.

13.2.4.2. Endpoint Definition

Long-term lead electrical performance is identified as the HB PCT at 12 months post-implant. Implant characteristics to be evaluated here include lead location, HB PCT at implant, and paced QRS duration at implant.

13.2.4.3. Analysis Methods

A multivariable regression analysis will be conducted to assess if there is any correlation between implant characteristics, including lead location, HB PCT, and QRS duration at implant, and the 12-month HB PCT.

13.2.5. Secondary Objective #5

13.2.5.1. Objective

This secondary objective is to characterize the occurrence of any complications related to the procedure or the lead for His bundle pacing up to 12 months post-implant.

13.2.5.2. Endpoint Definition

Procedure and the lead for His bundle pacing related complications will be reported via the Adverse Event eCRF. Examples include but are not limited to: lead dislodgement, exit block, loss of capture, or high threshold causing action.

13.2.5.3. Analysis Methods

The types of complications related to the procedure or the lead for His bundle pacing will be summarized using frequencies and percentages. The probability of a subject being free of a complication related to the procedure or the lead for His bundle pacing through 12 months post-implant will be estimated using the Kaplan-Meier method. In addition, the relationship between implant characteristics, including lead position, HB PCT at implant, and QRS duration at implant, and the occurrence of complications related to the procedure or the lead for His bundle pacing will be assessed using a Cox proportional hazard regression model.

13.3. Ancillary Objectives

Additional analyses may be done on data and images collected during the study as outlined below. These analyses are descriptive in nature and are intended to provide additional information about His bundle pacing with the Medtronic SelectSecure™ MRI SureScan™ Model 3830 lead.

13.3.1. Ancillary Objective #1

13.3.1.1. Objective:

This ancillary objective is to characterize the performance of existing delivery tools for the Medtronic SelectSecure™ MRI SureScan™ Model 3830 lead for HBP.

13.3.1.2. Endpoint Definition:

Physicians will report the performance of existing delivery tools for the 3830 lead for HBP via a Physician Questionnaire to be completed after each implant procedure.

13.3.1.3. Analysis Methods:

Responses to the Physician Questionnaire eCRF will be summarized using frequencies and percentages.

13.3.2. Ancillary Objective #2

13.3.2.1. Objective:

This ancillary objective is to summarize implant procedure information.

13.3.2.2. Endpoint Definition:

The implant procedure information to be characterized include: procedure times, number of fixation attempts, fluoroscopy time, delivery systems used.

13.3.2.3. Analysis Methods:

The implant procedure information will be summarized using descriptive statistics (mean, median, standard deviation, minimum, maximum for continuous variables, and frequencies and percentages for categorical variables).

13.3.3. Ancillary Objective #3

13.3.3.1. Objective:

This ancillary objective is to characterize the survival for subjects up to 12 months post-implant.

13.3.3.2. Endpoint Definition:

Deaths will be reported via the Adverse Event eCRF.

13.3.3.3. Analysis Methods:

The causes of death will be summarized using frequencies and percentages. The probability of subject survival through 12 months post-implant will be estimated using the Kaplan-Meier method.

14. Ethics

14.1. Statement(s) of Compliance

This study will be conducted in compliance with international ethical and scientific quality standards, known as good clinical practice (GCP). GCP includes review and approval by an independent IRB/Ethics Board before initiating a study, continuing review of an ongoing study by an IRB/Ethics Board and obtaining and documenting the freely given informed consent of a subject before initiating the study.

The study will be conducted according to federal, national and local laws, regulations, standards, and requirements of the countries where the study is being conducted. The study will also be conducted in accordance with the Declaration of Helsinki. The principles of the Declaration of Helsinki have been implemented through the subject IC process, IRB/Ethics Board approval, study training, clinical trial registration, preclinical testing, risk benefit assessment, and publication policy.

Ultimately, all sites will follow and comply with:

- Principles of Declaration of Helsinki
- 21 CFR Part 11 (Electronic Records, Electronic Signatures)
- The Clinical Trial Agreement
- The procedures described within this CIP
- Local independent institutional review board

The study will be conducted in compliance with 21 CRF Parts 50 (protection of human subjects) and 56 (Institutional Review Boards). Also, local laws and regulations will be applicable in the countries where the study is conducted.

The study will be publicly registered prior to first enrollment in accordance with the 2007 Food and Drug Administration Amendments Act (FDAAA) and Declaration of Helsinki on http://clinicaltrials.gov (PL 110-85, section 810(a)).

Approval of the CIP is required from the following groups prior to any study procedures at a study center:

- Medtronic
- Investigator (Investigator Agreement)
- An independent institutional review board

The Investigator will forward to the sponsor any action taken by an IRB/Ethics Board with respect to the investigation.

Subjects may be compensated for their time for this study if specified in the Agreement as agreed upon by the Investigator, site and Medtronic.

15. Study Administration

15.1. Monitoring

It is the responsibility of Medtronic to ensure proper monitoring of clinical studies as needed to secure Investigator compliance. Monitoring can occur on site or remotely. If deemed necessary by Medtronic, appropriately trained Medtronic personnel or delegates appointed by Medtronic may perform study monitoring at the study site to ensure that the study is conducted in accordance with the CIP, the Clinical Trial Agreement, and applicable regulatory and local requirements. Medtronic, or delegates, must therefore be allowed access to the subjects' case histories (clinic and hospital records, and other source data/documentation) upon request as per the subject Informed Consent, Research Authorization (where applicable) and Clinical Trial Agreement. The principal investigator should also be available during monitoring visits.

If monitoring occurs for this study, the frequency of monitoring visits will be based upon subject enrollment, duration of the study, study compliance number of deviations, findings from previous

monitoring visits and any suspected inconsistency in data that requires investigation. Regulatory documents may be reviewed at each study site. Any monitoring for the study will be done in accordance to the study-specific monitoring plan.

Should Medtronic decide monitoring visits are necessary, the visits will be conducted periodically to assess site study progress, the investigator's adherence to the CIP, regulatory compliance including but not limited to IRB/Ethics Committee approval and review of the study, maintenance of records and reports, and review of source documents against subject eCRFs. Monitors review site regulatory and study compliance by identifying findings of non-compliance and communicating those findings along with recommendations for preventative/corrective actions to site personnel. Monitors may work with study personnel to determine appropriate corrective action recommendations and to identify trends within the study or at a particular site.

15.2. Data Management

The eCRF data will be stored in a secure, password-protected database which will be backed up nightly. eCRF data will be collected via remote data capture and entered into an Oracle Clinical database. Data will be managed by Medtronic Core Clinical Solutions Data Management and External Partner Cognizant. At the end of the study, the data will be frozen and will be retained indefinitely by Medtronic.

All records and other information about subjects participating in this study will be treated as confidential. Data will be transferred and processed by Medtronic or a third party designated by Medtronic in a key coded form, unless it's impossible to make it anonymous. The CT scanned images, EP recording system files and electrical testing printouts will be de-identified when possible.

Procedures in the CIP require source documentation. Source documentation will be maintained at the site and copies of testing results and electrical data recordings will be sent to Medtronic. The eCRF may serve as source documentation if not available within the medical record.

15.3. Direct Access to Source Data/Documents

The sponsor or a regulatory authority may audit or inspect the study site to evaluate the conduct of the study. The clinical investigator(s)/institution(s) shall allow study related monitoring, audits, IRB/Ethics Board review and regulatory inspection by providing direct access to source data/documents.

15.4. Confidentiality

Subject confidential information may be accessed by Medtronic for this study. All records and other information about subjects participating in this study will be treated as confidential. Data will be transferred and processed by Medtronic in a key coded form, unless it's impossible to make it anonymous, for instance, where the patient's name cannot be removed from the data carrier, such as fluoroscopy images.

15.5. Liability

The study will be using market released products only. All product will be used under current indications and standard procedures.

15.6. CIP Amendments

If CIP revision is required, CIP amendment will not be implemented at the site until approval of the revised CIP is obtained from the Investigator, the Sponsor and the IRB/Ethics Board.

15.7. Record Retention

The investigator is responsible for the preparation (review and signature) and/or retention of the records cited below. The following records are subject to inspection and must be retained for a period of two years after study termination or closure:

- All correspondence that pertains to the investigation.
- Subject's case history records, including: signed/dated subject informed consent form, procedure date, and documentation of the dates and rationale for any deviation from the protocol
- IRB approval documents and documentation that the investigator did not participate in the approval process.
- Any other records that local regulatory agencies require to be maintained.

eCRFs must be maintained and signed electronically within the electronic data capture system during the study. Medtronic will provide electronic copies of CRFs (i.e. Patient Data Report) from the database upon request following study closure.

15.8. Publication and Use of Information

A publication committee may be formed during the course of the study if deemed necessary. Ideas for publications arising from findings of this study should be submitted in writing to the study sponsor. Unless otherwise provided in the Protocol, Investigator and Participating Institution shall submit any contemplated publication or presentation containing any information, data or results received or generated in the course of this study to Medtronic for review at least 60 days prior to submission, for a determination whether Confidential Information is disclosed. If notified by Medtronic within such 60-day period that such publication or presentation contains Confidential Information, Investigator and Participating Institution each agree to delete Confidential Information, other than Study results, prior to any publication or presentation.

Authorship will be selected on the basis of the following:

- A significant contribution to the design of the clinical study
- A significant contribution to subject enrollment in the clinical study
- High procedure volume and quality of data as determined by the clinical study requirements

15.9. Suspension or Early Termination

Early Termination of the Study is the closure of a clinical study that occurs prior to meeting defined objectives. This is possible for the whole study or a single site. Study Suspension is a temporary postponement of study activities related to enrollment and distribution of the product. This is possible for the whole study or a single site.

In the case of a study suspension, subject enrollment and follow-up must stop until the suspension is lifted by Medtronic.

Medtronic will promptly inform the clinical investigators of the termination or suspension and the reasons and inform the regulatory authority(ies) where required. In the case of study termination or suspension for reasons other than a temporary IRB/Ethic Board approval lapse, the investigator will promptly inform the IRB/Ethic Board. Subject follow-up will end in accordance with the plan specified at the time of the termination decision.

16. References

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17. Appendices

Appendix A: Draft data collection elements (Case Report Forms)

Draft Case Report Forms for the IMAGE-HBP study will be provided under separate cover. Final CRFs will be provided to sites via the electronic data management system after the site has fulfilled all requirements for database access.

Appendix B: Informed consent template

Informed consent template will be provided under separate cover.

Appendix C: Participating investigators and institutions

A complete list of participating investigators and institutions will be provided under separate cover upon request when available

Appendix D: IRB list

A complete list of participating IRBs and the Chairperson(s) will be distributed under a separate cover upon request when available.

18. Version History

Version	Summary of Changes	Author(s)/Title
1.0	Not Applicable, New Document	Lisa Hughes, Prin Field Clinical Engineer
2.0	Section 7.5: Adjusted Medtronic Delivery Catheter description to include commercially available delivery catheters Section 11.1: Removed 'or delivery system' from the second bullet to align with objectives and analysis plans	Lisa Hughes, Prin Field Clinical Engineer
3.0	Table 1: Updated to match table referenced in publication Section 6: Update number of sites from 3 to up to 5. Changed enrollment number to up to 70 enrollments to achieve approximately 62 implant attempts. Section 7.5 Lead: Removed specification of RA lead to allow real world use of a second lead as RA or RV. Section 7.5 DR220 Holter: Added the holter to be collected at the 3 month visit (or 6 month visit if missed at 3 month).	Lisa Hughes, Prin Field Clinical Engineer Tracy Bergemann, Sr Prin Statistician

	Section 8.3: Removed reference to ACC/AHA/HRS 2008 guidelines to allow most recent guidelines to be used by physician. Section 8.5: Changed center enrollment cap to half of the final study implant attempt enrollments. Table 2: Added Holter to 3 month visit and notation to allow collect at the 6 month visit if missed at the 3 month visit. Section 9.7: Adjusted to allow second lead instead of specifying RA lead. Corrected reference to the Implant Procedure Workbook. Test strips vs test results to be printed. Section 9.8.1: Test strips vs test results to be printed. Section 9.8.3: Addition of holter collection at 6 month visit if missed at 3 month visit. Test strips vs test results to be printed. Section 9.8.4: Addition of holter collection at 3 month visit. Test strips vs test results to be printed. Section 13.1.3: Sample size determination adjusted per new enrollment size. Table 8: Updated the Estimation Precision for Implant Success Proportion based on new sample size. Reference 15: Adjusted reference to match the correct publication for 15. Appendix D: Updated IRB list for CIP version 3	
4.0	Table 3: Cardiac CT Scan window end to 17 days	Lisa Hughes, Prin Field Clinical Engineer