Abbott	Clinical Investigation Plan Cover Page

NCT Number: NCT02877693
ASIA MRI ICD Study
A post-market clinical evaluation of St. Jude Medical™ MR Conditional ICD System on patients undergoing Magnetic Resonance Imaging
Study Document No: SJM-CIP-10163
Version B
Date: 04-Dec-2017

Sponsor

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Project Acronym: ASIA MRI ICD Study

Project Title: "A post-market clinical evaluation of St. Jude Medical™ MR Conditional ICD System on patients undergoing Magnetic Resonance Imaging"

CRD_889

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Clinical Investigation Plan (CIP)

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1 Introduction

This document is a clinical investigation plan (CIP) for the Asia MRI ICD clinical investigation. This clinical investigation is intended to assess the clinical performance of the St. Jude Medical™ MR Conditional ICD System in patients undergoing an elective thoracic MRI scan. This clinical investigation is sponsored by St. Jude Medical.

2 Background and Justification for clinical investigation

Magnetic resonance imaging (MRI) is a diagnostic method used 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 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. Examples of these hazards include unwanted cardiac stimulation, heating near lead electrodes, image artifacts, and forces being applied to implanted components.[2,7,8] Due to these issues, certain currently marketed implantable cardiac device systems, including ICDs, may be contraindicated for use in an MRI environment.

Over the past 10 years, there have been numerous patients with implanted devices who successfully underwent magnetic resonance imaging.[9-14]
In this post market study, St. Jude Medical plans to assess the clinical performance of the St. Jude Medical™ MR Conditional ICD System in patients undergoing an elective thoracic MRI scan (1.5T and 3.0T).

3 Clinical Investigation Design

3.1 Clinical Investigation Design

This clinical investigation is a prospective, multicenter, 2-phase, single arm, Asian study.

- In the 1st phase patients will be enrolled at least 60 days post successful implant with a St. Jude Medical™ MR Conditional ICD System approved for thoracic scan with 1.5 Tesla MRI scanning machines.
- In the 2nd phase patients will be enrolled at least 60 days post successful implant with a St. Jude Medical™ MR Conditional ICD System approved* for thoracic scan with 3.0 Tesla MRI scanning machines.

  *NOTE: The 2nd phase of this study will start only after receiving appropriate regulatory approval for MRI labelling at 3.0T and phase 1 enrollment has completed. The Sponsor will notify each ethics committee and site when Phase 2 may begin. Patient can be enrolled only in one of the two phases of the study.

A prospective, multi-center study design was chosen for generalizability of study results by enrolling subjects across multiple geographies and sites, with the minimum sample size required to demonstrate the safety of St. Jude Medical™ MR Conditional ICD System in an MRI environment with 1.5 Tesla and 3.0 Tesla scanning machines.

Enrollment of the study is expected to require 36 months. The anticipated duration of the study is 42 months, depending on the rate of enrollment and regulatory timelines (CE approval of St. Jude Medical™ MR Conditional ICD System for thoracic scan with 3.0 Tesla MRI scanning machines for 2nd Phase and phase 1 enrollment has completed).

The clinical investigation will enroll at least 396 subjects (198 in each phase) up to 40 centers across Asian Countries.

Subjects will be enrolled, undergo the study MRI scans, and followed for one month following the study MRI scan. The minimum duration of each subject's participation is approximately one month from the MRI scan (1 Month Post Scan visit).

3.2 Objectives

To assess the clinical performance of the St. Jude Medical™ MR Conditional ICD System in patients undergoing an elective thoracic MRI scan.

3.3 Endpoints

3.3.1 Primary Endpoint

Freedom from MRI-scan related complications* related to St. Jude Medical™ MR Conditional ICD System from MRI scan visit to 1 month post-MRI scan visit

**A complication is a serious adverse device effect (SADE) that requires an invasive intervention or leads to death.*

The primary endpoint analysis will be performed for each study phase separately.

3.3.2 Descriptive Endpoints

- Demographics and medical/surgical history such as gender, age, history of smoking, cardiac disease history, arrhythmia history, and indication for ICD implant, etc.
- Proportion of SJM high voltage lead implanted with SJM MR Conditional ICD with capture threshold increase of ≤ 0.5V @ 0.5ms from pre-MRI scan testing to 1 month post-MRI scan testing
- Proportion of SJM high voltage lead implanted with SJM MR Conditional ICD with sensing amplitude decrease of ≤ 50% from pre-MRI scan testing to 1 month post-MRI scan testing
- Average and Peak Specific Absorption Rate (SAR) during MRI scan, MRI visit duration in MRI laboratory and total MRI scan duration in MRI laboratory.
- Adverse events and death

3.4 Study Population

A subject is considered enrolled in the study after he/she signs the study consent, meets all of the inclusion criteria and none of the exclusion criteria verified during the enrollment visit.

The study population includes males and females implanted with St. Jude Medical™ MR Conditional ICD System. Vulnerable subjects, such as minors or those unable to provide consent, are excluded from participating.

3.4.1 Inclusion Criteria

To participate in this clinical investigation, the subject must meet all of the following inclusion criteria:

1. Subject is pectorally implanted with St. Jude Medical™ MR Conditional ICD System for at least 60 days
2. Subject is willing to undergo an elective MRI scan without sedation

   NOTE: Antianxiety agents (e.g. minor tranquilizers, etc.) may be used as long as the patient can communicate with site personnel during the MRI scan
3. Subject's ventricular bipolar capture threshold is stable < 2.5V @ 0.5ms

4. Subject's ventricular sensing is measurable (patient has underlying rhythm > 30bpm) and the sensing amplitude is stable > 4mV
5. Subject is able to provide informed consent for study participation (legal guardian or legally authorized representative is NOT acceptable)
6. Subject is willing and able to comply with the prescribed follow-up tests and procedures
7. Subject is not contraindicated for an MRI scan (per the MRI Screening Form)

3.4.2 Exclusion Criteria

To participate in this clinical investigation, the subject must meet none of the following exclusion criteria:

1. Subject is pacemaker dependent
2. Subject has a non SJM MRI compatible endocardial lead implanted or capped
3. Subject has another existing active implanted medical device, e.g., neurostimulator, infusion pump, etc. that has MR labeling that will not allow the MRI scans per this protocol to be completed.
4. Subject has a high voltage lead revision incidence < 60 days of the enrollment visit
5. Subject has other non-MRI compatible device or material implanted

NOTE: MRI compatible knee replacements, hip replacements, stents, etc. may be included as long as the labeling of these devices allow MRI scans conducted per this protocol

NOTE: MRI compatible mechanical, prosthetic, and bioprosthetic heart valves may be included as long as the labeling of these devices allow for MRI scans conducted per this protocol

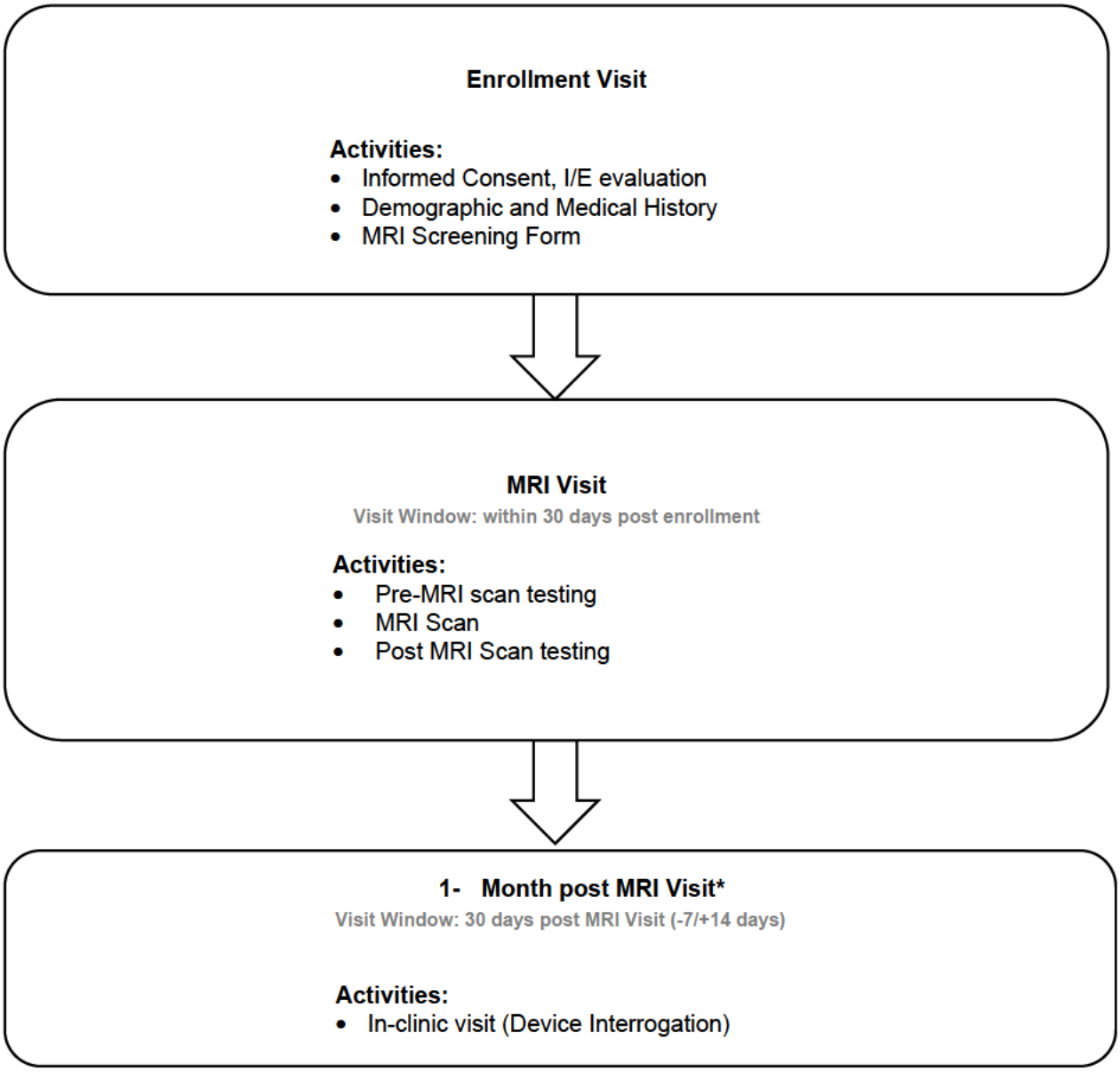
NOTE: Non-removable dental implants may be included

6. Subject has a lead extender, adaptor, or capped/abandoned lead
7. Subject is enrolled or intend to participate in a clinical drug and/or device study (investigational device, investigational drug, new indication for a device or drug or additional testing beyond standard of care procedures), which could confound the results of this trial as determined by SJM.
8. Subject is pregnant or planning to become pregnant during the duration of the subject's participation in the study
9. Subject has a life expectancy of less than 12 months due to any condition
10. Subject has exclusion criteria required by local law (e.g., age)

4 Procedures

4.1 Study Flowchart

The Study Flow Chart (Fig. 1) summarizes subject flow during this clinical investigation.



*This follow up visit is to be conducted in office, whether centers might use remote monitoring in their daily follow up is up to physicians' discretion by using Merlin.net

4.2 Study Procedures

This clinical investigation will be conducted in accordance with this clinical investigation plan (CIP). All parties involved in the conduct of the clinical investigation will be qualified by education, training, or experience to perform their tasks and this training will be documented appropriately.

The clinical investigation will not commence until Sponsor receives written approval from the IRB/EC and relevant regulatory authorities (if applicable) and all required documents have been collected from the investigational site(s).

Subjects who are pectorally implanted with a St. Jude Medical™ MR Conditional ICD System at least 60 days will be enrolled. Enrolled subjects will undergo an elective MRI scan within 30 days post enrollment. Post MRI visit all subjects will be followed up at 1-Month post MRI visit.

The following sections provide a detailed description of procedures required by this Clinical Investigation Plan.

Table-1 Specific Study Procedures & Data Collection

Study Visit	Visit Window	Study Procedures & Data Collection	Forms and CRFs
Enrollment		• Screen subject for enrollment eligibility • Obtain informed consent(s) • Complete MRI Screening Form • Obtain medical and surgical history • Collect demographic information • Document indication for implant of ICD • Obtain ICD system information: model and serial number of implanted St. Jude Medical™ MR Conditional ICD System, and if applicable, most recent lead revision information. • Evaluate subject Adverse Device Effect (ADE) and Serious Adverse Device Effect (SADE), and submit an AE CRF (as applicable).	• Signed and Dated Patient Informed Consent Form(s) • MRI Screening Form • Enrollment CRF

Study Visit	Visit Window	Study Procedures & Data Collection	Forms and CRFs
MRI Scan Visit	*Within 30 days post enrollment* The pre-MRI scan, MRI and post- MRI scan procedures should occur on the same day.	***Pre-MRI Scan testing:*** • Assess inclusion/exclusion criteria • Screen, clear and prepare subject for MRI scan • Complete MRI screening form (if MRI scan visit does not occur the same day as enrollment visit) • Complete MRI Hazard Checklist • Administer pregnancy test – can be done up to 7 days before MRI scan • Interrogate device • Perform capacitor maintenance • Obtain in-clinic lead measurements: ventricular bipolar capture threshold, ventricular sensing amplitude, ventricular pacing impedance and high voltage lead impedance*#$ • Setup and activate MRI Settings • Upload device session record (X-file) through the EDC study site portal ***During MRI Scan*** • Monitor subject with ECG, pulse oximetry, and verbal communication ***Post-MRI scan testing:*** • Interrogate device • Deactivate MRI Settings • Obtain in-clinic lead measurements: ventricular bipolar capture threshold, ventricular sensing amplitude, ventricular pacing impedance and high	• MRI Hazard Checklist • Pre-MRI Scan CRF • Pre-MRI Device session records (X-Files) • MRI Scan CRF • Post-MRI Device session records (X-Files) If applicable: • MRI Screening Form • AE CRF • Deviation CRF • Death CRF • Withdrawal CRF • Product Out of Service CRF

Study Visit	Visit Window	Study Procedures & Data Collection	Forms and CRFs
		voltage lead impedance*# • Evaluate subject Adverse Device Effect (ADE) and Serious Adverse Device Effect (SADE), and submit an AE CRF (as applicable). • Report deviations, death, withdrawal and out of service if applicable • Submit MRI scan results, e.g. scan time, sequences used, etc. • Upload device session record (X-file) through the EDC study site portal	
One Month Post- MRI Scan Visit	30 days post MRI scan (- 7/+14 days)	• Interrogate device • Obtain in-clinic lead measurements: ventricular bipolar capture threshold, ventricular sensing amplitude, ventricular pacing impedance and high voltage lead impedance*# • Evaluate subject Adverse Device Effect (ADE) and Serious Adverse Device Effect (SADE), and submit an AE CRF (as applicable). • Report deviations, death, withdrawal and out of service as applicable • Upload device session record (X-file) through the EDC study site portal	• Follow Up CRF • Device session records (X-Files) ***If applicable:*** • AE CRF • Deviation CRF • Death CRF • Withdrawal CRF • Product Out of Service CRF
Unscheduled (if applicable)	Any time after Enrollment visit (where the subject is seen in clinic due to an ADE, SADE)	• Interrogate device • Obtain in-clinic lead measurements: ventricular bipolar capture threshold, ventricular sensing amplitude, ventricular	• Follow Up CRF • Device session records (X-Files) • AE CRF

Study Visit	Visit Window	Study Procedures & Data Collection	Forms and CRFs
		pacing impedance and high voltage lead impedance*# • Evaluate subject Adverse Device Effect (ADE) and Serious Adverse Device Effect (SADE), and submit an AE CRF (as applicable). • Report deviations, death, withdrawal and out of service as applicable • Upload device session record (X-file) through the EDC study site portal	***If applicable:*** • Deviation CRF • Death CRF • Withdrawal CRF • Product Out of Service CRF
System Revision (if applicable)	Can occur any time after enrollment visit	• Interrogate device • Obtain in-clinic lead measurements: ventricular bipolar capture threshold, ventricular sensing amplitude, ventricular pacing impedance and high voltage lead impedance (HVLI)*# for cases where the lead was repositioned, or was replaced with another HVLI lead, or where the ICD was replaced with another ICD. • Evaluate subject Adverse Device Effect (ADE) and Serious Adverse Device Effect (SADE), and submit an AE CRF (as applicable). • Report deviations, death, withdrawal, out of service as applicable • Upload device session record (X-file) through the EDC study site portal	• System Revision CRF ***If applicable:*** • AE CRF • Deviation CRF • Death CRF • Withdrawal CRF • Product Out of Service CRF

[*]Lead capture thresholds are not required if a high ventricular rate (e.g. 110bpm) is present. If available, sites should use the automatically obtained pacing capture threshold from the most recent archival data as a substitute for the in clinic capture threshold.
[#]Lead sensing measurements are not required if the subject's intrinsic rate has been established to be at or below 30 beats per minute
[$]If the subject's intrinsic rate at MRI scan visit has been established to be at or below 30 beats per minute subject should be withdrawn from the study.

Table-2: List of all clinical investigation specific tests and procedures

Visit Study Activity	Enrollment	MRI Scan Visit ***(Within 30 days post enrollment)***	1 Month Post MRI FU ***(30 days post MRI scan (-7/+14 days))***	Unscheduled visit
Informed Consent Process	X			
Demographics	X			
Medical and Surgical History	X			
Implant Indication	X			
System Information	X			
Device Interrogation		X*	X	X
Device Programming		X**		
MRI Screening Form	X	X		
MRI Hazard Checklist		X		
Monitor subject with ECG, pulse oximetry, and verbal communication during MRI scan		X		
Adverse Event	(X)	(X)	(X)	X
Deviation	(X)	(X)	(X)	(X)
Withdrawal	(X)	(X)	(X)	(X)
Death	(X)	(X)	(X)	(X)

** Device interrogation (including capture threshold, sensing amplitude, pacing impedance and high voltage lead impedance testing)*

**MRI Scan Guidelines as per Appendix-E
(X) If applicable

4.3 Informed Consent Process

The principal investigator or his/her authorized designee will conduct the Informed Consent Process, as required by applicable regulations and the center's IRB/EC. This process will include a verbal discussion with the subject on all aspects of the clinical investigation that are relevant to the subject's decision to participate, such as details of clinical investigation procedures, anticipated benefits, and potential risks of clinical investigation participation. During the discussion, the principal investigator or his/her authorized designee will avoid any improper influence on the subject and will respect subject's legal rights. The subject shall be provided with the informed consent form that is written in a language that is understandable to the subject and has been approved by the center's IRB/EC. The subject shall have adequate time to review, ask questions and consider his/her participation.

If the subject agrees to participate, the Informed Consent form must be signed and dated by the subject and by principal investigator or delegated study personnel obtaining the consent. The signed original consent will be filed in the subject's hospital or research charts, and a copy will be provided to the subject.

The principal investigator or his/her authorized designee will document the informed consent process in the subject's hospital and/or research charts. The date of signature will be entered on an appropriate Case Report Form (CRF).

Failure to obtain informed consent from a subject prior to clinical investigation enrollment should be reported to Sponsor within 5 working days and to the reviewing center's IRB/EC according to the IRB's/ EC's reporting requirements.

The principal investigator or his/her authorized designee will inform the subject of any important new information about the clinical investigation.

4.3.1 Special circumstances for informed consent

Subject unable to read or write, if applicable: Subjects unable to read or write may be enrolled in this clinical investigation. Informed consent will be obtained through a supervised oral process. An independent witness will be present throughout the informed consent process. The written informed consent form and any other information will be read aloud and explained to the prospective subject will sign and personally date the informed consent form. The witness also signs and personally dates the informed consent form attesting that the information was accurately explained and that informed consent was freely given.

4.4 Point of Enrollment

Subject is considered enrolled in the clinical investigation from the moment the subject has provided a written Patient Informed Consent and has been confirmed to meet all inclusion criteria and none of the exclusion criteria verified during enrollment visit. Notification of enrollment to the Sponsor is considered to have occurred when the appropriate CRF has been received by the Sponsor.

If a subject does not meet all inclusion criteria or meets any of the exclusion criteria the subject cannot participate in the clinical investigation. The principal investigator is responsible for ensuring all clinical investigation data is collected as required per CIP scheduled procedures.

4.5 Enrollment visit

The subject is considered enrolled after the informed consent is signed.

The principal investigator or delegated study personnel will record enrollment information (name of the clinical investigation, date of consent and Inclusion/exclusion information) in the hospital records and complete and submit an Enrollment CRF in a timely manner.

Collect data on the subject including demographics and medical/surgical history such as gender, age, history of smoking, medical and surgical history, and indication for ICD implant, etc. To ensure the patient meets the requirements to undergo the study MRI scan, use the MRI Screening Form as part of the enrollment screening.

Data Submission

Complete and submit the appropriate forms to St. Jude Medical. Refer to **Table-1 Specific Study Procedures and Data Collection.**

4.6 Scheduled Follow-ups

After Enrollment visit, subjects will be seen for an MRI Scan Visit which should happen within 30 days post enrollment. During the MRI Scan Visit, the pre-MRI scan testing, MRI Scan and Post-MRI scan testing should all occur on the same day. Subjects will also be seen 1 Month Post MRI Scan Visit (-7/+14 days).

Refer to **Table-1 Specific Study Procedures and Data Collection.**

The Enrollment and MRI Scan Visit is allowed, but is not required, to be conducted on the same day.

4.6.1 MRI Scan Visit

IMPORTANT NOTE: Before the MRI Scan Visit, if the subject underwent a system revision since enrollment that resulted in

- implant of a lead or ICD other than St. Jude Medical™ MR Conditional ICD System or
- capping/abandoning a lead
- implant of a non-MRI compatible device or material, or
- any combination above,

the subject is no longer eligible to undergo the study MRI Scan. Do not proceed with any of the tests listed for the MRI Scan Visit and withdraw the patient. Refer to Section 4.9 System Revisions
Otherwise, follow the procedures outlined below for the MRI Scan Visit.

4.6.1.1 Pre-Scan Testing and Device Programming

Pregnancy Testing

Administer a pregnancy test (per institutional standard) to all female subjects of childbearing potential. The pregnancy testing may be done up to 7 days before the MRI scan. Document the results of the test. If the subject is pregnant, do not proceed any further and withdraw the patient.

Clearing the Subject for the Study MRI Scan

In order to safely perform an MRI scan on a subject with the implanted study system, the physician/clinician should do the following as stated in the Appendix E: MRI Scan Guideline for St. Jude Medical™ MR Conditional ICD System:

- Confirm that the patient has an MR Conditional System
- Confirm that no adverse conditions to MRI scanning are present (e.g. additional hardware)
- Review the potential adverse events
- Generate a report of the patient's permanently programmed parameters
- Select and Save MRI Settings
- Review the MRI Checklist and Program the MRI Settings using the Merlin® Patient Care System (PCS)
- Subject receives the MRI Scan
- Disable MRI Settings Using the Merlin® PCS

The radiologist or staff, a designated radiological member, must determine the subject's eligibility for an MRI scan prior to the MRI scan (per standard of practice). However, the ICD and lead (wires) contraindication item on the checklist do not apply if the subject is implanted with St. Jude Medical™ MR Conditional ICD Systems.

Complete MRI Screening Form again if the MRI scan visit does not occur the same day as enrollment.

The study MRI Hazard Checklist may be used to document a radiologist or designated member of the radiology department has cleared the subject for an MRI scan. Alternatively, the radiology department may use its own hazard checklist in lieu of the study MRI Hazard Checklist. This documentation should be maintained with the subject's medical and/or study records.

Device Assessment and Programming

Interrogate the ICD, and obtain the following for ventricular lead:

- In-clinic ventricular bipolar capture threshold at a pulse width of 0.5 ms. Either the manual decrement or automatic (in-clinic, programmer-based) method may be used to obtain the capture threshold. **Note: If the capture threshold is > 2.5V, then the patient does not meet inclusion criteria.**
- In-clinic ventricular bipolar sensing amplitude. Either the incremental or the automatic (in-clinic, programmer based) method may be used to obtain the sensing threshold. **Note: If the ventricular sensing is not measurable (patient has underlying rhythm < 30bpm) and the sensing amplitude is < 4mV, then the patient does not meet inclusion criteria.**
- In-clinic ventricular bipolar pacing impedance and high voltage lead impedance
- Upload device session record (X-file) through the EDC study site portal

NOTE: RV capture thresholds are not required to be obtained if a high ventricular rate is present (e.g. 110bpm). If available, sites should use the automatically obtained pacing capture threshold from the most recent archival data as a substitute for the in clinic capture threshold. RV sensing measurements are not required if the subject's intrinsic rate has been established to be ≤30 beats per minute, as patient doesn't meet inclusion criteria he/she should be withdrawn from the study.

If the device testing results do not meet the MRI conditions for scanning per the Appendix E: MRI Scan Guideline, also see below, or the patient's sensing threshold is not stable or not measurable or the sensing threshold is less than 4mV, the physician may choose to reschedule the subject to return for re-testing. The subject's 1 Month Post MRI Scan Visit will need to be rescheduled to correspond with the MRI Scan Visit where the MRI scan was completed.

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

- Ventricular Bipolar capture thresholds are stable at ≤2.5V@ 0.5 ms
- Bipolar pacing lead impedance is within range, i.e. ≥ 200 and ≤ 2000 ohms
- HVLI is within range, i.e. ≥20 and ≤200 ohms
- No additional hardware (adaptors, extenders, or abandoned leads)

Save the MRI Setting after the MRI Checklist has been reviewed, using the parameters listed in **Table 3: MRI** Parameters. Perform all other applicable tests and procedures.

Table 3: MRI Parameters

Parameters	Required Programmed Values
MRI Mode*	Pacing off
MRI Base Rate	n/a
MRI RV Pulse Configuration	n/a
MRI RV Pulse Amplitude	n/a
MRI RV Pulse Width	n/a
Tachy settings	Disabled

***Note:** When MRI Settings are enabled, sensing is disabled. Determine whether or not the subject requires pacing support during the MRI scan. When pacing support is needed, thoracic MRI scan cannot be performed, *as patient doesn't meet inclusion criteria he/she should be immediately withdrawn from the study.* When pacing support is not needed, set the MRI Mode to Pacing Off.

For more details, kindly refer to MRI Ready Systems Manual: MRI Procedure Information for the St. Jude Medical™ MR Conditional System.

In MR Conditional ICDs, tachytherapy is disabled when the MRI settings are programmed.

After the electrical measurements for the RV lead have been taken, capacitor maintenance has been performed, the MRI Checklist (on the programmer) verified and the MRI Setting saved, activate the MRI parameters.

Setting up Pulse Oximetry and ECG

Set up pulse oximetry and an ECG per standard of care.

Place the oximetry clip on the subject's finger or other any other appendage that results in valid pulse oximetry readings. Position MRI compatible surface electrodes on the subject to ensure the subject's heart rate can be continuously monitored during the scan. During the MRI scan, periodically record heart rate, and blood oxygen saturation levels. Visually examine the ECG during the MRI scan. Note any abnormalities observed in the cardiac rhythm. After the MRI scan, remove the subject from the MRI field.

Data Submission

Once required testing has been performed, complete and submit the appropriate forms to St. Jude Medical. Refer to **Table-1 Specific Study Procedures and Data Collection**

Upload pre-MRI scan device session records through the EDC study portal. It is recommended that the following device printouts and measurements be maintained at the site.

- FastPath Summary
- Test Results with Freezes, Include Battery & Leads
- Wrap-up Overview with full parameters
- Upload device session record (X-file) through the EDC study site portal

4.6.1.2 The MRI Scan

After confirmation by the electrophysiologist or device specialist that all pre-MRI system checks (mentioned above) have been met, subjects will have their MRI scan completed by a radiology staff member. **Note: If the patient does not pass the Pre-MRI scan System Check specified above, then the patient should not undergo an MRI scan. The patient can be rescheduled to come back to repeat the Pre-MRI scan System Check testing within the visit window.**

Protocol required MRI scan sequences for each subject undergoing an MRI scan are described in detail in Appendix E. It is recommended that the MRI scan be set up on the MRI scanner in advance of the first subject scheduled for a study scan to ensure the scan has been appropriately programmed, and to provide adequate time to address any questions or issues that may arise.

Subjects will undergo Thoracic MRI scan for the study. The thoracic scan is RF intensive should be set up to last about 6 minutes and 15 seconds. The thoracic scan will need to be repeated four times to ensure the subject is scanned approximately 25 minutes.

In addition to study specific Thoracic MRI Scan, an optional non-study MRI scan (either a brain, cardiac or lumbar scan without administration of contrast agents or sedation) may be run per discretion of Investigator to provide a MRI report to subjects. These optional scans will occur after the study scan and will not have a scan time greater than 5 minutes. Sites will be provided with a guidance document for Optional MRI Scan set-up.

Further details about the set-up, programming and ways to adjust the parameters for MRI scans can be found in Appendix E: MRI Scan Guidelines.

The subject may be in the bore or near the vicinity of the magnet for approximately 60 minutes. The actual amount of time the subject will be scanned is approximately 30 minutes (including Optional MRI Scan).

In conditions where the time of RF exposure is stretched above 30 minutes, the scan will be interrupted and patient will be taken out of the MRI bore. MRI scan can be continued again once waiting period of 30 minutes is completed.

The MRI scan is not intended to be diagnostic in nature and therefore the administration of contrast fluids or sedation are not permitted.

Consult the “MRI Ready Systems Manual: MRI Procedure Information for the St. Jude Medical™ MR Conditional System” for guidelines and `precautions related to conducting an MRI scan with the implanted study ICD system.

NOTE: MRI scan in this study is being performed to demonstrate performance of St. Jude Medical™ MR Conditional ICD System for an MRI scan, and is not meant to be diagnostic in nature. The MRI scan will not be read by the radiologist.

If subject movement causes distortion on the MRI, do not repeat the MRI scan.

Cardiac Monitoring

During the entire MRI scan, the subject’s cardiac function must be monitored using pulse oximetry and an ECG by a 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 subject must also take place to assess and/or confirm any clinically significant changes noted in the subject’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 MRI 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 subject’s hemodynamic function is compromised during the MRI scan, discontinue the MRI procedure and take proper measures to restore the subject’s hemodynamic function.

Handling of Subjects Unable to Tolerate an MR Scan

In cases where the scan cannot be tolerated by the subject, remove the subject from the scanner. Assess the subject for possible adverse events, and treat the subject's reported symptoms according to your institution's standard of practice. Document the reason for the intolerance. At a minimum, information related to the sequence used to perform the scan, the length of time the subject 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. The subject is not withdrawn from the study. The subject should be scheduled to return for their 1 month post MRI scan visit.

4.6.1.3 Post- MRI Scan Testing

Device Assessment and Programming

Following the MRI Scan, remove the subject from the MRI bore. Interrogate the ICD. Disable the MRI Settings. **Note: MRI settings must be disabled to ensure that tachyarrhythmia therapy is turned back on.** Obtain the following for the ventricular lead:

- In-clinic ventricular bipolar capture threshold at a pulse width of 0.5 ms. Either the manual decrement or automatic (in-clinic, programmer-based) method may be used to obtain the capture threshold.
- In-clinic ventricular bipolar sensing amplitude. Either the incremental or the automatic (in-clinic, programmer based) method may be used to obtain the sensing threshold.
- In clinic ventricular bipolar lead impedance
- In-clinic High Voltage Lead impedance

NOTE: RV capture thresholds are not required to be obtained if a high ventricular rate is present. RV sensing measurements are not required if the subject's intrinsic rate is established to be ≤30 beats per minute.

Reporting of MRI Scan-Related Adverse Device Effects

An ADE or SADE related to the following should be reported as soon as possible 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 ADEs or SADEs related to or caused by the MRI scan are appropriately captured, before starting the scan, verbally instruct the subject 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, room air blood oxygen saturation, and/or

respiration rate that occur during the MRI scan that may suggest an ADE or SADE 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 ADE or SADE 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 ECG
(2) A 2-view chest X-ray (PA and Lateral).
(3) Room air blood oxygen saturation
(4) A transthoracic echocardiogram.

If the subject reports pocket discomfort, ask the subject for additional descriptive information and determine if the pocket is discolored or warm to the touch. ECG, 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.

Data Submission

Once required testing has been performed, complete and submit the appropriate forms to St. Jude Medical. Refer to **Table-1 Specific Study Procedures and Data Collection.**

Export the study MRI scan onto a CD, or other form of electronic media in DICOM format as source document. Upload post MRI scan device session records through the EDC study portal. It is recommended that the following device printouts and measurements be maintained at the site.

- FastPath Summary
- Test Results with Freezes, Include Battery & Leads
- Wrap-up Overview with full parameters
- Upload device session record (X-file) through the EDC study site portal

4.6.2 One (1) Month Post Scan Visit

Testing

Interrogate the ICD and obtain the following for the ventricular lead:

- In-clinic ventricular bipolar capture threshold at a pulse width of 0.5 ms. Either the manual decrement or automatic (in-clinic, programmer-based) method may be used to obtain the capture threshold.
- In-clinic ventricular bipolar sensing amplitude. Either the incremental or the automatic (in-clinic, programmer based) method may be used to obtain the sensing threshold.

- In clinic ventricular bipolar lead impedance
- In-clinic High Voltage Lead impedance

Evaluate the subject for ADE & SADE and submit an AE CRF if applicable.

NOTE: RV capture thresholds are not required to be obtained if a high ventricular rate (e.g. 110bpm) is present. If available, sites should use the automatically obtained pacing capture threshold from the most recent archival data as a substitute for the in clinic capture threshold. RV sensing measurements are not required if the subject's intrinsic rate is established to be ≤30 beats per minute.

Data Submission

Once required testing has been performed, complete and submit the appropriate forms to St. Jude Medical. Refer to **Table-1 Specific Study Procedures and Data Collection.** It is recommended that the following device printouts and measurements be maintained at the site.

- FastPath Summary
- Test Results with Freezes, Include Battery & Leads
- Wrap-up Overview with full parameters
- Upload device session record (X-file) through the EDC study site portal

4.7 Unscheduled Visits

An unscheduled visit is defined as a visit that occurs after Enrollment visit where the subject is seen in clinic due to an ADE or, SADE associated with St. Jude Medical™ MR Conditional ICD System.

Where possible, perform a device interrogation for ventricular lead(s) to obtain:

- In-clinic ventricular bipolar capture threshold at a pulse width of 0.5 ms.
- In-clinic ventricular bipolar sensing amplitude. Either the incremental or the automatic (in-clinic, programmer based) method may be used to measure the sensing threshold.
- In-clinic ventricular bipolar lead impedance
- In-clinic High Voltage lead impedance

Data Submission

Once testing has been performed, complete and submit the appropriate forms to St. Jude Medical. Refer to **Table-1 Specific Study Procedures and Data Collection.**

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

- FastPath Summary
- Test Results with Freezes, Include Battery & Leads
- Wrap-up Overview with full parameters
- Upload device session record (X-file) through the EDC study site portal

4.8 Complete System Explants

If the subject has the entire ICD system removed at any time during the study, and the subject will not receive a replacement St. Jude Medical™ MR Conditional ICD System, follow the subject for 30 days, and withdraw the subject from the study. Complete a Product Out of Service CRF and submit through EDC. A System Revision CRF is not required to be submitted.

4.9 System Revisions

In cases where only the device pocket is revised (leads are not repositioned, leads have not been disconnected from the ICD), a System Revision CRF is not required to be submitted. A System Revision CRF should be completed for all other types of revisions such as pulse generator replacement, lead replacement and lead repositioning. The subject's follow up schedule is not affected in any way.

A system revision is defined as a replacement of or repositioning of one or more components of the study ICD system (ventricular lead, compatible ICD) that occurs after the subject has been consented into the study. Because all components of the study ICD system are market-released, all procedures related to the revision should be performed according to standard of care. The revision may be performed by either a study investigator or other clinician qualified to perform such procedures.

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 CRF.
Refer to **Table-1 Specific Study Procedures and Data Collection** to determine which case report forms need to be completed and submitted.

4.10 Description of activities performed by Sponsor Representatives

Trained sponsor personnel may perform certain activities to ensure compliance to the clinical investigational plan and may provide technical expertise. Sponsor field clinical engineers may perform the following activities:

- Interrogation of and testing the implanted ICD system at any study visit (scheduled or unscheduled): capture threshold, sensing amplitude, pacing impedance and high voltage lead impedance measurements,
- Verifying MRI scan parameters on the programmer at the MRI Scan Visit,
- Programming of the ICD per protocol, and/or as directed by the investigator/designee.

While sponsor representatives may perform these activities, the principal investigator remains responsible for ensuring all study data is collected as required per protocol. Deviations resulting from failure to comply with protocol requirements will be reported through completion of a Deviation CRF.

4.11 Subject Study Completion

The minimum duration of each subject's participation is approximately one month from the MRI scan (1 Month Post Scan visit). When the subject's participation in the clinical study has been completed the subject will return to standard medical care as per physician's recommendation.

4.12 Subject Withdrawal

Subjects must be informed about their right to withdraw from the clinical investigation at any time and for any reason without sanction, penalty or loss of benefits to which the subject is otherwise entitled. Withdrawal from the clinical investigation will not jeopardize their future medical care or relationship with the investigator. Subjects will be requested to specify the reason for the request to withdraw. The investigator must make all reasonable efforts to retain the subject in the clinical investigation until completion of the clinical investigation.

The investigator may decide to withdraw a subject from the clinical investigation at any time if participation is no longer medically appropriate or due to other rationale. The subject's future care will not be influenced by this decision.

Reasons for subject's withdrawal include, but are not limited to::

- Subject and/or Family Request Withdrew Consent
- Subject Lost to Follow-up
- System Explant with no system replacement (i.e. with another Durata or Optisure lead and Ellipse ICD) →Please complete a Product Out of Service Form
- Subject Death → Please complete Death, Product Out Of Service and an Adverse Event Form
- Subject Non-compliance
- Other

If a subject withdraws from the clinical investigation, the site will record reasons for withdrawal, on a Withdrawal CRF.

The status of the subject's condition should be documented at the time of withdrawal.

4.13 Requirements for Clinical Laboratories

Participating center should have a certified MRI laboratory & radiologist. To full fill the CIP requirement, center should be equipped with both 1.5 (For Phase 1) and 3.0 Tesla (For Phase 2) or have an associated Laboratory with required study set-up.

4.14 Study Committees

4.14.1 Steering committee

The Steering Committee will be used to advise the Sponsor during a clinical investigation, such as in the development of the CIP, during the conduct of the study, during data analysis and/or presentation/publication of the clinical investigation results. Membership may include site investigators for the clinical investigation under review.

5 Statistical Considerations

The following section describes the statistical methods for the clinical investigation and justification of the design.

5.1 Primary Endpoint

5.1.1 Primary Endpoint and Hypothesis

The primary endpoint is the Freedom from MRI scan-related complications related to St. Jude Medical™ MR Conditional ICD System from MRI scan to 1 month post MRI scan

Hypothesis

The hypothesis is formally expressed as:

H_0: $P_{MRI\text{-}Scan} \leq 90\%$

H_a: $P_{MRI\text{-}Scan} > 90\%$

Where $P_{MRI\text{-}Scan}$ is the freedom from MRI scan-related complications(s) related to St. Jude Medical™ MR Conditional ICD System from MRI scan to 1 month post-MRI scan visit.

The hypothesis will be tested at the 2.5% significance level. The null hypothesis will be rejected if the 97.5% lower confidence bound (LCB) for $P_{MRI\text{-}Scan}$ is greater than 90%.

5.1.1.1 Analysis Methodology

The freedom from MRI scan related complications for the SJM MR Conditional ICD system from MRI scan to 1 month Post MRI scan will be estimated using binomial proportion. The 97.5% lower confidence

bound will be calculated by the exact (Clopper-Pearson) method for binomial probabilities. The primary endpoint analysis will be performed for each study phase separately.

5.1.1.2 Sample Size Determination

[redacted]

5.1.1.3 Analysis Populations

The analysis will be conducted on subjects who meet all of the following criteria:

- Implanted with the SJM MR Conditional ICD system
- Sign informed consent
- Meet the MRI Conditions of Use
- Undergo a MRI scan
- Have 1 month post MRI scan visit or have MRI-scan related complication(s) related to SJM MR Conditional ICD system before the 1 month post MRI scan visit

5.1.1.4 Subgroup Analysis

There are no subgroup analyses planned for this study.

5.1.1.5 Missing Data

The primary endpoint will be evaluated with data available. No imputations are planned for missing data for primary endpoint.

5.2 Descriptive Endpoints

- Demographics and medical/surgical history such as gender, age, history of smoking, cardiac disease history, arrhythmia history, and indication for ICD implant, etc. Continuous variables will be summarized as sample size, mean, standard deviation, minimum and maximum. For categorical variables, the counts and percentages of subjects will be summarized for each category.

- Proportion of SJM high voltage lead implanted with SJM MR Conditional ICD with capture threshold increase of ≤ 0.5V @ 0.5ms from pre-MRI scan testing to 1 month post-MRI scan testing.

  This proportion will be calculated as number of subjects who had high voltage lead with

[redacted]

capture threshold increased of ≤ 0.5V @ 0.5ms from pre-MRI scan testing to 1 month post-MRI scan testing divided by total number of subjects who had high voltage lead implanted, undergo a MRI scan and with both pre-MRI scan and 1 months Post MRI scan capture threshold available.

- Proportion of SJM high voltage lead implanted with SJM MR Conditional ICD with sensing amplitude decrease of ≤ 50% from pre-MRI scan testing to 1 month post-MRI scan testing. This proportion will be calculated as number of subjects who had high voltage lead with sensing amplitude decrease of ≤ 50% from pre-MRI scan testing to 1 month post-MRI scan testing divided by total number of subjects who had high voltage lead implanted, undergo a MRI scan and with both pre-MRI scan and 1 months Post MRI scan sensing amplitude available.

- Average and Peak Specific Absorption Rate (SAR) during MRI scan, MRI visit duration in MRI laboratory and total MRI scan duration in MRI laboratory
  Average and Peak Specific Absorption Rate (SAR) during MRI scan, MRI visit duration in MRI laboratory and total MRI scan duration in MRI laboratory will be summarized as mean, standard deviation, minimum, median and maximum.

- Adverse events and death
  The number of events, number of subjects who encountered the events will be summarized for each event category for ADE and SADE separately. The number of death will be summarized as counts and percentages for each primary cause.

5.3 Justification of Clinical Investigation Design

This is a prospective, multi-center study intended to evaluate the safety of SJM MR Conditional ICD system in an MRI environment with 1.5 Tesla and 3.0 Tesla scanning machines by demonstrating the superiority of freedom of MRI-scan related complications for ICD system from MRI scan to 1 month post MRI scan against the performance goal of 90%. The time point for evaluation the endpoint is designed to capture MRI scan related complications related to ICD system which are most likely occurred within one month of scan.

5.4 Multiplicity Adjustment

The primary endpoint will be evaluated for each phase separately at 2.5% significance level. Therefore, no multiplicity adjustment is planned for this study.

5.5 Overall Sample Size

Minimum 396 subjects (198 in each phase) will be enrolled in this study in order to meet the minimum target requirement for primary endpoint for each phase.

5.6 Timing of Analysis

The analysis will be conducted for each phase separately. The dataset will be frozen for analysis for each phase when 168 subjects have completed the 1 month post MRI scan visit.

Success Criteria

Success will be assessed for SJM MR Conditional ICD system in an MRI environment for each phase separately, i.e. safety of SJM MR Conditional ICD system will be established if the primary endpoint is met for each phase, respectively.

5.7 Interim Analysis

There are no interim analyses planned for this study.

5.8 Statistical Criteria for Termination

There are no statistical criteria for termination of this study.

5.9 Deviations from Statistical Plan

If any deviations from the original statistical plan occur, such deviations will be documented in the clinical study report or statistical report containing the analysis results.

6 Device(s) under investigation

The following market-released devices* will be used in this clinical investigation in an MRI environment according to MRI-conditional labeling.

Table- 4: Identification of Devices* under Investigation

Device name	Model/Type/Description	Manufacturer	Region/ Country	Investigational or Market Released
Ellipse VR	CD1377-36QC/ICD/Single Chamber	SJM	Outside US	Market Released
Ellipse VR	CD1377-36Q/ICD/Single Chamber	SJM	Outside US	Market Released
Ellipse DR	CD2377-36QC//ICD/Dual Chamber	SJM	Outside US	Market Released
Ellipse DR	CD2377-36Q/ICD/Dual Chamber	SJM	Outside US	Market Released
Durata	7120Q/Lead/Active fixation, dual shock, 17 cm spacing, DF4	SJM	Outside US	Market Released

	connector, 58/65cm length			
Durata	7122Q/Lead/Active fixation, single shock, DF4 connector, 58/65 cm length	SJM	Outside US	Market Released
Optisure	LDA220Q/Lead/Active fixation, dual shock, 17 cm spacing, DF4 connector, 58/65cm length	SJM	Outside US	Market Released
Optisure	LDA210Q/Lead/Active fixation, single shock, DF4 connector, 58/65 cm length	SJM	Outside US	Market Released
Tendril MRI	LPA 1200M/Lead/ Active fixation, Bipolar, Pacing 46/52/58cm length	SJM	Outside US	Market Released

*Apart from the devices listed in Table 4; any other CE-marked St. Jude Medical MRI compatible ICD system market released in participating countries approved for Thoracic MRI scan with 1.5 Tesla (1st Phase of enrollment) & 3.0 Tesla (2nd Phase of enrollment) scanning machines can be used for this clinical investigation.

6.1 Device Description and Intended purpose

6.1.1 Ellipse ICD

The Ellipse ICD is supported by the St. Jude Medical Merlin Patient Care System (Merlin PCS) with software Model 3650, Software Model 3330 version 20.X (or higher). The Ellipse ICD is intended to provide ventricular antitachycardia pacing and ventricular defibrillation for automated treatment of life-threatening ventricular arrhythmias.

Instructions for use, storage and handling instructions, preparation for use and any precautions can be found in the User's Manual for the Ellipse ICD.

6.1.2 Durata Lead

The Durata Models 7120Q, and 7122Q leads are market-released 7 French, transvenous, steroid eluting, bipolar, DF4 compatible (single connector with four electrical terminals), active fixation leads intended for permanent sensing and pacing of the right ventricle and the delivery of cardioversion/defibrillation therapy when used with a compatible St. Jude Medical pulse generator with a DF4-LLHH or DF4-LLHO lead receptacle designation.

Instructions for use, storage and handling instructions, preparation for use and any precautions can be found in the User's Manual for the Durata lead.

6.1.3 Optisure Lead

The Optisure Models LDA220Q and LDA210Q transvenous leads are market-released leads indicated for use with compatible pulse generators (refer to the applicable defibrillator manual for system indications). They provide pacing and sensing and deliver cardioversion/defibrillation therapy to the heart.

Instructions for use, storage and handling instructions, preparation for use and any precautions can be found in the User's Manual for the Optisure Lead.

6.1.4 Tendril MRI Lead

The Tendril MRI Lead Models LPA 1200M 46/52/58cm length transvenous leads are market-released leads indicated for use with compatible pulse generators (refer to the applicable manual for system indications). They provide pacing and sensing to the heart.

Instructions for use, storage and handling instructions, preparation for use and any precautions can be found in the User's Manual for the Tendril MRI Lead.

6.2 Device Handling & Storage

This study involves use of market approved products. Physicians should consult the User's manual for device handling and storage.

7 Risks and Benefits of the clinical study

7.1 Anticipated Adverse Device Effects

The below list of anticipated adverse device effects represents the summary of the most common events observed and documented in literature associated with the patient medical condition and associated with the medical device exposure.

The St. Jude Medical™ MR Conditional ICD System are market-released devices. Risks associated with the use St. Jude Medical™ MR Conditional ICD System are anticipated to be comparable to those associated with the use of other market-released defibrillation leads, pacing leads, and ICDs. Subjects participating in this study are indicated for or implanted with an ICD as part of their standard medical management and are subject to the risks associated with these devices independent of the subject's participation in the study.

The St. Jude Medical™ MR Conditional ICD System are being tested in an MRI environment, and subjects participating in the study are required to undergo the study MRI scans which are investigational for the purposes of investigating the effect the scan has on the implanted ICD system. The subjects are therefore exposed to, but not limited to, an incremental risk of experiencing the events listed below.

Table-5: Anticipated Events and Anticipated Adverse Device Effects

Event	Mitigation
Potential MRI Related 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 subject 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: a. the system to fail to detect or treat irregular heartbeats b. the system to treat the subject'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	These risks are mitigated through the selection of investigators who are qualified by training and/or experience to evaluate and treat subjects implanted with an ICD system. In addition, study investigators will be trained on the study protocol to ensure the proper procedures are followed to assure subject safety during the study MRI scan. This includes continuous monitoring of the subject using pulse oximetry, ECG and verbal communication during the scan. Advanced Cardiac Life Support (ACLS) procedures will be in place to address situations where a life threatening arrhythmia and/or hemodynamic collapse occurs. The programmer will be used outside the American College of Radiology (ACR) defined Zone 4 magnet room. If the subject's hemodynamic function is compromised during the MRI scan, the MRI scan will be stopped, and proper measures will be taken to restore the subject's hemodynamic function.
Potential ICD Related Events	
• Refer to the Device user's manual for a full list of potential adverse events (Refer to Appendix-I)	The ICD which will be used in this investigation are a market-released ICD. The adverse events associated with this ICD are

Event	Mitigation
	the same as those associated with other market-released ICDs. These risks are mitigated through the selection of investigators who are qualified by training and/or experience to evaluate and treat subjects implanted with an ICD.
Potential Lead Related Events	
• Refer to the lead user's manual for a full list of potential adverse events (Refer to Appendix-I)	The high voltage leads are market released transvenous, steroid-eluting defibrillation leads. The adverse events associated with these leads are the same as those associated with other market-released transvenous defibrillation leads. These risks are mitigated through the selection of investigators who are qualified by training and/or experience to evaluate and treat subjects implanted with an ICD system.

In addition, subjects may also experience unavoidable events related to the MRI scan. An unavoidable event is an event related to the MRI scan that is expected to occur for a projected duration in all subjects. Unavoidable events are not reportable unless the condition worsens or continues beyond the time frame listed below. Unavoidable events do not need to be reported on an adverse event form if they are resolved within the time frame specified. These events are expected to occur with any MRI scan, including the study MRI scans.

Table 6: Unavoidable events 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
• Sensation of warmth at device pocket not arising to the level of discomfort	• During and < 1 hour post MRI scan
• Hearing impairment	• < 24 hours
• Body stiffness related to immobility	• < 48 hours

7.1.1 Risks associated with Clinical Investigation participation

Potential risks associated with the study MRI scan are the same as or comparable to those associated with MRI scans of an implanted medical device powered by a battery or other electrical source of power including, but not limited to, those listed in the Adverse Events and Adverse Device Effects section of the protocol.

7.2 Risk Control Measures

The risks associated with MRI scanning of subjects implanted with implantable active medical devices have been identified through clinical evaluation, including an exhaustive literature search.

Risks normally associated with ICDs and transvenous leads will be minimized in the study by selecting investigators who are experienced in treating subjects implanted with ICDs, evaluating implanted ICD systems, and who are trained in the Asia MRI ICD Study. Subjects will be actively monitored during the study scan using verbal communication, ECG, and continuous pulse oximetry monitoring. The investigator or other ACLS-certified personnel who have been trained on the study protocol will be present during the study MRI scan to address cases of asystole or hemodynamic collapse that may occur during the study MRI scan. In addition, because the study MRI scan is not meant to be diagnostic in nature, contrast agents will not be used, thereby eliminating the risk of allergic or adverse reactions to contrast agents.

Risks will also be minimized by careful assessment of each subject prior to enrollment. After enrollment, subjects in the study will be followed as specified in this CIP to monitor the condition of the implanted system and the battery after the subject has undergone the study MRI scan.

In order to safely perform an MRI scan on a subject with the implanted study system, the physician/clinician should do the following as stated in the MRI Ready Systems Manual: MRI Procedure Information for the St. Jude Medical™ MR Conditional System:

- Confirm that the patient has an MR Conditional System
- Confirm that no adverse conditions to MRI scanning are present (e.g. additional hardware)
- Review the potential adverse events
- Generate a report of the patient's permanently programmed parameters
- Select and Save MRI Settings
- Review the MRI Checklist and Program the MRI Settings using the Merlin® PCS
- Subject receives the MRI Scan
- Disable MRI Settings Using the Merlin® PCS

After the MRI scan and at the 1 Month Post Scan visit, the ICD will be interrogated to verify appropriate ICD function, to evaluate pacing and sensing characteristics, and to assess any adverse events.

Overall, the clinical study design, subject selection process, and procedures developed for scanning and monitoring of the subject during the MRI scan have all been designed to minimize risks to the subject.

While steps have been taken to identify and reduce or minimize risks associated with the study MRI scan and participation in the study, there may be risks that are unknown at this time.

7.3 Possible interactions with concomitant treatments

Other than the study MRI scans, there are no treatments that the subject would not otherwise receive as part of the subject's medical management related to having an implanted ICD system. While an MRI scan is not part of the usual treatment regimen for subjects implanted with an ICD, it is an accepted imaging modality used in the diagnosis of diseases or other medical condition.

The MRI scanner, methods used to scan the subject (scan sequences), and monitoring procedures in and of themselves are not investigational. As such, there are no anticipated interactions with concomitant medical treatments or concurrent medical interventions associated with the study MRI scan.

The device checks at each study visit are standard of care, or involve testing of the device and lead that are normally done at a routine device check. As such, there are no anticipated interactions with concomitant medical treatments or concurrent medical interventions associated with the study visits.

7.4 Anticipated Benefits

The information collected in this clinical investigation will provide further understanding the effects of Thoracic MRI scans on ICDs. Individual subjects will not receive any direct benefit as a result of their participation in this investigation.

8 Requirements for Investigator records and reports

8.1 Deviations from CIP

A deviation is defined as an event where the clinical investigator, site personnel, Sponsor or Sponsor representative did not conduct the clinical investigation according to the CIP. The investigator is not allowed to deviate from the CIP, except as specified under emergency circumstances to protect the rights, safety and well-being of the subject.

Regulations require Investigators obtain approval from the Sponsor and the IRB/EC (if required) before initiating changes in or deviations from the CIP. The Principal Investigator may call or email and discuss the potential deviation with the Sponsor. Deviation to the CIP necessary to protect the life or physical well-being of a subject shall be documented and reported to the Sponsor and the IRB/EC as soon as possible, but no later than 5 working days.

In some cases, failure to comply with the CIP may be considered failure to protect the rights, safety and well-being of subjects, since the non-compliance exposes subjects to unreasonable risks. For example, failure to adhere to the inclusion/exclusion criteria, failure to perform safety assessments intended to detect adverse events. Investigators should seek minimization of such risks by adhering to the CIP.

Regulations require that the PI maintain accurate, complete, and current records, including documents showing the date of and reason for every deviation from the CIP. Relevant information for each deviation will be documented as soon as possible on the appropriate CRF. The site will submit the CRF to the Sponsor.

8.2 Safety reporting

The safety reporting performed both by the investigator and Sponsor will start as soon as the study procedure begins. This is defined as from the time the subject enrolled under this clinical investigation date of signature of the informed consent – or definition of “enrolled” in the CIP).

The safety surveillance and the safety reporting will continue until the last investigational visit has been performed, the subject is deceased, the subject/investigator concludes his participation into the clinical investigation or the subject withdrawal from the clinical investigation.
All Adverse Device Effects (serious or non-serious) are to be documented and reported to the sponsor as soon as possible after becoming aware of the event.

Adverse Event (AE)

Any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device under clinical investigation.

This definition includes events related to the investigational medical device or the comparator.
This definition includes events related to the procedures involved.

Serious Adverse Event (SAE)
An adverse event that led to:

- Death
- A serious deterioration in the health of the subject, that either resulted in:
  - A life-threatening illness or injury OR
  - A permanent impairment to a body structure or a body function OR
  - An in-patient or prolonged hospitalization OR
  - A medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function OR
- Fetal distress, fetal death or a congenital abnormality or birth defect

A planned hospitalization for a pre-existing condition, or a procedure required by the CIP is not considered a serious adverse event.

Adverse Device Effect (ADE)
An adverse event related to the use of an investigational medical device.
This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device.
This definition includes any event resulting from the use error or from intentional misuse of the investigational medical device.

Serious Adverse Device Effect (SADE)
Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.

Additional information may be requested by the Sponsor in order to support the reporting of ADEs or SADEs to regulatory authorities as applicable.

NOTE: If an adverse device event is documented at the subject's last follow up visit, both the notification and follow-up information on the AE CRF are to be provided to the sponsor.

Adverse device events will be monitored until they are adequately resolved or the subject has ended his/her participation in the trial, whichever comes first. The status of the subject's condition should be documented at each visit.

For the purposes of this clinical investigation the following events will be reported: ADEs, SADEs and Death events.

Reportable events shall be submitted to the Sponsor. The Sponsor will ensure that all applicable events are reported to the relevant authorities as per regulations. The sites should notify the Sponsor of reportable adverse events by creating and saving the applicable case report form within the electronic data capture system. Additional information may be requested by the Sponsor in order to support the reporting of ADEs, SADEs and Deaths to regulatory authorities. The investigator must notify the IRB/EC, if appropriate, in accordance with national and local laws and regulations, of the ADEs or SADEs reported to the Sponsor.

8.2.1 Subject Death

All subject deaths are to be documented and reported to the Sponsor as soon as possible and as per local laws and regulations) after becoming aware of the event.
Should death occur, the investigator is requested to record death information in the hospital records and immediately document the information on the Death form. By completing the form the sponsor will be notified.

In case of EDC failure, notify Sponsor via AdverseEvent@sjm.com or via Fax (please refer to the Investigator Site Binder, for further details about Fax numbers).
Patient Death can be an outcome of a serious adverse event (SAE).

- All efforts to obtain the details should be made and the Adverse Event form must be completed.
- The patient's death is an Early Conclusion of the subject's participation in the investigation. Therefore, the investigator is requested to complete the Termination form.

- The investigator must notify the EC / IRB, if appropriate, in accordance with national and local laws and regulations.

8.2.2 Complaints if applicable

A complaint is any written, electronic, or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness, or performance of a device after it is released for distribution.

If the complaint does not involve a reportable adverse event per protocol the investigator should notify the SJM Product Surveillance Department through one of the methods listed below as soon as possible after becoming aware of a complaint.
Email address: SVcomplaints@sjm.com
Toll Free: 800-722-3774
Direct US: 818-364-1506

Complaints will be collected and reported by St. Jude Medical according to our product reporting process.

8.3 Source records

Source documents will be created and maintained by the investigational site team throughout the clinical investigation. The data reported on the CRFs will be derived from, and be consistent with, these source documents, and any discrepancies will be explained in writing.
The following data needs to be filed in patient file at the site:

- Device interrogation report
- MRI Scan images in DICOM Format
- Other source documents (to support SAEs)

8.4 Records retention

The Sponsor and the Principal Investigators will maintain the clinical investigation documents as required. They will take measures to prevent accidental or premature destruction of these documents. The Principal Investigator or the Sponsor may transfer custody of records to another person/party and document the transfer at the investigational site or the Sponsor's facility.

These documents must be retained by the investigational site for a period of 2 years after clinical investigation conclusion (or as per local regulatory requirement) and made available for monitoring or auditing by the Sponsor's representative or representatives of the applicable regulatory agencies.

All original source documents must be stored for the longest possible time permitted by the local regulations at the hospital, research institute, or practice in question. If archiving of original source documents can no longer be maintained at the site, the investigator will notify the Sponsor.

9 Clinical Data Handling

Overall, the Sponsor will be responsible for the data handling. The Sponsor and/or its affiliates will be responsible for compiling and submitting all required reports to governmental agencies. Data will be analyzed by the Sponsor and may be transferred to the Sponsor's locations outside of Asia and/or any other worldwide regulatory authority in support of a market-approval application.

9.1 Protection of Personally Identifiable Information

St. Jude Medical respects and protects personally identifiable information collected or maintained for this clinical investigation. The privacy of each subject and confidentiality of his/her information will be preserved in reports and when publishing any data. Confidentiality of data will be observed by all parties involved at all times throughout the clinical investigation. All data will be secured against unauthorized access.

9.2 Data Management Plan

A detailed Data Management Plan (DMP) will be established to ensure consistency of handling the data. This document will include procedures used for data review, database cleaning, and issuing and resolving data queries. If appropriate, the DMP may be updated throughout the clinical investigation duration. All revisions will be tracked and document controlled.

CRF data will be captured in a validated electronic database management system hosted by the Sponsor. Only authorized site personnel will be permitted to enter the CRF data through the electronic data capture (EDC) system deployed by St. Jude Medical. An electronic audit trail will be used to track any subsequent changes of the entered data.

9.3 Document and Data Control

9.3.1 Traceability of Documents and Data

The investigator will ensure accuracy, completeness, legibility and timeliness of the data reported to the Sponsor on the CRFs and in all required reports.

9.3.2 Recording Data

The eCRF will be reviewed by the authorized site personnel. An appropriate comment will be provided for any change to data reported on eCRF.

10 Monitoring

It is the responsibility of the Sponsor of the clinical investigation to ensure the clinical investigation is conducted, recorded, and reported according to the approved CIP, subsequent amendment(s), applicable regulations, and guidance documents. Monitoring will be conducted according to the St. Jude Medical Clinical Monitoring working instruction.

Prior to beginning the clinical investigation, the Sponsor will contact the investigator or designee to discuss the clinical investigation and data requirements. A designated monitor will periodically review the subject records and associated source documents.

The investigator shall make subject and clinical investigation records available to the clinical monitor for monitoring.

Centralized monitoring will occur through routine internal data review. This monitoring is designed to identify missing and inconsistent data, data outliers, and potential CIP deviations that may be indicative of site non-compliance.

11 Compliance Statement

11.1 Statement of Compliance

This clinical investigation will be conducted in compliance with the most current regional and local laws and regulations. Principles of Good Clinical Practice will be followed as based on the most current version of the World Medical Association (WMA) Declaration of Helsinki.

The investigator will not start enrolling subjects or requesting informed consent from any subject prior to obtaining IRB/EC approval and Competent Authority approval, if applicable, and authorization from the sponsor in writing for the clinical investigation. If additional requirements are imposed by the IRB/EC or Competent Authority, those requirements will be followed. If any action is taken by an IRB/EC or a Competent Authority with respect to the clinical investigation, that information will be forwarded to the Sponsor.

As the Sponsor, St. Jude Medical has taken up general liability insurance in accordance with the requirements of the applicable local laws. Appropriate country representative will be utilized to understand the requirements for the type of insurance that will be provided for subjects, such information will be incorporated into the site informed consent, as applicable. If required, additional subject coverage or a clinical investigation specific insurance will be provided by the Sponsor.

11.2 Quality Assurance audits and Regulatory Inspections

The investigator and/or delegate should contact the Sponsor immediately upon notification of a regulatory authority inspection at the site. A monitor or designee will assist the investigator and/or delegate in preparing for the audit. The Sponsor may perform quality assurance audits, as required.

The Principal Investigator or institution will provide direct access to source data during and after the clinical investigation for monitoring, audits, IRB/EC review and regulatory authority inspections, as required. The Principal Investigator or institution will obtain permission for direct access to source documents from the subject, hospital administration and national regulatory authorities before starting the clinical investigation.

11.3 Repeated and Serious Non-Compliance

In the event of repeated non-compliance or a one-time serious non-compliance, as determined by the Sponsor, a monitor or designee will attempt to secure compliance by one or more of the following actions:

- Visiting the investigator,
- Contacting the investigator by telephone,
- Contacting the investigator in writing,
- Retraining of the investigator.

If an investigator is found to be repeatedly non-compliant with the signed agreement, the CIP or any other conditions of the clinical investigation, the Sponsor will either secure compliance or, at its sole discretion, terminate the investigator's participation in the clinical investigation. In case of termination, the Sponsor will inform the responsible regulatory authority, as required, and ensure that the IRB/EC is notified, either by the Principal Investigator or by the Sponsor.

12 Publication Policy

The results of the clinical investigation will be submitted, regardless of the outcome of the clinical investigation.

A 'Publication Agreement' will be signed between the Principal Investigator and the Sponsor either as a separate Publication Agreement or within the Clinical Trial Agreement.

For more information on publication guidelines, please refer to the International Committee of Medical Journal Editors (ICMJE) on www.icmje.org.

This clinical investigation and its results will be posted on ClinicalTrials.gov as required.

This clinical investigation will be registered on ClinicalTrials.gov prior to IRB/EC submission. A full report of the pre-specified outcomes, including any negative outcomes, will be made public through the ClinicalTrials.gov website no later than 12 months after clinical investigation completion, as required by Section 801 of the FDA Amendments Act. If this clinical investigation is terminated early, the Sponsor will make every effort to hasten the release of the pre-specified outcomes through the ClinicalTrials.gov website.

13 Suspension or premature termination of the clinical investigation

The Sponsor reserves the right to stop the clinical investigation at any stage, with appropriate written notice to the investigators, IRB/ ECs and Competent authorities, if required.

A Principal Investigator, IRB/EC or regulatory authority may suspend or prematurely terminate participation in a clinical investigation at the investigational sites for which they are responsible. The investigators will follow the requirements specified in the Clinical Trial Agreement.

If suspicion of an unacceptable risk to subjects arises during the clinical investigation or when so instructed by the IRB/EC or regulatory authority, the Sponsor may suspend the clinical investigation as appropriate while the risk is assessed. The Sponsor will terminate the clinical investigation if an unacceptable risk is confirmed. If the Sponsor concludes an analysis of the reasons for the suspension, implements the necessary corrective actions, and decides to lift the temporary suspension, the Sponsor will inform the Principal Investigators, IRB/EC, or regulatory authority, where appropriate, of the rationale, providing them with the relevant data supporting this decision. Approval from the IRB/EC or regulatory authority, where appropriate, will be obtained before the clinical investigation resumes. If subjects have been informed of the suspension, the Principal Investigator or authorized designee will inform them of the reasons for resumption.

If the Sponsor suspends or prematurely terminates the clinical investigation at an individual investigational site in the interest of safety, the Sponsor will inform all other Principal Investigators.

If suspension or premature termination occurs, the Sponsor will remain responsible for providing resources to fulfill the obligations from the CIP and existing agreements for following up the subjects enrolled in the clinical investigation, and the Principal Investigator or authorized designee will promptly inform the enrolled subjects at his/her investigational site, if appropriate.

14 Clinical Investigation Conclusion

The clinical investigation will be concluded when:

- All sites are closed AND
- The Final report has been provided to investigators or the Sponsor has provided formal documentation of clinical investigation closure.

Appendix A: CIP Revisions

[redacted]

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Appendix B: Definitions

Non-study Specific Definitions

Adverse Device Effect (ADE)
An adverse event related to the use of an investigational medical device.
This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device.
This definition includes any event resulting from the use error or from intentional misuse of the investigational medical device.

Serious Adverse Device Effect (SADE)
Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.

Vulnerable Subject
Vulnerable subject is defined as individual whose willingness to volunteer in a clinical investigation could be unduly influenced by the expectation, whether justified or not, of benefits associated with participation or of retaliatory response from senior members of a hierarchy in case of refusal to participate
EXAMPLE Individuals with lack of or loss of autonomy due to immaturity or through mental disability, persons in nursing homes, children, impoverished persons, subjects in emergency situations, ethnic minority groups, homeless persons, nomads, refugees, and those incapable of giving informed consent. Other vulnerable subjects include, for example, members of a group with a hierarchical structure such as university students, subordinate hospital and laboratory personnel, employees of the Sponsor, members of the armed forces, and persons kept in detention.

Appendix C: Abbreviations

Abbreviation	Term
ACLS	Advanced Cardiac Life Support
ACR	American College of Radiology
ADE	Adverse Device Effect
AE	Adverse Event
ASADE	Anticipated Serious Adverse Device Effect
CA	Competent Authority
CCI	Clinical Coordination Investigator
CE	Conformité Européene
CIP	Clinical Investigation Plan
CRF	Case Report Form
CTA	Clinical Trial Agreement
CTR	Clinical Trial Registration
DMP	Data Management Plan
EC	Ethics Committee
ECG	Electrocardiogram
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
EMEA	Europe, Middle East, Africa
GCP	Good Clinical Practice
GP	General Practitioner
HVLI	High Voltage Lead Impedance
ICD	Implantable Cardioverter Defibrillator
ICMJE	International Committee of Medical Journal Editors
I/E	Inclusion/Exclusion criteria
IRB	Institutional Review Board
ISB	Investigator Site Binder
ISO	International Organization for Standardization
ILAR	Legally Acceptable Representative
Merlin PCS	Merlin Patient Control System
MFG	Manufacturing Group
MP	Monitoring Plan
MR	Magnetic Resonance

MRI	Magnetic Resonance Imaging
NA	Not Applicable
PI	Principal Investigator
RDC	Remote Data Capture
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SAR	Specific Absorption rate
SC	Steering Committee
SJM	St. Jude Medical
US	United States
USADE	Unanticipated Serious Adverse Device Effect
VT/VF	Ventricular Tachycardia/Ventricular Fibrillation
WMA	World Medical Association

[redacted]

Appendix D: Declaration of Helsinki

The most current version of the document will be followed.

Appendix E: MRI Scan Guidelines

Instructions and guidelines for performing MRI scans for the ASIA MRI ICD Study are kept under separate cover, and will be provided to study centers by St. Jude Medical.

Appendix F: MRI Screening Forms

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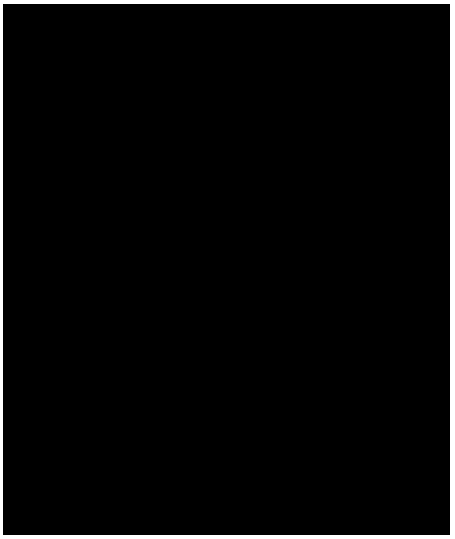

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Appendix- H: Sample Informed Consent

(Final Informed Consent Template is kept under separate cover)

Appendix I: Product Instructions for Use

The Product Instructions for Use, User Manual and CE Certificates are kept under a separate cover, and will be provided to study centers by St. Jude Medical.

Appendix J: Bibliography

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