INVESTIGATIONAL PLAN
FOR THE

MRI Study
Accent MRI™ Pacemaker and Tendril MRI™ Lead IDE Study

IDE Number: G100096

July 10, 2014

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REVISION CHANGE HISTORY

Revision #	Reason for Revision
xxxxxxxx.xx	• Initial draft for internal review
60028820/A	• First doc controlled version of protocol submitted to FDA May 19, 2010
60028820/B draft	**Date and revision of document updated to reflect current date/version** • Added table of tables, and table of figures • Correction of grammatical and typographical errors throughout document for readability • Revised section 3.0: Description of Device to reflect usage of MRI devices outside of the U.S.A • Clarified capability of MRI activator • Increased number of centers to minimum of 50, maximum of 75 centers • Expanded scope of study to include centers out of the U.S.A • Increase sample size to a minimum of 363 patients, based on negotiations with FDA • Increased duration of study to 34 months based on increase in sample size • Removed 1 week and 1 month post implant follow up visits • Revised study flow diagram to reflect change in follow up requirements • Revised primary endpoints to reflect • New sample size of 363, including providing criteria for analysis of the primary endpoints based on negotiations with FDA • Total of 9 primary endpoints • Lead endpoints partitioned into 2 phases: acute and chronic • Patients will be followed for a minimum of 12 months for the lead safety endpoint • Provide additional details on analysis of secondary endpoints based on negotiations with FDA • Added details on collection of additional data: communication challenges between MRI and cardiology personnel, availability of equipment at MRI visit, incidence of aberrant behavior of device in MRI mode, loss/lapse of monitoring during an MRI scan, MRI image analysis, number of non-study related MRI scans, summary of AE data on first 44 patients who complete the 1 month post MRI visit • Added list of definitions to be used in MRI study • Revised inclusion criteria to make explicit patient must provide consent ; legal guardian consent is not acceptable • Revised exclusion criteria to clarify patient should not come into contact with magnet façade inside MRI bore, removed requirement for patient to be 18 or older, allow patients to undergo non-study MRI scans while enrolled in the study • Added section 4.5 to clarify neither study personnel nor patient will be blinded to randomization assignment • Added clarification at study visits of when RA and RV lead measurements are not required to be obtained

Revision #	Reason for Revision
	• Clarified study requirements and data submission at each study visit • Removed PSA measurement for both RA and RV leads at implant visit • Added language at each study visit on method to be used when performing capture and sensing threshold testing for the RA and RV lead. • Added option non-endpoint visits can be performed via remote monitoring. • Clarified actions to be taken with respect to follow up visit scheduling and retention in the study if a patient undergoes a system revision procedure prior to or after the MRI visit • Provided separate sets of instructions for MRI Control and MRI Scan Group procedures and data collection at the MRI visit • Provided separate sets of instructions for MRI Control and MRI Scan Group procedures and data collection at the MRI visit • Added language to Unscheduled MRI section to clarify data to be collected for medically indicated scans performed while the patient is participating in the study • Added section 18.0 to provide information on publication of study on clinicaltrials.gov website. • Revised MRI Scan sequence (Appendix B) to provide clarity on scan sequences and parameters to be used for MRI study scans • Added statement in consent form to inform patients they may be asked to participate in a post approval study after completion of the IDE study
60028820/B	• Doc controlled version of protocol with changes incorporated based on feedback from FDA. Protocol was doc controlled, but not submitted to FDA due to additional changes that were requested by FDA based on pre-IDE meetings after the protocol was doc controlled.
60028820/C draft	**Updated footer to reflect current date and revision of investigational plan.** • Added IDE identifier to cover page of investigational plan • Removed data collection requirements not affecting endpoints of study • Total procedure time • Total fluoroscopy time • Pulse oximetry/ECG monitoring for MRI Control Group • Added note to MRI Scan Sequences for the MRI IDE Study - Appendix B on maximum spatial gradient determined safe for Accent MRI system • Revised consent form to clarify the amount of time the MRI control group is required to wait between the initial check to the final check of the implanted Accent MRI pacemaker system • Removed pulse oximetry/ECG monitoring explanation for MRI Control Group in consent form.
60028820/C	• Doc controlled version of protocol submitted to FDA on October 28, 2011.
60028820/D draft	**Updated footer to reflect current date and revision of investigational plan.** **Based on negotiations with and feedback from FDA** • Protocol structured into Lead and MRI portions. • Number of sites increased: minimum of 60, maximum of 80 • Sample size increased to minimum of 800 • Enrollment duration increased to 12 months

Revision #	Reason for Revision
	• Revision of flow diagram to reflect MRI portion of study will be initiated only upon approval from FDA • Clarification in endpoint analysis methods per FDA request • Additional analyses added to the primary MRI Efficacy endpoints **Section 4.2 – Objectives/Study Endpoints** • Updated/revise end point analysis to coincide with the increase in sample size. • Identified a sample size of 363 for the MRI portion • Additional Data (sec 4.2.5) – added Lead Handling Characteristics and updated image qualitative analysis. **Section 4.3 – Patient Selection** • Added Exclusion: "Are medically indicated for an MRI scan at time of enrollment. **Section 4.4 – Randomization** • Updated randomization language to coincide with timing of FDA approval to begin MRI scans. **Section 4.7 – Study Procedures** • Split Schedule of Evaluation Tables into two tables: Table 1 specific to the Lead Safety part and Table 2 specific to the MRI scan evaluation part. • Added "Death Form, if applicable" to data submission forms for study visits • Expanded 6 month visit window to 60 days to maintain consistency of visit window with other visits at or after 6 months post implant. • Moved MRI related study procedures and requirements to section 4.7.6 **Appendix B: MRI Sequences** • Part 4 – added additional language to Image Sequence Parameter Summary related to clinically useful scans. **Appendix C: Patient Informed Consent** • Removed MRI related testing, risks, etc. The primary consent will address the lead part of the study. • Created an addendum to the consent for the MRI portion of the study. Described in the Protocol under "Appendix D: Patient Informed Consent Addendum: MRI Consent. **Appendix D: Patient Informed Consent Addendum: MRI Consent** • New appendix **Appendix E: MRI Conditional Notification to Patients** • New appendix
60028820/D	• Doc controlled version submitted to FDA on February 2, 2012.
60028820/E draft	**Updated footer to reflect current date and revision of investigational plan.** • Flow diagram updated to reflect re-attempt is allowed after an unsuccessful re-implant attempt • Clarified patients with Tendril MRI lead implanted in or through jugular are not eligible to participate in MRI portion of study. • Added forms that are required to be submitted at each study visit: medication log, death form and withdrawal form • Revised lead to reflect a minimum enrollment of 800 patients. • Added wording to section 4.2.4 to indicate that gender comparisons and gender by

Revision #	Reason for Revision
	treatment interaction assessments will be done at the 0.15 level of significance. • Added statement of unforeseeable risks in Risk section lead consent form • Clarified in MRI consent addendum the study doctor or staff may also perform the MRI screening assessment in addition to radiology staff • Removed statement cardiologist WILL be available during MRI scan • Reworded statement under MRI consent addendum stating benefits of participating in MRI portion of study to make it clearer to patient benefits of having an MRI compatible pacemaker system implanted – if needed, patient can undergo MRI scan.
60028820/E	• Doc controlled version of investigational plan submitted in April 2012 to FDA related to conditions of approval stated in FDA letter stamped MAR 7, 2012, marked as Dated: February 2, 2012; Received: February 6, 2012.
60028820/F final draft	**Updated footer to reflect current date and revision of investigational plan.** • Flow diagram updated to reflect MRI phase of study is happening in parallel to lead phase of study • Updated text through-out document removing references to initiation of MRI scans upon FDA approval of MRI phase of study; MRI scans performed that are not required by the protocol will not be considered protocol deviations. Text also updated to allow randomization to take place as early as the implant visit to allow adequate time for sites to schedule the MRI scan. • Updated flow diagram to reflect patients may be enrolled in MRI phase of study starting at enrollment visit of lead phase of study, allowance of multiple implant attempts, and randomization starting at the implant visit • Window for MRI visit revised to match with revised flow diagram; window now opens at 1 week after 2 months post implant or a system revision procedure, and closes at 12 months post implant. • Window for 2 month post implant visit revised to ±7 days vs.-7days/+0 days. • "Bipolar" added throughout document to identify endpoints are based on bipolar measurements • Text in Primary Lead Safety Endpoint section updated to reflect sample size of 400 RA leads and 800 RV leads. • Additional Analyses text added to section 4.2.2.3 Change in bipolar atrial sensing thresholds before and after the MRI scan and 4.2.2.4: Change in bipolar ventricular sensing thresholds before and after the MRI scan – as requested by FDA. • Inclusion Criteria – added clarifier to inclusion criteria #6 – "Applies only to those patients who will participate in the MRI portion of the study." • Exclusion Criteria – added clarifier to exclusion criteria #'s 2 & 3 - "Applies only to those patients who will participate in the MRI portion of the study." • Exclusion Criteria #2 has been modified; "inactive" has been removed. The exclusion now reads, "Have an existing active implanted medical device, e.g., neurostimulator, infusion pump, etc." • Updated text throughout as it relates to inclusion/exclusion clarification. • Table 1: Schedule of Evaluations Summary: Accent MRI Lead Safety - updated Notes at the bottom of the table; RA/RV sensing measurements are not required if the patient's intrinsic rate has been established to be below 30 beats per minute. Added "RV capture thresholds are not required if a high ventricular rate is present." Updated notes can be found throughout as they apply to lead testing at each study

<table>
<tr><th>Revision #</th><th>Reason for Revision</th></tr>
<tr><td></td><td>visit.
• Unipolar capture and sensing threshold measurements for the RA and/or RV lead added at the MRI and 1 Month Post MRI visit under Additional Data to be collected for the study; requirement also added under the corresponding schedule of evaluations (Table and text at the specified visits).
• Medically indicated MRI scan removed as exclusion criterion
• Forms renamed throughout document, where applicable, to reflect type of data collected on the forms:
➢ Randomization changed to MRI Enrollment to allow collection of MRI enrollment information on the form
➢ MRI Termination changed to MRI Discontinuation eliminate confusion between withdrawal from the study versus discontinued participation in the MRI phase of the study
➢ MRI Form changed to MRI Scan Group Testing Form and MRI Control Group Testing Form to reflect data being collected for each group
➢ Unscheduled MRI Form changed to Non-study MRI Form to reflect medically indicated scans (non-study MRI scans) are usually scheduled
• Clarified personnel needed to be present at the MRI visit
• Removed text stating radiologist or designated staff is required to determine if a Control patient is eligible for an MRI scan at the MRI visit since the MRI Control patient is not undergoing an MRI scan at the MRI visit.
• Added event below to Unavoidable AEs related to the MRI Scan Table
<table><tr><th>Event</th><th>Time Frame post – MRI scan</th></tr><tr><td>Sensation of bodily warmth</td><td>During and < 1 hour post MRI scan</td></tr></table></td></tr>
<tr><td></td><td>• Removed event below from Potential Pacing System Adverse Events and added to Potential MRI System Adverse Events to reflect event is related to Potential MRI System Adverse Events
➢ Lead heating resulting in thrombus formation or embolism
• Added clinicaltrials.gov registration number under Publications section: NCT01576016
• MRI scan sequence instructions revised to provide clearer instructions on how scans should be performed, and what regions need to be scanned. Duplicate rows of Clinical Scan Sequence table deleted. MRI Scan tables moved to before text; manufacture specific tables added – GE, Phillips and Siemens.
• Table 5: MRI Parameters – removed Accent ST MRI DR as a device option and added Accent MRI SR as a device option. Also added VOO & Pacing Off a programming options and VOO as the Nominal Value.
• Lead Phase Patient informed consents updated to reflect sponsor personnel may be present at study visits. Name/signature of person obtaining consent added, along with other minor clarifications.
• Revised MRI consent addendum to reflect MRI part of study will be fully implemented with implementation of Rev F of the investigational plan. Patient compensation changed from $100/MRI visit and $50/1 month post MRI visit to $60/MRI visit to comply with current sponsor guidelines on reimbursement related to patient expenses. Removed references to Accent MRI system not being MR conditional and MRI scans not being allowed until FDA grants approval.</td></tr>
</table>

Revision #	Reason for Revision
	Name/signature of person obtaining consent added, along with other minor clarifications.
60028820/F	• Doc controlled version of investigational plan intended for submission to FDA in May 2012 in response to ➢ conditions of approval stated in FDA letter stamped MAR 7, 2012, Dated: February 2, 2012; Received: February 6, 2012 ➢ disapprovals stated in FDA letter stamped NOV 30 2011; Dated: October 28, 2011; Received: October 31, 2011
60028820/G	• Date and document revision number updated in document footer per sponsor internal process • Added "Lessons Learned" as additional being collected per FDA request. • Deleted "Accent" from table label for Schedule of Evaluations Summary for lead safety part of study • Corrected intrinsic heart rate typo to "below 30 beats per minute" in notes that state RA/VR sensing threshold measurements are not required to be obtained for pacemaker dependent patients. • Added the following statement, per FDA request, at the MRI and 1 Month Post MRI Visit where data for the efficacy endpoint are being collected: *If the RA capture and sensing thresholds could not be obtained due to a patient's atrial fibrillation or flutter, and if the patient's atrial fibrillation or flutter is transient, for data analysis purposes, the pacing capture threshold and sensing threshold from the next study visit, if available, will be used.* • Revised text in protocol to clarify all patients agreeing to participate in the MRI portion of the study will be rescreened and the pre-MRI safety screening form will be completed for each of those patients per FDA request. • MRI Visit Window revised to allow for the MRI Visit to be conducted any time after the patient receives a randomization assignment for those patients participating in the MRI portion of the study • MRI Parameter Table revised to clarify the pacing options listed are individual, selectable options under the MRI mode for the Accent MRI single and dual chamber pacemakers • Moved MRI Hardware and Software Requirements Summary information to MRI Scan Sequence document in Appendix B. • Clarified instructions related the non-diagnostic nature of the study MRI scans • Added text detailing purpose of clinical and non-clinical MRI scans • Reinstated requirement of advanced cardiac life support trained clinician to be present during the MRI scan under the MRI visit per FDA requirement • Clarified instructions on reporting of arrhythmias that occur during an MRI scan at the MRI visit • MRI scan sequence, Appendix B, revised to provide clearer instructions on performing non-clinical and clinical MRI scans for the study. Due to extensive reformatting and movement of information, as well as the addition of instructions related to clinical study MRI scans, the Appendix was replaced in its entirety. The document is intended to be used as a guideline by the radiologist or MR technologist • Added line listing of risks associated with implant procedure and Accent MRI system to lead safety consent

Revision #	Reason for Revision
	• In the MRI Consent Addendum ➢ Added type of scan – clinical and non-clinical - that will be performed on patients randomized to the MRI Scan Group ➢ Added clarification that patients may need to return for the MRI visit depending on the outcome of the testing of the Accent MRI pacemaker. • Added risks associated with MRI Scans of Patients Implanted with Cardiac Devices to MRI Conditional Notification to Patients per FDA request
60028820/H	• Date and document revision number updated in document footer per sponsor internal process • Instructions on MRI scan-related AE reporting inserted under MRI Visit in response to FDA request.
60028820/J	**NOTE**: "I" is not utilized as a revision number due to Sponsor internal document control restrictions; the next sequential letter, J, was used. • Date and document revision number updated in document footer per sponsor internal process • Instructions on handling of patients who cannot tolerate an MR scan added under the MRI Visit, the Non-Clinical Scan Sequences and Clinical Sequence instructions in response to FDA request. • Instructions related to MRI scan-relate AE reporting and diagnostic testing to be performed for pre-specified MRI scan-related AEs that may occur during or immediately after an MRI scan updated in response to FDA request. • Instructions on splitting RF intensive scan into 4 exposure windows added per FDA request. • Correction of typo in Non-Clinical Scan Sequence instructions
60028820/K	• Date and document revision number updated in document footer per sponsor internal process • Reference to randomization removed throughout document per agreement with FDA to structure study utilizing objective performance criteria (OPC) for the MRI-related primary endpoints. • MRI Control and MRI Scan Group nomenclature removed throughout document as appropriate to reflect OPC study. • Study flow diagram updated to reflect new study design; MRI CONTROL Group patients may return for an MRI scan and corresponding 1 Month Post MRI Visit. • MRI-related Primary Safety and Efficacy endpoints updated to an OPC. Corresponding analyses details updated to align with utilization of OPCs for the MRI-related primary endpoints. • Section on Randomization, Blinding and Cross Over removed as the study is no longer a randomized study. • Removed data collection requirements for MRI Control Group under the MRI visit since an MRI Control Group is no longer applicable. • Revised Safety Screening Form and MRI Hazard Checklist to provide more clarity on patient eligibility for the MRI Phase. • Correction of typo of parameter name ("Measurements" changed to "Phases" in GE scanner table. "Phases" is the equivalent parameter name for "Measurements") in scan sequence for GE scanner in Non-Clinical Scan Sequence instructions • Updated MRI Consent Addendum to reflect change of study from Randomized,

Revision #	Reason for Revision
	Controlled to OPC-based. MRI Control Group information removed. Added statement in signature block to clarify patients previously randomized to CONTROL are now agreeing to undergo the study MRI scan by signing the consent addendum.

1.0 Introduction

Magnetic resonance imaging (MRI) is a diagnostic method to view high quality two and three dimensional images of the body.[1, 2] MRI does not use radiation, has few side effects and is very useful to view soft tissue. In 2007, an estimated 27.5 million MRI procedures were performed in the U.S. in 7,195 hospital and non-hospital sites.[3]

According to the 2005 World Survey of cardiac pacing and cardioverter defibrillators, 223,425 new pacemakers were implanted in the United States in 2005.When compared to a similar survey conducted in 2001, the 2005 survey showed an increase in the number of pacemakers and defibrillators implanted throughout the world, a trend that is likely to continue into the future.[4,5] It is estimated that 50-75% of the patients with implantable cardiac devices will develop an indication for an MRI scan during the lifetime of their device.[6]

Magnetic resonance imaging systems generate three electromagnetic fields that are used to produce an image. These include a static magnetic field, a time varying gradient magnetic field, and an RF field. All three of these fields interact with implanted devices and could create hazards for the device, the patient, or both.[7] Examples of these hazards include unwanted cardiac stimulation, heating near lead electrodes, image artifacts, and forces being applied to implanted components.[2,8,9] Due to these issues, currently marketed pacemaker systems may be contraindicated for use in an MRI environment.

In initial MRI studies involving patients implanted with cardiac devices, there were anecdotal reports of device malfunction or patient death associated with an MRI scan.[10] None of these deaths occurred during physician supervised procedures.[11] Over the past 10 years, there have been numerous patients with implanted devices who successfully underwent magnetic resonance imaging.[12,13,14,15,16] Although many patients with implanted devices have undergone MRI scans successfully and without incident, physicians and regulators have made the point that "failing to identify an adverse event is not equivalent to demonstrating safety – especially when only a limited number of patients are studied".[17, 18] In order to validate that MRI scans are safe for patients with implantable cardiac devices, these devices need to be specifically designed and developed to mitigate the hazardous interactions in an MRI environment. St. Jude Medical has developed a system, the Accent MRI™ system, comprised of the Accent™ device and the Tendril MRI™ lead, and an investigational MRI Activator™, designed to mitigate such interactions.

2.0 Purpose

The intent of this IDE study is to evaluate the safety and efficacy of the implanted Accent MRI™ system, which includes the investigational St. Jude Medical Tendril

MRI™ lead and Accent MRI™ pacemaker. An MRI Activator™, also investigational, will be used in conjunction with the Accent MRI system. The MRI Activator is a handheld device that allows the user to enable and disable the MRI Setting, as well as check the status of the MRI Setting in the pacemaker. The patient population under study includes patients with a standard bradycardia pacing indication.

3.0 Description of Device

In this IDE study, the investigational St. Jude Medical Tendril MRI™ lead will be implanted with the investigational Accent MRI pacemaker Model PM2218 and Model PM1224 or other models with similar functionality; devices implanted outside the United States will utilize different device models. The Accent MRI pacemaker is supported by the St. Jude Medical Merlin Patient Care System (Merlin PCS) with software Model 3330 version 11.1 .1(or higher). The investigational system includes the Accent MRI pacemaker and Tendril MRI™ lead. The MRI Activator Device (Model EX4000 or higher) or programmer can program the Accent MRI pacemaker into and out of the MRI Setting. The MRI Activator is also investigational.

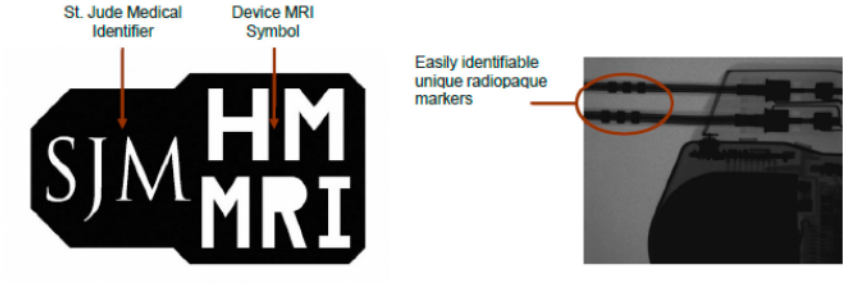
The Accent MRI pacemaker is based on the market approved Accent pacemaker. All commercially available features of the Accent pacemaker are included in the MRI device. However, the Patient Notifier feature is permanently disabled if the patient has an MRI scan.

The MRI pacemaker has new hardware and firmware to prevent unintended stimulation due to electromagnetic fields created by the MRI scanner. The new hardware and firmware include

- Reduction in feed-through capacitance to mitigate gradient-induced stimulation
- Addition of a band-stop filter (MR filter assembly) to limit the ingress of MRI-specific frequencies which otherwise could result in RF rectification and/or other interference.

The device shape and size is modified to accommodate the MRI filter assembly. The Accent MRI pacemaker also has a unique MRI radiopaque x-ray marker – see Figure 1 below.

Figure 1: Accent™ MRI Pacemaker System X-Ray Markers



Due to the noise created by the MRI environment, sensing must be disabled for the duration of an MRI scan. Therefore, firmware and programmer software will include the capability to program the device to MRI conditionally safe settings. The MRI Mode will provide the physician with two options – either asynchronous pacing or pacing off. The MRI Setting consists of nonprogrammable and programmable pacing parameters. The Merlin PCS programmer software will include:

- Ability for the user to pre-set the MRI parameters in advance and save these in the device as an "MRI Setting"
- Checklist feature allowing the user to confirm that the system meets all conditions required for safe MRI scanning
- Capability to program the device into MRI Setting, out of MRI Setting, and back into the previously programmed settings
- Ability to set an MRI Ready status in the device for future use with the MRI Activator
- Collection of diagnostics from the MRI Setting (time in MRI setting, etc.) and display via MRI-related reports.

The Tendril MRI lead is an endocardial, bipolar, active fixation lead with an IS-1 connector based on the currently marketed Tendril™ Model 1888TC lead. The Tendril MRI lead incorporates filters to mitigate MRI induced RF tissue heating near the lead electrodes. It has a radiopaque identification marker built into the connector end allowing the physician to identify the lead as MRI compatible via x-ray. The lead's body has a co-axial design and uses MP35N coils and an Optim outer insulation. The lead has been designed to fit through an 8F introducer without a retained guide wire and is available in lengths of 46, 52 and 58 cm.

In addition to the programmer, the external MRI Activator is a handheld device that allows the user to enable or disable the MRI Setting in the Accent MRI pacemaker if the checklist conditions have been verified and the use of the MRI Activator has been approved and enabled by the physician. The MRI Activator hardware is based on the commercially available St. Jude Medical Confirm® Patient Activator hardware. The MRI Activator firmware will include the capability to program the MRI Setting on

and off, and back into the previously programmed settings if the pacemaker has been made MRI ready.

4.0 Clinical Protocol

4.1 Study Design and Scope

This is a prospective, multi-center, clinical study designed to evaluate the safety and efficacy of the Accent MRI System in a patient population indicated for implant of a pacemaker within and outside of the MRI environment.

The study will be conducted at a minimum of 60 centers and a maximum of 80 centers worldwide. The minimum requirement for completing this study is 800 patients. A maximum of 120 (15% of the total) enrollments will be allowed per center. It is anticipated that at least 30% of enrollments will include patients implanted with the Tendril MRI lead in the right atrium.

Within the MRI environment, The Accent MRI system will be evaluated in conjunction with the MRI Activator. The MRI Activator performance will be evaluated qualitatively during this phase of the study. Up to 363 patients, including patients who were randomized to the MRI Control Group in previous versions of the investigational plan, will be enrolled in this phase of the study.

Enrollment in the MRI clinical study is expected to take approximately 12 months. The anticipated duration of this study is 32 to 34 months, depending on the rate of enrollment. All patients will be implanted with an Accent MRI pacemaker and a Tendril MRI lead. Devices implanted outside the United States will utilize different device model numbers.

The following study evaluations will occur after implant:

- Post implant follow up (pre-discharge)
- 2 month visit (post implant, in-office)
- 6 month visit (post implant, in-office)
- 12 months visit (post implant, in-office)
- Every 6 months post implant until study completion

MRI visits will consist of:

- MRI visit which includes:
  - Pre-MRI scan testing
  - MRI scan
  - post MRI testing
- 1 month post MRI visit

The schedule of follow up visits for the lead safety component of the study is based on the date of implant of the Accent MRI System. The follow up schedule for the MRI visit is based on the date of implant or revision of an MRI lead until the MRI visit; the MRI visit should take place no sooner than one week after the 2 month post implant or system revision procedure where the Tendril MRI lead was implanted, repositioned or replaced. The one month post MRI follow up visit is based on the MRI visit.

Figure 2: Lead Safety Phase Flow Diagram

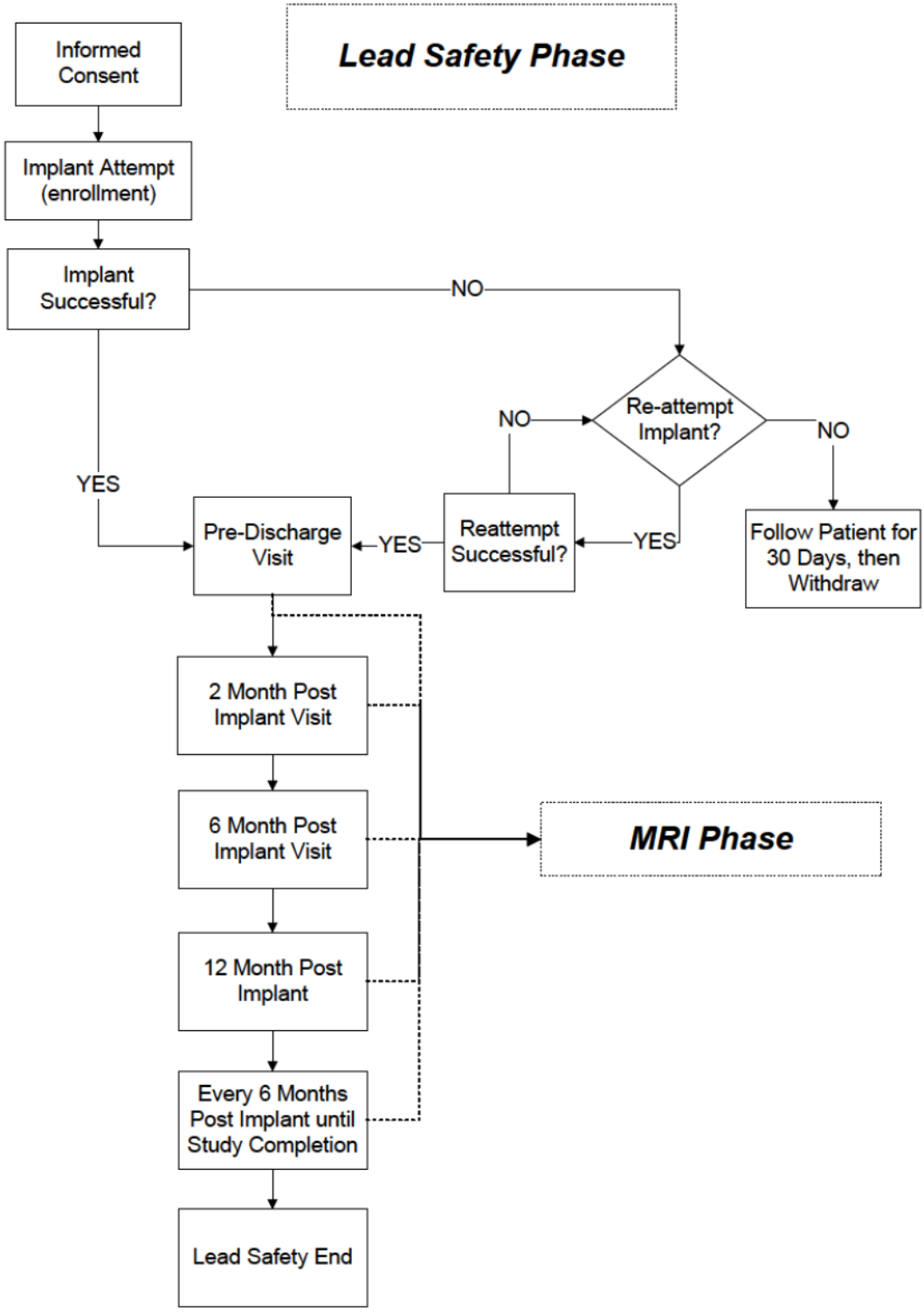
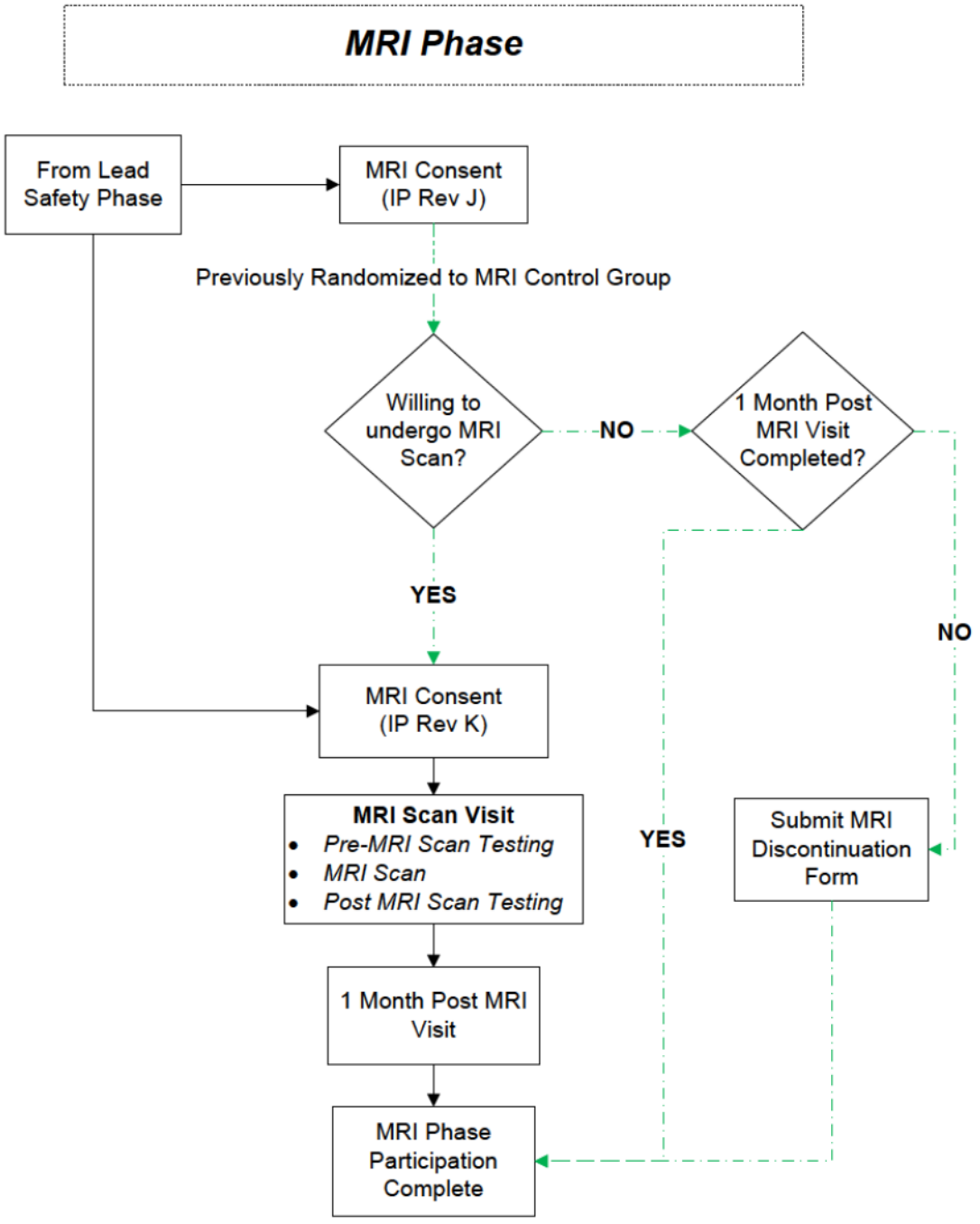


Figure 3: MRI Phase Flow Diagram



4.2 Objectives/Study Endpoints

The primary objectives of this study are to assess the safety and efficacy of the Accent MRI™ system in a patient population that is indicated for a pacemaker.

Primary Endpoints
Lead Safety
Safety of the Tendril MRI™ lead will be evaluated in terms of freedom from RA and RV lead-related complications for the acute (implant to 2 month visit) and chronic (2 month visit through the 12 month visit) timeframes.

MRI Safety
The safety of the Accent MRI system will be evaluated in terms of freedom from MRI scan related complications in the month following the MRI scan.

Lead Efficacy
Efficacy of the Tendril MRI™ lead will be evaluated in terms of the change in bipolar atrial and ventricular capture and sensing thresholds before and after the MRI scan.

Secondary Endpoints
Safety
Safety of the Accent MRI™ system will be evaluated in terms of freedom from system-related complications through the 12 month visit.

Efficacy
Efficacy of the Tendril MRI™ lead will be evaluated in terms of the bipolar atrial and ventricular capture thresholds at the MRI Visit.

4.2.1 Primary Lead Safety Endpoints

4.2.1.1 Freedom from RA lead-related complications in the acute period

4.2.1.2 Freedom from RV lead-related complications in the acute period

The lead safety endpoint will be assessed separately for the RA and RV leads and for an acute (implant to 2 months) period.

The hypothesis is formally expressed as:

H_0: Freedom from lead related complications from implant up to 2 month visit $\leq 92\%$

Ha: Freedom from lead related complications from implant up to the 2 month visit $> 92\%$

The objective performance criterion of 92% used for this objective denotes the minimum level of adequate safety for the RA or RV leads in the acute time period. This endpoint will be tested separately for the RA and the RV leads. Only those complications occurring by the 2 month visit and adjudicated by the Clinical Events Committee as RA lead or RV lead complications will be used in the estimation of these endpoints.

Sample Size

Simulation was used to calculate the sample size requirements for testing the Kaplan-Meier estimated survival probability for the freedom-from-complication endpoint. The SCORE Registry, containing patients who were implanted with a St. Jude Medical RA and RV market approved Tendril™ family of leads, was used to estimate freedom from lead related complications in the acute time period. Using these estimates derived from the SCORE Registry data, the expected proportion of patients free from RA lead related complications from implant to 2 months is 0.995 with 95% lower confidence bound of 0.994. Similarly, for the RV lead, the expected proportion of patients free from RV lead related complications from implant to 2 months is 0.993 with 95% lower confidence bound of 0.991. Taking a conservative expected complication free rate of 0.97, with a study size of 800 RV leads and 400 RA leads patients and a Type 1 error rate for the acute time period hypothesis test of $\alpha = 0.025$ for a one-sided test, the power is greater than 98%.

Patient Group

All patients that have had an attempted implant or a successful implant of an Accent MRI system will be included in this endpoint.

Patients who are lost to follow-up or withdrawn prior to the 2 month follow-up visit due to an RA or RV lead related complication will be analyzed as having experienced a complication at the date the complication occurred. Patients who withdraw for reasons unrelated to an RA or RV lead related complication will be censored at the date of withdrawal.

Analysis

The desired outcome is to reject both null hypotheses for the RA and RV endpoints. The RA and RV hypothesis will be tested separately. The null hypothesis for the RA or RV endpoints will be rejected at the 2.5% significance level if the 95% lower limit of a two-sided confidence interval for the freedom from RA or RV lead-related complications by 2 months is greater than 92%. The confidence

interval will be constructed using the log-log transformation of the event free estimate at 2 months.

4.2.1.3 Freedom from RA lead-related complications in the chronic time period

4.2.1.4 Freedom from RV lead-related complications in the chronic time period

The lead safety endpoint will be assessed separately for the RA and RV leads for the chronic (2 months through the 12 month visit) time period.

The hypothesis is formally expressed as:

H_0: Freedom from lead related complications from the 2 month through the 12 month visit $\leq 95\%$

Ha: Freedom from lead related complications from the 2 month through the 12 month visit $> 95\%$

The objective performance criterion of 95% used for this objective denotes the minimum level of adequate safety for the RA or RV leads in the chronic time period. This endpoint will be tested separately for the RA and the RV leads. Only those complications occurring by the 12 month visit and adjudicated by the Clinical Events Committee as RA lead or RV lead complications will be used in the estimation of these endpoints.

Sample Size

Simulation was used to calculate the sample size requirements for testing the Kaplan-Meier estimated survival probability for the freedom-from-complication endpoint. The SCORE Registry, containing patients who were implanted with an RA and RV market approved Tendril™ family of leads, was used to estimate freedom from lead related complications in the chronic time period. Using these estimates derived from the SCORE registry data, the expected proportion of patients free from RA lead related complications from 2 months post-implant through 12 months is 0.996 with a 95% lower confidence bound of 0.994. Similarly, for the RV lead, the expected proportion of patients free from RV lead related complications from 2 months post-implant through 12 months is 0.998 with 95% lower confidence bound of 0.997. Taking a conservative expected complication free rate of 0.98, with a study size of 800 RV leads and 400 RA leads patients and a Type 1 error rate for the chronic time

period hypothesis test of $\alpha = 0.025$ for a one-sided test, the power is greater than 98% for the RV leads and greater than 85% for the RA leads.

Patient Group
All patients who have had an attempted implant or a successful implant of an Accent MRI system will be included in this endpoint.

Patients who are lost to follow-up or withdrawn prior to the 12 month follow-up visit due to an RA or RV lead related complication will be analyzed as having experienced a complication at the date of the complication. Patients who withdraw for reasons unrelated to an RA or RV lead related complication will be censored at the date of withdrawal.

Analysis
The desired outcome is to reject both null hypotheses for the RA and RV endpoints. The RA and RV hypothesis will be tested separately. The null hypothesis for the RA or RV endpoints will be rejected at the 2.5% significance level if the 95% lower limit of a two-sided confidence interval for the freedom from RA or RV lead-related complications between 2 months and 12 months is greater than 95%. The confidence interval will be constructed using the log-log transformation of the event free estimate at 12 months.

4.2.2 Primary MRI Safety Endpoint: Freedom from MRI Scan-Related complications

An MRI Scan-Related complication is a complication caused by the interaction between the investigational pacing system and the MRI system that occurs during the MRI scan, including the time the patient is within the 5 Gauss line of the MRI system, up through the patient's 1 month post MRI visit. In addition, complications occurring due to the patient's MRI programming will be considered MRI scan related by the Clinical Events Committee (CEC).

The hypothesis is formally expressed as:

H_0: Proportion of patients who are free from MRI scan-related complications between the MRI scan and one month post MRI visit $\leq 90\%$

H_a: Proportion of patients who are free from MRI-scan related complications between the MRI scan and one month post MRI visit $> 90\%$

The comparison criterion of 90% used for this objective denotes the minimum level for adequate safety following the MRI scan. Complications that can be attributed to the MRI scan are expected to occur within one month of the scan.[19] Therefore, assessing this objective one month post-MRI scan will capture all MRI scan-related complications following the MRI scan procedure.

Sample Size

The expected proportion of patients free from complications under the null hypothesis is 0.90, and the Type 1 error rate is set at $\alpha = 0.025$ for the one-sided test. Assuming the portion of patients free from complications of.0.97, a sample size of 133 MRI patients provides a power level of 90% for this endpoint.

In another manufacturer's study involving an MRI conditional pacemaker, the complication free rate as observed to be 100%.[19] Therefore, an assumption of 97% complications-free rate is assumed in the sample size calculation.

The objective will be evaluated using a one-sided z-test with variance of the test statistic based on the hypothesized value of 0.90 for the binomial proportion. The desired outcome is to reject the null hypothesis.

Patient Group

All patients implanted with the Accent MRI system who undergo an MRI scan and have completed their 1 month post MRI visit, or have an MRI-related complication before the end of the 1 month post MRI visit date will be included in the analysis of this endpoint.

Analysis

The analysis will be conducted on the per-protocol (PP) population. The per-protocol population includes patients who meet the following criteria:

- Successfully implanted with the Accent MRI system
- Have MRI visit data
- Meet the MRI Conditions of Use
- Received an MRI scan
- Have 1-month post MRI visit data

All individual primary safety endpoints must be successful (reject the null hypothesis at the $\alpha = 2.5\%$ level) for the safety endpoint to be successful.

A supporting analysis will also be performed using all patients who undergo an MRI scan For this analysis, each missing data point will be replaced by a failure one at a time. Each time a new failure is added the analysis will be re-run. This continues until either all missing data has been replaced with a failure or the test becomes non-significant (i.e. the interpretation of the results changes). The proportion of missing data that would need to be a failure in order to change the analysis results will be reported and discussed.

4.2.3 Primary MRI Efficacy Endpoints

4.2.3.1 Proportion of patients free of atrial capture threshold increase of > 0.5V at 0.5ms from before and to one month after the MRI scan

4.2.3.2 Proportion of patients free of ventricular capture threshold increase of > 0.5V at 0.5ms from before to one-month after the MRI scan

The hypothesis is formally expressed as:

H_0: Proportion of patients with threshold increase of $\leq$ 0.5V at 0.5ms from before to one month post MRI visit $\leq$ 90%

H_a: Proportion of patients with a threshold increase of$\leq$0.5V at 0.5ms form before to one month post MRI visit > 90%

The desired outcome is to reject the null hypothesis. The null hypothesis is rejected at 2.5% significance level if the lower bound of the two-sided 95% confidence bound on the proportion of patients with a threshold increase of $\leq$ 0.5V at 0.5ms from before to one month post MRI visit is greater than 90%.

Sample Size

A success (Post-MRI scan Threshold – Pre-MRI scan Threshold) is defined as a patient who experiences an increase in threshold less than or equal to 0.5 volts at the 1 month post-MRI visit compared to their pre-MRI testing (MRI visit). In this case post MRI capture Threshold $\leq$ pre MRI capture Threshold + 0.5 volts.

The % of Success (Post-MRI scan Threshold – Pre-MRI scan Threshold) is defined as the number of patients with successes divided by the analyzable patients.

In another manufacturer's study involving an MRI conditional pacemaker, the proportion of patients with an increase in threshold less than or equal to 0.5 volts at the 1 month post-MRI visit compared to their pre-MRI testing was 100%.[19] Therefore, an assumption of 98% of successes (Post MRI scan-Pre-MRI scan threshold) in the atrium and ventricle is assumed in the sample size calculation.

A sample size of 93 patients provides 90% power to demonstrate a success rate greater than 90% for the atrial and ventricular endpoints, respectively, at the 2.5% significance level.

Analysis

The analysis will be conducted on the per-protocol population. The per-protocol population includes patients who meet the following criteria:

- Successfully implanted with the Accent MRI system
- Have MRI visit data
- Meet the MRI Conditions of Use
- Received an MRI scan
- Have 1 month post MRI visit data
- Have a pacing threshold difference not exceeding 0.5 V at 0.5 ms between the two-month and MRI visit device pre-check, in cases where the MRI visit occurs approximately 9-12 weeks after the implant or system revision procedure since such short-term variability in pacing performance can be indicative of an abnormal lead/tissue interface that could confound analyses of MRI related effects.
- Have an atrial lead to be included in the '% success (change in atrial capture threshold)' endpoint analysis and/or a ventricular lead to be included in the '% success (change in ventricular capture threshold)' endpoint analysis
- Are not in AF at the time of atrial capture threshold measurements. Note: If atrial arrhythmias persist throughout the visit window for the MRI and/or 1 Month Post MRI visit, and no atrial capture threshold value can be obtained either at the MRI and/or 1 Month Post MRI visit, measured atrial capture threshold values from the next nearest timed visit may be substituted.

The proportion of patients not experiencing increases of 0.5V at 0.5ms for both atrial and ventricular capture thresholds will be calculated separately along with the associated 2.5% lower confidence bound. The lower bound for both of these proportions will be compared to the

OPC of 90%. The endpoints will be considered successful if the lower bound is greater than 90%.

Additional Analyses
A sensitivity analysis of the endpoint will be conducted using the ITT population, where both a worst and best case analysis will be performed. The worst case analysis will consist of treating all missing data as failures. The best case analysis will treat all missing data as successes.

4.2.3.3 Proportion of patients with atrial sensing amplitude decrease of ≤ 50% and a sensing amplitude at 1-month post MRI visit of ≥ 1.5mV

The hypothesis for the atrial sensing threshold is formally expressed as:

H_0: Proportion of patients with an atrial sensing amplitude decrease of ≤ 50% and atrial sensing amplitude at 1-month post MRI visit of >1.5 mV ≤ 85%

H_a: Proportion of patients with an atrial sensing amplitude decrease of ≤ 50% and atrial sensing amplitude at 1-month post MRI visit of ≥ 1.5 mV > 85%

The null hypothesis is rejected at 2.5% significance level if the lower bound of the two-sided 95% confidence interval on the proportion of patients with an atrial sensing amplitude decrease of ≤ 50% and atrial sensing amplitude at 1-month post MRI visit of ≥ 1.5mV is greater than 85%.

4.2.3.4 Proportion of patients with ventricular sensing amplitude decrease of ≤ 50% and a sensing amplitude at 1-month post MRI visit of ≥ 5mV

The hypothesis for the ventricular sensing threshold is formally expressed as:

H_0: Proportion of patients with a 'ventricular sensing amplitude decrease of ≤ 50% and ventricular sensing amplitude at 1-month post MRI visit of >5 mV' ≤ 87%

H_a: Proportion of patients with a 'ventricular sensing amplitude decrease of ≤ 50% and atrial sensing amplitude at 1-month post MRI visit of ≥ 5 mV' >87%

The null hypothesis is rejected at 2.5% significance level if the lower bound of the two-sided 95% confidence interval on the proportion of patients with a 'ventricular sensing amplitude decrease of ≤ 50% and ventricular sensing amplitude at 1-month post MRI visit of ≥5mV' is greater than 87%.

Sample Size

A success is defined as a patient who experiences a decrease in sensing amplitude not exceeding 50%, and a sensing amplitude not less than 5 mV for ventricular measurements and not less than 1.5mV for atrial measurements at the 1 month post-MRI visit from the pre-MRI testing (at MRI visit).

The % of Success (Post-MRI scan Amplitude – Pre-MRI scan Amplitude) is defined as the number of patients with successes divided by the number of analyzable patients.

In another manufacturer's study involving MRI conditional pacemaker, proportion of patients with 'sensing amplitude decrease of ≤ 50% and atrial sensing amplitude at 1-month post MRI visit of ≥ 1.5mV' was approximately 93%. In the same study, the proportion of patients with 'sensing amplitude decrease of ≤ 50% and ventricular sensing amplitude at 1-month post MRI visit of ≥ 5mV' was approximately 95%.[19] Therefore, an assumption of 93% for successes in the atrium and 95% successes in the ventricle is assumed

A sample size of 165 patients provides 90% power for the atrial endpoint and 138 patients provides 90% power for the ventricular endpoint at the 2.5% significance level.

Analysis

The analysis will be conducted on the per-protocol population. The per-protocol population includes patients who meet the following criteria:

- Successfully implanted with the Accent MRI™ system
- Have MRI visit data
- Meet the MRI Conditions of Use
- Received an MRI scan (if in the MRI group)
- Have 1-month post MRI visit data
- Have a pacing threshold difference not exceeding 0.5V between the two-month and three month post-implant (MRI scan pre-check), in cases where the MRI visit takes place approximately 9-12 weeks after an implant or system revision procedure since such short-term variability in pacing

performance can be indicative of an abnormal lead/tissue interface that could confound analyses of MRI related effects.

- Have a pre-MRI/pre-waiting period sensing amplitude greater than or equal to 5.0 mV in the ventricle or greater than or equal to 1.5 mV in the atrium.
- Have an atrial lead to be included in the '% success (change in atrial sensing amplitude)' endpoint analysis and/or a ventricular lead to be included in the '% success (change in ventricular sensing amplitude)' endpoint analysis
- Are not in AF at the time of atrial sensing amplitude measurements
- Have an intrinsic heart rate ≥ 30 beats per minute at the time of ventricular and/or atrial capture threshold measurements

The proportion of patients not experiencing an atrial sensing amplitude decrease of ≤ 50% and atrial sensing amplitude at 1-month post MRI visit of >1.5 mV will be calculated. The associated 2.5% lower confidence bound will also be derived. This lower bound will be compared to the OPC of 85% and the endpoint will be considered successful if the lower bound is greater than 85%.

The proportion of patients not experiencing a ventricular sensing amplitude decrease of ≤ 50% and ventricular sensing amplitude at 1-month post MRI visit of > 5 mV will be calculated. The associated 2.5% lower confidence bound will also be derived. This lower bound will be compared to the OPC of 87% and the endpoint will be considered successful if the lower bound is greater than 87%.

All individual primary efficacy endpoints must be successful (reject the null hypothesis at the $\alpha = 2.5\%$ level) for the efficacy endpoint to be successful.

Additional Analyses

The same additional analyses described above in section 4.2.3.1 and 4.2.3.2 will be completed for this endpoint if required.

The overall success for the primary endpoints is achieved if all primary safety and primary efficacy endpoints are successful.

4.2.4 Secondary Endpoints

The secondary endpoints will be assessed only if all primary safety and efficacy endpoints were significant. The secondary endpoints will be tested sequentially in the order of: system related complications at 12 months, followed by the atrial capture threshold at the MRI visit, and finally the mean ventricular capture threshold at the MRI visit. At the point where a secondary endpoint fails to achieve significance, all further testing of secondary endpoints will stop.

4.2.4.1 Freedom from system-related complications

The hypothesis is formally expressed as:

H_0: Freedom from system related complications through the 12 month visit $\leq 80\%$

H_a: Freedom from system related complications through the 12 month visit $> 80\%$

The desired outcome is to reject the null hypotheses. The null hypothesis will be rejected at the 5% significance level if the 95% lower confidence limit for the freedom from system related complications at 12 months is greater than 85%.

Simulation was used to calculate the sample size requirements for testing the Kaplan-Meier estimated survival probability for the freedom-from-complication endpoint. The expected proportion of patients free from system related complications at 12 months is 0.975 (95% CI: 0.924, 0.992) using data from the VICTORY pulse generator IDE study (G050191). For a study size of 800 patients and a Type 1 error rate for the hypothesis test of $\alpha = 0.05$ for a one-sided test, the power is greater than 98%.

Patient Group
All patients that have had an attempted implant or a successful implant of an Accent MRI system will be included in this endpoint.

Patients who are lost to follow-up or withdrawn prior to the 12 month follow-up visit due to a system related complication will be analyzed as having experienced a complication at the date of withdrawal. Patients who withdraw for reasons unrelated to a system related complication will be censored at the date of withdrawal.

4.2.4.2 Bipolar atrial capture threshold at the MRI visit

The hypothesis is formally expressed as:

H_0: The proportion of patients with atrial capture threshold ≤2.0V at MRI visit is ≤ 85%

H_a: The proportion of patients with atrial capture threshold is ≤2.0V at MRI visit > 85%

The proportion of patients with atrial capture threshold ≤2.0V at the MRI visit endpoint will be evaluated using a one-sided z-test, with variance calculated using the OPC of 85% at the $\alpha = 2.5\%$ level. The desired outcome is to reject the null hypothesis.

Patient Group
All patients implanted with the Tendril MRI™ lead with pre-MRI testing atrial capture threshold measurements at the MRI visit.

4.2.4.3 Bipolar ventricular capture threshold at the MRI visit

The hypothesis is formally expressed as:

H_0: The proportion of patients with ventricular capture threshold ≤ 2.0 V at MRI visit is ≤ 85%

H_a: The proportion of patients with ventricular capture threshold ≤2.0 V at MRI visit is > 85%

The proportion of patients with ventricular capture threshold ≤2.0V at MRI visit endpoint will be evaluated using a one-sided z-test with variance calculated using the OPC of 85% at the $\alpha = 2.5\%$ level. The desired outcome is to reject the null hypothesis.

Patient Group
All patients implanted with the Tendril MRI™ lead with pre-MRI ventricular capture threshold measurements at the MRI visit.

4.2.4.4 Additional Secondary Endpoint Analyses

As supporting analyses for each of the three secondary endpoints, a tipping point analysis will be provided. In sequential fashion, each missing data point will be replaced by a "failure" after which the analysis will be re-run. This continues until either all missing data has been replaced with a "failure" or the test becomes non-significant (i.e.

the interpretation of the results changes). The proportion of missing data that would need to be a failure in order to change the analysis results will be reported and discussed.

4.2.5 Sub-group Analyses

Gender Analysis

The primary and secondary endpoints will be re-analyzed comparing the estimates for males and females. All relevant summary statistics will be reported.

Additionally, for the primary endpoints of freedom from RV/RA lead related complications in both the acute and chronic timeframes, a Kaplan-Meier analysis comparing freedom from lead complications between males and females will be provided. Note that with the large sample size associated with these endpoints, clinically irrelevant differences may be detected. This same type of analysis will also be done on the endpoint of freedom from MRI scan related complications.

All comparisons of gender will be done at the 0.15 level of significance.

4.2.6 Additional Data

- Ability to identify radiopaque identification marker on the pacemaker and lead through X-ray review by a cardiologist and radiologist
- Adverse Events – system, lead, and implant procedure related events (not including the primary safety endpoint)
- Atrial and ventricular bipolar capture thresholds immediately after MRI scan
- Atrial and ventricular unipolar capture thresholds before and after the MRI scan
- Atrial and ventricular bipolar lead impedance through the 1 month post MRI visit
- Atrial and ventricular bipolar sensing thresholds immediately after MRI scan
- Cardiac medications
- Challenges and lessons learned in communication between the MRI/Radiology and Cardiology teams

- Demographics: gender, age, ethnicity, race, cardiac disease history, arrhythmia history, indication for pacemaker implant, history of smoking, etc.
- Inadequate equipment availability during MRI scan
- Incidence of aberrant or undesirable behavior of the device while in the MRI mode.
- Incidence of MRI related arrhythmias and asystole
- Lead handling characteristics
- Loss or lapses in patient monitoring during the MRI scan
- Mortality
- MRI Activator performance and usability
- MRI image qualitative analysis; St. Jude Medical will provide data on the image quality/presence of artifact for the first 20 MRI scans performed. Each participating site will be asked to submit the first five MRI scans performed (up to 5 scans maximum) until 20 total scans have been submitted.
- Number of non-study related MRI scans
- Preliminary study phase small cohort - St. Jude Medical will summarize the adverse event data on the first 44 patients who complete the one month post MRI scan (29 MRI, 15 Control). This summary will be provided to the FDA.

4.2.7 Definitions to be used in the MRI study

Abnormal Lead Pacing Impedance: Measured pacing impedances with values $\leq 200\ \Omega$ or $\geq 2000\ \Omega$

Adverse Event: Any unfavorable clinical event which impacts, or has the potential to impact the health or safety of a patient caused by or associated with a study device or intervention. Adverse events are classified as complications or observations.

Complication: An adverse event caused by or associated with the study device, system component(s), and or procedure that requires invasive intervention (e.g. lead dislodgment requiring repositioning).

Cardiac Tamponade: Confirmed or suspected accumulation of fluid in the pericardial space

Cardiac Perforation: An excursion of the lead through the cardiac muscle. Signs and symptoms of a perforation by an intra-cardiac lead

may include radiographic evidence of excursion of the lead into the pericardial sac, abnormal echocardiography indicative of a perforation, the accumulation of fluid in the pericardium, cardiac tamponade, or patient symptoms such as chest pain and discomfort

Diaphragmatic/Phrenic Nerve Stimulation: Electrical activation of the diaphragm muscle by the device output pulse. The abrupt diaphragmatic contraction is noted clinically as hiccups associated with each pacing stimulus. The pacing stimulus may stimulate the diaphragm either directly or indirectly via the phrenic nerve.

Elevated Pacing Thresholds: Pacing thresholds > 2.0 V at 0.5 ms at implant. Following lead maturation at 6-8 weeks, an increase in pacing thresholds of 1.2 V at 0.5 ms or greater between visits. This definition is intended to serve as a guideline and it is understood that individual patients may have unique situations

Lead Dislodgement: The movement of a pacing lead from its originally implanted position resulting in elevated pacing thresholds or a decrease in sensing

Lead Fracture: A break in a conduction coil of a pacing or defibrillation lead typically evidenced by an increase in impedance, intermittent or complete loss of capture, intermittent or complete loss of sensing, noise on the intra-cardiac electrogram and visual signs of conductor coil fracture on x-ray

Lead Insulation Damage: A disruption to the integrity of the lead insulation without disruption of the conductor coil. An insulation break may be indicated by a drop in impedance, and can cause loss of capture or sensing problems

Loss of Capture: The inability of the device's output pulse to result in depolarization and contraction of the appropriate cardiac chamber. Causes include insufficient stimulus strength, separation of the electrode from the myocardium and placement of the stimulating electrode in contact with a non-responsive portion of the myocardium such as scar tissue. Delivery of an output pulse at a time when the myocardium is physiologically refractory is not loss of capture, since capture is not physiologically feasible

Loss of Sensing: A condition in which the pulse generator is unable to sense intrinsic cardiac signals

Observation: An adverse event caused by or associated with the study device, system component(s), and or procedure that does not requires invasive intervention (e.g. oversensing or loss of pacing capture requiring reprogramming).

Oversensing: The detection of inappropriate electrical signals by the pulse generator's sense amplifier. These signals, such as myopotentials, electromagnetic interference, T waves or crosstalk between atrial and ventricular channels, must be of sufficient duration to interfere with normal device function

Pneumothorax: An accumulation or suspected accumulation of air in the pleural cavity

Undersensing: The failure of the pulse generator to sense P or R waves, causing delivery of inappropriately timed, asynchronous or competitive output pulses. Undersensing can sometimes be corrected by programming the device to a more sensitive setting, i.e., decreasing the millivolt value

4.3 Patient Selection

4.3.1 Inclusion Criteria

Eligible patients will meet **all** of the following:

1. Have an approved indication per ACC/AHA/HRS guidelines for implantation of a pacemaker
2. Will receive a new pacemaker and lead
3. Be willing to undergo an elective MRI scan without sedation
4. Be able to provide informed consent for study participation (legal guardian is NOT acceptable)
5. Be willing and able to comply with the prescribed follow-up tests and schedule of evaluations
6. *Is not contraindicated for an MRI scan (per the pre-MRI safety screening form)

4.3.2 Exclusion Criteria

Patients will be excluded if they meet **any** of the following:

1. Have an existing pacemaker or ICD. A new pacemaker and lead is required for enrollment

2. *Have an existing active implanted medical device, e.g., neurostimulator, infusion pump, etc.
3. *Have a non-MRI compatible device or material implanted (e.g., intracranial aneurysm clip, non-MRI compatible devices or material, metals or alloys, etc.)
4. Have a lead extender or adaptor
5. Be unable to fit in MRI bore; will come into contact with the magnet façade inside the MRI bore.
6. Have a prosthetic tricuspid heart valve
7. Are currently participating in a clinical investigation that includes an active treatment arm
8. Are allergic to dexamethasone sodium phosphate (DSP)
9. Are pregnant or planning to become pregnant during the duration of the study
10. Have a life expectancy of less than 12 months due to any condition
11. Patients with exclusion criteria required by local law (e.g., age)
12. Are unable to comply with the follow up schedule

***Applies only to those patients who will participate in the MRI portion of the study.**

4.4 Study Procedures

All required study procedures at each specified interval are outlined in the sections below. Refer to Table 1 and Table 2 for an overview of the required study procedures at each interval or study visit.

Table 1: Schedule of Evaluations Summary: MRI Lead Safety

Evaluation	Cardiology Staff						
	Standard Study Visits						
	Enrollment	Implant	Post Implant (Pre-Discharge)	2 month post implant visit	6 month visit	12 month visit	Every 6 months until Study Completion
Informed Consent & Inclusion/ Exclusion Evaluation	√						
Cardiovascular history	√						
Cardiac medications	√		√	√	√	√	√
Pre-MRI Safety Screening (MRI Safety Screening Form)	√						
Bipolar capture threshold testing @ 0.5msec, bipolar sensing amplitude & lead impedance for RA and RV leads *		√	√	√	√	√	√
Chest X-ray (PA and lateral view of final lead placement)			√				
X – ray analysis by cardiologist and radiologist			√				

** Note: RA lead measurements are not required if a single chamber device is implanted. RA capture and sensing thresholds are not required if a patient is in atrial fibrillation or atrial flutter.*

RA/RV sensing measurements are not required if the patient's intrinsic rate has been established to be below 30 beats per minute. RV capture thresholds are not required if a high ventricular rate is present.

Table 2: Schedule of Evaluations Summary: MRI-Related Visits

Evaluation	Radiology & Cardiology Staff				
	MRI Visit Schedule				
		MRI visit			
	Prior to MRI Visit	Pre- MRI Period Testing	MRI Period	Post-MRI Testing	1 Month Post MRI
Informed Consent & Inclusion/ Exclusion Evaluation+	√+				
Bipolar capture threshold testing @ 0.5msec, bipolar sensing amplitude & lead impedance for RA and RV leads *		√		√	√
Unipolar capture threshold testing @ 0.5msec, for RA and RV leads*		√		√	√
Cardiac medications		√			√
Pre-MRI Safety Screening (MRI Safety Screening Form)		√			
MRI Hazard Checklist		√			
Pregnancy Test		√			
Pulse Oximetry			√		
ECG			√		
Save MRI Setting		√			
Use MRI Activator to activate MRI Setting			√		
Use MRI Activator to deactivate MRI Setting				√	

** Note: RA lead measurements are not required if a single chamber device is implanted. RA capture and sensing thresholds are not required if a patient is in atrial fibrillation or atrial flutter. If the RA capture and sensing thresholds could not be obtained due to a patient's atrial fibrillation or flutter, and if the patient's atrial fibrillation or flutter is transient, for data analysis purposes, the pacing capture threshold and sensing threshold from the next study visit, if available, will be used.*

RA/RV sensing measurements are not required if the patient's intrinsic rate has been established to be below 30 beats per minute. RV capture thresholds are not required if a high ventricular rate is present.

+Study site must verify that the MRI consent has been signed and patient meets criteria to undergo MRI scan

4.4.1 Enrollment Requirements

4.4.1.1 Enrollment

Consider all patients for participation in this study regardless of gender. Screen patients as outlined by the inclusion/exclusion criteria. Obtain informed consent from the patient. Collect data on the patient including gender, age, ethnicity, race, cardiac disease history, cardiac medications, arrhythmia history, smoking history, and indication for pacemaker implant. It is required that the pre-MRI safety screening form be completed as part of the enrollment screening for all patients to ensure there are no current contraindications for an MRI scan; this will apply to all patients agreeing to participate in the MRI portion of the study of the study (see Appendix A). Patients who meet the inclusion, and do not meet the exclusion criteria, sign an IRB approved informed consent and have an attempted implant will be considered enrolled in the study.

Once eligibility screening is completed, informed consent has been obtained, and the Accent MRI system has been implanted, or an attempt was made to implant the system (refer to the Implant Procedures section for further details), complete and submit the forms listed under the Implant Procedures to St. Jude Medical via Electronic Data Capture (EDC).

4.4.2 Implant Procedures

Perform the device and lead implant procedure according to standard of care. Do not implant a dual chamber device with only one lead. Consult the User's Manual for implantation guidelines, appropriate lead/device connections and general handling information. The Accent MRI system will be considered successfully implanted if, at a minimum, the Accent MRI pacemaker and a Tendril MRI lead are implanted.

4.4.2.1 Lead Placement and Testing

Implant one Tendril MRI™ Lead (Model LPA1200M) in the right ventricle and one in the right atrium for dual chamber pacemakers. Implant one Tendril MRI™ lead in the right ventricle for single chamber pacemakers. The physician can use any appropriate delivery system that is legally marketed from St. Jude Medical or any other manufacturers.

- Only Tendril MRI™ leads are permitted (abandoned leads, additional leads and non-Tendril MRI™ leads are not permitted). If non-Tendril MRI™ leads are implanted, complete a protocol deviation form.
- Use of lead extenders or adaptors is not permitted. If used, complete a protocol deviation form.
- The atrial or ventricular port cannot be plugged. If either port is plugged, complete a protocol deviation form.

After the lead(s) are connected to the device, obtain the following electrical measurements for the RA and/or RV leads.

- Manual bipolar capture threshold at a pulse width of 0.5 ms using the Decrement Threshold test method. Pace at least three cycles per step, and confirm at least three consecutive beats have capture before recording the capture threshold results.
- Bipolar sensing amplitude using the Incremental Test Method. Set the required sensed beats to at least 3 cycles per step. Confirm at least three consecutive beats are sensed before recording the sensing threshold results.
- Bipolar lead impedance

Note: RA lead measurements are not required if a single chamber device is implanted. RA capture and sensing thresholds are not required if a patient is in atrial fibrillation or atrial flutter.

RA/RV sensing measurements are not required if the patient's intrinsic rate has been established to be below 30 beats per minute. RV capture thresholds are not required if a high ventricular rate is present.

Data Submission
Once required testing has been completed at the Implant Visit, complete and submit the forms listed below to St. Jude Medical. Upload device session records through the EDC study site portal. Device session records may also be sent to St. Jude Medical, CRMD Sylmar, CA.

- Enrollment Form
- Implant Form
- Medication Log
- Adverse Event Form, if applicable

- Protocol Deviation Form, if applicable
- Product Out of Service Form, if applicable
- Death Form, if applicable

It is recommended that the following device printouts and measurements be maintained at the site.

- FastPath Summary
- Test Results with Large Freezes, Include Battery & Leads
- Wrap-up Overview with full parameters

4.4.3 Unsuccessful Implant

Unless the implant will be re-attempted, for patients who have an unsuccessful implantation of a St. Jude Medical Accent MRI system, follow the patient for a period of 30 days for adverse events, and then withdraw the patient. The physician must document the nature of the unsuccessful implant on the implant form. Only those individuals who are successfully implanted with the Accent MRI system are permitted to undergo an MRI scan.

Data Submission
Once information has been collected and required testing has been completed at the Implant Visit, complete and submit the forms listed below to St. Jude Medical. If applicable, upload device session records through the EDC study site portal. Device session records may also be sent to St. Jude Medical, CRMD Sylmar, CA.

- Implant Form
- Medication Log
- Withdrawal Form
- Adverse Event Form, if applicable
- Protocol Deviation Form, if applicable
- Product Out of Service Form, if applicable
- Death Form, if applicable

It is recommended that the following device printouts and measurements be maintained at the site.

- FastPath Summary, if applicable
- Test Results with Large Freezes, Include Battery & Leads, if applicable

- Wrap-up Overview with full parameters, if applicable

4.4.4 Complete System Explants

If the patient has the entire Accent MRI system removed at any time during the study, and the patient will not receive a replacement Accent MRI system, follow the patient for 30 days, and withdraw the patient from the study. Complete and submit the forms listed below to St. Jude Medical. A system revision form is not required to be submitted.

- Withdrawal Form
- Product Out of Service Form
- Adverse Event Form, if applicable
- Death Form, if applicable

4.4.5 Follow-Up Requirements – Lead Safety

Patients will be seen at the following intervals:

- System Revision, if applicable
- Pre-Discharge
- 2 month visit (post implant)
- 6 month visit (post implant)
- 12 month (and every 6 months thereafter until completion of the study) (post implant)

The schedule of follow up visits is based on the date of the successful implant for all visits for the lead safety component of the study.

Table 3: Study Time Interval Windows – Lead Safety

Post Implant (Pre-Discharge)	2 months post implant	6 months post implant	12 month post implant	Every 6 months post implant after until study completion
+ 7 days	±7 days	± 60 days	± 60 days	± 60 days

4.4.5.1 System Revisions

A system revision is defined as capping a lead, plugging a port, repositioning or explanting (with or without replacement) of the implanted pacemaker and/or leads.

If the patient undergoes a system revision that results in:

- a complete Accent MRI system explant with replacement of another Accent MRI system within the same procedure, OR
- replacement of one or more MRI components with another MRI component(s), OR
- repositioning of one or more MRI leads,
- capping of the MRI or any other implanted lead(s),
- plugging of a port, or
- implant of a non-MRI lead or device, OR
- any combination above, AND
- at least 1 MRI component is still implanted,

perform the testing as outlined in section 4.4.2.1. Only MRI leads that are repositioned or newly implanted during the revision procedure need to be tested. Any explanted devices or leads (including damaged leads, lead segments and lead fragments) should be returned to St. Jude Medical promptly for analysis. Document any change to the status of the lead and device (e.g. capped, removed) on the Product Out of Service Form.

Note: RA lead measurements are not required if a single chamber device is implanted. RA capture and sensing thresholds are not required if a patient is in atrial fibrillation or atrial flutter.

RA/RV sensing measurements are not required if the patient's intrinsic rate has been established to be below 30 beats per minute. RV capture thresholds are not required if a high ventricular rate is present

Data Submission

Complete a Protocol Deviation form for each of the applicable items: capping of lead, implant of a non-MRI component, plugging a port. Complete and submit the forms listed below to St. Jude Medical. Upload device session records through the EDC study site portal. Device session records may also be sent to St. Jude Medical, CRMD Sylmar, CA.

- System Revision Form

- Adverse Event Form, if applicable
- Deviation Form, if applicable
- Product Out of Service Form, if applicable
- Death Form, if applicable
- Withdrawal Form, if applicable

It is recommended that the following device printouts and measurements be maintained at the site.

- FastPath Summary
- Test Results with Large Freezes, Include Battery & Leads
- Wrap-up Overview with full parameters

Retention and Follow Up
Retain the patient in the study. Follow the patient as outlined in Table 1.

4.4.5.2 Pre-Discharge

A Posterior/Anterior (P/A) and Lateral view chest x-ray of the final lead position must be obtained at pre-discharge to confirm the presence of MRI radiopaque identification markers on the leads and pacemaker, ensure that the radiopaque identification markers are easily identifiable, and to ensure no lead dislodgment or lead fracture is present. The x-ray must be reviewed by a radiologist and cardiologist.

- Fluoroscopic, printed angiographic pictures or other methods to confirm lead placement are not to be used as an alternative to the Posterior/Anterior (P/A) and Lateral view x-rays.
- Follow-up chest x-rays are recommended in the case of a lead revision per standard of practice.

Document cardiac medications. Evaluate the patient for adverse events. Perform a device interrogation, and obtain the following electrical measurements for the RA and/or RV leads.

- Manual bipolar capture threshold at a pulse width of 0.5 ms using the Decrement Threshold test method. Pace at least three cycles per step, and confirm at least three consecutive beats have capture before recording the capture threshold results.
- Bipolar sensing amplitude using the Incremental Test Method. Set the required sensed beats to at least 3 cycles per step.

Confirm at least three consecutive beats are sensed before recording the sensing threshold results.

- Bipolar lead impedance

Note: RA lead measurements are not required if a single chamber device is implanted. RA capture and sensing thresholds are not required if a patient is in atrial fibrillation or atrial flutter.

RA/RV sensing measurements are not required if the patient's intrinsic rate has been established to be below 30 beats per minute. RV capture thresholds are not required if a high ventricular rate is present.

Data Submission
Once required testing has been performed, complete and submit the forms listed below to St. Jude Medical. If an adverse event has occurred since the Implant, complete an Adverse Event Form. Upload device session records through the EDC study site portal. Device session records may also be sent to St. Jude Medical, CRMD Sylmar, CA.

- Pre-Discharge Follow Up Form
- Adverse Event Form, if applicable
- Protocol Deviation Form, if applicable
- Product Out of Service Form, if applicable
- Death Form, if applicable
- Withdrawal Form, if applicable

It is recommended that the following device printouts and measurements be maintained at the site.

- FastPath Summary
- Test Results with Large Freezes, Include Battery & Leads
- Wrap-up Overview with full parameters

4.4.5.3 2 Month Visit (Post Implant)

Document cardiac medications. Evaluate the patient for adverse events. Perform a device interrogation, and obtain the following electrical measurements for the RA and/or RV leads.

- Manual bipolar capture threshold at a pulse width of 0.5 ms using the Decrement Threshold test method. Pace at least three

cycles per step, and confirm at least three consecutive beats have capture before recording the capture threshold results.

- Bipolar sensing amplitude using the Incremental Test Method. Set the required sensed beats to at least 3 cycles per step. Confirm at least three consecutive beats are sensed before recording the sensing threshold results.
- Bipolar lead impedance

Note: RA lead measurements are not required if a single chamber device is implanted. RA capture and sensing thresholds are not required if a patient is in atrial fibrillation or atrial flutter.

RA/RV sensing measurements are not required if the patient's intrinsic rate is established to be below 30 beats per minute. RV capture thresholds are not required if a high ventricular rate is present.

If required testing was unable to be performed within the protocol specified criteria (e.g., 0.5 ms pulse width for capture thresholds) please reschedule the patient to return for re-testing. If possible, bring the patient back for re-testing within the visit window.

Data Submission
Once required testing has been performed, complete and submit the forms listed below to St. Jude Medical. If an adverse event has occurred since the Implant, complete an Adverse Event Form. Upload device session records through the EDC study site portal. Device session records may also be sent to St. Jude Medical, CRMD Sylmar, CA.

- Follow Up Form
- Medication Log
- Adverse Event Form, if applicable
- Protocol Deviation Form, if applicable
- Product Out of Service Form, if applicable
- Death Form, if applicable
- Withdrawal Form, if applicable

It is recommended that the following device printouts and measurements be maintained at the site.

- FastPath Summary
- Test Results with Large Freezes, Include Battery & Leads
- Wrap-up Overview with full parameters

4.4.5.4 6 Month Visit (Post Implant)

Document cardiac medications. Evaluate the patient for adverse events. Perform a device interrogation, and obtain the following electrical measurements for the RA and/or RV leads.

- Manual bipolar capture threshold at a pulse width of 0.5 ms using the Decrement Threshold test method. Pace at least three cycles per step, and confirm at least three consecutive beats have capture before recording the capture threshold results.
- Bipolar sensing amplitude using the Incremental Test Method. Set the required sensed beats to at least 3 cycles per step. Confirm at least three consecutive beats are sensed before recording the sensing threshold results.
- Bipolar lead impedance

Note: RA lead measurements are not required if a single chamber device is implanted. RA capture and sensing thresholds are not required if a patient is in atrial fibrillation or atrial flutter.

RA/RV sensing measurements are not required if the patient's intrinsic rate is established to be below 30 beats per minute. RV capture thresholds are not required if a high ventricular rate is present.

Data Submission
Once required testing has been performed, complete and submit the forms listed below to St. Jude Medical. If an adverse event has occurred since the last study visit, complete an Adverse Event Form. Upload device session records through the EDC study site portal. Device session records may also be sent to St. Jude Medical, CRMD Sylmar, CA.

- Follow Up Form
- Medication Log
- Adverse Event Form, if applicable
- Protocol Deviation Form, if applicable
- Product Out of Service Form, if applicable
- Death Form, if applicable
- Withdrawal Form, if applicable

It is recommended that the following device printouts and measurements be maintained at the site.

- FastPath Summary
- Test Results with Large Freezes, Include Battery & Leads
- Wrap-up Overview with full parameters

4.4.5.5 12 Month Visit (Post Implant) (and every 6 months thereafter)

The 12 month visit must be completed in-office. Document cardiac medications. Evaluate the patient for adverse events. Perform a device interrogation, and obtain the following electrical measurements for the RA and/or RV leads.

- Manual bipolar capture threshold at a pulse width of 0.5 ms using the Decrement Threshold test method. Pace at least three cycles per step, and confirm at least three consecutive beats have capture before recording the capture threshold results.
- Bipolar sensing amplitude using the Incremental Test Method. Set the required sensed beats to at least 3 cycles per step. Confirm at least three consecutive beats are sensed before recording the sensing threshold results.
- Bipolar lead impedance

Note: RA lead measurements are not required if a single chamber device is implanted. RA capture and sensing thresholds are not required if a patient is in atrial fibrillation or atrial flutter.

RA/RV sensing measurements are not required if the patient's intrinsic rate is established to be below 30 beats per minute. RV capture thresholds are not required if a high ventricular rate is present.

For the 12 Month Visit, if required testing was unable to be performed within the protocol specified criteria (e.g., 0.5 ms pulse width for capture thresholds) please reschedule the patient to return for re-testing. If possible, bring the patient back for re-testing within the visit window.

Data Submission
Once required testing has been performed, complete and submit the forms listed below to St. Jude Medical. If an adverse event has occurred since the last study visit, complete an Adverse Event Form. Upload device session records through the EDC study site portal.

Device session records may also be sent to St. Jude Medical, CRMD Sylmar, CA.

- Follow Up Form
- Medication Log
- Adverse Event Form, if applicable
- Protocol Deviation Form, if applicable
- Product Out of Service Form, if applicable
- Death Form, if applicable
- Withdrawal Form, if applicable

It is recommended that the following device printouts and measurements be maintained at the site.

- FastPath Summary
- Test Results with Large Freezes, Include Battery & Leads
- Wrap-up Overview with full parameters

4.4.5.6 Unscheduled Follow-up Visits

An unscheduled visit is defined as a visit between two specified study interval visits where the patient is seen in clinic due to an adverse event associated with the Accent MRI system. Where possible, document cardiac medications, and perform a device interrogation to obtain the following electrical measurements for the RA and/or RV leads.

- Manual bipolar capture threshold at a pulse width of 0.5 ms using the Decrement Threshold test method. Pace at least three cycles per step, and confirm at least three consecutive beats have capture before recording the capture threshold results.
- Bipolar sensing amplitude using the Incremental Test Method. Set the required sensed beats to at least 3 cycles per step. Confirm at least three consecutive beats are sensed before recording the sensing threshold results.
- Bipolar lead impedance

Note: RA lead measurements are not required if a single chamber device is implanted. RA capture and sensing thresholds are not required if a patient is in atrial fibrillation or atrial flutter.

RA/RV sensing measurements are not required if the patient's intrinsic rate is established to be below 30 beats per minute. RV capture thresholds are not required if a high ventricular rate is present.

Data Submission
Complete and submit the forms listed below to St. Jude Medical
Upload device session records through the EDC study site portal.
Device session records may also be sent to St. Jude Medical, CRMD Sylmar, CA.

- Follow Up Form
- Medication Log, if applicable
- Adverse Event Form
- Protocol Deviation Form, if applicable
- Product Out of Service Form, if applicable
- Death Form, if applicable
- Withdrawal Form, if applicable

It is recommended that the following device printouts and measurements be maintained at the site.

- FastPath Summary
- Test Results with Large Freezes, Include Battery & Leads
- Wrap-up Overview with full parameters

4.4.6 Follow-Up Requirements – MRI Visits

Patients participating in the MRI portion of the study will be seen at the following intervals:

- System Revisions, if applicable
- MRI visit
- 1 Month post MRI visit

The MRI visit is based on the date of the successful implant or successful revision of the MRI lead. Please refer to section 4.4.6.2 on when to enroll subjects into the MRI portion of the study, and section 4.4.6.3 on when to schedule the MRI visit. The 1 month post MRI visit is based on the date of the MRI visit.

4.4.6.1 MRI-Related Visit Windows

Table 4: Study Time Interval Windows – MRI-Related Visits

MRI Visit		1 month post MRI visit
Window Opens	Window Closes	
1 week after 2 month visit (post implant or successful system revision)	Not Applicable	± 7 days

4.4.6.2 Enrolling Patients into the MRI Phase of the Study

Consider all patients for participation in the MRI portion of the study regardless of gender. It is required that the MRI safety screening form be completed as part of the MRI screening for all patients who agree to participate in the MRI portion of the study to ensure there are no current contraindications for an MRI scan (See Appendix A). If a patient is contraindicated for the MRI scan based on the study exclusion criteria, the patient is NOT eligible for participation in the MRI portion of the study.

Obtain informed consent from the patient.

Important Note: MRI Control Patients enrolled under Revision J of the Protocol: This revision of the protocol, Revision K, allows patients previously enrolled into the MRI Phase under Revision J and who were randomized to the MRI Control Group, to now undergo the study MRI scans. To do so, obtain informed consent from the patient.

Patients enrolled and randomized under protocol Revision J to the MRI Control Group who have not completed an MRI Visit or a 1 Month Post MRI visit, AND who do not want to undergo the study MRI scans should be discontinued from the MRI Phase. To do so, complete and submit the MRI Discontinuation Form under the MRI Control visit in RDC.

Patients who have a Tendril MRI lead(s) implanted in or through the jugular are NOT eligible for participation in the MRI portion of the study.

Data Submission
Complete and submit the forms listed below to St. Jude Medical.

- MRI Enrollment Form

- MRI Discontinuation Form, if applicable

It is recommended that the following completed forms be maintained at the site:

- MRI Safety Screening Form
- MRI Hazard Checklist

4.4.6.3 Scheduling the MRI Visit

Schedule the MRI visit no sooner than one week after the 2 month post implant visit or successful system revision procedure where the MRI lead was repositioned or implanted (refer to sections 4.4.6.4 and 4.4.6.5 to determine whether the patient is eligible for a study MRI scan after the patient's MRI system has been revised).

4.4.6.4 System Revisions Before the MRI Visit: Scenario One

If the patient undergoes a system revision that results in:

- a complete Accent MRI system explant with replacement of another Accent MRI system within the same procedure, OR
- replacement of one or more Accent MRI system components with another Accent MRI system component(s), OR
- repositioning of one or more MRI leads,

perform the testing as outlined in section 4.4.2.1. Only MRI leads that are repositioned or newly implanted during the revision procedure need to be tested. Any explanted devices or leads (including damaged leads, lead segments and lead fragments) should be returned to St. Jude Medical promptly for analysis. Document any change to the status of the lead and device (e.g. capped, removed) on the Product Out of Service Form.

Note: RA lead measurements are not required if a single chamber device is implanted. RA capture and sensing thresholds are not required if a patient is in atrial fibrillation or atrial flutter.

RA/RV sensing measurements are not required if the patient's intrinsic rate is established to be below 30 beats per minute. RV capture thresholds are not required if a high ventricular rate is present.

Data Submission
Complete and submit the forms listed below to St. Jude Medical. Upload device session records through the EDC study site portal.

Device session records may also be sent to St. Jude Medical, CRMD Sylmar, CA.

- System Revision Form
- Adverse Event Form, if applicable
- Product Out of Service Form, if applicable
- Death Form, if applicable
- Withdrawal Form, if applicable

It is recommended that the following device printouts and measurements be maintained at the site.

- FastPath Summary
- Test Results with Large Freezes, Include Battery & Leads
- Wrap-up Overview with full parameters

Retention and Follow Up
Retain the patient in the MRI component of the study. Schedule and perform a follow up visit 2 months after the system revision date. Schedule the MRI visit no sooner than one week after the 2 month post implant visit or successful system revision procedure where the MRI lead was repositioned or implanted, and schedule the 1 Month Post MRI visit accordingly. The patient is still a candidate to undergo the study MRI scan after the system revision procedure if all of the items below are met:

- The patient has a complete Accent MRI™ system implanted
- All leads and pacemaker are implanted for more than 9 weeks
- Bipolar capture thresholds are stable at ≤ 2.5V @ 0.5 ms
- Bipolar pacing lead impedances are within range, i.e. ≥ 200 and ≤ 2000 ohms
- Patient undergoes another chest X-ray to ensure no lead dislodgment or lead fracture is present and that the pacemaker and lead are labeled with the radiopaque identification marker. *Note: The cardiologist and radiologist must confirm the presence of MRI radiopaque identification markers on the leads and PG only if a new MRI lead and/or device was implanted*
- There are no abandoned/capped non-Tendril MRI™ leads from the previous implant/explant

4.4.6.5 System Revisions Before the MRI Visit: Scenario Two

If the patient undergoes a system revision that results in:

- capping of the MRI or any other implanted lead(s),
- plugging of a port, or
- implant of a non-MRI lead or device, OR
- any combination above, AND
- at least 1 MRI component is still implanted

perform the testing as outlined in section 4.4.2.1. Only MRI leads that are repositioned or newly implanted during the revision procedure are required to be tested. Any explanted devices or leads (including damaged leads, lead segments, and lead fragments) should be returned to St. Jude Medical promptly for analysis. Document any changes to the status of the lead and device (e.g. capped, removed) on the Product Out of Service form.

Note: RA lead measurements are not required if a single chamber device is implanted. RA capture and sensing thresholds are not required if a patient is in atrial fibrillation or atrial flutter.

RA/RV sensing measurements are not required if the patient's intrinsic rate is established to be below 30 beats per minute. RV capture thresholds are not required if a high ventricular rate is present.

Data Submission

Complete a Protocol Deviation form for each of the applicable items: capping of lead, implant of a non-MRI component, plugging a port. Complete and submit the forms listed below to St. Jude Medical. Upload device session records through the EDC study site portal. Device session records may also be sent to St. Jude Medical CRMD Sylmar, CA.

- System Revision Form
- MRI Discontinuation Form
- Protocol Deviation Form
- Product Out of Service Form
- Adverse Event Form, if applicable
- Death Form, if applicable
- Withdrawal Form, if applicable

It is recommended that the following device printouts and measurements be maintained at the site.

- FastPath Summary
- Test Results with Large Freezes, Include Battery & Leads
- Wrap-up Overview with full parameters

Retention and Follow Up
Discontinue the patient from the MRI component of the study by completing an MRI Discontinuation form. However, retain the patient in the lead safety portion of the study. Bring the patient back for follow up as outlined in Table 1 for the 2 Month visit, if applicable, and all remaining study visits for the lead safety portion of the study.

4.4.6.6 MRI Visit

IMPORTANT NOTE: For patients participating in the MRI portion of the study, prior to the MRI visit, if the patient underwent a system revision that resulted in

- capping of the MRI lead(s),
- plugging of a port, or
- implant of a non-MRI lead or device, OR
- any combination above,

the patient is not eligible to undergo a study MRI Scan. Do not proceed with any of the tests listed for the MRI Visit. If not already done, discontinue the patient from the MRI component of the study. Refer to section 4.4.6.5 for further details.

Otherwise, follow the procedures outlined below for the MRI Visit.

Cardiac Medications and Pregnancy Testing
Document all cardiac medications. Administer a pregnancy test to all female patients of childbearing potential.

Pre-MRI Scan: Pacemaker Device Measurements
Evaluate the patient for adverse events. Perform a device interrogation, and obtain the following electrical measurements for the RA and/or RV leads.

- Manual **unipolar** capture threshold at a pulse width of 0.5 ms using the Decrement Threshold test method. Pace at least three cycles per step, and confirm at least three consecutive beats have capture before recording the capture threshold results.

- Manual **bipolar** capture threshold at a pulse width of 0.5 ms using the Decrement Threshold test method. Pace at least three cycles per step, and confirm at least three consecutive beats have capture before recording the capture threshold results.
- Bipolar sensing amplitude using the Incremental Test Method. Set the required sensed beats to at least 3 cycles per step. Confirm at least three consecutive beats are sensed before recording the sensing threshold results.
- Bipolar lead impedance

Note: RA lead measurements are not required if a single chamber device is implanted. RA capture and sensing thresholds are not required if a patient is in atrial fibrillation or atrial flutter. If the RA capture and sensing thresholds could not be obtained due to a patient's atrial fibrillation or flutter, and if the patient's atrial fibrillation or flutter is transient, for data analysis purposes, the pacing capture threshold and sensing threshold from the next study visit, if available, will be used.

RA/RV sensing measurements are not required if the patient's intrinsic rate is established to be below 30 beats per minute. RV capture thresholds are not required if a high ventricular rate is present.

If required testing was unable to be performed within the protocol specified criteria (e.g., 0.5 ms pulse width for bipolar capture thresholds, the change in the ventricular and/or atrial bipolar capture threshold is > 0.5 V at 0.5 ms since the last study visit), please reschedule the patient to return for re-testing. The patient's follow up schedule may need to be revised depending on the nature of the missing data. **Please contact St. Jude Medical personnel to determine if the patient's follow up schedule needs to be revised. Do not proceed any further with the procedures below.**

Data Submission

Once required testing has been performed, complete and submit the forms listed below to St. Jude Medical. If an adverse event has occurred since the last study visit, complete an Adverse Event Form. Upload device session records through the EDC study site portal. Device session records may also be sent to St. Jude Medical, CRMD Sylmar, CA.

- MRI Visit Follow Up Form
- Medication Log

- Adverse Event Form, if applicable
- Protocol Deviation Form, if applicable
- Product Out of Service Form, if applicable
- Death Form, if applicable
- Withdrawal Form, if applicable

It is recommended that the following device printouts and measurements be maintained at the site.

- FastPath Summary
- Test Results with Large Freezes, Include Battery & Leads
- Wrap-up Overview with full parameters

If all device measurements were obtained per protocol, proceed with the rest of the procedures as indicated below.

Pre-MRI Safety Screening Assessment

Prior to the MRI scan, complete an MRI Safety Screening assessment to ensure compliance with inclusion/exclusion criteria for the study for patients who previously have not consented to participate in the MRI Phase of the study. For patients who were previously randomized to the MRI Control Group, the MRI Safety Screening assessment does not need to be completed again. (Please see Appendix A). The radiologist or a designated radiological staff member must determine the patient's eligibility for an MRI scan prior to the MRI scan (per standard of practice). However, the pacemaker contraindication item on the checklist does not apply if the patient is implanted with the St. Jude Medical Accent MRI system and is currently enrolled in this clinical study.

Complete the following forms:

- MRI Safety Screening Form (only applies to newly consented patient who did not previously receive a randomization assignment under prior versions of the protocol).
- MRI Hazard Checklist

Review the MRI checklist on the programmer. Verify the following conditions before saving the MRI Setting.

- Bipolar capture thresholds are stable at $\leq$2.5V@ 0.5 ms
- Bipolar pacing lead impedance is within range, i.e. $\geq$ 200 and $\leq$ 2000 ohms
- Device and Leads are labeled for MRI

- No additional hardware (adaptors, extenders, or abandoned leads)

Save the MRI Setting after the MRI Checklist has been reviewed. If the patient is pregnant, do not perform the MRI scan. Perform all other applicable tests and procedures.

Table 5: MRI Parameters

Parameters	Selectable Options	Nominal Values
MRI Mode Accent MRI DR	 AOO VOO DOO Pacing OFF	DOO
Accent MRI SR	VOO Pacing Off	VOO
MRI Base Rate	30-120 bpm, in steps of 5 bpm	85 bpm
MRI Paced AV Delay	25 msec 30-200 msec, in steps of 10 msec 225-300 msec, in steps of 25 msec 350 msec	120 msec
MRI Atrial Pulse Configuration	Bipolar	[non-programmable]
MRI Atrial Pulse Amplitude	5.0 V, 7.5 V	5.0 V
MRI Atrial Pulse Width	1.0 msec	[non-programmable]
MRI RV Pulse Configuration	Bipolar	[non-programmable]
MRI RV Pulse Amplitude	5.0 V, 7.5 V	5.0 V
MRI RV Pulse Width	1.0 msec	[non-programmable]

Pacemaker Programming, Pulse Oximetry and ECG
After the electrical measurements for the RA and/or RV leads have been taken, the Pre-MRI Safety screening assessment completed, the MRI Checklist verified and the MRI Setting saved, activate the MRI parameters with the MRI Activator. Consult the MRI Activator™ User Manual for use of the MRI Activator. Interrogate the device to confirm that the MRI parameters above have been programmed.

Note: the St. Jude Medical Merlin programmer and MRI Activator are not MRI safe and must be used for programming purposes outside of the American College of Radiology (ACR) defined Zone 4 (magnet room).

Set up pulse oximetry and an ECG per standard of care. Capture a real-time ECG/EGM at 25mm/sec.

The MRI scans are not intended to be diagnostic in nature and therefore the administration of contrast fluids or sedation, or the application of saturation bands or water and fat saturation techniques are not permitted. Multiple MRI scans will be conducted for a total magnet duration of approximately 60 minutes. Please review Appendix B for MRI scan sequences.

During the MRI scan sequences, if patient movement causes distortion (documented by a radiologist) on the MRI, the MRI scan will not be repeated (the scan is not meant to be diagnostic) unless it is a clinical scan sequence being performed for image artifact assessment for the MRI study.

Position MRI compatible surface electrodes to continuously monitor the patient's heart rate. During the MRI scan, for monitoring purposes, take pulse oximetry measurements and an ECG. Visually examine the ECG during the MRI scan. Note any abnormalities observed in the cardiac rhythm. After the MRI scan, remove the patient from the MRI field.

Pre-MRI Scan System Checks Summary

- Verify that all items on the pre-MRI safety screening form are satisfied for the patient
- Patient must have a St. Jude Medical Accent MRI lead system implanted, which can be verified by the Patient ID card, patient records, or the radiopaque identification markers on the pacemaker and leads as shown on X-ray.
- The Tendril MRI lead(s) have stable bipolar capture thresholds at $\leq$ 2.5 V@ 0.5 ms.
- Only Tendril MRI leads are allowed (No additional hardware – adaptors, extenders, or abandoned leads)
- Leads are electrically intact. Check that no lead fractures or other damage to the leads has occurred. Bipolar pacing lead impedance is within range, i.e. $\geq$ 200 and $\leq$ 2000 ohms
- Patient is not pregnant (All women of child bearing age must undergo a pregnancy test prior to the MRI Scan)

MRI Scan
After confirmation by the electrophysiologist or device specialist that all pre-MRI system checks (mentioned above) have been met, patients will have their MRI scan completed by a radiology staff member. Protocol required MRI scan sequences for each patient undergoing an MRI scan are described in detail in Appendix B.

Non-Clinical MRI Scans
The goal is to have the patient complete all aspects of testing in Appendix B for the non-clinical scans. Multiple MRI scans will be conducted, and the patient may be in the bore or near the vicinity of the magnet for a total magnet duration of approximately 60 minutes. The minimum amount of scan time that the patient needs to complete is 30 minutes. Consult the MRI procedure information manual for guidelines and precautions.

NOTE: The non-clinical MRI scan is being performed to demonstrate safety and MRI compatibility of the Accent MRI system for an MRI scan, and is not meant to be diagnostic in nature. The MRI scan will not be read by the radiologist.

Clinical MRI Scans
In addition to the non-clinical MRI scan, at least 20 clinical scans will be performed to collect information on image quality and artifact as outlined in Appendix B. Depending on the area being scanned, the scan duration time is approximately 5-10 minutes. Consult the MRI procedure information manual for guidelines and precautions.

The clinical MRI scan is being performed to assess image quality and artifact. The MRI scan should be reviewed for obvious abnormalities by a radiologist, and reported to the patient's physician (per standard of care by the facility performing the MRI scan). A copy of the documentation of the abnormality discovered on the MRI scan should be kept in the patient's file. The review of the MRI scan is not meant to be diagnostic.

Cardiac Monitoring during the MRI scan
During the entire MRI scan, the patient's cardiac function must be monitored using pulse oximetry and an ECG by an Accent MRI study trained electrophysiologist, cardiologist, or Advanced Cardiac Life Support (ACLS) trained personnel capable of delivering external cardiac pacing defibrillation and advanced cardiac life support. Verbal communication with the patient must also take place to assess and/or confirm any clinically significant changes noted in the patient's

oxygen saturation or heart rate, as well as any clinically significant complaints not obvious with pulse oximetry. Record these changes and complaints during the scan.

ACLS procedures must be in place to address situations where a life threatening arrhythmia and/or hemodynamic collapse occurs. The programmer must be used outside the American College of Radiology (ACR) defined Zone 4 magnet room. If the patient's hemodynamic function is compromised during the MRI scan, discontinue the MRI procedure and take proper measures to restore the patient's hemodynamic function.

Life–threatening Ventricular Arrhythmia and Asystole Assessment

Monitoring of spontaneous ventricular arrhythmias and asystole must be conducted via an ECG during the MRI scans. Any sustained ventricular arrhythmias or asystole must be documented on an Adverse Event form. Non-sustained ventricular tachycardias (NSVT) or premature ventricular contractions (PVCs) do not need to be reported as an adverse event. However, if an arrhythmia reproducibly occurs (occurring more than one time) while the patient is actively being scanned, report the event on an Adverse Event form.

Definitions:

- *Sustained Ventricular Arrhythmia:* Heart Rate >150bpm for > 30 seconds
- *Asystole:* A standstill > 6 seconds in electrical activity of the heart (i.e., no heart rate for 6 seconds or more)

Handling of Patients Unable to Tolerate an MR Scan

In cases where the scan cannot be tolerated by the patient, remove the patient from the scanner. Assess the patient for possible adverse events, and treat the patient's reported symptoms according to your institution's standard of practice. Note the reason for the intolerance. At a minimum, information related to the sequence used to perform the scan, the length of time the patient was scanned, and the whole body SAR level reached should be collected and submitted to St. Jude Medical. A repeat scan is not required to be completed.

Test the patient's device as outlined below.

Post-MRI Scan Testing

Immediately following the MRI scan, restore the original programmed values on the pacemaker by pressing the red button on the MRI Activator. Interrogate the pacemaker and confirm the original

programmed values have been restored. Obtain the following electrical measurements for the RA and/or RV leads.

- Manual **unipolar** capture threshold at a pulse width of 0.5 ms using the Decrement Threshold test method. Pace at least three cycles per step, and confirm at least three consecutive beats have capture before recording the capture threshold results.
- Manual **bipolar** capture threshold at a pulse width of 0.5 ms using the Decrement Threshold test method. Pace at least three cycles per step, and confirm at least three consecutive beats have capture before recording the capture threshold results.
- Bipolar sensing amplitude using the Incremental Test Method. Set the required sensed beats to at least 3 cycles per step. Confirm at least three consecutive beats are sensed before recording the sensing threshold results.
- Bipolar lead impedance

Note: RA lead measurements are not required if a single chamber device is implanted. RA capture and sensing thresholds are not required if a patient is in atrial fibrillation or atrial flutter.

RA/RV sensing measurements are not required if the patient's intrinsic rate is established to be below 30 beats per minute. RV capture thresholds are not required if a high ventricular rate is present.

Reporting of MRI Scan-Related Adverse Events
Adverse events related to the following should be reported as soon as possible, but no later than 10 working days, to St. Jude Medical: clotting, pulmonary embolism, or heating of the device pocket during the MRI scan. These events are likely to be associated with symptoms occurring during or immediately following the MRI scan and may manifest as chest pain, shortness of breath, or changes in vital signs during or immediately following the MRI scan.

To ensure all adverse events related to or caused by the MRI scan are appropriately captured, before starting the scan, verbally instruct the patient to report symptoms of chest pain, shortness of breath or pocket discomfort that he/she experiences while being scanned or immediately after exiting the scanner. Note changes in vital signs such as changes in heart rate, blood pressure, room air blood oxygen saturation, and/or respiration rate that occur during the MRI scan that may suggest an AE has occurred due to clotting, pulmonary embolus or related to lead tip or device pocket heating.

If symptoms during or immediately after the MRI scan suggest that an AE has occurred due to clotting, pulmonary embolus or related to lead tip or device pocket heating, test to assess possible causes. Diagnostic testing may be performed in any order deemed appropriate by the investigator; if any test was not performed, provide medical justification for not performing that test:

(1) A 12-lead EKG
(2) A 2-view chest X-ray (PA and Lateral).
(3) Room air blood oxygen saturation
(4) A transthoracic echocardiogram.

If the patient reports pocket discomfort, ask the patient for additional descriptive information and determine if the pocket is discolored or warm to the touch. EKG, chest x-ray, room air blood oxygen saturation, or transthoracic echocardiogram testing are not required to be performed for symptoms related to device pocket heating.

Sites should report an AE if the patient experiences a significant rise in pacing threshold (as defined in section 4.4.6.6 of the study protocol) from pre-MRI scan to one month post-MRI scan.

Data Submission
Once required testing has been performed, complete and submit the forms listed below to St. Jude Medical. If an adverse event has occurred since the last study visit, complete an Adverse Event Form. Upload device session records through the EDC study site portal. Device session records may also be sent to St. Jude Medical, CRMD Sylmar, CA.

If possible, export the study MRI scan onto a CD, DVR or other form of electronic media, and send to St. Jude Medical.

- MRI Scan Group Testing Form
- MRI Survey Form
- MRI Scan Image for image artifact/image quality analysis (St. Jude Medical will notify sites of when to submit the scan)
- Adverse Event Form, if applicable
- Protocol Deviation Form, if applicable
- Product Out of Service Form, if applicable
- Death Form, if applicable
- Withdrawal Form, if applicable

It is recommended that the following device printouts and measurements be maintained at the site.

- FastPath Summary
- Test Results with Large Freezes, Include Battery & Leads
- Wrap-up Overview with full parameters

4.4.6.7 1 Month Post-MRI Visit

For all patients enrolled in the MRI portion of the study, document cardiac medications. Evaluate the patient for adverse events. Perform a device interrogation, and obtain the following electrical measurements for the RA and/or RV leads.

- Manual **unipolar** capture threshold at a pulse width of 0.5 ms using the Decrement Threshold test method. Pace at least three cycles per step, and confirm at least three consecutive beats have capture before recording the capture threshold results.
- Manual **bipolar** capture threshold at a pulse width of 0.5 ms using the Decrement Threshold test method. Pace at least three cycles per step, and confirm at least three consecutive beats have capture before recording the capture threshold results.
- Bipolar sensing amplitude using the Incremental Test Method. Set the required sensed beats to at least 3 cycles per step. Confirm at least three consecutive beats are sensed before recording the sensing threshold results.
- Bipolar lead impedance

Note: RA lead measurements are not required if a single chamber device is implanted. RA capture and sensing thresholds are not required if a patient is in atrial fibrillation or atrial flutter. If the RA capture and sensing thresholds could not be obtained due to a patient's atrial fibrillation or flutter, and if the patient's atrial fibrillation or flutter is transient, for data analysis purposes, the pacing capture threshold and sensing threshold from the next study visit, if available, will be used.

RA/RV sensing measurements are not required if the patient's intrinsic rate is established to be below 30 beats per minute. RV capture thresholds are not required a high ventricular rate is tracking present.

If required testing was unable to be performed within the protocol specified criteria (e.g., 0.5 ms pulse width for capture thresholds)

please reschedule the patient to return for re-testing. If possible, bring the patient back for re-testing within the visit window.

Data Submission
Once required testing has been performed, complete and submit the forms listed below to St. Jude Medical. If an adverse event has occurred since the last study visit, complete an Adverse Event Form. Upload device session records through the EDC study site portal. Device session records may also be sent to St. Jude Medical, CRMD Sylmar, CA.

- Follow Up Form
- Medication Log
- Adverse Event Form, if applicable
- Protocol Deviation Form, if applicable
- Product Out of Service Form, if applicable
- Death Form, if applicable
- Withdrawal Form, if applicable

It is recommended that the following device printouts and measurements be maintained at the site.

- FastPath Summary
- Test Results with Large Freezes, Include Battery & Leads
- Wrap-up Overview with full parameters

4.4.6.8 Non-Study MRI Scan

A non-study MRI scan is defined as a scan occurring at any time following enrollment up to the completion of the study, excluding the MRI scan performed during the MRI Visit. Non-study MRI scans should be performed per each center's standard of care.

For non-study MRI scans performed at the study center, the same safety data collection and safety precautions outlined at the MRI visit should be followed. However, if procedures or data are not followed or collected as presented on the non-study MRI form during a non-study MRI scan, it will not be considered a protocol deviation.

MRI Scan Analysis
The MRI scan should be reviewed for obvious abnormalities by a radiologist, and reported to the patient's physician (per standard of care by the facility performing the MRI scan).

The following data should be collected, and reported to St. Jude Medical for non-study MRI scans:

- Date of scan
- Type of scan performed
- Documentation of any Adverse Events
- Device diagnostics, if available
- MRI Scan report, if available
- Fast Path Summary, if available

Data Submission
If the patient undergoes a non-study MRI scan at any time during the study, please complete and submit the forms listed below to St. Jude Medical. Upload device session records, if applicable and available, through the EDC study site portal. Device session records may also be sent to St. Jude Medical CRMD, Sylmar, CA.

- Non-study MRI Scan Form
- Adverse Event Form, if applicable
- Death, if applicable
- Withdrawal Form, if applicable

It is recommended that the following forms, device printouts and measurements be maintained at the site.

- MRI Safety Screening Form
- MRI Hazard Checklist
- FastPath Summary
- Test Results with Large Freezes, Include Battery & Leads
- Wrap-up Overview with full parameters

5.0 Protocol Deviations

Investigators are required to adhere to the investigational plan, signed Investigator's Agreement, applicable federal (national) or state/local, laws and regulations, and any conditions required by the IRB/MEC or applicable regulatory authorities.

A protocol deviation is used to describe situations in which the clinical protocol was not followed. All deviations from the investigational plan must be reported to St. Jude Medical per 21 CFR §812.150. In addition, all deviations must be reported to the reviewing IRB per the IRB's reporting requirements.

The investigator must notify St. Jude Medical and the reviewing IRB of any deviation from the investigational plan to protect the life or physical well-being of a patient in an emergency as soon as possible, but not later than 5 working days after the deviation has occurred, or no later than 5 working days after the investigator becomes aware of the deviation.

6.0 Adverse Events

A Clinical Events Committee (CEC) will review and adjudicate all Adverse Events. The CEC will base their final adjudication on the information provided on the case report forms, medical records, and their clinical knowledge and experience.

Adverse events (AEs) are any unfavorable clinical event which impacts, or has the potential to impact the health or safety of a patient caused by or associated with a study device or intervention. Adverse events will be classified as complications or observations.

Complications: Adverse events that require invasive intervention (e.g. lead dislodgment requiring repositioning).

Observations: Adverse events that can be managed without invasive intervention (e.g., oversensing or loss of pacing capture, which is remedied by reprogramming of the pacemaker).

Should an adverse event occur, complete an Adverse Event form and submit to St. Jude Medical. Report the adverse event to the IRB/MEC per the IRB/MEC policy. Any explanted devices or leads should be returned to St. Jude Medical for analysis.

Unavoidable AE: An unavoidable AE is defined as an adverse event related to the implant procedure or the MRI scan that is expected to occur for a projected duration in all patients. Unavoidable AEs are not reportable unless the condition worsens or continues beyond the time frame listed below. Unavoidable AEs, listed below, do not need to be reported if they are resolved within the time frame specified.

Table 6: Unavoidable AEs related to the Implant Procedure

Event	Time Frame post-Implant
Anesthesia related nausea/vomiting	<24 hours
Low-grade fever (<100 degree Fahrenheit fever or < 37.8 degree Celsius	< 48 hours
Pocket site/incision pain	< 72 hours
Mild to moderate bruising/ecchymosis at pocket site	< 72 hours
Sleep problems (insomnia)	< 72 hours
Back pain related to laying on the table	< 72 hours

Table 7: Unavoidable AEs related to the MRI Scan

Event	Time Frame post – MRI scan
Claustrophobia	During MRI scan
Mild diaphoresis	During and < 1 hour post MRI scan
Sensation of bodily warmth	During and < 1 hour post MRI scan
Hearing impairment	< 24 hours
Body stiffness related to immobility	< 48 hours

Definitions of AE relatedness:

Pacing system related: An AE that results from the presence or performance of the system under investigation.

Implant procedure related: An AE that occurs due to the implant procedure.

MRI scan related: An AE which is caused by the interaction between the investigational pacing system and the MRI system that occurs during the MRI scan and includes the time the patient is within the 5 Gauss line of the MRI system and up through the patient's 1 month post MRI scan follow up visit. In addition, AE's occurring due to the patient's MRI programming will be considered MRI scan related.

Potential MRI System Adverse Events:

- Lead electrode heating and tissue damage resulting in loss of sensing or capture or both
- Lead heating resulting in thrombus formation or embolism
- Device heating resulting in tissue damage in the implant pocket or patient discomfort or both
- Induced currents on leads resulting in continuous capture, VT/VF, hemodynamic collapse, or all three
- Damage to the device or leads causing:

  - the system to fail to detect or treat irregular heartbeats
  - the system to treat the patient's condition incorrectly
  - Damage to the functionality or mechanical integrity of the device resulting in the inability of the device to communicate with the programmer
- Movement or vibration of the device or leads
- Lead dislodgment
- Competitive pacing and potential for VT/VF induction due to ambulatory asynchronous pacing in MRI mode
- Pulmonary Embolism

Potential Pacing System Adverse Events:

- Air embolism
- Body rejection phenomena
- Cardiac tamponade or perforation
- Hematoma, bleeding hematoma, seroma
- Formation of fibrotic tissue; local tissue reaction
- Inability to interrogate or program due to programmer or device malfunction
- Infection/erosion
- Interruption of desired pulse generator function due to electrical interference either electromyogenic or electromagnetic
- Loss of capture or sensing due to lead dislodgement or reaction at the electrode/tissue interface
- Loss of desired pacing and/or sensing due to lead displacement, body reaction at electrode interface, or lead malfunction (fracture or damage to insulation)
- Lead malfunction due to conductor fracture or insulation degradation
- Loss of normal pacemaker function due to battery failure or component malfunction
- Pacemaker migration, pocket erosion
- Pectoral muscle stimulation
- Phrenic nerve or diaphragmatic stimulation
- Pneumothorax/hemothorax
- Endocarditis
- Excessive bleeding
- Induced atrial or ventricular arrhythmias
- Myocardial irritability
- Pericardial effusion
- Pericardial rub
- Pulmonary edema
- Rise in threshold and exit block
- Valve damage

Potential lead related adverse events

- Cardiac tamponade
- Diaphragmatic/phrenic nerve stimulation
- Embolism
- Excessive bleeding
- Induced ventricular ectopy
- Infection
- Loss of pacing and/or sensing due to dislodgement or mechanical malfunction of the pacing lead
- Thrombosis

Complications reported with direct subclavian venipuncture include pneumothorax, hemothorax, laceration of the subclavian artery, arteriovenous fistula, neural damage, thoracic duct injury, cannulation of other vessels, massive hemorrhage and rarely, death.

As defined in 21 CFR §812.3, **UNANTICIPATED ADVERSE DEVICE EFFECTS (UADE)** are defined as any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of patients.

If an **UNANTICIPATED ADVERSE DEVICE EFFECT** occurs, the investigator must notify St. Jude Medical and the IRB/MEC immediately, but no later than 10 working days of the investigator's knowledge of the event, as required by 21 CFR §812.150. St. Jude Medical will take any steps necessary to investigate the event, and will be responsible for notifying FDA and all other participating IRBs/MECs and investigators.

Should St. Jude Medical determine, either through physician reports or in-house testing, that an unanticipated adverse event presents an unreasonable risk to participating patients, St. Jude Medical will suspend the clinical investigation and notify all participating investigators, IRBs/MECs and the FDA.

6.1 Data Safety Monitoring Board (DSMB)

An independent, unblinded DSMB will be established to review safety data. The DSMB will consist of at least 3 members with study-related backgrounds. Members will include at least one statistician, one cardiologist and one radiologist or cardiologist with MRI experience. St. Jude Medical will appoint members of the DSMB and the chairperson. St. Jude Medical may facilitate the DSMB meeting, but will not be voting members.

7.0 Other Reported Events

Other Reported Events are any other clinical event that is submitted by the investigator which is not caused by or associated with the study device and/or system component(s) and/or defined as an Adverse Event in section 6.0.

8.0 Deaths

A Mortality Committee will review and classify all patient deaths. All patient deaths that occur during this investigation must be reported to St. Jude Medical as soon as possible. Notification of death should include a detailed statement of the pertinent events and be signed by the investigator in addition to the appropriate case report forms (Patient Death form, Patient Withdrawal form, and Product Out of Service form). It is the investigator's responsibility to notify the IRB/MEC per the IRB/MEC policy. Details of death and the following information, if available, should be provided in a letter to St. Jude Medical by the investigator summarizing the patient's course since enrollment in the study:

- Date and time of death
- Place death occurred (e.g. hospital, nursing home, patient's home)
- If death was witnessed
- Identification of the rhythm at the time of death, if known (include any available documentation)
- Cause of death
- Any other circumstances surrounding the death
- Approximate time interval to death from the initiating event.
- Autopsy report (if performed)
- Whether it was device and/or procedure related
- Whether it was related to the study
- Device configuration at the time of death

If any of the above information is not available, provide an explanation in the death narrative of what attempts (and how many) were made to obtain the information, and the outcome of those attempts. At a minimum, two (2) phone calls should be placed, followed by a certified letter, to the patient's next of kin. Provide clinical notes and witness statements. If possible, interrogate the pacemaker. Retrieve and print all episode diagnostics, IEGMs, and programmed parameters. If applicable, the pacemaker should then be programmed **OFF.**

Every attempt should be made to explant the pacemaker and/or leads intact. Any explanted devices or leads should be returned to St. Jude Medical for analysis

promptly. In the event that the device is not explanted, the above procedure must be followed to retrieve the data. The reason the pacemaker and/or lead(s) are not being returned to St. Jude Medical must be stated clearly on the case report form.

9.0 Withdrawals

Withdrawal is defined as termination of participation of a patient from a clinical trial. All reasonable efforts should be made to retain the patient in the clinical trial until completion of the clinical trial. Reasons for withdrawal include, but are not limited to the following:

- Patient Death
- Patient and/or Family Request
- Patient Lost to Follow-Up: Patient will be considered "lost to follow-up" after a minimum of 2 documented phone calls by personnel at the investigational center to the patient or emergency contact and a certified letter is sent to the last known address
- Patient Participation terminated by Investigator
- Sponsor Request
- Unsuccessful Implant
- If a system explant occurs without replacement of an Accent MRI™ system and an MRI scan has not been performed after implant.

A **WITHDRAWAL** Case Report Form should be completed and sent to St. Jude Medical CRMD, Sylmar, CA.

10.0 Risk Analysis

The risks associated with the use of the Accent MRI™ system are anticipated to be comparable to those associated with the use of other currently available pacemakers and leads. Patients participating in this study are indicated for a pacemaker as part of their standard medical management and are patient to the risks associated with these devices (refer to Section 6.0).

Risks normally associated with pacemakers, transvenous leads and their implant procedure will be minimized in the MRI study by selecting investigators who are experienced in treating patients indicated for pacemakers, who have experience with the procedures required to implant pacemakers and leads, and who are trained in the Accent MRI Pacemaker and Tendril MRI Lead IDE Study. In addition, investigators will be actively involved in the implantation and follow-up of the patients implanted with the pacemaker system.

Risks will be minimized by careful assessment of each patient prior to, during and after implant of the pacemaker. After implantation, patients in the MRI study will be

followed at regular intervals to monitor the condition of the implanted system and the battery. At each follow up, the pacemaker must be interrogated to verify appropriate pacemaker function and to evaluate pacing and sensing characteristics and to assess any adverse events.

In order to safely perform an MRI scan on a patient with the Accent MRI system, the physician/clinician should do the following as stated in the MRI Procedure Information for the St. Jude Medical® MR Conditional pacing system:

- Review the MRI Conditional Contraindications
- Review the MRI Procedure Considerations
- Verify the Presence of Additional Hardware
- Select and Save MRI Setting
- Review the Checklist and Enable MRI Setting Using the Merlin® PCS
- Review the Checklist and Enable the Use of the St. Jude Medical MRI Activator® handheld device
- Patient receives the MRI Scan
- Disable MRI Setting Using the Merlin® PCS

Also, during the MRI scans the Patients will be monitored by a health care professional to further reduce risks.

11.0 Investigator Information

This clinical investigation will be conducted by investigators with experience and/or willingness to be trained in the use of the device therapy for the treatment of bradyarrhythmias and an MRI Environment. A principal investigator should have experience in and/or will be responsible for:

- Conducting the clinical investigation in accordance with the signed agreement with St. Jude Medical, the investigational plan, all applicable FDA regulations (21 CFR Parts 50, 54, 56, 812), GCP guidelines, and any conditions of approval imposed by the IRB/MEC
- Providing signed Investigator/Co-Investigator (s) Agreement
- Providing signed Financial Disclosure Form for Clinical Investigators
- Providing IRB/MEC Approved Informed Consent
- Collection and archiving of data obtained pursuant to the requirements of the investigational plan during the course of the study and after the study has been completed
- Strict adherence to the Investigational Plan testing requirements.

- Screening and selecting appropriate Patients

It is acceptable for the principal investigator to delegate one or more of the above functions to an associate or co-investigator, however, the principal investigator remains responsible for the proper conduct of the clinical investigation, complying with the investigational plan and collecting all required data. In clinical investigations involving active implantation of an investigational product, the investigation is not transferable to other implant centers attended by the investigator unless prior approval is obtained from St. Jude Medical.

12.0 Monitoring Procedures

St. Jude Medical will serve as the "sponsor" of the MRI Study clinical investigation. It is the responsibility of St. Jude Medical as the "sponsor" of the study to ensure proper monitoring of the investigation and to see that all the clinical requirements are met.

Prior to beginning the study, a St. Jude Medical monitor will contact the investigator or designee to discuss the investigational plan and to review the data requirements in detail. A St. Jude Medical monitor will visit the investigator or designee periodically during the study to monitor progress, to assist in gathering the required data and to answer any questions. During these visits, the clinical monitor will review the patient's records to verify that all records and files are up to date, and to assure compliance with all requirements of the protocol and FDA regulations.

The investigator will make patient and study records available to the clinical monitor for periodic inspection. Clinical monitoring will be conducted under the St. Jude Medical standard operating procedure 9.4.3 (Clinical Monitoring Procedure).

Responsibility for overall study management will be held by the Sr. VP of Clinical Affairs, St. Jude Medical, CRMD.

Clinical Affairs
St. Jude Medical CRMD
15900 Valley View Court
Sylmar, CA 91342
TEL:
FAX:

FDA Inspections

The investigator and /or designee should contact St. Jude Medical in Sylmar, CA within 24 hours upon being notified of an impending FDA inspection. A clinical monitor may assist and review study documentation with the investigator and/or designee to prepare for the audit.

An investigator shall permit authorized FDA employees, at reasonable times and in a reasonable manner, to enter and inspect any establishment where investigational devices are used and to inspect and copy all records relating to an investigation.

An investigator shall permit authorized FDA employees to inspect and copy records that identify patients, upon notice that FDA has reason to suspect that adequate informed consent was not obtained, or that reports required to be submitted by the investigator to the sponsor or IRB have not been submitted or are incomplete, inaccurate, false, or misleading.

13.0 Labeling

(Please refer to User's Manual and MRI Procedure Information document)

14.0 Consent Materials

See attached consent in Appendix C.

Failure to obtain informed consent from a patient prior to study enrollment should be reported to St. Jude Medical within 5 working days and to the reviewing IRB consistent with the IRB's reporting requirements.

15.0 IRB Information

IRB approval for the study and informed consent will be required prior to beginning the study. A copy of the IRB approval and corresponding informed consent must be forwarded to St. Jude Medical prior to authorization of the institution to begin the study. Any withdrawal of IRB approval should be reported to St. Jude Medical within 5 working days of the withdrawal of approval.

Institutional Review Board (IRB) for participating Institutions

A list of IRBs for Institutions participating in the Clinical Investigation will be provided upon request.

16.0 Other Institutions

The name and address of each institution, at which a part of the investigation may be conducted, that has not been identified under IRB information, will be provided upon request.

17.0 Records and Reports

Clinical investigators of St. Jude Medical investigational products are required to maintain records, prepare and submit reports , and permit FDA Bioresearch Monitoring Inspections relating to the investigator's participation in and conduct of the study, as described in 21 CFR §812.150. St. Jude Medical will provide demographic and safety data to the FDA on an annual basis.

17.1 Custody

An investigator may withdraw from the responsibility to maintain records for the period required and transfer custody of the records to any other person who will accept responsibility for them as described, including the requirements regarding FDA inspection. Notice of transfer shall be given to St. Jude Medical and FDA no later than ten working days after transfer occurs.

17.2 Retention Period

Clinical investigators of St. Jude Medical investigational products are required to maintain records during the investigation and for a period of two years after the latter of the following two dates: the date on which the investigation is terminated or completed, or the date that the records are no longer required for purposes of supporting a premarket approval application or a notice of completion of a product development protocol.

18.0 Publication

This study will be posted on ClinicalTrials.gov and results will be posted on ClinicalTrials.gov as required. The clinicaltrials.gov identifier is NCT01576016.

19.0 Appendix A: MRI Screening Checklist

Example of Pre-MRI Safety Screening form[18,19] from the American College of Radiology Blue Ribbon Panel on MRI Safety.

Safety Screening Form for
Magnetic Resonance Imaging Procedure

Site Name: _____

Patient ID: _____

check one: ☐ MRI Phase Screening ☐ MRI Visit ☐ MRI Phase Screening + MRI Visit on same day

Questions to ask Patient	**YES**	**NO**
1. Why are you having this examination (medical problem)? – *Participating in MRI Phase of MRI Study?*.....	____	____
2. Have you ever had an MRI examination before and had a problem? …….....	____	____
If YES, please describe_____		
3. Have you ever had a surgical operation or procedure of any kind? ……..……..……	____	____
If YES, please list all prior surgeries and dates *(any surgeries that resulted in the use of metallic material that is not MRI compatible at ≥4 W/kg or is not MRI safe that remains implanted in the patient disqualifies the patient for participation in the MRI Phase):*		
_____		
_____		
4. Have you ever been injured by a metal object/foreign body (e.g., bullet, BB, shrapnel) or have metal in your eyes? ……..……....	____	____
If YES, was the metal removed?.....	____	____
5. Do you have any drug allergies that would prevent you from getting the study MRI scan?	____	____
If YES, please list drugs _____		
6. Are you a female of child-bearing potential? *If "yes" complete questions 7-9*……..……	____	____
7. Are you pregnant or suspect you may be pregnant? ……..……..……..	____	____
8. Are you breast-feeding? *(Answering YES does not disqualify patient for participation in the MRI Phase.)*……....	____	____
9. Date of last menstrual period_____		

The purpose of this form is to ensure the patient meets the criteria to undergo the study MRI scan(s). All information on this form should be verifiable against the patient's medical records and/or study records. Complete this form for each patient enrolled into the MRI Phase. A second form should be filled out at the time of the MRI Visit. If screening for the MRI Phase was done on the same day as the MRI Visit, a second form is not required to be completed.

YES may be answered for some of the questions above, but does not disqualify the patient for enrollment into the MRI Phase. If YES has been answered to any of the questions above, has it been verified that the patient is currently eligible for an MRI scan per the protocol requirements?

☐ Yes, the patient **IS** eligible for a study MRI scan(s).

☐ The patient **is NOT** eligible for a study MRI scan(s).

Study Personnel Completing Form:

Print Name:_____ Signature:_____ Date:_____

Sample MRI Hazard Checklist

THE FOLLOWING ITEMS MAY BE HARMFUL TO YOU DURING YOUR MRI SCAN OR MAY INTERFERE WITH THE MRI EXAMINATION

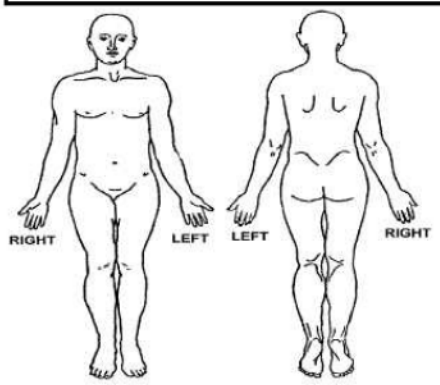
Please mark on the drawings provided the location of any metal inside your body or site of surgical operation.

You must provide a Yes or No for every item. Please indicate if you have or have had any of the following?

YES NO

____ ____Any type of electronic, mechanical or magnetic implant (Type _____)
____ ____Cardiac pacemaker (Accent MRI pacemaker is OK)
____ ____Aneurysm clip(s)
____ ____Implantable cardiac defibrillator
____ ____Neurostimulator
____ ____Biostimulator (Type_____)
____ ____Any type of internal electrode(s) or wire(s) (Tendril MRI leads are OK)
____ ____Cochlear implant
____ ____Hearing aid
____ ____Implanted drug pump (e.g. insulin, Baclofen, chemotherapy, pain medication)
____ ____Halo vest
____ ____Spinal fixation device
____ ____Spinal fusion procedure
____ ____Any type of coil, filter, or stent (Type_____)
____ ____Any type of metal object (e.g., shrapnel, bullet, BB)
____ ____Artificial heart valve
____ ____Penile implant
____ ____Artificial eye
____ ____Eyelid spring
____ ____Any type of implant held in place by a magnet (Type_____)
____ ____Any type of surgical clip or staple
____ ____Any I.V. access port (e.g. Broviac, Port-a-Cath, Hickman, Picc line)
____ ____Medication patch (e.g., Nitroglycerine, nicotine)
____ ____Shunt
____ ____Artificial limb or joint (What and where_____)
____ ____Tissue expander (e.g., breast)
____ ____Removable dentures, false teeth or partial plate
____ ____Diaphragm, IUD, Pessary (Type_____)
____ ____Surgical mesh (Location_____)
____ ____Body piercing (Location_____)
____ ____Wig, hair implants
____ ____Tattoos or tattooed eyeliner
____ ____Radiation seeds (e.g., cancer treatment)
____ ____Any implanted items (e.g., pins, rods, screws, nails, plates, wires)
____ ____Any hair accessories (e.g., bobby pins, barrettes, clips)
____ ____Jewelry
____ ____Any other type of implanted item (Type_____)

Please mark on the figure(s) below the location of any implant or metal inside of or on your body.



Instructions for patients

1. You are urged to use the ear plugs or headphones that we supply for use during your MRI examination since some patients may find the noise levels unacceptable and the noise levels may affect your hearing.
2. Remove all jewelry (e.g., necklaces, pins, rings).
3. Remove all hair pins, bobby pins, rings).
4. Remove all dentures, false teeth, partial dental plates.
5. Remove all hearing aids.
6. Remove eyeglasses.
7. Remove your watch, pager, cell phone, credit and bank cards, and all other cards with a magnetic strip.
8. Remove body piercing objects.
9. Use gown, if provided, or remove all clothing with metal fasteners, zippers.

I attest that the above information is correct to the best of my knowledge. I have read or have had the questions read to me, understand the entire contents of this form, and I have had the opportunity to ask questions regarding the information on this form.

Patient signature_____

This document is not a substitute for medical records or a source document and is intended as a checklist to ensure the patient is able to undergo a study scan. The form that is dated closest to and on or before the MRI Visit will be used as the form of record for the MRI Phase of the study. Complete a form for each patient enrolled into the MRI Phase of the study.

A YES to one or more of the questions above does not automatically disqualify the patient from participating in the MRI Phase. If YES has been answered to any of the questions above, ensure that all removable items are removed, and that implanted materials or devices can be scanned according to the study protocol, *i.e.* per protocol inclusion/exclusion criteria and protocol procedures - the material or device(s) can undergo an MRI scan at a specific absorption rate (SAR) of 4 W/kg or higher in addition to any other conditions specified by the manufacturer of the material or device.

Check one: ☐ The patient is eligible for the study MRI scans. ☐ The patient is NOT eligible for the study MRI scan.

Study Personnel Completing Form

- Print Name:_____
- Signature:_____ Date_____

Hazard Checklist for Radiology Personnel

For MRI Site Use Only

☐ ***Check this box if a site specific checklist was used. Remainder of form does not need to be completed.***

The standard form used by the MRI department at the site may be used in lieu of completing this section. If one is used, provide a copy to Cardiology for maintenance in the study records. Include the patient ID and Date that form was completed. It is expected that the patient should not have any of the items below.

YES	NO		YES	NO	
___	___	Endotracheal tube	___	___	Foley catheter with temperature sensor and/or metal clip
___	___	Swan-Ganz catheter	___	___	Rectal probe
___	___	Extraventricular device	___	___	Esophageal probe
___	___	Arterial line transducer	___	___	Tracheotomy tube
			___	___	Guidewires

Comments

_____

_____

_____

_____

Is the patient cleared to undergo an MRI scan per your center's standard of practice?

☐ Yes, the patient meets criteria to undergo an MRI scan per standard of practice.

Radiology Personnel Completing Checklist (MRI Personnel Section)

- Print Name:_____ Signature_____ Date:_____

20.0 Appendix B: MRI Scan Sequences

The following are instructions and guidelines for performing MR scans for the MRI study. Updated instructions and/or sequences for the non-clinical and clinical scans may be provided to study centers by St. Jude Medical under separate cover.

4 W/kg Whole-Body SAR Non-Clinical Scan Sequences

Table 8: GE MRI Scanner – 4 W/kg Whole Body SAR Non-Clinical Sequences

Requirements		Value	
System		1.5 T, horizontal bore	
Magnetic Field Polarization			
		Sequence	FIESTA Sequence
RF Intensive Sequence		Value to be Programmed	Value to be Programmed
TE	ms	8	
Gradient Intensive Sequence / Parameters			Diffusion Weighted Echo Planer Imaging
Echo Time (TE)			

Requirements	Value
b-values	

Table 9: Philips MRI Scanner – 4 W/kg Whole Body SAR Non-Clinical Sequences

Requirements	Value
System	1.5 T, horizontal bore
Magnetic Field Polarization	Record (North or South)

Parameter Name	Units	TSE (Turbo Spin Echo) Sequence	Balanced FFE Sequence
RF Intensive Sequence		**Value to be Programmed**	**Value to be Programmed**
TE (Echo Time)	ms		

Gradient Intensive Sequence / Parameters		Diffusion Weighted Echo Planer Imaging
Echo Time (TE)	ms	

Table 10: Siemens MRI Scanner – 4 W/kg Whole Body SAR Non-Clinical Sequences

Requirements	Value

Parameter Name	Units	TSE (Turbo Spin Echo) Sequence	True FISP Sequence
RF Intensive Sequence		Value to be Programmed	Value to be Programmed
Length		4	N/A
			NA (only one slice)

Gradient Intensive Sequence / Parameters	Diffusion Weighted Echo Planer Imaging

Gradient Intensive Sequence / Parameters	Diffusion Weighted Echo Planer Imaging

4 W/kg Whole Body SAR Non-Clinical Scan Sequence Instructions

1. Introduction

The purpose of having patients implanted with an Accent MRI system undergo an MRI scan is to demonstrate the MRI scan will not adversely affect the functionality of the Accent MRI system. To do so, the Accent MRI system will be exposed to two worst case MRI scan scenarios, one involving an RF intensive MRI scan sequence at 4 W/kg whole body SAR level, and one involving a gradient intensive MRI scan sequence. The goal is not to obtain images for diagnostic purposes, but to expose the implanted Accent MRI system to two severe testing scenarios. The parameters relevant for the MRI system selection and selected scan sequences will be discussed in detail.

The MRI scans are not intended to be diagnostic in nature and therefore the administration of contrast agents or sedation, or the application of saturation bands or water and fat saturation techniques are not permitted. During the MRI scan sequences, if patient movement causes distortion on the MRI, do not repeat the MRI scan (the scan is not meant to be diagnostic).

2. Patient Screening and Safety

The patient presenting for this MRI scan has been pre-screened by the cardiology team to ensure the patient has met the criteria set by St. Jude Medical to undergo an MRI scan for the MRI Study. This includes review and verification of the following:

Pacemaker Device Requirements:

- Bipolar capture thresholds are stable at $\leq$2.5V@ 0.5 ms
- Bipolar pacing lead impedance is within range, i.e. $\geq$ 200 and $\leq$ 2000 ohms
- Device and Leads are labeled for MRI
- No additional hardware (adaptors, extenders, or abandoned leads)

MRI Scan Equipment Requirements:

In additon to the screening above, before proceeding with any MRI scans, ensure the patient is not contra-indicated for an MRI scan, and that the MRI scanner meets the criteria below.

- Scanner Manufacturer: General Electric (GE), Siemens or Philips with the following operating characteristics:
    - Horizontal closed bore scanner working in
        - Normal Operating Mode or
        - First Level Controlled Operating Mode
        - with Whole Body Specific Absorption Rate (SAR) $\leq$ 4.0 W/kg
        - and Head SAR $\leq$ 3.2 W/kg
    - A static magnetic field strength of 1.5 Tesla
    - Maximum gradient slew rate of 200 T/m/s per axis
    - An RF excitation frequency in the range of 63.75 $\pm$ 0.5 MHz (corresponding to 1.5 Tesla scanners using hydrogen-based imaging)

Follow your institution's standard guidelines and procedures to ensure it is safe for the patient to undergo an MRI scan, including verifying implanted MRI-compatible and/or MRI-safe materials may be scanned at up to a 4 W/kg whole body SAR scan.

3. RF Exposure: Sequence and Landmark

The purpose of the RF intensive sequence is to expose the pacemaker system to

1). A 4 W/kg SAR sequence,
2). The highest possible flip angle amplitude, (i.e. peak B1 value).

The 4 W/kg SAR limit is only achievable in the "first level controlled mode." The peak B1 value will depend on the flip angle amplitude used.

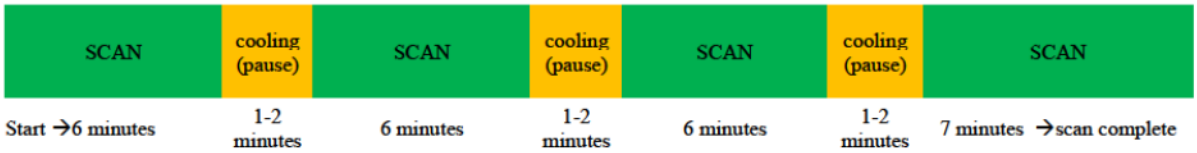
Refer to the parameters in the Non-Clinical Sequences tables (Tables 8 thru 10) and to the descriptions below to achieve the required 4 W/kg SAR and high flip angle amplitude. Refer to the appropriate table, e.g. if the MRI scanner is a GE scanner, refer to the GE table. Select ONE sequence, and program the values for each parameter outlined in the table. Store a copy of this sequence on the scanner if possible for future study scanning.

The sequence parameters in the table have been shown to result in 4 W/kg. If you are not able to prescribe the sequence parameters as given, follow the provided guidelines for ways to reach the proper SAR value; differences in patient weight will change SAR values. Therefore, please ensure the SAR for each patient is 4 W/kg or the highest achievable SAR for each patient within the defined SAR limits for the scanner, as defined by the scanner reported whole body SAR.

Please be aware the scan sequence was designed using one slice to simplify the number of adjustments needed to be made to achieve the 4 W/kg whole body SAR limit due to interleaving when more than one slice is utilized. Additional NEX/averages and/or measurements can be added to achieve the required scan duration; additional slices should not be used to increase scan duration.

To ensure the patient is not subjected to unnecessary MR exposure, the 25 minute scan duration will be split into three 6 minute segments and one 7 minute segment to reach a cumulative scan duration of 25 minutes. To allow for patient cooling, 1-2 minutes of no scanning must follow each scan segment. The total time for the procedure will be approximately 28-31 minutes, 25 minutes of scan time plus the additional wait time.

Figure 4: RF Sequence Scanning and Cooling Segments



There are two sequences prescribed for each scanner (GE, Philips, Siemens) to achieve the required RF intensive exposure. Only ONE (1) RF intensive sequence is required to be completed:

1) TSE (Turbo Spin Echo)(Philips/Siemens scanners)/FSE (Fast Spin Echo)(GE scanners)
2) TrueFISP(Siemens scanners)/FIESTA (GE scanners)/balanced FFE(Philips scanners)

TSE/FSE Guidelines:
The TSE/FSE sequence uses an excitation pulse followed by a train of refocusing pulses to accelerate the image acquisition. To achieve a 4 W/kg SAR with a high flip angle, the following guidelines should be used.

TrueFISP/FIESTA/balanced FFE Guidelines:
The TrueFisp sequence is a gradient recalled echo sequence that applies a fixed flip angle RF pulse α to achieve steady state imaging. To achieve a 4 W/kg SAR with a high flip angle, the following guidelines should be used.

Landmark:
Position the patient table bed such that the **patient's heart is at iso-center**; this will result in the highest RF field exposure of the implant. Follow your institution's standard operating procedures for performing a thoracic region scan, making sure to prepare the patient for pulse oximetry and ECG monitoring.

4. Gradient Exposure: Sequence and Landmark
The purpose of the gradient exposure sequence is to expose the pacemaker system to the maximum time varying magnetic field (dB/dt) which is produced by the gradients coils during ramp up and ramp down time.

The slice selection direction must be sagittal and the phase encoding direction must be in the Head-Foot direction to ensure that the readout is the Y-direction (AP), which will maximize the gradient in the Y-direction.

Note: The maximum spatial gradient for which the Accent MRI system has been determined safe is 10 T/m.

Landmark:
Position the patient table bed such that the implanted pacemaker is at the edge of the superoinferior extent of the gradient coils of your system to ensure the device is exposed to the highest gradient field (dB/dt). Follow your institution's standard operating procedures for performing a head scan, making sure to prepare the patient for pulse oximetry and ECG monitoring.

5. Patient Monitoring and Safety:
Before the start of the scan, instruct the patient to verbalize any discomfort or pain he/she may experience while in the MRI bore.

During the entire MRI scan, the patient's cardiac function must be monitored using pulse oximetry and an ECG by an Accent MRI study trained electrophysiologist, cardiologist, or Advanced Cardiac Life Support (ACLS) trained clinician who is capable of delivering external cardiac pacing defibrillation and advanced cardiac life support. Verbal communication with the patient must also take place to assess and/or confirm any clinically significant changes noted in the patient's oxygen saturation or heart rate, as well as any clinically significant complaints not obvious with pulse oximetry. Record these changes and complaints.

Life–threatening Ventricular Arrhythmia and Asystole Assessment:
Monitoring of spontaneous ventricular arrhythmias and asystole must be conducted via an ECG during the MRI scans. Any sustained ventricular arrhythmias or asystole must be documented on an Adverse Event form. Non-sustained ventricular tachycardias (NSVT) or premature ventricular contractions (PVCs) do not need to be reported as an adverse event. However, if an arrhythmia reproducibly occurs (occurring more than one time) while the patient is actively being scanned, report the event on an Adverse Event form.

Definitions:

- *Sustained Ventricular Arrhythmia:* Heart Rate >150bpm for > 30 seconds
- *Asystole:* A standstill > 6 seconds in electrical activity of the heart (*i.e.,* no heart rate for 6 seconds or more)

ACLS procedures must be in place to address situations where a life threatening arrhythmia and/or hemodynamic collapse occurs. The programmer must be used outside the American College of Radiology (ACR) defined Zone 4 magnet room. If the patient's hemodynamic function is compromised or the patient experiences a medical emergency during the MRI scan, stop the MRI scan and take proper measures to restore the patient's hemodynamic function and/or the appropriate steps per your institution's standard operating procedures to addressing the medical emergency.

Handling of Patients Unable to Tolerate an MR Scan
In cases where the scan cannot be tolerated by the patient, remove the patient from the scanner. Assess the patient for possible adverse events, and treat the patient's reported symptoms according to your institution's standard of practice. Note the reason for the

intolerance. Information related to the sequence used to perform the scan, the length of time the patient was scanned, and the whole body SAR level reached should be collected and submitted to St. Jude Medical. A repeat scan is not required to be completed.

6. Image Sequence Parameter Summary

The preceding Non-Clinical Sequences tables (Appendix B) show the imaging parameters for a 4 W/kg whole body SAR level scan RF and gradient intensive sequences. The total imaging time should last approximately 30 minutes, with 25 minutes of cumulative RF intensive scanning and 5 minutes of gradient intensive scanning.

If needed, and/or as requested by St. Jude Medical, additional clinically useful scans will be performed for the purposes of conducting analyses on MR image quality and artifact. These scans should be performed until a total of 20 analyzable study-wide scans have been collected. St. Jude Medical will notify your study center which patients need to undergo these additional scan sequences. Supplemental instructions will be provided for these sequences prior to the first MRI scan to those centers with eligible patients scheduled for an MRI scan.

If the need arises, updated instructions and/or sequence tables for the non-clinical and clinically useful scans will be provided to your study center by St. Jude Medical under separate cover.

2 W/kg Whole Body SAR Non-Clinical Scan Sequences

Table 11: GE MRI Scanner – 2 W/kg Whole Body SAR Non-Clinical Sequences

Requirements	Value
System	
Gradient Intensive Sequence Parameters / Sequence	Diffusion weighted Echo Planer Imaging
Echo Time (TE)	ms

Gradient Intensive Sequence Parameters / Sequence	Diffusion weighted Echo Planer Imaging	
b-values		1000,
	min	

Table 12: Philips MRI Scanner – 2 W/kg Whole Body SAR Non-Clinical Sequences

Requirements	Value
System	1.5 T, horizontal bore

Parameter Name		TSE (Turbo Spin Echo) Sequence	Balanced FFE Sequence
RF Intensive Sequence	Units	Value to be Programmed	Va e to be Programmed
TE (Echo Time)	ms		

Gradient Intensive Sequence Parameters / Sequence	Diffusion weighted Echo Planer Imaging

Table 13: Siemens MRI Scanner – 2 W/kg Whole Body SAR Non-Clinical Sequences

Requirements	Value
System	1.5 T, horizontal bore

Parameter Name		TSE (Turbo Spin Echo) Sequence	True FISP Sequence
RF Intensive Sequence Parameters	Units	Value to be Programmed	Value to be Programmed
TE (Echo time)	ms		

Gradient Intensive Sequence Parameters / Sequence		Diffusion weighted Echo Planer Imaging
Echo Time (TE)	ms	

Gradient Intensive Sequence Parameters / Sequence	Diffusion weighted Echo Planer Imaging
b-values	

2 W/kg Whole Body SAR Non-Clinical Scan Sequence Instructions

1. Introduction

The purpose of having patients implanted with an Accent MRI system undergo an MRI scan is to demonstrate the MRI scan will not adversely affect the functionality of the Accent MRI system. To do so, the Accent MRI system will be exposed to two worst case MRI scan scenarios at a 2 W/kg whole body SAR level, one involving an RF intensive MRI scan sequence, and one involving a gradient intensive MRI scan sequence. The goal is not to obtain images for diagnostic purposes, but to expose the implanted Accent MRI system to these two severe testing scenarios. The parameters relevant for the MRI system selection and selected scan sequences will be discussed in detail.

The MRI scans are not intended to be diagnostic in nature and therefore the administration of contrast agents or sedation, or the application of saturation bands or water and fat saturation techniques are not permitted. During the MRI scan sequences, if patient movement causes distortion on the MRI, do not repeat the MRI scan (the scan is not meant to be diagnostic).

2. Patient Screening and Safety

The patient presenting for this MRI scan has been pre-screened by the cardiology team to ensure the patient has met the criteria set by St. Jude Medical to undergo an MRI scan for the MRI Study. This includes review and verification of the following:

Pacemaker Device Requirements:

- Bipolar capture thresholds are stable at $\leq$2.5V@ 0.5 ms
- Bipolar pacing lead impedance is within range, i.e. $\geq$ 200 and $\leq$ 2000 ohms
- Device and Leads are labeled for MRI
- No additional hardware (adaptors, extenders, or abandoned leads)

MRI Scan Equipment Requirements:

In additon to the screening above, before proceeding with any MRI scans, ensure the patient is not contra-indicated for an MRI scan, and that the MRI scanner meets the criteria below.

- Scanner Manufacturer: General Electric (GE), Siemens or Philips with the following operating characteristics:
    - Horizontal closed bore scanner working in
        - Normal Operating Mode or
        - First Level Controlled Operating Mode
        - with Whole Body Specific Absorption Rate (SAR) $\leq$ 2.0 W/kg
        - and Head SAR $\leq$ 3.2 W/kg
    - A static magnetic field strength of 1.5 Tesla
    - Maximum gradient slew rate of 200 T/m/s per axis
    - An RF excitation frequency in the range of 63.75 $\pm$ 0.5 MHz (corresponding to 1.5 Tesla scanners using hydrogen-based imaging)

Follow your institution's standard guidelines and procedures to ensure it is safe for the patient to undergo an MRI scan, including verifying implanted MRI-compatible and/or MRI-safe materials may be scanned at up to a 2 W/kg whole body SAR scan.

3. RF Exposure: Sequence and Landmark

The purpose of the RF intensive sequence is to expose the pacemaker system to

1). A 2 W/kg SAR sequence,
2). The highest possible flip angle amplitude, (i.e. peak B1 value).

The 2 W/kg SAR limit is achievable in the "normal operating mode." The peak B1 value will depend on the flip angle amplitude used.

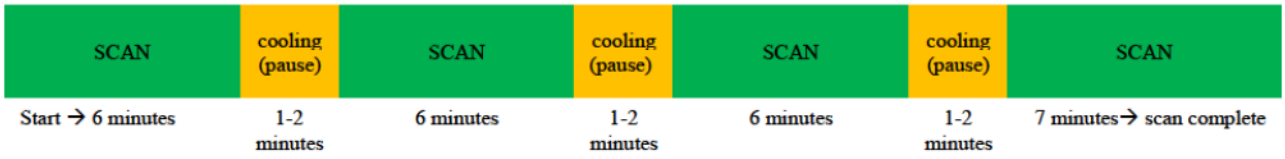
Refer to the parameters in the 2 W/kg Whole Body SAR Non-Clinical Sequence tables and to the descriptions below to achieve the required 2 W/kg SAR and high flip angle amplitude. Refer to the appropriate table, e.g. if the MRI scanner is a GE scanner, refer to the GE table. Select ONE of the two sequences, and program the values as shown in the table. Store a copy of this sequence on the scanner if possible for future study scanning.

The sequence parameters in the table have been shown to result in 2 W/kg. If you are not able to prescribe the sequence parameters as given, follow the provided guidelines for ways to reach the proper SAR value. Differences in patient weight will change SAR values. Therefore, please ensure the SAR for each patient is 2 W/kg or the highest achievable SAR for each patient within the defined SAR limits for the scanner, as defined by the scanner reported whole body SAR.

Please be aware the scan sequence was designed using one slice to simplify the number of adjustments needed to achieve the 2 W/kg whole body SAR limit due to interleaving when more than one slice is utilized. Additional NEX/averages and/or measurements can be added to achieve the required scan duration; additional slices should not be used to increase scan duration.

To ensure the patient is not subjected to unnecessary MR exposure, the 25 minute scan duration will be split into three 6 minute segments and one 7 minute segment to reach a cumulative scan duration of 25 minutes. To allow for patient cooling, 1-2 minutes of no scanning must follow each scan segment. The total time for the procedure will be approximately 28-31 minutes, 25 minutes of scan time plus the additional wait time.

Figure 3: RF Sequence Scanning and Cooling Segments



There are two possible sequences that can be prescribed to achieve the required RF intensive exposure. Only ONE (1) RF intensive sequence is required to be completed:

1) TSE (Turbo Spin Echo)(Philips/Siemens scanners)/FSE (Fast Spin Echo)(GE scanners)
2) TrueFISP(Siemens scanners)/FIESTA (GE scanners)/balanced FFE(Philips scanners)

TSE/FSE Guidelines:
The TSE/FSE sequence uses an excitation pulse followed by a train of refocusing pulses to accelerate the image acquisition. To achieve a 2 W/kg SAR with a high flip angle, the following guidelines should be used. The flip angle of the excitation pulse is fixed at 90°. The flip angle of the refocusing pulses must be set to 180°. This will achieve the highest possible flip angle for the TSE/FSE sequence. If you are not able to obtain to exact sequence parameters as prescribed in the Table specific to your scanner, and/or the sequence does not result in 2 W/kg, please refer to the guidelines below for ways to increase the SAR .

Ways to Increase SAR:
The prescribed sequence will result in a higher SAR when you use the shortest possible TR and TE.

TrueFisp/FIESTA/balanced FFE Guidelines:
The TrueFisp sequence is a gradient recalled echo sequence that applies a fixed flip angle RF pulse α to achieve steady state imaging. To achieve a 2 W/kg SAR with a high flip angle, the following guidelines should be used. The flip angle should be set to the maximum allowed by the scanner to achieve the SAR limit of 2 W/kg. If you are not able to obtain to exact sequence parameters as prescribed in Table specific to your scanner, and/or the sequence does not result in 2 W/kg with a high flip angle, please refer to the guidelines below for ways to increase the SAR.

Ways to Increase SAR:
It is important to increase the TR in order to achieve the highest flip angle possible. Often the TR is not a user-adjusted variable for this type of pulse sequence.

Landmark:
Position the patient table bed such that the **patient's heart is at iso-center**; this will result in the highest RF field exposure of the implant. Follow your institution's standard operating procedures for performing a thoracic region scan, making sure to prepare the patient for pulse oximetry and ECG monitoring.

4. Gradient Exposure: Sequence and Landmark
The purpose of the gradient exposure sequence is to expose the pacemaker system to the maximum time varying magnetic field (dB/dt) which is produced by the gradients coils during ramp up and ramp down time.

Select a diffusion weighted EPI sequence and refer to the parameters in the Non-Clinical Sequences Tables specific to your scanner and to the descriptions below to achieve a gradient intensive sequence. Select the appropriate table, e.g. if the MRI scanner is a GE scanner, refer to the GE table, and program the values as shown in the table. Store a copy of this sequence on the scanner if possible for future study scanning.

The sequence parameters in the table have been shown to result a gradient intensive sequence however, if you are not able to prescribe the sequence parameters as given please follow the guidelines for ways to reach the proper gradients. The required scan duration is 5 minutes and should be easily achieved using a single sequence. If you are not able to obtain to exact sequence parameters as prescribed in the Table specific to your scanner, refer to the guidelines below to ensure the sequence has maximized the gradient exposure.

The slice selection direction must be sagittal and the phase encoding direction must be in the Head-Foot direction to ensure that the readout is the Y-direction (AP), which will maximize the gradient in the Y-direction.

Ensure the field of view is small while the gradient encoding matrix is as large as possible. The readout bandwidth should be as high as possible in order to increase the gradient slew rate in the Y-direction. The b-values of 1000, 1500, and 2000 were chosen to create large diffusion weighted gradients and should be maintained as high as possible. The gradient stimulation monitor may require you to reduce some of these parameters if the stimulation threshold has been exceeded. If the gradient stimulation threshold is reached, then the first choice should be to increase the slice thickness, and second choice should be to decrease the phase encoding matrix size.

If the programming the values as outlined in the Gradient Intensive scan sequence results in a predicted whole body SAR that is > 2W/kg, the RF exposure should be reduced to the extent that would allow the Gradient Intensive scan to be performed. This can be achieved using low flip angle set to a minimum value that minimizes RF exposure.

Note: The maximum spatial gradient for which the Accent MRI system has been determined safe is 10 T/m.

Landmark:
Position the patient table bed such that the implanted pacemaker is at the edge of the superoinferior extent of the gradient coils of your system to ensure the device is exposed to the highest gradient field (dB/dt). Follow your institution's standard operating procedures for performing a head scan, making sure to prepare the patient for pulse oximetry and ECG monitoring.

5. Patient Monitoring and Safety:
Before the start of the scan, instruct the patient to verbalize any discomfort or pain he/she may experience while in the MRI bore.

During the entire MRI scan, the patient's cardiac function must be monitored using pulse oximetry and an ECG by an Accent MRI study trained electrophysiologist, cardiologist, or Advanced Cardiac Life Support (ACLS) trained clinician who is capable of delivering external cardiac pacing defibrillation and advanced cardiac life support. Verbal communication with the patient must also take place to assess and/or confirm any clinically significant changes noted in the patient's oxygen saturation or heart rate, as well as any clinically significant complaints not obvious with pulse oximetry. Record these changes and complaints.

Life–threatening Ventricular Arrhythmia and Asystole Assessment:
Monitoring of spontaneous ventricular arrhythmias and asystole must be conducted via an ECG during the MRI scans. Any sustained ventricular arrhythmias or asystole must be documented on an Adverse Event form. Non-sustained ventricular tachycardias (NSVT) or premature ventricular contractions (PVCs) do not need to be reported as an adverse event. However, if an arrhythmia reproducibly occurs (occurring more than one time) while the patient is actively being scanned, report the event on an Adverse Event form.

Definitions:

- *Sustained Ventricular Arrhythmia:* Heart Rate >150bpm for > 30 seconds
- *Asystole:* A standstill > 6 seconds in electrical activity of the heart (i.e., no heart rate for 6 seconds or more)

ACLS procedures must be in place to address situations where a life threatening arrhythmia and/or hemodynamic collapse occurs. The programmer must be used outside the American College of Radiology (ACR) defined Zone 4 magnet room. If the patient's hemodynamic function is compromised or the patient experiences a medical emergency during the MRI scan, stop the MRI scan and take proper measures to restore the patient's hemodynamic function and/or the appropriate steps per your institution's standard operating procedures to addressing the medical emergency.

Handling of Patients Unable to Tolerate an MR Scan

In cases where the scan cannot be tolerated by the patient, remove the patient from the scanner. Assess the patient for possible adverse events, and treat the patient's reported symptoms according to your institution's standard of practice. Note the reason for the intolerance. Information related to the sequence used to perform the scan, the length of time the patient was scanned, and the whole body SAR level reached should be collected and submitted to St. Jude Medical. A repeat scan is not required to be completed.

6. Image Sequence Parameter Summary

The preceding Non-Clinical Sequences tables (Appendix B) show the imaging parameters for the RF and gradient intensive sequences. The total imaging time should last approximately 30 minutes, with 25 minutes of RF intensive scanning and 5 minutes of gradient intensive scanning.

If needed, and/or as requested by St. Jude Medical, additional clinically useful scans will be performed for the purposes of conducting analyses on MR image quality and artifact. These scans should be performed until a total of 20 analyzable study-wide scans have been collected. St. Jude Medical will notify your study center which patients need to undergo these additional scan sequences. Supplemental instructions will be provided for these sequences prior to the first MRI scan to those centers with eligible patients scheduled for an MRI scan.

If the need arises, updated instructions and/or sequence tables for the non-clinical and clinically useful scans will be provided to your study center by St. Jude Medical under separate cover.

Image Quality and Artifact Clinical Scan Sequence Instructions

1. Introduction

The sequences provided are intended to be a reference sequence for a cardiac, thoracic spine, cervical spine, and shoulder joint scan, and are clinically relevant scan sequences. St. Jude Medical will provide confirmation on which area should be scanned for up to the first 5 patients to undergo an MRI scan at each study center.

The goal of the clinical scan is to obtain scan images for the purposes of image quality and artifact analysis. If needed, updated instructions or refinements to the sequences may be provided by St. Jude Medical under separate cover.

The MRI scan should be reviewed for any obvious abnormalities by a radiologist within a reasonable timeframe. Any obvious abnormalities that are noted must be reported to the patient's physician (per standard of care by the facility performing the MRI scan). A copy of the documentation of the abnormality discovered on the MRI scan should be kept in the patient's file and/or study records. The review of the MRI scan is not meant to be diagnostic.

2. Scan Sequence Selection

After receiving the clinical scan assignment confirmation from St. Jude Medical, refer to the specific scanner table, e.g. GE, Philips and Siemens. Each table contains sequences for cardiac, thoracic spine, cervical spine, and shoulder joint scans. You may use the sequence parameters given in the tables to perform the scan for which the patient has been assigned to receive. Alternatively, you may use similar clinically relevant sequences that are available and used on the scanner at your center.

The MRI scans are intended to generate clinically relevant images for the purpose of analyzing those images for quality and artifact. However, the administration of contrast agents or sedation is not permitted. During the MRI scan sequences, if patient movement causes distortion on the MRI, it is acceptable to repeat the MRI scan.

3. Scan Data / Images

Save and export the scan images. Provide a copy of the images and programmed parameter values to St. Jude Medical.

Refer to the instructions below to perform the scan.

4. Patient Screening and Safety

The patient presenting for this MRI scan has been pre-screened by the cardiology team to ensure the patient has met the criteria set by St. Jude Medical to undergo a clincally relevant MRI scan for the MRI Study. This includes review and verification of the following:

Pacemaker Device Requirements:

- Bipolar capture thresholds are stable at $\leq$2.5V@ 0.5 ms
- Bipolar pacing lead impedance is within range, i.e. $\geq$ 200 and $\leq$ 2000 ohms

- Device and Leads are labeled for MRI
- No additional hardware (adaptors, extenders, or abandoned leads)

MRI Scan Equipment Requirements:
In additon to the screening above, before proceeding with any MRI scans, ensure the patient is not contra-indicated for an MRI scan, and that the MRI scanner meets the criteria below.

- Scanner Manufacturer: General Electric (GE), Siemens or Philips with the following operating characteristics:
  - Horizontal closed bore scanner working in
    - Normal Operating Mode or First Level Controlled Operating Mode
    - with Whole Body Specific Absorption Rate (SAR) $\leq$ 2.0 W/kg
    - and Head SAR $\leq$ 3.2 W/kg
  - A static magnetic field strength of 1.5 Tesla
  - Maximum gradient slew rate of 200 T/m/s per axis
  - An RF excitation frequency in the range of 63.75 $\pm$ 0.5 MHz (corresponding to 1.5 Tesla scanners using hydrogen-based imaging)

Follow your institution's standard guidelines and procedures to ensure it is safe for the patient to undergo an MRI scan, including verifying implanted MRI-compatible and/or MRI-safe materials may be scanned according to the applicable manufacturer's labeling.

5. Landmark
Position the patient table bed such that the area being scanned is at iso-center. Follow your institution's standard operating procedures to perform a scan, making sure to prepare the patient for pulse oximetry and ECG monitoring.

6. Patient Monitoring and Safety
Before the start of the scan, instruct the patient to verbalize any discomfort or pain he/she may experience while in the MRI bore.

During the entire MRI scan, the patient's cardiac function must be monitored using pulse oximetry and an ECG by an Accent MRI study trained electrophysiologist, cardiologist, or Advanced Cardiac Life Support (ACLS) trained clinician who is capable of delivering external cardiac pacing defibrillation and advanced cardiac life support. Verbal communication with the patient must also take place to assess and/or confirm any clinically significant changes noted in the patient's oxygen saturation or heart rate, as well as any clinically significant complaints not obvious with pulse oximetry. Record these changes and complaints.

Life–threatening Ventricular Arrhythmia and Asystole Assessment:
Monitoring of spontaneous ventricular arrhythmias and asystole must be conducted via an ECG during the MRI scans. Any sustained ventricular arrhythmias or asystole must be

documented on an Adverse Event form. Non-sustained ventricular tachycardias (NSVT) or premature ventricular contractions (PVCs) do not need to be reported as an adverse event. However, if an arrhythmia reproducibly occurs (occurring more than one time) while the patient is actively being scanned, report the event on an Adverse Event form.

Definitions:

- *Sustained Ventricular Arrhythmia:* Heart Rate >150bpm for > 30 seconds
- *Asystole:* A standstill > 6 seconds in electrical activity of the heart (i.e., no heart rate for 6 seconds or more)

ACLS procedures must be in place to address situations where a life threatening arrhythmia and/or hemodynamic collapse occurs. The programmer must be used outside the American College of Radiology (ACR) defined Zone 4 magnet room. If the patient's hemodynamic function is compromised or the patient experiences a medical emergency during the MRI scan, stop the MRI scan and take proper measures to restore the patient's hemodynamic function and/or the appropriate steps per your institution's standard operating procedures to addressing the medical emergency.

Handling of Patients Unable to Tolerate an MR Scan

In cases where the scan cannot be tolerated by the patient, remove the patient from the scanner. Assess the patient for possible adverse events, and treat the patient's reported symptoms according to your institution's standard of practice. Note the reason for the intolerance. Information related to the sequence used to perform the scan, the length of time the patient was scanned, and the whole body SAR level reached should be collected and submitted to St. Jude Medical. A repeat scan is not required to be completed.

Image Quality and Artifact Clinical Scan Sequences

Table 14: GE MRI Scanner – MRI Study Clinical Sequences

C-SPINE SEQUENCES	Unit	T2 FSE	T1 FSE	-
Slices	mm	13	13	13
Slice thickness	mm		3	3
T-SPINE SEQUENCES		T2 FSE	T1 FSE	-
Slices	mm	22	15	15

SHOULDER JOINT	Unit	T2 FSE	T1 FSE	T2 Propeller	PD FSE
Slices	mm	27	27	20	24

CARDIAC SEQUENCES	Unit	FIESTA	SPGR	Perfusion EPI	Delayed Enhancement	Single-Shot FSE Blackblood
Slices	mm	1	1	1	1	24
Slice thickness	mm	6	6	10	8	5

Table 15: Philips MRI Scanner – MRI Study Clinical Sequences

C-SPINE SEQUENCES	Unit	T2_TSE	T1_TSE	Real IR
Slices	mm	13	13	13
Slice thickness	mm	3	3	3

T-SPINE SEQUENCES		T2_TSE	T1_TSE	Real IR
Slices	mm	22	15	15
Slice thickness	mm	4	3	3
NSA		2	2	1

SHOULDER JOINT	Unit	T2_TSE	T1_TSE	T2_MultiVane	PD_TSE
Slices	mm	27	27	20	24
Slice thickness	mm	3	3	4	3

CARDIAC SEQUENCES	Unit	Balanced FFE	T1-FFE	Perfusion EPI	Delayed Enhancement	Single-Shot TSE Blackblood
Slices	mm	1	1	1	1	24
Slice thickness	mm	6	6	10	8	5

Table 16: Siemens MRI Scanner – MRI Study Clinical Sequences

C-SPINE SEQUENCES	Unit	T2 TSE	T1 TSE	T1 TIRM
Slices	mm	13	13	13
T-SPINE SEQUENCES		T2 TSE	T1 TSE	T1 TIRM
Slices	mm	22	15	15
Slice thickness	mm	4	3	3

SHOULDER JOINT	Unit	T2 TSE	T1 TSE	T2 BLADE	PD TSE
Slices	mm	27	27	20	24
Slice thickness	mm	3	3	4	3

CARDIAC SEQUENCES	Unit	TrueFISP	FLASH	Perfusion EPI	Delayed Enhancement	HASTE Blackblood
Slices	mm	1	1	1	1	24
Slice thickness	mm	6	6	10	8	5

21.0 Appendix C: Patient Informed Consent

Patient Informed Consent for the

Accent MRI™ Pacemaker and Tendril MRI™ Lead IDE Study

Introduction

You are being asked to take part in this research study because your doctor has determined that you may qualify to take part in the Accent MRI™ (magnetic resonance image) Pacemaker and Tendril MRI™ Lead IDE (investigational device exemption) study. This form explains why this research is being done and what your role will be if you decide to participate. This form also talks about the possible risks that may happen if you take part in this study. This study is sponsored by St. Jude Medical.

Please read this form, and ask your study doctor any questions about the study so that you can have your questions answered before you decide if you want to take part in the study. Please take your time and talk about this information with your family, friend, or family doctor.

This consent form may contain some words that you do not understand. Please ask the study doctor or the study staff to explain any words or information that you do not understand.

If you agree to be in the study, you will need to sign this form. Taking part in this study is entirely voluntary. You may decide not to participate without penalty or loss of benefits to which you are otherwise entitled

What is the purpose of this study?

The purpose of this IDE study is to evaluate the short and long term safety of the Tendril MRI lead and the Accent MRI pacemaker, together known as the Accent MRI system. There are two parts to this study. One part of the study will look at how the Accent MRI system performs independent of an MRI scan. This part of the study will be referred to as the lead part of the study.

The second part of the study will look at how the Accent MRI system works after it has undergone an MRI scan. This part of the study will be referred to as the MRI part of the study. Additionally, the MRI Activator Device (Model EX4000), a small hand-held device that will be used to change the settings in the Accent MRI pacemaker in preparation for an MRI scan, will also be evaluated in this study. You may be asked if you wish to participate in that part of the study in addition to your participation in the lead part of the study. If you do, you will be asked to sign a separate consent form.

In comparison to FDA approved St. Jude Medical™ pacemakers and leads, there are changes to the design of both the investigational Accent MRI pacemaker and the Tendril MRI lead. The MRI Activator is also investigational. These changes are listed below:

- The Accent MR pacemaker has new hardware to prevent an MRI scanner from changing certain settings in your pacemaker. The shape and size of the device has been changed to hold this new hardware. The device has an X-ray marker built into it so that your doctor can identify that the device is MRI compatible.
- The Tendril MRI lead has also been modified to prevent the MRI scanner from heating the lead. The lead has an X-ray identification marker built into it so that your doctor can identify the lead is MRI compatible.
- The MRI Activator (portable handheld device) is used by the study staff to turn the MRI functions of the Accent MR pacemaker on or off before and after the MRI scan.

What will happen if you take part in this research study?

If you decide to take part in this study, you will be asked a series of questions about whether or not you've had any MRI scans in the past and other relevant information that will help your doctor determine if you qualify the study. Based on your answers and your medical history, your doctor will decide if you qualify to take part in the Accent MRI™ Pacemaker and Tendril MRI™ Lead IDE study.

If your doctor determines that you qualify, and you decide to take part in this study, the procedure(s) described below will be performed for the lead portion of the study.

There may be a representative of the sponsor at your study visits and the representative may carry out some of the study procedures. The study doctor may direct a representative from the sponsor to collect information from your implanted device. At the study doctor's direction, the sponsor representative may also program your device or run tests to see if your device is working as expected. The sponsor's representative will work under the direction of your study doctor or other care provider.

At each scheduled study visit, your study doctor or staff will ask you about the medications that you take every day.

All patients will be implanted with the Accent MRI pacemaker and at least one Tendril MRI lead during a procedure in the Electrophysiology Laboratory (EP Lab) or in the Operating Room (OR). The total estimated time for a pacemaker procedure is approximately 1 hour. This implant procedure is similar to the implant procedure for any approved pacemaker system (pacemaker and pacing leads). Your doctor will insert the pacing lead(s) into the vein, and gently guide the lead(s) through the vein into your heart. Once the lead(s) are in your heart, your doctor will test the lead(s) to see if they are in a good place. Your doctor will connect the lead(s) into the pacemaker, and place the pacemaker into a small pocket made just beneath the skin on your upper chest before closing the pocket with stitches.

Part One: Lead Evaluation

You will be required to return for follow-up study visits to have your implanted pacemaker and leads checked. These visits will be done at the following times:

- Pre-Discharge (following implant before you are sent home from the hospital)
- 2 months after implant
- 6 months after implant
- 12 months after implant
- Every 6 months after the 12 month visit until the study is finished

You may also need to return for additional visits not listed above if your MRI lead(s) need to be repositioned or replaced. Your study doctor or study personnel will work with you to schedule those extra visits if they are needed.

The following tests will be done at the follow-up study visits:

1. **Pre-Discharge**
   - The study doctor or staff will ask you about the medications that you take every day
   - Your Pacemaker device will be tested using a programmer in the same way as at a regular clinical check-up. You should not feel any discomfort during this procedure.
   - A chest x-ray will be performed to check the position of the leads (wire) in your heart. An x-ray technician will ask you to hold your breath for 5 seconds when the x-ray is taken. This procedure should take approximately 15 minutes.

2. **2 Month Visit (after implant)**
   - The study doctor or staff will ask you about the medications that you take every day
   - Your Pacemaker device will be tested using a programmer (a computer and a wand) in the same way as at a regular clinical check-up. You should not feel any discomfort during this procedure.

3. **6 months, 12 months, and every 6 months after implant until study completion Visits**

   - The study doctor or staff will ask you about the medications that you take every day
   - Your Pacemaker device will be tested using a programmer in the same way as at a regular clinical check-up. You should not feel any discomfort during this procedure. A sponsor representative may also program your device or collect information from your device under a physician's supervision.

How long will the study last?

A minimum of 800 patients at up to 80 investigational centers in and outside of the United States will take part in this IDE study. This study will last for approximately 34 months. You will take part in this study for about 34 months for active follow-up or less depending on when the last person is enrolled in the study.

Additionally, you will be asked to participate in a post-approval study following the completion of the MRI IDE study. Your participation in the post-approval study may last for up to 5 years starting from the day you provide informed consent for the post-approval study.

What are the possible discomforts and risks?

Risks associated with a standard pacemaker system and surgery
Your doctor will review the risks related to a standard pacemaker surgery. The risks related to the use of a pacemaker system are expected to be similar to those related to any other FDA approved pacemaker system. These adverse events include, but are not limited to:

Potential Pacing System Adverse Events:

- Air embolism
- Body rejection phenomena
- Cardiac tamponade or perforation
- Hematoma, bleeding hematoma, seroma
- Formation of fibrotic tissue; local tissue reaction
- Inability to interrogate or program due to programmer or device malfunction
- Infection/erosion
- Interruption of desired pulse generator function due to electrical interference either electromyogenic or electromagnetic
- Loss of capture or sensing due to lead dislodgement or reaction at the electrode/tissue interface
- Loss of desired pacing and/or sensing due to lead displacement, body reaction at electrode interface, or lead malfunction (fracture or damage to insulation)
- Lead malfunction due to conductor fracture or insulation degradation
- Loss of normal pacemaker function due to battery failure or component malfunction
- Pacemaker migration, pocket erosion
- Pectoral muscle stimulation
- Phrenic nerve or diaphragmatic stimulation
- Pneumothorax/hemothorax
- Endocarditis
- Excessive bleeding
- Induced atrial or ventricular arrhythmias
- Myocardial irritability
- Pericardial effusion
- Pericardial rub
- Pulmonary edema

- Rise in threshold and exit block
- Valve damage

Potential lead related adverse events

- Cardiac tamponade
- Diaphragmatic/phrenic nerve stimulation
- Embolism
- Excessive bleeding
- Induced ventricular ectopy
- Infection
- Loss of pacing and/or sensing due to dislodgement or mechanical malfunction of the pacing lead
- Thrombosis

Complications reported with direct subclavian venipuncture include pneumothorax, hemothorax, laceration of the subclavian artery, arteriovenous fistula, neural damage, thoracic duct injury, cannulation of other vessels, massive hemorrhage and rarely, death.

Study procedures may also involve risks that are currently unforeseeable.

Risks for Women of Childbearing Age

If you are pregnant or plan to become pregnant in the next 20 months, you should discuss your participation with your study doctor. Patients who become pregnant while taking part in the study should contact the study doctor right away.

What are the possible benefits to you or to others?

If you decide to take part in this study, you may benefit from the ability to safely undergo MRI scans with an implanted pacemaker system, but there is no guarantee that this will happen. The information gathered in this study will add to the understanding of treatment options for patients with slow heart rates who require MRI scans. We expect patients implanted with an Accent MRI™ Pacemaker system to receive the same benefit as patients implanted with other St. Jude Medical pacemaker systems.

The sponsor of this study is paying for cost of data capture and items that are not deemed standard of care/routine care in the study. St. Jude Medical will pay the study center where the study is being conducted.

If you do not want to take part in this study, what other options are available to you?

Your doctor will discuss other options available to you, including the possibility of receiving another market approved pacemaker.

How will your privacy and the confidentiality of your research records be protected?

If you decide to take part in this study, your medical records and personal information will be kept private to the extent allowed by federal, state, and local law. No personal information about you, your illness, or your treatment will be made public.

Information (data) collected from the study will be sent to St. Jude Medical. A special code (letter and number combination) will be used to identify your personal information.

The data may be given to governmental agencies, for example: the Food and Drug Administration (FDA) or similar government agencies in other countries. Only information about your medical condition as it relates to the Accent MRI™ system will be provided to St. Jude Medical. In order to verify study data, monitors from governmental agencies (for example: FDA), St. Jude Medical, and the Institutional Review Board (IRB)/Ethics Committee (EC) will also have the right to review your medical records as they relate to this study. In addition, publication(s) using data collected during the study will not include your name or any information that can identify you.

A description of this study will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This web site will not include information that can identify you. At most, the web site will include a summary of the results. You can search this web site at any time.

St. Jude Medical may export data to countries where different data protection laws apply.

If you receive medical care from a doctor other than your study doctor while taking part in this study, you agree that your medical records will be made available for the collection of data related to this study.

If you choose to take part in this study, will it cost you anything?

You and your insurance company are responsible for the costs of all standard of care tests, procedures, and devices. There is no guarantee that your insurance company will cover 100% of these costs. You should check with your insurance company to verify coverage or payments of these procedures.

Will you receive compensation (payment) for taking part in this study?

You will not receive any compensation for your participation in part one of the study.

What if the device needs to be removed?

In the event your Accent MRI™ system or any part has to be removed, it will be returned to St. Jude Medical for analysis. Should you withdraw from this study and choose to have your Accent MRI™ system or any part of it removed, the cost will be your responsibility.

In the event of your death, your implanted Accent MRI™ system may be removed and returned to St. Jude Medical for analysis. The study doctor will get your family's approval prior to removing the device.

What if you are injured because of the study?

If you are injured as a direct result of taking part in this study, medical treatment will be available to you. You, or your insurance company, will be responsible for all costs incurred as a result of that treatment. No other arrangement has been made for financial payments or other forms of compensation (such as lost wages, lost time or discomfort) with respect to such injuries. You do not waive any legal rights by signing this consent form.

During the study, if you experience any medical problems or illnesses from taking part in this study, please contact Dr. _____ at ___-___-_____.

What are your rights if you decide to take part in this study?

Your signature on this consent form means that you have received information about this research study and that you agree to be a part of the study.

You may stop taking part in the study at any time without penalty or loss of benefits to which you are otherwise entitled. If you wish to stop taking part in this research study for any reason, you should contact Dr. _____ at ___-___-_____. A decision to withdraw or to not take part in the study will not affect the quality of medical care that you receive. Your decision will not result in any penalty or loss of benefits to which you are otherwise entitled or affect your future medical care.

Your doctor or the sponsor, St Jude Medical, may decide to withdraw you from the study at any time without your consent. If it is felt to be in your best interest, or if the study is stopped, your doctor may withdraw you from this research. If you have a problem as described in the risks section, or if you become ill during the research, you may have to stop participating in the study, even if you would like to continue. Your study doctor will make this decision. Your study doctor or designee will discuss with you what follow-up is required if you decide to withdraw, or are withdrawn from the study before the study is finished. Early consequences include inability for another non-study site to interrogate the device.

If important information is learned during the course of this study, your doctor will be notified by St. Jude Medical. You will be told of any important new information that is learned during the course of this research study that may affect your condition or your willingness to continue to take part in this study.

Who can you contact for study information?

If you have any questions about the study or taking part in this study, please contact Dr. _____ at ___-___-_____.

In addition, if you have questions about your rights as a research patient, or if you have complaints, concerns, or questions about the research, please contact _____ at -___-___-_____.

Signature

You are making a decision on whether or not to take part in the study. Your signature indicates that you have read the information in this form and have decided to take part in the Lead Safety Portion of the study. You will be given a signed copy of this form to keep.

_____
Printed Name of Patient

_____ _____
Signature of Patient Date

_____
Print Name of Person Obtaining Consent

_____ _____
Signature of Person Obtaining Consent Date

22.0 Appendix D: Patient Informed Consent Addendum: MRI Consent

Patient Informed Consent Addendum: MRI consent

ACCENT MRI™ PACEMAKER AND TENDRIL MRI™ LEAD IDE STUDY

Introduction

You were asked to and agreed to participate in the Accent MRI™ (magnetic resonance image) Pacemaker and Tendril MRI™ Lead IDE (investigational device exemption) research study because your doctor had determined that you qualified to take part in the lead portion of the study. Because you have an Accent MRI system implanted, you may be eligible to participate in the MRI portion of the study.

If you decide to take part in the MRI portion of this study, you will be asked a series of questions about whether or not you've had any MRI scans in the past and other relevant information that will help your doctor determine if you qualify for the MRI portion of the study. Based on your answers and your medical history, your doctor will decide if you qualify to take part in the MRI portion of the study.

When you agreed to take part in the lead portion of the study, FDA may not yet have granted permission for your study doctor to perform MRI scans for the study. If that was the case, you were not allowed to undergo an MRI scan until now. FDA is now allowing your study doctor to perform MRI Scans for the study; your Accent MRI system is now MR Conditional. This means you may undergo MRI scans with your implanted Accent MRI system.

This consent addendum covers information related to the MRI scan, including what will happen during the MRI visits, the risks associated with an MRI scan and your implanted Accent MRI system. It will also cover information related to and costs associated with the MRI Scan and MRI visits, along with other information related to the MRI and 1 Month Post MRI visits. Please refer to your original consent form for other information such as your rights as a study participant.

In order to participate in the MRI related visits, you must sign and date this consent form.

Please read this form, and ask your study doctor any questions about the study so that you can have your questions answered before you decide if you want to take part in this portion of the study. Please take your time and talk about this information with your family, friend, or family doctor. Taking part in this portion of the study is entirely voluntary.

Part Two: MRI Study Visits

All patients who agree to complete the MRI and 1 Month Post MRI visits of the study will undergo the tests and procedures described below.

There may be a representative of the sponsor at your study visits and the representative may carry out some of the study procedures. The study doctor may direct a representative from the sponsor to collect information from your implanted device. At the study doctor's direction, the sponsor representative may also program your device or run tests to see if your device is working as expected. The sponsor's representative will work under the direction of your study doctor or other care provider.

1. MRI Visit

The section below describes the procedures that will occur. You may be asked to come back on a different day to complete your MRI visit depending on the outcome of the testing of your pacemaker device.

Please note: There are two types of scans that may be performed for the MRI study. One is a non-clinical scan. This MRI scan is being performed to demonstrate safety and MRI compatibility of the Accent MRI system for MRI scans for the purposes of this study. This MRI scan is not meant to be diagnostic in nature. You will receive this type of scan.

The second type of scan that will be performed is a clinical scan. This type of scan is being performed to collect information on the image quality of the MRI scan and to see if there is any artifact on the MR image. This MRI scan is not meant to be diagnostic in nature. This type of scan will be performed until at least 20 scans are collected that can be analyzed for image quality and artifact. Your study doctor or study staff will inform you if you will receive the clinical scan.

Before the MRI Scan:

- The study doctor or staff will ask you about the medications that you take every day
- A pregnancy test will be given (for women of child bearing age)
- Before the actual MRI scan, your Pacemaker device will be tested using a programmer in the same way as at a regular clinical check-up. You should not feel any discomfort during this procedure.
- A member of your study doctor's staff or the radiological team will ask you a series of questions (MRI Screening Assessment) to make sure you meet the safety requirement to receive the MRI scan.
- Your device settings will be adjusted for the MRI scan. The MRI Activator will be used to turn on the MRI Setting in the pacemaker device. The programmer will be used to double check that the MRI feature was turned on by the MRI Activator.

During the MRI scan

Once approved to have an MRI, you will be placed on a padded table and positioned for your exam. Electrodes (sticky pads) will be placed on your chest, and the electrodes will be connected to an electrocardiogram machine (ECG). The ECG allows the MRI staff to monitor your heart rhythm during the exam. A pulse oximeter (a painless finger clip to measure the amount of oxygen in your body) will be put on your finger tip. This allows the doctor to monitor the oxygen content in your blood during the MRI. During the exam, the MRI staff is able to see and hear you. You will be able to hear the MRI staff.

Depending on the type of MRI you are having, a soft padded coil may be placed at the area where the pictures will be taken. The table on which you are lying will be moved to the center of the MRI magnet, which looks like a short narrow tube. Even though the tube is open, some people feel confined in small places. If this bothers you, please notify the MRI staff. When MRI pictures are taken, radio signals and magnetic fields are used. When this happens, it is normal for the MRI machine to make loud, banging, and clicking noises. You may be asked to wear earplugs or headphones for your comfort during the exam.

When the MRI exam is finished, the pulse oximeter and ECG electrodes will be removed.

After the MRI Scan
After the MRI scan, the MRI Activator will be used to turn the MRI Setting off in the pacemaker. The programmer will be used to double check that the MRI Setting was turned off by the MRI Activator. After you have your scan, your device will be checked (an external evaluation with a computer and "wand") again, and reset to your regular settings. Your Pacemaker device will be tested using a programmer. Your device settings may be adjusted if changes occurred during the MRI.

2. **1 Month Post MRI Visit**
    - The study doctor or staff will ask you about the medications that you take every day
    - Your Pacemaker device will be tested using a programmer in the same way as at a regular clinical check-up. You should not feel any discomfort during this procedure. A sponsor representative may also program your device or collect information from your device under a physician's supervision.

How long will the MRI part of study last?

Up to 363 patients (including patients randomized to the MRI Control Group under previous versions of the protocol) will be enrolled. Your participation in the MRI Phase of the study will last approximately one to two months, roughly the amount of time from when you come in for your MRI visit to when you return for your 1 month check after the MRI visit. Your participation may last longer if you need to have your MRI lead repositioned or replaced before you complete an MRI visit.

If you need to have your Accent MRI system, either the pacemaker or an MRI lead to be repositioned or replaced and your study doctor decides that the MRI lead will no longer be used, or if your study doctor plugs one of the ports on your device before you complete your MRI visit, you will no longer be able to participate in the MRI part of the study. You will be withdrawn from the MRI part of the study. You will, however, still continue to participate in Part One, the lead portion, of the study if you still have the Accent MRI pacemaker and at least one working Tendril MRI lead implanted.

What are the possible discomforts and risks?

Risks associated with MRI scans of patients with Cardiac Devices:
The following risks have been associated with MRI scans of patients with implanted cardiac devices:

a) **Potential MRI Scan Adverse Events:**

- Claustrophobia (fear of enclosed spaces)
- Mild diaphoresis (sweating)
- Hearing impairment (difficulty hearing)
- Sensation of bodily warmth
- Body stiffness related to immobility

There will be emergency personnel and equipment on hand for your safety. Please tell the study doctor, nurse or technician if you experience any unusual sensations or discomfort during the scan.

b) **Potential MRI System Adverse Events:**

- Lead electrode heating and tissue (heart muscle) damage resulting in loss of sensing or capture or both
- Device heating resulting in tissue damage in the implant pocket or patient discomfort or both
- Induced currents on leads resulting in continuous capture, VT/VF, hemodynamic collapse, or all three
- Damage to the device or leads causing:
    - the system to fail to detect or treat irregular heartbeats
    - the system to treat the patient's condition incorrectly
- Damage to the functionality or mechanical integrity of the device resulting in the inability of the device to communicate with the programmer
- Movement or vibration of the device or leads
- Lead dislodgment (lead comes loose from the heart)
- Competitive pacing and potential for VT/VF induction due to ambulatory asynchronous pacing in MRI mode

These risks would also apply if you undergo a non-study MRI scan.

There may be other risks to you that are not known at this time.

If you do not want to take part in this portion of the study, what other options are available to you?

Your doctor will discuss other options available to you, including not participating in this part of the study.

If you choose to take part in this study, will it cost you anything?

You and your insurance company are responsible for the costs of all standard of care tests, procedures, and devices. There is no guarantee that your insurance company will cover 100% of these costs. You should check with your insurance company to verify coverage or payments of these procedures.

The cost of the MRI scan performed at the MRI visit will be covered through the study.

Will you receive compensation (payment) for taking part in this study?

You will receive a payment of $60 to compensate you for your travel, time, meals, and parking related to your MRI visit.

What are the possible benefits to you or to others?

If you agree to participate in the study, you will be able to undergo an MRI if it were needed to help your doctor confirm a diagnosis. The Accent MRI system was designed to be MRI compatible. The information gathered in this study will add to the understanding of treatment options for patients with implanted pacemaker systems who need to have an MRI scan performed.

The sponsor of this study is paying for cost of data capture and items that are not deemed standard of care/routine care in the study. St. Jude Medical will pay the study center where the study is being conducted

Signature

You are making a decision on whether or not to take part in the MRI Phase of the study. Your signature indicates that you have read the information in this form and have decided to take part in the MRI Phase of the study. You will be given a signed copy of this form to keep.

If you previously consented to participate in the MRI Phase of the study, by signing this consent form, you are making a decision on whether or not to undergo the study MRI scan in the MRI Phase of the MRI Study. Your signature indicates that you have read the information in this form and have decided to undergo the study MRI scan. All the tests and procedures outlined in this consent form are the same as the tests and procedures in previous versions of the consent form for the MRI Phase of the study. You will be given a signed copy of this form to keep.

☐ Please check this box if the patient was previously enrolled in the MRI Phase under Revision J of the Protocol and was randomized to the MRI Control Group.

Printed Name of Patient

_____ _____

Signature of Patient Date

_____

Print Name of Person Obtaining Consent

_____ _____

Signature of Person Obtaining Consent Date

23.0 Appendix E: MRI Conditional notification to Patients

Patient Notification of MRI Conditional status of Accent MRI System

Accent MRI™ Pacemaker and Tendril MRI™ Lead IDE Study

Dear <insert patient name and/or study ID>:

You are receiving this notice because you are participating in the Accent MRI™ Pacemaker and Tendril MRI™ Lead IDE Study at <insert study center name>. At the time of your enrollment into the study, your implanted pacemaker system was not MR conditional. This meant that you were not allowed to have an MRI scan.

The Food and Drug Administration, FDA, has now granted permission for your study doctor to perform MRI scans on your pacemaker system for the study. What this means is you are now allowed to undergo an MRI scan, if you need one. If you need to have an MRI scan not related to the study, you should speak with and ask your doctor about the risks associated with MRI scans of patients with implanted cardiac devices. A list of the risks is provided below for your reference. These are the same risks that could occur during a study MRI scan. There may be other risks that could occur.

1. Risks associated with MRI Scans of Patients with Implanted Cardiac Devices:
The following risks have been associated with MRI scans of patients with implanted cardiac devices:

a) **Potential MRI Scan Adverse Events:**

- Claustrophobia (fear of enclosed spaces)
- Mild diaphoresis (sweating)
- Hearing impairment (difficulty hearing)
- Sensation of bodily warmth
- Body stiffness related to immobility

b) **Potential MRI System Adverse Events:**

- Lead electrode heating and tissue (heart muscle) damage resulting in loss of sensing or capture or both
- Device heating resulting in tissue damage in the implant pocket or patient discomfort or both
- Induced currents on leads resulting in continuous capture, VT/VF, hemodynamic collapse, or all three
- Damage to the device or leads causing:

  - the system to fail to detect or treat irregular heartbeats
  - the system to treat the patient's condition incorrectly
- Damage to the functionality or mechanical integrity of the device resulting in the inability of the device to communicate with the programmer
- Movement or vibration of the device or leads
- Lead dislodgment (lead comes loose from the heart)
- Competitive pacing and potential for VT/VF induction due to ambulatory asynchronous pacing in MRI mode

You may be asked by your study doctor if you want to participate in the MRI part of the study. Your study doctor or his staff may ask you this question at your next study visit, or he/she may call you or contact you by other means to determine if you are interested. Please contact Dr. <insert investigator name> or his study staff at <insert phone number> if you have any questions about the content of this letter.

Sincerely,

<insert name of site>

References

[1] Rogulin A, Schwitter J, Vahlhaus C, Lombardi M, Brugada J, Vardas P, *et al*. Magnetic resonance imaging in individuals with cardiovascular implantable electronic devices. Europace 2008;10:336-346.
[2] Duru F, Luechinger R, Scheidegger M, et al. Pacing in magnetic resonance imaging environment: Clinical and technical considerations on compatibility. Eur heart J 2001;22:113-124.
[3] imv Medical Information Division.. 2007 MRI Market Summary Report. Prepared for St. Jude Medical June 2008.
[4] Mond H G, Irwin M, Ector H, and Proclemer A. The world survey of cardiac pacing and cardioverter- defibrillators: calendar year 2005 an International Cardiac Pacing and Electrophysiology Society (ICPES) Project. PACE 2008 Sep;31(9):1202-12.
[5] Mond H G, Irwin M, Morillo C, Ector H. The world survey of cardiac pacing and cardioverter- defibrillators: Calendar year 2001. PACE 2004 Feb;27:955-64
[6] Kalin R and Stanton R. Current Clinical Issues for MRI Scanning of Pacemaker and Defibrillator Patients. PACE 2005;28(4):326-328.
[7] A Primer on Medical Device Interactions with MRI Systems; http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm107721.htm#overview], 9-Feb-10
[8] Pinski S L and Trohman R G. Interference in implanted cardiac devices, Part II. Journal of Pacing and Clinical Electrophysiology. 2002 Oct; 25(10): 1496-1509.
[9] Roguin A. Magnetic resonance imaging in patients with implantable cardioverter-defibrillators and pacemakers. Journal of the American College of Cardiology. 2009 Aug; 54(6): 556-557.
[10] Levine P. Industry viewpoint: St. Jude medical: Pacemakers, ICDs and MRI. PACE 2005;28(4):266-267.
[11] Shellock F G, et al. Cardiac pacemaker: In vitro assessment at 1.5 T. American Heart Journal. 2006 Feb; 151(2): 436-443.
[12] Gimbel J R, Johnson D, Levine P A, Wilkoff B L. Safe performance of magnetic resonance imaging on five patients with permanent cardiac pacemakers. PACE 1996;19:913-919.
[13] Valhaus C, Sommer T, Lewalter T. et al. Inteference with cardiac pacemakers by magnetic resonance imaging : Are there irreversible changes at 0.5 Tesla? PACE 2001; 24: 489-495.
[14] Luechinger R, Duru F, Scheidegger, M B, et al. Force and torque effects of a 1.5Tesla MRI scanner on cardiac pacemakers and ICDs. PACE 2001; 24:199-205.
[15] Loewy J, Loewy A, and Kendall EJ. Reconsiderations of pacemakers and MR imaging. RadioGraphics 2004; 24:1257-1268.
[16] Roguin A, Zviman M M, Meininger G T, et al. Modern pacemaker and implantable cardioverter defibrillator system scan be magnet safe : In vitro and in vivo assessment of safety and function at 1.5T. Circulation 2004; 110:475-482.
[17] Gimbel J R and Kanal E. Can patients with implantable pacemakers safely undergo magnetic resonance imaging? Journal of the American College of Cardiology. 2004 April; 43(7): 1325-1327.

[18] Faris O, Shein M. Government viewpoint: US Food & Drug Administration: Pacemakers, ICDs and MRI. PACE 2005; 28(4) 268-269.
[19] Wilkoff B L, Bello D, Taborsky M, Vymazal J, Kanal E, Heuer H, *et al.* EnRhythm MRI SureScan Pacing System Study Investigators, Magnetic Resonance Imaging in Patients with a Pacemaker System Designed for the MR Environment, Heart Rhythm (2009), doi: 10.1016/j.hrthm.2010.10.002..