Abbott	Clinical Investigation Plan Cover Page

NCT Number: NCT03828357
China MRI
Evaluation of ICD Defibrillation Systems in a 1.5T Magnetic Resonance Imaging (MRI) Environment in China CIP/SAP
Study Document No: ABT-CIP-10238/ CL1005886
Version D/ Version C
Date: 30-SEP-2019/ 11-MAY-2020

Sponsor

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Annex Ⅳ

Clinical Study Protocol of Medical Device

Protocol No.: CRD_930 Study Specific Doc No: ABT-CIP-10238 Ver. D

Clinical Study Protocol for the Evaluation of ICD Defibrillation Systems in a 1.5T Magnetic Resonance Imaging (MRI) Environment in China

Name of the medical device:

Generators: Ellipse VR®, Ellipse DR®, and Quadra Assura MP™

Leads: Durata®, Optisure™®, Tendril™ STS, Isoflex™, and Quartet™

Model/specification:

TABLE 1: STUDY DEVICE

Device name	Model/Type	Manufacturer	Region/ Country	Investigational or Market Released
Generators				
Ellipse VR	CD1377-36Q/QC	St. Jude Medical	China	Market Released
Ellipse DR	CD2377-36Q/QC	St. Jude Medical	China	Market Released
Quadra Assura MP	CD3371-40Q/QC	St. Jude Medical	China	Market Released
Leads				
Durata	7120Q 7122Q	St. Jude Medical	China	Market Released
Optisure	LDA210Q	St. Jude Medical	China	Market Released
Tendril STS	2088TC	St. Jude Medical	China	Market Released
Isoflex	1944	St. Jude Medical	China	Market Released
Quartet	1456Q 1458Q 1458QL	St. Jude Medical	China	Market Released

Management categories of investigational medical device:

Class III medical device that needs NMPA approval for the conduct of clinical investigations in China
☐Yes ☑No

Similar products available in Chinese market
☐Yes ☑No

Protocol version No. and date: Ver. D 30SEP2019

Lead Clinical study institution: The First Affiliated Hospital of Zhejiang Coordinating Investigator: [redacted], Professor, MD

Sponsor: St. Jude Medical Coordination Center BVBA and St. Jude Medical Cardiac Rhythm Management Division (now Abbott)

Deputy: Abbott Medical (Shanghai) Co., Ltd.

[redacted]

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1. Sponsor Information

St. Jude Medical Coordination Center BVBA and St. Jude Medical Cardiac Rhythm Management Division (now Abbott)

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2. Objectives, Endpoints, and contents of clinical study

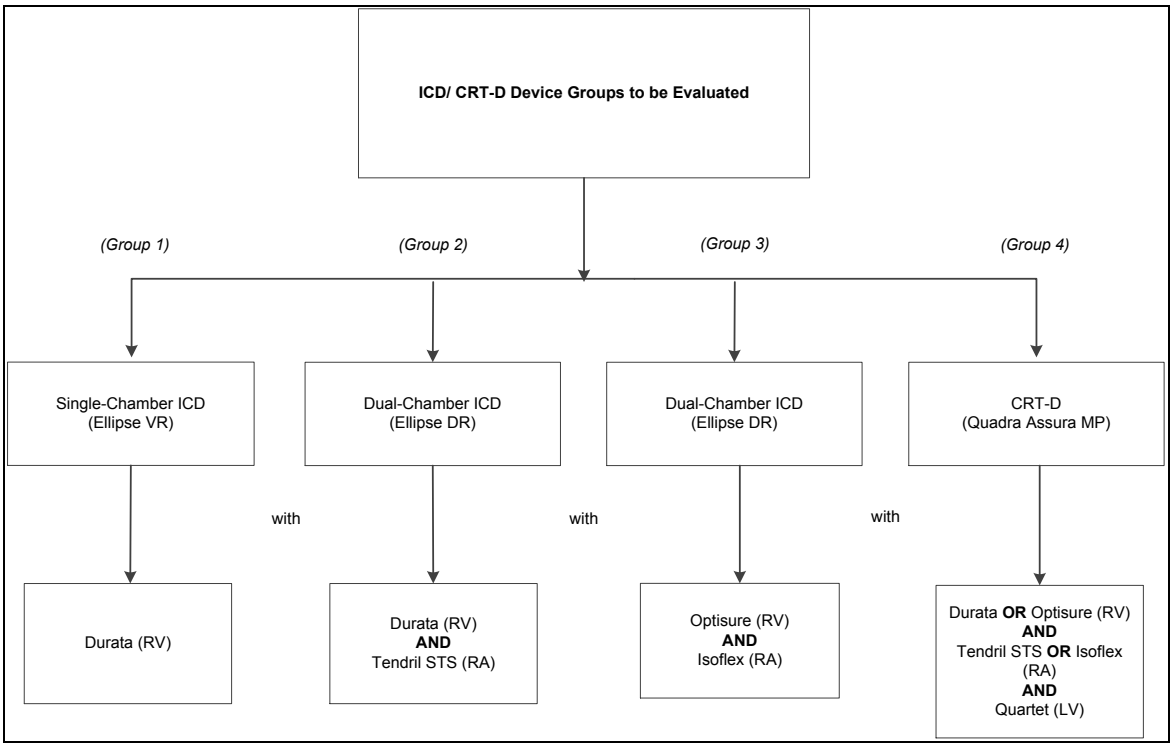
2.1. Objectives

The objective of this clinical study is to evaluate the safety and effectiveness of the Ellipse VR/DR implantable cardiac defibrillators (ICDs) and the Quadra Assura MP cardiac resynchronization therapy defibrillators (CRT-Ds), with Durata or Optisure defibrillation leads, Tendril STS or Isoflex pacing leads, and the Quartet quadripolar leads in a 1.5T MRI environment for MR-conditional labeling expansion of these market-approved ICD/CRT-D systems in China.

There are four device combination groups in this clinical study as outlined below:

- **Group 1:** Ellipse VR single-chamber ICD with a Durata lead in the right ventricle (RV).
- **Group 2:** Ellipse DR dual-chamber ICD, with a Durata lead in the RV and a Tendril STS lead in the right atrium (RA).
- **Group 3:** Ellipse DR dual-chamber ICD with a Optisure lead in the RV and a Isoflex lead in the RA.
- **Group 4:** Quadra Assura MP CRT-D with a Durata or Optisure lead in the RV, a Tendril STS or Isoflex lead in the RA, and a Quartet lead in the left ventricle (LV).

FIGURE 1: STUDY GROUP OVERVIEW



2.2. Primary Endpoints

- Safety: Freedom from MRI-scan related complications related to the ICD/ CRT-D device and/or leads from the time of the MRI scan to 1-month post-MRI scan testing.
- Effectiveness: Proportion of leads with a capture threshold increase of ≤ 0.5V at 0.5ms for RA and RV leads and ≤1.0V at 0.5ms for LV leads from pre-MRI scan to 1-month post-MRI scan testing.
- Effectiveness: Proportion of leads with a sensing amplitude decrease of ≤ 50% from pre-MRI scan testing to 1-month post-MRI scan.

2.3. Descriptive Endpoint(s)

Descriptive endpoints are reported using only summary statistics and no hypothesis tests will be performed.
The following data will be collected:

1. Demographics: gender, age, ethnicity, race, cardiac disease history, arrhythmia history, indication for ICD/CRT-D implant, history of smoking, etc.
2. Device electrical measurements at the MRI Scan Visit (pre- and post-scan) and at the 1 Month Post Scan Visit
3. ADE, SADE, USADE
4. Mortality
5. Number of non-study MRI scans
6. Summarize number of subjects that returned to usual programming after the MRI scan and number of subjects, if any, experiencing delays in reprogramming

2.4. Contents

This document is a clinical investigation plan (CIP) for the observational clinical study of the safety and effectiveness of the Ellipse VR/DR implantable cardiac defibrillators (ICDs) and the Quadra Assura MP cardiac resynchronization therapy- Defibrillators (CRT-Ds), with Durata or Optisure defibrillation leads, Tendril STS or Isoflex pacing leads, and the Quartet quadripolar lead in a 1.5T MRI environment in China. This clinical study is intended to support MR conditional labeling expansion approval from the China National Medical Products Administration (NMPA) for these market approved ICD/CRT-D systems in China. This clinical study is sponsored by Abbott.

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

3. Background information of the clinical study

Magnetic resonance imaging (MRI) is a non-invasive imaging technique capable of providing high-quality images of the whole human body. MRI can provide images of excellent spatial resolution together with functional and tissue characterization information without the use of damaging ionizing radiation and potentially nephrotoxic iodinated contrast agents in two and three dimensions.[1] For these reasons, MRI is the imaging modality of choice in a wide spectrum of diseases, not only for diagnosis but also for staging and follow-up of affected patients, including those with involvement of the neurological, musculoskeletal, oncological, and cardiovascular systems. This has led to a recent rapid increase of the number of MRI scans performed.[2] 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 2009 World Survey of cardiac pacing and cardioverter defibrillators, 235,567 new pacemakers were implanted in the United States in 2009. When compared to a similar survey conducted in 2005, the 2009 survey showed an increase in the number of pacemakers and defibrillators implanted throughout the world, a trend that is likely to continue.[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.[7,8] Due to these issues, certain currently marketed implantable cardiac device systems, including ICDs and CRT-Ds, may be contraindicated for use in an MRI environment. There is a specific need for device manufacturers to give clinical evidence that MR conditional systems provide evidence of patient safety who receive MRI scans. [9]

Over the past 10 years, there have been numerous patients with implanted devices who successfully underwent magnetic resonance imaging.[10,11,12,13,14,15]

In this study, Abbott plans to evaluate the safety and effectiveness of the Ellipse VR/DR, ICDs, the Quadra Assura MP CRT-Ds, with Durata or Optisure defibrillation leads, Tendril STS or Isoflex pacing leads, and the Quartet quadripolar left heart lead in a 1.5T MRI environment for MR-conditional labeling expansion of these market-approved ICD systems in China.

4. Features of product, structure and composition, operating principle, mechanism of action and scope of study

4.1. Features of product

This study involves use of market approved products that will be provided by the Sponsor. Although these products are already market approved to be implanted in patients who meet the indications for use, these products are not approved for use in an MRI environment. Therefore, the study procedure i.e. MRI scan, is considered investigational in nature.

4.2. Structure and composition, operating principle and function mechanism of product

- The Ellipse ICDs are intended to provide ventricular antitachycardia pacing and ventricular defibrillation for automated treatment of life-threatening ventricular arrhythmias. In cases where AF Suppression™ is available, AF Suppression pacing is indicated for suppression of paroxysmal or persistent atrial fibrillation in patients with the above ICD indication and sinus node dysfunction. The Ellipse ICDs are supported by the St. Jude Medical Merlin Patient Care System (Merlin PCS) with software Model 3650, Software Model 3330 v. 20.X (or higher).
- The Quadra Assura MP CRT-D devices are intended to provide ventricular antitachycardia pacing and ventricular defibrillation for automated treatment of life-threatening ventricular arrhythmias, they are also intended to resynchronize the right and left ventricles in patients with congestive heart failure. They are equipped with an IS4-LLLL low voltage connector to facilitate implantation of an IS4 LV four electrode lead. Also, devices with a Q suffix have a high voltage DF4-LLHH bore that allows the use of a high voltage lead with a DF4 connector. The Quadra Assura MP CRT-D devices deliver 40J of energy and are supported by the St. Jude Medical Merlin Patient Care System (Merlin PCS) with software Model 3330 version 16.1.1 (or higher).
- The Durata Models 7120 and 7122Q leads are 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.
- The Optisure Model LDA220Q 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.
- The Tendril STS Model 2088TC pacing lead is a market-released MR conditional active-fixation lead indicated for permanent sensing and pacing of the heart.

- The Isoflex Model 1944 is a J-shaped, market-released, passive-fixation leads indicated for permanent sensing and pacing of the heart.
- The Quartet Models 1456Q, 1458Q, and 1458QL leads are 5.1 French, transvenous, steroid eluting, quadripolar, IS4 compatible (single connector with four electrical terminals), passive fixation leads intended for permanent sensing and pacing of the left ventricle when used with a compatible St. Jude Medical biventricular system with an IS4-LLLL lead receptacle designation.

4.3. Scope of study

This is a study in at least 60 subjects from at least 6 study centers in China who provide consent to have any of the four defibrillation system combination groups implanted (See **Figure 1**), undergo a non-diagnostic MRI scan, and complete follow-up through 1-month post-MRI scan.

5. Indications, contraindications and precautions of product

Please refer to the products Instructions For Use (IFU) for the indications, contraindications, and precautions of each device.

6. Device handling and storage

This study involves use of market approved products; the study procedure i.e. MRI scan, is considered investigational in nature. Device handling and storage should be done according to the Instructions for Use. Due to the devices being supplied by the Sponsor, it is required that they be stored in a secure area to prevent unauthorized access or use.

7. Device accountability

Study system devices will be provided by the sponsor to study sites. The Principal Investigator or an authorized designee must maintain records of device information as defined by sponsor and such study devices can only be used in patients that are enrolled into the study.

The Sponsor will maintain accountability documentation for all used study devices.

8. Overall design

This is a prospective, multi-center, single-arm study to evaluate the safety and effectiveness of the Ellipse VR/DR ICDs, and the Quadra Assura MP CRT-D, with Durata or Optisure defibrillation leads, Tendril STS or Isoflex pacing leads, and the Quartet quadripolar LV lead in a 1.5T MRI environment for MR-conditional labeling expansion in China.

This study will be conducted in at least 6 centers in China and at least 60 subjects who provide consent for participation will be enrolled. Subjects will be considered enrolled after providing consent. Subjects will be implanted with any one of the device/lead combination groups outlined in **Figure 1,** depending on their clinical need as determined by the Investigators. At least 15 subjects will be enrolled in each group**.**

- **Group 1** will have at least 15 enrolled subjects with the Ellipse VR single-chamber ICD with a Durata lead in the RV.
- **Group 2** will have at least 15 enrolled subjects with the Ellipse DR dual-chamber ICD with a Durata lead in the RV and a Tendril STS lead in the RA.
- **Group 3** will have at least 15 enrolled subjects with the Ellipse DR dual-chamber ICD with a Optisure lead in the RV and a Isoflex lead in the RA.
- **Group 4** will have at least 15 enrolled subjects with a Quadra Assura MP CRT-D and an Optisure or Durata lead in the RV, an Isoflex or Tendril STS lead in the RA, and a Quartet lead in the LV.

The enrollment group and group 4 lead pairing will be at the discretion of the Investigator, dependent on patient needs in conjunction with study needs to fulfill study goals.

At least forty-five (45) days after system implantation or after a system revision, subjects will have a baseline visit followed by an MRI visit; subjects will undergo a study-related MRI scan at 1.5T. Subjects will have a 1-month follow-up after the study MRI scan. The minimum duration of each subject's participation is approximately 2.5 months from enrollment. The expected duration of enrollment is approximately 14 months. The total duration of clinical study is expected to be 16.5 months.

8.1. Clinical study design

8.1.1. Clinical study objective

The objective of this clinical study is to evaluate the safety and effectiveness of the Ellipse VR/DR, implantable cardiac defibrillators (ICDs), and the Quadra Assura MP CRT-Ds, with Durata or Optisure defibrillation leads, Tendril STS or Isoflex pacing leads, and the Quartet quadripolar leads in a 1.5T MRI environment for MR-conditional labeling expansion of these market-approved ICD systems in China.

8.1.2. Selection of clinical study method and rationale

A prospective, multi-center, non-randomized, open-label, single arm clinical study design was chosen to generalize the study results by enrolling subjects across multiple sites and limit the sample size to the minimum number required by the NMPA to receive MR labeling approval. This study intends to provide clinical data from a local Chinese population to supplement IDE clinical data from a population in the United States and

Europe for submission to the NMPA in support of a marketing application of MRI labeling expansion for these ICD/CRT-D systems in China.

The selection of this local clinical study method was based on discussions with the NMPA and the Sponsor during a pre-market workshop meeting held on November 9th and 10th, 2016 in China.

8.1.3. Measures for reducing and avoiding bias

Measures to reduce and avoid bias in this study include: allowing all subjects who meet the eligibility criteria specified in this CIP may be enrolled in this study, the Sponsor will approach sites for participation without bias or consideration for specific demographic subgroups; additionally, clinical events (adverse device effects and deaths) occurring after the MRI settings have been programmed, will be adjudicated by an independent Clinical Events Committee (CEC).

The CEC is an independent adjudication body comprised of qualified physicians who are not participants in the clinical investigation. The CEC will review and adjudicate pre-specified events reported by investigators or identified by Safety personnel for the clinical investigation as defined in the CEC charter and according to definitions provided in this CIP.

8.1.4. Investigational medical device and reference medical device/reference diagnosis/therapeutic method (if any)

Devices and reference numbers are listed in **Table 1: Study Device** above.

8.1.5. Selection of subjects

The study population includes male and female Chinese nationals that meet the eligibility requirements and give consent for the study. Vulnerable subjects, such as minors or those unable to provide consent are excluded from participating.

8.1.6. Inclusion criteria

Assessment for general eligibility criteria is based on medical records of the site and interview with a candidate patient. If some of the clinical and laboratory tests are not included in site standard tests, they must be done but after written informed consent is obtained. Patients must meet ALL the inclusion criteria to be considered for the clinical study. If ANY of the exclusion criteria are met, the patient is excluded from the clinical study and cannot be enrolled.

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

- Have an approved indication for implantation of an ICD, or CRT-D
- Be a Chinese national
- Will be implanted with one of the following device/lead combinations evaluated in this study:
    - Group 1: Ellipse VR single-chamber ICD with a Durata lead in the RV
    - Group 2: Ellipse DR dual-chamber ICD, with a Durata lead in the RV and a Tendril STS lead in the RA
    - Group 3: Ellipse DR dual-chamber ICD with a Optisure lead in the RV and a Isoflex lead in the RA
    - Group 4: Quadra Assura MP CRT-D and an Optisure or Durata lead in the RV, an Isoflex or Tendril STS lead in the RA, and a Quartet lead in the LV
- Be willing to undergo an elective MRI scan without sedation ≥ 45 days after implant

  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
- Be able to provide informed consent for study participation (legal guardian or legally authorized representative is NOT acceptable)
- Be willing and able to comply with the prescribed follow-up tests and procedures
- Are not contraindicated for an MRI scan (per the MRI Screening Form)
- Subjects who are at least 18 years of age (or older, required by local law)

8.1.7. Exclusion criteria

Subjects who meet any of the following exclusion criteria must be excluded from the clinical investigation:

- Have a competitor's MRI compatible endocardial lead implanted or capped
- Have 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.
- Have other non-MRI compatible device or material implanted. The following examples may be included as long as labelling of these devices allow MRI scans conducted per this protocol:
    - MRI compatible knee replacements, hip replacements, stents, etc.
    - MRI compatible mechanical, prosthetic, and bio prosthetic heart valves
    - Non-removable dental implants
- Have a lead extender, adaptor, or capped/abandoned lead
- 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 study as determined by Abbott.

- Pregnant or planning to become pregnant during the duration of the subject's participation in the study
- Have a life expectancy of less than 12 months due to any condition

8.1.8. Criteria and procedures for study/study treatment termination

No formal statistical rule for early termination of the clinical study for insufficient effectiveness of the device/ MRI procedures under investigation is defined.

The Sponsor reserves the right to discontinue the clinical study at any stage or reduce the follow-up period with suitable written notice to the investigator. Possible reason(s) may include, but are not limited to:

- Unanticipated adverse device effect (e.g., UADE) occurs and it presents an unreasonable risk to the participating subjects
- Any oversight committee (e.g., Steering/Executive Committee, Data Monitoring Committee) makes a recommendation to stop or terminate the clinical study (such as higher frequency of anticipated adverse device effects)
- Further product development is cancelled

Should the clinical study be discontinued by the Sponsor, subjects will be followed per routine hospital practice with device-related AEs reported to the Sponsor as per vigilance/commercial reporting requirements.

Should this occur, the investigator shall return all clinical investigation materials (including devices) to the Sponsor and provide a written statement as to why the premature termination has taken place to the IRB/EC (if applicable). All applicable clinical study documents shall be subject to the same retention policy as detailed in section **18.1** of the CIP.

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

If the Sponsor suspends or prematurely terminates the clinical study at an individual 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 the subjects enrolled in the clinical study, and the Principal Investigator or authorized designee will promptly inform the enrolled subjects at his/her site, if appropriate.

The clinical study 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 study closure.

8.1.9. Time of enrollment

The expected duration of enrollment is approximately 14 months.

8.1.10. Anticipated duration of clinical study and the reasons for determination

With an expected duration of enrollment of 14 months, the 45-day post-implant stabilization period, and the 1-month post-MRI scan visit, the total duration of clinical study is expected to be 16.5 months from the time of first enrollment.

8.1.11. Anticipated participation duration of each subject

Each subject is anticipated to participate in this clinical investigation for 2.5 months from the time of enrollment. This accounts for the 45-day post-implant stabilization period and 30 days for completion of the 1-month post-MRI visit.

8.1.12. Number of subjects required for clinical study

A minimum of 60 total subjects will be enrolled in this study. Fifteen (15) subjects for each of the 4 main device groups (See **Figure 1**) will be enrolled in this study to meet the minimum required 10 subjects per device arm, as requested by the NMPA for each group accounting for attrition of anticipated 5 subjects for each group in this study.

8.2. Effectiveness evaluation method

There are two primary effectiveness endpoints to be evaluated in this study.

8.2.1. Description of the effectiveness endpoints

- Proportion of leads with a capture threshold increase of ≤ 0.5V at 0.5ms for RA and RV leads and ≤ 1.0V at 0.5ms for LV leads from pre-MRI scan to 1-month post-MRI scan testing.
- Proportion leads with a sensing amplitude decrease of ≤ 50% from pre-MRI scan testing to 1-month post-MRI scan.

8.2.2. Selection of method and time for evaluation, recording and analysis of the effectiveness endpoints

Since the objective is to evaluate the effect of MRI exposure for the ICD/ CRT-D device groups included in this study, the effectiveness parameters were selected to compare abnormal changes in device performance from pre- to 1-month post- MRI scan. The pre-MRI measurements are collected within the same day prior to the MRI scan. The 1-month post-MRI scan measurements are collected at 30 days post-MRI scan (within +14 days) to ensure any effect of the MRI exposure is captured.

The effectiveness parameters are recorded directly from the device. The device measurements will be obtained using the Merlin programmer to interrogate the device during study visits. The analysis of the effectiveness parameters will be conducted on all subjects with complete data from pre- to 1-month post-MRI scan.

8.3. Safety evaluation method

There is one primary safety endpoint to be evaluated in this study.

8.3.1. Description of the safety endpoint

Freedom from MRI-scan related complications from the time of the MRI scan to 1-month post-MRI scan testing.

8.3.2. Selection of method and time for evaluation, recording and analysis of the safety endpoints

Since the objective is to evaluate the effect of MRI exposure for the ICD/ CRT-D device groups included in this study, the safety parameters were selected to include only MRI-scan related complications from the time of device programming for an MRI scan to 1-month post-MRI scan. An independent physician CEC will adjudicate all adverse device effects during this period to determine the relatedness to the MRI scan.

Safety surveillance within this study and the safety reporting, both performed by the investigator, starts as soon as the subject completes the pre-MRI visit testing and the MRI Settings have been programmed according to the protocol. The safety surveillance and the safety reporting will continue until the last study visit has been performed, the subject is deceased, the subject/investigator concludes his participation into the clinical study or the subject withdrawal from the clinical study.

8.4. Study procedures

The clinical study will be conducted in accordance with the CIP. All parties participating in the conduct of the clinical study will be qualified by education, training, or experience to perform their tasks and this training will be documented appropriately.

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

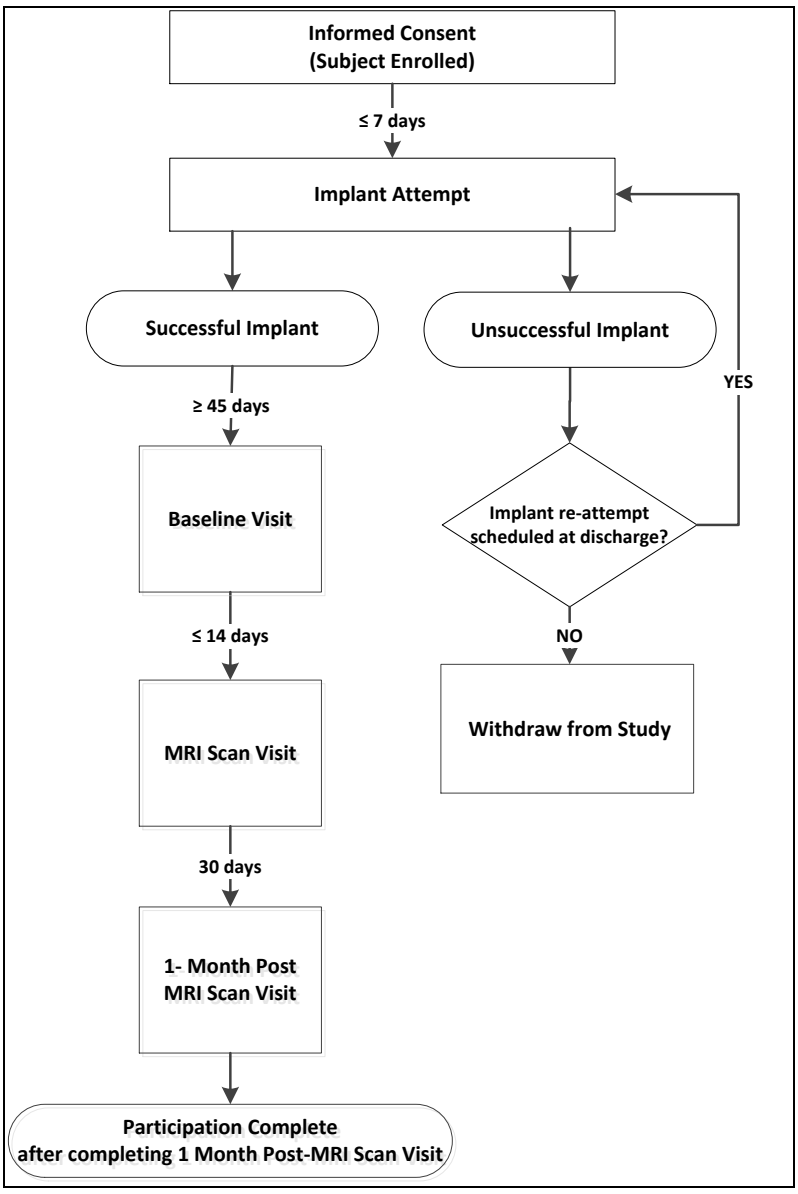
Approval from the Sponsor must be received prior to initiating study procedures.

Enrolled subjects (as defined in section **8.4.3**) will have undergone a successful implant procedure with the study ICD/ CRT-D and study leads. Forty-five (45) days after discharge from hospitalization post successful implant procedure, the subject will have a MRI Scan Visit, followed by a one-month post MRI Scan Visit. Upon completion of the one-month post MRI scan visit, the subject will be considered to have completed the follow-up requirements of this clinical study. The Principal Investigator should arrange for appropriate care of subjects following study completion.

The following sections provide a detailed description of procedures required by this CIP.

8.4.1. Study flow chart

FIGURE 2: STUDY FLOW CHART



8.4.2. Patient recruitment

All patients presenting at the study site may be screened by a member of the study team previously trained on the CIP and delegated to do so. Patients who do not meet the inclusion/exclusion criteria will not be eligible to participate in this study. Patients meeting the inclusion/exclusion criteria will be fully informed about the study and asked to review and sign informed consent. In case the subject agrees, a duly signed and dated Patient Informed Consent will be obtained. Qualifying patients will be approached with the study consent at all participating study centers.

8.4.3. Point of enrollment

Subjects are considered enrolled after the study consent has been signed (Refer to section **14.5** for the Informed Consent Process).

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 applicable CRF in a timely manner. Notification of enrollment to the Sponsor is considered to have occurred when the Sponsor has received the applicable CRF.

8.4.4. Scheduled procedures

The Principal Investigator is responsible for ensuring all clinical study data is collected as required per CIP scheduled procedures.

All required study procedures at each specified interval are outlined in the sections below. Refer to **Table 2: Schedule of Evaluations Summary: Study visits, Table 3: Schedule of Evaluations Summary: MRI Related visits,** and **Table 4: Subject visit data collection summary** for an overview of the required study procedures at each interval or study visit.

TABLE 2: SCHEDULE OF EVALUATIONS SUMMARY: STUDY VISITS

Evaluation	Cardiology Staff					
	Study Visits					
	Enrollment	Implant	Baseline	MRI Scan	1-month visit	Unscheduled (as necessary)
Time frame from previous visit (window) in days	0	≤ 7 post enrollment	45 (+7) post implant	≤ 14 post Baseline	30 (+14) post MRI Scan	-
Informed Consent	√					
Inclusion/ Exclusion Evaluation	√					
Demographics and Medical History	√					
Verify ICD/ CRT-D and lead combination (group) post-implantation		√				
Pre-MRI Safety Screening (MRI Safety Screening Form)	√		√	√*		
Capture ICD/ CRT-D system information		√				
Device Interrogation/ Device Measurements**			√	√	√	√
Collect Study Specific AEs				√	√	√

** re-verify if not done same day as Baseline*

*** Capture bipolar capture, sense, pacing, and HVLI impedances*

Note: *RA lead capture only for subjects with Tendril STS or Isoflex leads. 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 most recent archival measurement, if available, will be used.*

TABLE 3: SCHEDULE OF EVALUATIONS SUMMARY: MRI RELATED VISITS

Evaluation	Radiology & Cardiology Staff			
	MRI Visit Schedule			
	MRI visit			1 Month Post MRI
	Pre- MRI Period Testing	MRI Period	Post-MRI Testing	
Re-assess Inclusion/Exclusion Criteria	√			
Device Interrogation/ Device Measurements*	√		√	√
Pre-MRI Safety Screening (MRI Safety Screening Form)	√			
MRI Hazard Checklist	√			
Pregnancy Test	√			
Pulse Oximetry (optional)		√		
ECG		√		
Save MRI Setting	√			
Activate MRI Setting		√		
Deactivate MRI Setting			√	

** Capture bipolar capture, sense, pacing, and HVLI impedances*

***Note:** RA lead capture only for subjects with Tendril STS or Isoflex leads. 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 most recent archival measurement, if available, will be used.*

TABLE 4: SUBJECT VISIT DATA COLLECTION SUMMARY

Study Visit	Visit Window	Study Procedures and Data Collection
Enrollment	Up to or same day before Implant	• Screen patient for enrollment eligibility • Obtain informed consent • Obtain medical and surgical history • Collect demographic information • Document indication for implant of ICD/ CRT-D

Study Visit	Visit Window	Study Procedures and Data Collection
		• Determine ICD/ CRT-D and lead combination (group) for the subject to be implanted
Implant	No greater than 7 days after enrollment visit Re-attempt scheduled at time of discharge (if applicable)	• Implant ICD/ CRT-D and leads within 7 days of obtaining consent • Obtain ICD/ CRT-D system information: model and serial number of implanted ICD/ CRT-D system • If implant is unsuccessful and no re-attempt to implant is attempted subject should be withdrawn from the study • If implant is unsuccessful and re-attempt to implant is attempted subject should continue in the study to the MRI Scan Visit 45(+7) days from the successful implant date.
Baseline/ MRI Scan Visit	45 (+7) days after implantation or after most recent lead revision MRI scan should occur within 14 days of Baseline visit. 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 prep subject for MRI scan • Complete MRI screening form • 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: bipolar capture, sense, pacing and HVLI impedances[1,2] • Setup and activate MRI Settings During MRI Scan • Monitor subject with ECG, or pulse oximetry, and verbal communication Post-MRI scan testing • Interrogate device • Deactivate MRI Settings • Obtain in-clinic lead measurements: bipolar capture, sense, pacing and HVLI impedances[1,2] • Evaluate subject for any adverse events (serious and non-serious) and submit an AE CRF (as applicable). • Report deviations, screening failure/withdrawal and out of service as applicable • Submit MRI scan results, e.g. scan time, sequences used, etc. • Upload device session records through the EDC study site portal
1-Month Post MRI Scan Visit	30 days after MRI scan (0/+14 days)	• Interrogate device • Obtain in-clinic lead measurements: bipolar capture, sense, pacing and HVLI impedances[1,2]

Study Visit	Visit Window	Study Procedures and Data Collection
		• Evaluate subject for any adverse events and submit an AE CRF (as applicable). • Report deviations, withdrawal and out of service as applicable • Upload device session records through the EDC study site portal
System Revision (if applicable)	Can occur any time after implant	• Interrogate device • Obtain applicable in-clinic lead measurements: bipolar capture[1], sense[2], and pacing and HVLI impedances for cases where the lead was repositioned, or was replaced with another Durata/Optisure or Tendril/Isoflex, Quartet lead, or where the ICD/ CRT-D was replaced with another Ellipse ICD/ Quadra Assura MP CRT-D. • Evaluate subject for any adverse events and submit an AE CRF (as applicable). • Report deviations, withdrawal and out of service as applicable • Upload device session records through the EDC study site portal
Unscheduled (if applicable)	Any time after the MRI scan visit before the 1 Month Post MRI Scan Visit	• Interrogate device. • Obtain applicable in-clinic lead measurements: bipolar capture, sense, pacing and HVLI impedances[1,2] • If an unscheduled visit occurs prior to the 1-month post MRI visit, evaluate subject for any adverse events and submit an AE CRF (as applicable). If an unscheduled event occurs after the 1-month post MRI visit, then the AE events do not need to be submitted in CRF, instead device-related AEs must be reported to the Sponsor as per vigilance/commercial reporting requirements. • Report deviations, withdrawal and out of service as applicable • Upload device session records through the EDC study site portal

8.4.4.1. 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. Obtain demographic, medical, and surgical history. Document indication for the ICD/ CRT-D system to be implanted and determine ICD/ CRT-D lead combination to be implanted. The principal investigator or delegated study personnel are responsible for screening all potential subjects to determine subject eligibility for the study and for

determining the ICD/ CRT-D lead combination (study group) for the subjects. This visit may occur up to or on the same day as the implant visit. The study implant ICD/ CRT-D and leads will be implanted within 7 days of obtaining consent.

8.4.4.2. Implant

Perform the device and lead implant procedure according to standard of care. Consult the User's Manual for implantation guidelines, appropriate lead/device connections and general handling information. The ICD/ CRT-D system will be considered successfully implanted if; at a minimum, the Ellipse VR/ DR, or Quadra Assura MP generator and a Durata, Optisure, Tendril STS, Isoflex, or a Quartet lead are implanted according to the study group for the subject.

Unsuccessful Implant- if applicable
Enrolled subjects who have an unsuccessful implantation of the study device and lead (see definition for successful implant above) will be withdrawn from the study unless the implant will be re-attempted and is scheduled at the time of discharge. The physician may re-attempt the implantation of study devices at his/her discretion.

8.4.4.3. Baseline and MRI scan visit

The Baseline visit must occur the latter of:

- ≥45 days after lead implant AND
- ≥45 days after most recent lead revision, if applicable

The MRI Scan Visit should occur ≤14 days after the baseline visit or may be performed on the same day as the Baseline visit.

To ensure the patient meets the requirements to undergo the study MRI scan, use the MRI Screening Form for reverification. Prior lead measurements performed at the Baseline visit may be used to evaluate inclusion criteria at the MRI visit.

The MRI visit is composed of 3 sections: Pre-MRI Scan Testing, MRI scan, and Post-MRI Scan.

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

- implant of a non-study generator or lead, or
- capping/abandoning of 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. The subject should be withdrawn. Refer to section **8.4.5** for further details.

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

8.4.4.4. Pre-MRI scan testing

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. The subject should be withdrawn.

Clearing the Subject for the Study Scan
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 Procedure Information for the St. Jude Medical® MR Conditional defibrillation 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

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/ CRT-D and lead (wires) contraindication item on the MRI hazard checklist do not apply if the subject is implanted with any one of the four main device systems included in this study.

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/ CRT-D and obtain the following for the Study leads:

- In-clinic bipolar and unipolar* 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 at 0.5ms for RA and RV leads or >2.0V at 0.5 ms for LV leads, then the subject does not meet pre-MRI screening criteria.
- In-clinic 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 pre-MRI screening criteria.
- In-clinic atrial and ventricular bipolar and unipolar* lead impedance

***NOTE:** Unipolar and bipolar configurations should be collected for LV leads*

***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.*

If the device testing results do not meet the MRI conditions for scanning per the MRI Procedure manual (also see below), or the patient's sensing threshold is 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.

- Bipolar capture thresholds are stable at ≤2.5V@ 0.5 ms for RA and RV leads or >2.0V @0.5ms for LV leads.
- 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 5** for ICDs and **Table 6** for CRT-Ds. Perform all other applicable tests and procedures.

TABLE 5: MRI PARAMETERS-ICD

Parameters	Selectable Options	Nominal Values
MRI Mode*	VOO Pacing Off	Pacing off
MRI Base Rate	30-100 bpm, in steps of 5 bpm	n/a

Parameters	Selectable Options	Nominal Values
MRI RV Pulse Configuration	Bipolar	n/a
MRI RV Pulse Amplitude	5.0 V, 7.5 V	n/a
MRI RV Pulse Width	1.0 msec	n/a
Tachy settings	Disabled	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, set the MRI Mode to the asynchronous pacing mode (VOO). When pacing support is not needed, set the MRI Mode to Pacing Off.* *Some subjects may be susceptible to cardiac arrhythmia induced by competitive pacing when an asynchronous MRI Mode is selected. For these subjects, it is important to select an appropriate MRI pacing rate to avoid competitive pacing and then minimize the duration of the asynchronous pacing operation.* *In MR Conditional ICDs, tachytherapy is disabled when the MRI settings are programmed.* *After the electrical measurements for the RA lead and/or 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.*		

TABLE 6: MRI PARAMETERS- CRT-D

Parameters	Selectable Options	Nominal Values
MRI Mode*	DOO Pacing off	DOO
MRI Base Rate	30-100 bpm	85 bpm
MRI paced AV delay	25-120ms	120 ms
MRI RV Pulse Configuration	Bipolar	n/a
MRI RV Pulse Amplitude	5.0 V, 7.5V	n/a
MRI RV Pulse Width	1.0 msec	n/a
MRI V pacing chamber	RV only	RV only
Tachy settings	Disabled	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, set the MRI Mode to the dual chamber asynchronous pacing mode (DOO).* *Some subjects may be susceptible to cardiac arrhythmia induced by competitive pacing when an asynchronous MRI Mode is selected. For these subjects, it is important to select an appropriate MRI pacing rate to avoid competitive pacing and then minimize the duration of the asynchronous pacing operation.* *In MR Conditional CRT-Ds, tach therapy is disabled when the MRI settings are programmed.* *After the electrical measurements for the RA lead and/or RV lead, and/or LV 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.*		

8.4.4.5. MRI Scan procedures

Monitor subject with ECG and/or pulse oximetry and verbal communication.

Setting up Pulse Oximetry and/or ECG
Set up pulse oximetry and/or 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. Or, 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. After the MRI scan, remove the subject from the MRI field.

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 subject does not pass the Pre-MRI scan System Check specified above, then the subject should not undergo an MRI scan. The subject 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 the MRI Scan Guidelines. 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 two different scans for the study, both of which will expose the ICD/ CRT-D to extreme scanning conditions: (1) a thoracic scan that is RF intensive, and (2) a head scan that is gradient intensive. The thoracic scan should be set up to last about 6 minutes and 15 seconds, and the head scan should be set to get as close as possible to 5 minutes without being under 5 minutes. The thoracic scan will need to be repeated 4 times to ensure the subject is scanned approximately 25 minutes. Further details about the set-up, programming and ways to adjust the parameters for MRI scans can be found in the 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 about 30 minutes: 25 minutes for the thoracic scan, and 5 minutes for the head scan.

These two MRI scans are not intended to be diagnostic in nature and therefore the administration of contrast fluids or sedation, or the application of water and fat saturation techniques 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/ CRT-D system.

NOTE: The study MRI scan is being performed to demonstrate safety and MRI compatibility of the ICD/ CRT-D system being evaluated in this trial 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.

An optional non-study MRI scan sequence may be conducted at the request of the subject and discretion of the Investigator and radiologist. This optional non-study MRI scan sequence must be done in accordance with the guidelines and precautions in the MRI Ready Systems Manual.

Cardiac Monitoring

During the entire MRI scan, the subject's cardiac function must be monitored using pulse oximetry and/or ECG by a study trained electrophysiologist, cardiologist 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.

Advanced cardiac lifesaving 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 Abbott. A repeat scan is not required to be completed but may be rescheduled. The subject is not withdrawn from the study. The subject should be scheduled to return for their 1-month post MRI scan visit.

8.4.4.5.1. Data Submission

Once required testing has been performed, complete and submit the appropriate forms to Abbott. Refer to **Table 4: Subject visit data collection summary**.
Upload the 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
- Device MRI summary report

8.4.4.6. Post MRI scan testing

Device Assessment and Programming
Following the MRI Scan, remove the subject from the MRI bore. Interrogate the ICD/ CRT-D. Disable the MRI Settings. **Note: MRI settings must be disabled to ensure that tachyarrhythmia therapy is turned back on.** Obtain the following for the study leads: Interrogate the ICD/ CRT-D, and obtain the following for the Study leads:

- In-clinic bipolar and unipolar* 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 bipolar sensing amplitude. Either the incremental or the automatic (in-clinic, programmer based) method may be used to obtain the sensing threshold.
- In-clinic atrial and ventricular bipolar and unipolar* lead impedance

***NOTE:** Unipolar and bipolar configurations should be collected for LV leads*

***NOTE:** RV capture thresholds are not required to be obtained if a high ventricular rate 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.*

Reporting of MRI Scan-Related Adverse Events
An ADE or SADE related to the following should be reported as soon as possible, but no later than 24 hours after the site becomes aware of the event, to Abbott: 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 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.

Sites should report an ADE or SADE if the subject experiences a significant rise in pacing threshold (1.25V @0.5ms or greater) from pre-MRI scan to one-month post-MRI scan.

8.4.4.6.1. Data submission

Once required testing has been performed, complete and submit the appropriate forms to Abbott. Refer to **Table 4: Subject visit data collection summary**.
Export the study MRI scan onto a CD, or other form of electronic media in DICOM format, and send to Abbott. 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
- Device MRI summary report

8.4.4.7. One (1) month post scan visit

8.4.4.7.1. Testing

Interrogate the ICD/ CRT-D and obtain electrical lead measurements.

- In-clinic bipolar and unipolar* 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. If a significant rise in pacing threshold (1.25V @0.5ms or greater) from pre-MRI scan to one-month post MRI scan has occurred, then complete an AE form.
- In-clinic bipolar sensing amplitude. Either the incremental or the automatic (in-clinic, programmer based) method may be used to obtain the sensing threshold.
- In-clinic atrial and ventricular bipolar and unipolar* lead impedance
- Evaluate the subject for ADE and SADE and submit an AE CRF- if applicable.

***NOTE:** Unipolar and bipolar configurations should be collected for LV leads*

***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.*

8.4.4.7.2. Data submission

Once required testing has been performed, complete and submit the appropriate forms to Abbott. Refer to **Table 4: Subject visit data collection summary**.
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
- Device MRI summary report

If an ADE or SADE events has occurred, submit an AE CRF (as applicable). Report withdrawal and out of service as applicable. Upload device session records through the EDC study site portal (as applicable).

8.4.5. Situations where subject does not meet enrollment criteria

If a subject does not meet all inclusion criteria or meets any of the exclusion criteria, the subject cannot participate in the study and cannot be enrolled.

In case the subject was already consented to participate in the study, but did not meet inclusion/exclusion criteria, the following actions will be taken (**Table 7**). The EC/IRB should be notified of deviations according to each respective entity's guidelines.

TABLE 7: ACTIONS FOR INCLUSION/EXCLUSION CRITERIA ISSUES OCCURING POST CONSENT

Issues where patient was consented, but did not meet inclusion/exclusion criteria	Action
If the subject did not have a successful implant procedure or successful re-attempt to implant with the study devices	• Document consenting information (name of the study, date of consent and inclusion/exclusion) in the subject's medical and/or study records • Complete the withdrawal CRF. The subject is withdrawn.
If the MRI Pre-Scan Visit has taken place, the MRI Settings was NOT programmed and the study MRI scan was NOT completed (e.g. Subject changed their mind about undergoing MRI scan, etc.)	• Document enrollment (name of the study, date of consent and inclusion/exclusion), MRI Scan Visit and study MRI scan information in the subject's medical and/or study records • Complete the Pre-MRI Scan Form • Note that the subject did not have the MRI Settings programmed on the pre-MRI CRF. • Complete deviation for inclusion/exclusion criteria not met • Complete the Withdrawal CRF. The patient is withdrawn.
If the MRI Pre-Scan Visit has taken place, the MRI Settings WERE programmed but the study MRI scan was NOT completed (e.g. Subject changed their mind about undergoing MRI scan, etc.)	• Document enrollment (name of the study, date of consent and inclusion/exclusion), MRI Scan Visit and study MRI scan information in the subject's medical and/or study records • Complete the Pre-MRI Scan Form • Complete deviation for inclusion/exclusion criteria not met • Complete the Withdrawal CRF. The patient is withdrawn.

8.4.6. Complete system explants

If the subject has the entire study ICD/ CRT-D system removed at any time during the study, and the subject will not receive a replacement study ICD/ CRT-D system, 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.

8.4.7. System revisions

In cases where only the device pocket is revised (leads are not repositioned, leads have not been disconnected from the ICD/ CRT-D), 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 generator replacement, lead replacement and lead repositioning has been performed.

8.4.7.1. Revisions before the MRI scan

A system revision is defined as a replacement of or repositioning of one or more components of the study ICD/ CRT-D system that occurs after the subject has been consented into the study. Because all components of the study ICD/ CRT-D 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 Abbott 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 4** to determine which case report forms need to be completed and submitted. Refer to **Table 8: System Revisions Scenarios Prior to MRI Scan** below to determine what actions need to be performed.

8.4.7.2. Revisions after the MRI scan

If a system revision occurs after the MRI scan, then the subject will remain in the study until the subject completes the 1 Month Post Scan visit.

Any explanted devices or leads (including damaged leads, lead segments and lead fragments) should be returned to Abbott 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 9: System Revisions Scenarios After MRI Scan below to determine what actions need to be performed.

TABLE 8: SYSTEM REVISIONS SCENARIOS PRIOR TO MRI SCAN

System Revisions that occur prior to MRI Scan	Action	Data Submission
Revisions where the study ICD/ CRT-D system is still implanted: • Study lead(s) or the ICD/ CRT-D is repositioned or replaced, AND • The study ICD/ CRT-D and study lead(s) are still implanted, AND • No other non-MRI compatible material has been implanted	Obtain (if possible): • In-clinic bipolar and unipolar* capture threshold at a pulse width of 0.5 ms. for the applicable lead(s). Either the manual decrement or automatic (in-clinic, programmer based) method may be used to obtain the capture threshold. • In-clinic bipolar sensing amplitude for the applicable lead(s). Either the incremental or the automatic (in-clinic, programmer based) method may be used to obtain the sensing threshold. • In clinic atrial and ventricular bipolar and unipolar* lead impedance for the applicable lead • Retain the subject in the study. If the MRI scan visit has not occurred yet, then wait at least 45 days from the successful revision before completing the MRI scan visit. If the MRI scan visit has occurred, then follow the subject through the 1 Month Post Scan visit. ***NOTE:** Unipolar and bipolar configurations should be collected for LV leads*	Complete and submit the appropriate forms to Abbott. Refer to **Table 4**. 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
Revisions where the study ICD/ CRT-D system is not retained, and the MRI Settings have not been programmed	The subject will be withdrawn from the study.	Document consenting information (name of the study, date of consent and inclusion/exclusion) in the subject's medical and/or study records.

System Revisions that occur prior to MRI Scan	Action	Data Submission
• Study leads, or study ICD/ CRT-D was explanted but was not replaced with another study lead or study ICD/ CRT-D, and/or • A non-MRI compatible material(s) or device(s) was implanted		Submit the Screen Failure CRF. Submit Deviation or Product Out of Service CRFs if applicable. 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
Revisions where the study ICD/ CRT-D system is not retained, and the MRI Settings were programmed Study leads, or study ICD/ CRT-D was explanted but was not replaced with another study lead or study ICD/ CRT-D, and/or A non-MRI compatible material(s) or device(s) was implanted	The subject will be withdrawn from the study.	Document consenting information (name of the study, date of consent and inclusion/exclusion) in the subject's medical and/or study records. Submit the Pre-MRI CRF, and Withdrawal CRF. Submit Deviation or Product Out of Service CRFs if applicable. 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

TABLE 9: SYSTEM REVISIONS SCENARIOS AFTER MRI SCAN

System Revisions that occur after the MRI Scan	Action	Data Submission
Revisions where the study ICD/ CRT-D system is still implanted • The study ICD/ CRT-D and study lead(s) are still implanted, BUT • A non-MRI compatible material(s) or device(s) has been implanted OR Revisions where the study ICD/ CRT-D system is still implanted • Study ICD/ CRT-D and study lead(s) is repositioned or replaced, AND • The study ICD/ CRT-D and study lead(s) are still implanted, AND • No other non-MRI compatible material has been implanted	Obtain (if possible): • In-clinic bipolar and unipolar* capture threshold at a pulse width of 0.5 ms. for the applicable lead(s). Either the manual decrement or automatic (in-clinic, programmer based) method may be used to obtain the capture threshold. • In-clinic bipolar sensing amplitude for the applicable lead(s). Either the incremental or the automatic (in-clinic, programmer based) method may be used to obtain the sensing threshold. • In clinic bipolar and unipolar* lead pacing impedance for the applicable lead(s) • Continue to follow the patient until the subject completes the 1 Month Post scan visit. ***NOTE:** Unipolar and bipolar configurations should be collected for LV leads*	Once required testing has been performed, complete and submit the appropriate forms to Abbott. Refer to **Table 4**
Revisions where the study lead(s) is not retained • Study lead(s) is replaced with another lead, AND • The study ICD/ CRT-D is still implanted, AND	The subject will be withdrawn from the study.	Document consenting information (name of the study, date of consent and inclusion/exclusion) in the subject's medical and/or study records. Submit the Pre-MRI CRF, MRI CRF, System Revision CRF and Withdrawal CRF. Submit

System Revisions that occur after the MRI Scan	Action	Data Submission
• A non-MRI compatible material(s) or device(s) has been implanted		Deviation, Product Out of Service, Adverse Event CRFs if applicable. 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

8.4.8. Unscheduled visits

An unscheduled visit is defined as a visit that occurs after the MRI Scan Visit where the subject is seen in clinic due to an ADE or SADE associated with the study lead(s) and study ICD/ CRT-D. Where possible, perform a device interrogation for the applicable lead(s) to obtain:

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

***NOTE:** Unipolar and bipolar configurations should be collected for LV leads*

8.4.9. Data submission

Once testing has been performed, complete and submit the appropriate forms to Abbott. Refer to **Table 4.** 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

8.4.10. Non-Study MRI Scans

A non-study MRI scan is defined as an MRI scan occurring at any time following the study MRI scan to the conclusion of the subject's participation in the study. Non-study MRI scans should be performed per each center's standard of care. A non-study scan may be performed 30 minutes after the study scan on the same day, if the Investigator and Subject choose to have one performed.

For non-study MRI scans performed at the study center, the same safety data collection and safety precautions outlined at the MRI Scan Visit should be followed. However, if procedures or data are not followed or collected as presented on the non-study MRI Case report 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 subject's physician (per standard of care by the facility performing the MRI scan).

The following data should be collected and reported to Abbott for non-study MRI scans.

- Date of scan
- Type of scan performed

- Documentation of any Adverse Device Effects
- Device diagnostics, if available
- MRI Scan report, if available
- Fast Path Summary, if available

9. Standards for device use

The product labeling for the study devices, instructions for use and packaging are kept under a separate cover and will be provided to the NMPA in the application.

10. Monitoring plan

Sponsor and/or designee will monitor the clinical study over its duration according to the CIP-specific monitoring plan which will include the planned extent of source data verification.

Prior to initiating any procedure, the Sponsor monitor (or delegate) will ensure that the following criteria are met:

- The investigator understands and accepts the obligation to conduct the clinical study according to the CIP and applicable regulations and has signed the Clinical Trial Agreement.
- The Investigator and his/her staff should have sufficient time and facilities to conduct the clinical study and should have access to an adequate number of appropriate subjects to conduct the clinical study.
- Source documentation (including original medical records) must be available to substantiate proper informed consent procedures, adherence to CIP procedures, adequate reporting and follow-up of adverse events, accuracy of data collected on case report forms, and device information.
- The Investigator/site will permit access to such records. A monitoring visit sign-in log will be maintained at the site. The Investigator will agree to dedicate an adequate amount of time to the monitoring process. The Investigator and/or research coordinator will be available for monitoring visits. It is expected that the Investigator will provide the monitor with a suitable working environment for review of clinical study-related documents.

11. Statistical considerations

This study is an observational study to meet the requirements for device approval by the NMPA. There is no endpoint hypotheses testing planned in this study. The endpoints, demographics, safety and device data will be summarized using descriptive statistics as outlined in the Statistical Analysis Plan (SAP).

Any major changes to the SAP will be documented in an amendment to the SAP. Less significant changes to the planned analyses will be documented in the final report(s).

12. Data management

Study data will be handled according to China Device GCP (Order 25). The Leading PI and his/her associated organization (leading Unit) will be responsible for compiling and submitting all required reports to governmental agencies.

Before the submission, Leading PI and his/her associated organization (leading Unit) should allow sponsor to have a copy of the above reports for reviewing and providing comments for Leading PI and his/her associated organization consideration.

Data will be analyzed by the Leading PI and his/her associated organization (leading Unit) and/or its affiliates. The Leading PI and his/her associated organization (leading Unit)'s also agree that data may be transferred to the Sponsor's locations worldwide and/or any other worldwide regulatory authority in support of a market-approval application.

13. Quality control of clinical study

13.1. 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 investigator/institution will permit direct access to source data/documents for the purpose of performing clinical study-related monitoring, audits, IRB/EC review and regulatory inspections.

Subjects providing informed consent are agreeing to allow clinical study monitors or regulatory authorities to review, in confidence, any records identifying the subjects in this clinical study. This information may be shared with regulatory agencies; however, Sponsor undertakes not to otherwise release the subject's personal and private information.

13.2. 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 study, the Sponsor will either secure compliance or, at its sole discretion, terminate the investigator's participation in the clinical study. 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.

13.3. Complaints

During the study, the investigator will be responsible for reporting all complaints. A complaint is defined as 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 AE as defined in this protocol, the investigator must notify the Post Market Surveillance Department by submitting the information on the device via email to SVcomplaints@sjm.com or by phone toll free: 001-800-722-3774 as soon as possible after becoming aware of the complaint. This information will not be collected on a CRF for the study.

If the complaint involves a reportable AE as defined in this protocol, the investigator must complete an AE CRF, including the information on the complaint and submit to the Sponsor as soon as possible.

13.4. 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.

13.5. Recording Data

The CRF will be reviewed by the authorized site personnel. An appropriate comment will be provided to explain changes to data reported on the CRF.

14. Ethical issues and informed consent of clinical study

14.1. Ethical considerations

This clinical study will be conducted in accordance with this Clinical Investigation Plan, the Declaration of Helsinki and the Good Clinical Practice (GCP) guidelines of the China National Medical Products Administration (NMPA) Order No.25. The most stringent

requirements, guidelines or regulations must always be followed. The conduct of the clinical study will be approved by the appropriate Ethics Committee (EC) of the respective clinical site and as specified by local regulations.

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

14.2. Description of the Methods that will be used to Address Potentially Confounding Factors in the Clinical Study Design

The effectiveness endpoints are change in bipolar ventricular capture and sensing threshold from pre-MRI scan to 1 Month Post Scan for the study lead(s) implanted with the study ICD/ CRT-D. Each subject therefore acts as his/her own control. Therefore, there is no concern for confounding factors for the effectiveness endpoint

14.3. Any Known or Foreseeable Factors that May Compromise the Outcome of the Clinical Study or the Interpretation of the Results

There are no foreseeable factors that may compromise the outcome of the clinical study or the interpretation of the results.

14.4. Approval of study protocol

The lead Investigator and the Sponsor will give approval for this protocol in collaboration with the NMPA. The protocol will be submitted to the study site's research governing bodies for approval and approved before any study activities occur.

14.5. Informed consent process and informed consent form

The 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 study that are

relevant to the subject's decision to participate, such as details of clinical study procedures, anticipated benefits, and potential risks of clinical study participation. Subjects must be informed about their right to withdraw from the clinical study 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 study will not jeopardize their future medical care or relationship with the investigator.

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 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 participation. The Principal Investigator or his/her authorized designee will make efforts to ensure that the subject understands the information provided. If the subject agrees to participate, the Informed Consent form must be signed and dated by the subject and thereafter by the person obtaining the consent prior to any clinical study-specific procedures. The signed original will be filed in the subject's hospital or research charts, and a copy will be provided to the subject.

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.

If, during the clinical investigation, new information becomes available that can significantly affect a subject's future health and medical care, the Principal Investigator or his/her authorized designee will provide this information to the subject. If relevant, the subject will be asked to confirm their continuing informed consent in writing.

14.6. Criteria and Procedures for Subject Withdrawal

Each enrolled subject shall remain in the clinical study until completion of the required follow-up period; however, a subject's participation in any clinical study is voluntary and the subject has the right to withdraw at any time without penalty or loss of benefit. Conceivable reasons for discontinuation may include, but not be limited to, the following:

- Subject death
- Subject voluntary withdrawal
- Subject lost-to follow-up as described below
- Subject's follow-up is terminated according to Section **23.1**.

The Sponsor must be notified of the reason(s) for subject discontinuation. The site will provide this information to the Sponsor. Investigators must also report this to their respective IRB/EC as defined by their institution's procedure(s).

No additional follow–up will be required or data recorded from subjects once withdrawn from the clinical study, except for the status (deceased/alive).

However, if a subject withdraws from the study due to problems related to the safety or performance of the device under investigation, the investigator shall ask for the subject's permission to follow his/her status/condition outside of the clinical study.

In case of subject withdrawal, the site should make attempts to schedule the subject for a final clinical study visit. At this final follow-up visit, the subject will undergo the following assessments:

- Device assessment including:
    - Fast Path Summary
    - Test results with Freezes, include battery and leads
    - Wrap-up overview with full parameters
    - Device MRI summary report (if performed)

Lost-to-Follow-up

If the subject misses two consecutive scheduled follow-up time points and the attempts at contacting the subject detailed below are unsuccessful, then the subject is considered lost-to-follow-up. Site personnel shall make all reasonable efforts to locate and communicate with the subject (and document these efforts in the source documents), including the following, at each contact time point:

- A minimum of two telephone calls on different days over the specified follow-up windows to contact the subject should be recorded in the source documentation, including date, time and initials of site personnel trying to make contact.
- If these attempts are unsuccessful, a letter (certified if applicable) should be sent to the subject.
- If a subject misses one or more non-consecutive follow-up contact time points, it will be considered a missed visit. The subject may then return for subsequent visits. If the subject misses two consecutive time points and the above-mentioned attempts at communicating with the subject are unsuccessful, the subject will be considered lost-to-follow-up.

Note: Telephone contact with General Practitioner, non-clinical investigation cardiologist or relative without the presence of the subject or indirect documentation obtained via discharge letters will not be considered as subject contact.

15. Risks and benefits

The risk analysis included an objective review of published and available unpublished medical and scientific data. The sections below provide an overview of residual risks identified in the risk management report and anticipated benefits of the medical device.

The additional tests and assessments required by the clinical study were analyzed for additional risks and are incorporated in the sections below.

15.1. Description of the Subject Population

This clinical study will enroll Chinese national male and female subjects 18 years of age or older from the general cardiology population with the medical need for an implanted Durata or Optisure leads, Tendril STS or Isoflex leads, Quartet quadripolar lead, and Ellipse VR/DR ICD or Quadra Assura MP CRT-D , as described under the Device Descriptions section of this document. Subjects must meet all eligibility criteria and provide written informed consent prior to conducting any study-specific procedures not considered standard of care.

15.2. Anticipated benefits

For the purposes of this study, an MRI Setting has been created, and will be enabled in the Ellipse VR/DR ICDs, and Quadra Assura MP CRT-Ds for the study MRI scan. The MRI Setting allows for the programming of pre-specified parameters that can be saved and utilized for MRI scanning without the need to individually program individual parameters every time a subject needs to undergo an MRI scan; the parameters in the MRI Setting are also all available individually in the Ellipse ICDs, and the Quadra Assura MP CRT-Ds.

Additionally, the study will potentially show that MRI scans can be safely completed in subjects implanted with these leads and devices resulting in MRI conditional labeling of these systems implanted in the subjects.

15.3. Risks associated with the device under investigation

The Durata, Optisure, Tendril STS, Isoflex, Quartet leads and the Ellipse VR/DR ICDs, and Quadra Assura MP CRT-Ds are market-released devices. Risks associated with the use of these devices are anticipated to be comparable to those associated with the use of other market-released defibrillation leads, pacing leads, ICDs, and CRT-Ds. Subjects participating in this study are indicated for or implanted with an ICD/CRT-D 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 Durata, Optisure, Tendril STS, Isoflex, Quartet leads and the Ellipse VR/DR ICDs, and Quadra Assura MP CRT-Ds 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/CRT-D system. The subjects are therefore exposed to, but not limited to, an incremental risk of experiencing the events listed in **Table 10: Anticipated Events and Anticipated Adverse Device Effects**.

15.4. Residual risks associated with the device under investigation

All risk regions were evaluated, and all the system risks were deemed acceptable. While steps have been taken to identify risks associated with the study MRI scan and participation in the study, there may be risks that are unknown at this time.

15.5. Risks associated with participation in the clinical study

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.

15.6. 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/CRT-D system. While an MRI scan is not part of the usual treatment regimen for subjects implanted with an ICD/ CRT-D, 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.

15.7. Risk-to-benefit rationale

There may be no direct clinical benefit to the subject for participating in this study; no direct therapy is being provided as part of the study procedures, i.e. the study MRI scan. However, these data will help to establish the safety and effectiveness of the Durata, Optisure, Tendril STS, Isoflex, and Quartet leads and the Ellipse VR/DR ICDs, or Quadra Assura MP CRT-Ds in an MRI environment, which, upon approval, will provide patients who need an ICD/ CRT-D to have the option to be safely scanned should these patients need to undergo an MRI in the future.

16. Provisions for adverse event and device defect reporting

16.1. Adverse events

To comply with worldwide standards and guidelines on clinical study adverse event reporting, the Sponsor has adopted uniform and worldwide applicable standard definitions and reporting timelines to be used and adhered to by the investigators.

Safety surveillance within this study and the safety reporting, both performed by the investigator, starts as soon as the subject's MRI Settings have been programmed during the MRI visit.

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

Reportable events shall be submitted to the Sponsor. The Sponsor will ensure that all applicable events and device deficiencies 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 CRF within the electronic data capture (EDC) system. Additional information may be requested by the Sponsor to support the reporting of AEs to regulatory authorities. The investigator must notify the IRB/EC, if appropriate, in accordance with national and local laws and regulations, of the AEs reported to the Sponsor.

All study related adverse events will be reported as per applicable regulatory requirements. The Sponsor will also notify all the other medical institutions conducting the clinical study and Ethics committees of the occurrence of SAEs.

Unchanged, chronic, non-worsening or pre-existing conditions are not AEs and should not be reported.

16.1.1. Criteria and Guidelines for Non-Reportable Events

Except as otherwise noted in the CIP, the following events are not reportable to the sponsor:

- Events that occur prior to the MRI settings have been programmed at the MRI study visit.

  NOTE: Since all products in the study are market released and will be used per the approved indication prior to programming MRI settings, the Principal investigator will be responsible for reporting these events as device complaints as they would for any market approved product (See Section 13.3).

- Events not related to the procedure remove, replace or reposition the study lead or ICD/ CRT-D.
- Unavoidable events, as listed in **Table 11** that resolve within the timeframes specified.

16.1.2. Criteria and Guidelines for Reportable Events

Records relating to the subject's subsequent medical course must be maintained and submitted (as applicable) to the Sponsor until the event has subsided or, in case of permanent impairment, until the event stabilizes, and the overall clinical outcome has been ascertained. Adverse events will be monitored until they are adequately resolved. The status of the subject's condition should be documented at each visit.

The investigator will report the event to the IRB/EC per their reporting requirements. Reportable events to sponsor are considered:

- ADEs and SADEs caused by or associated with the study MRI scan (except unavoidable events related to the MRI scan)
- Unavoidable ADEs occurring after MRI setting have been programmed at the MRI study visit whose conditions worsen or continue beyond the time frame listed in the Unavoidable events tables.
- All ADEs and SADEs that are not associated with the MRI scan after MRI settings have been programmed at the MRI study visit.

All above events will be reported to the Sponsor, as soon as possible, but no later than 24 hours of first learning of the event. A list of foreseeable adverse events and anticipated adverse device effects include, but are not limited to, those listed in **Table 10: Anticipated Events and Anticipated Adverse Device Effects.**

The Sponsor will ensure that all adverse events are reported to the relevant authorities as per regulations. The description of the adverse event, date of the adverse event, treatment and resolution of the reportable adverse events will be reported, as applicable, to the relevant authorities per regulations. Additional information may be requested, when required, by the Sponsor to support the reporting of AE CRFs to regulatory authorities. The investigator must notify the IRB, if appropriate, in accordance with national and local laws and regulations, of the AE CRFs reported to the Sponsor.

TABLE 10: 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	These risks are mitigated through the selection of investigators who are qualified by training and/or experience to

Event	Mitigation
• 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	evaluate and treat subjects implanted with an ICD/ CRT-D 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 lifesaving 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/ CRT-D Related Events	
• Refer to the Ellipse VR/DR and Quadra Assura MP user's manual for a full list of potential adverse events	The Ellipse VR/DR ICDs, and Quadra Assura MP CRT-Ds are market-released. The adverse events associated with these devices are the same as those associated with other market-released ICDs/ CRT-Ds. 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/ CRT-D.
Potential Lead Related Events	
• Refer to the Durata, Optisure, Tendril STS, Isoflex, and Quartet lead user's manual for a full list of potential adverse events	The Durata, Optisure, Tendril STS, Isoflex, and Quartet leads are market released transvenous, steroid-eluting

Event	Mitigation
	leads. The adverse events associated with these leads are the same as those associated with other market-released transvenous 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/ CRT-D 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 11: 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

SAE Reporting

The investigator should report all SAEs occurring after MRI settings have been programmed at the MRI study visit to the Sponsor as soon as possible but no later than outlined below.

Clinical Site	Reporting timelines
All Sites	SAEs should be reported to regulatory authorities and the Sponsor no later than 24 hours from the day the site personnel became aware of the event or as per the investigative site's local requirements, if the requirement is more stringent than those outlined.

[redacted]

The date the site staff became aware the event met the criteria of an SAE must be recorded in the source document. The Investigator will further report the SAE to the local IRB/EC according to the institution's IRB/EC reporting requirements.

16.1.3. Subject Death

Subject deaths will be documented and reported to the Sponsor as soon as possible (but no later than 24 hours) after becoming aware of the event via the applicable AE CRF, Withdrawal CRF, and Product Out of Service CRF.

17. Provisions for deviation from clinical study protocol and the revision of clinical study protocol

17.1. Deviations from CIP

The Investigator should not deviate from the CIP for any reason except in cases of medical emergencies when the deviation is necessary to protect the rights, safety and well-being of the subject or eliminate an apparent immediate hazard to the subject. In that event, the Investigator will notify Sponsor immediately by phone or in writing.

No waivers for CIP deviations will be granted by the Sponsor. All deviations must be reported to the Sponsor using the Deviation CRF. The occurrence of CIP deviations will be monitored by the Sponsor for evaluation of investigator compliance to the CIP and regulatory requirements and dealt with according to written procedures. Investigators will inform their IRB/EC or equivalent committee of all CIP deviations in accordance with their specific IRB/EC or equivalent committee reporting policies and procedures.

In the event of repeated non-compliance, as determined by the Sponsor, a Sponsor's monitor or company representative will attempt to secure compliance by one or more of the following (and not limited to):

- Visiting the investigator and/or delegate
- Telephoning the investigator and/or delegate
- Corresponding with the investigator and/or delegate

Repeated non-compliance with the signed agreement, the CIP or any other conditions of the clinical investigation may result in further escalation in accordance with the Sponsor's written procedures, including securing compliance or, at its sole discretion, Sponsor may terminate the investigator's participation in the clinical investigation.

17.2. Protocol revisions

Approved CIP amendments will be provided to the Investigators by the Sponsor prior to implementing the amendment. The Principal Investigator is responsible for notifying the IRB/EC or equivalent committee of the CIP amendment (administrative changes) or obtaining IRB's/EC's approval of the CIP amendment (changes in subject care or safety), according to the instructions provided by the Sponsor with the CIP amendment.

Acknowledgement/approval by the IRB/EC of the CIP amendment must be documented in writing prior to implementation of the CIP amendment. Copies of this documentation must also be provided to the Sponsor. Rationale will be included with each amended version in the revision history table below. The version number and date of amendments will be documented.

TABLE 12: PROTOCOL REVISION HISTORY

Amendment Number	Version	Date	Rationale	Details
[redacted]				

18. Direct access to source data/documents

Regulations and GCP require the Investigator to maintain information in the subject's original medical records that corroborates data collected on the CRFs. To comply with these regulatory requirements/GCP, the following information should be included in the subject record at a minimum and if applicable to the clinical study:

- Medical history/physical condition of the subject before involvement in the clinical study sufficient to verify CIP entry criteria
- Dated and signed notes on the day of entry into the clinical study referencing the Sponsor, CIP number, subject ID number and a statement that informed consent was obtained
- Dated and signed notes from each subject visit (for specific results of procedures and exams)
- Adverse events reported and their resolution, including supporting documents, such as discharge summaries, catheterization laboratory reports, ECGs, and lab results including documentation of site awareness of SAEs and of investigator assessment of device relationship for SAEs.
- CIP-required laboratory reports and 12-lead ECGs, reviewed and annotated for clinical significance of out of range results (if applicable).
  Note: With electronic medical records some clinical sites may be able to annotate that the labs or ECG have been reviewed in the system. For those sites that do not have such capability, the labs or ECG may be able to be printed or signed. Each project team should include CIP language regarding these processes that is most suitable for the specific clinical investigation.
- Notes regarding CIP-required and prescription medications taken during the clinical study (including start and stop dates).
- Subject's condition upon completion of or withdrawal from the clinical study.
- Any other data required to substantiate data entered in the CRF

18.1. Records retention

The Sponsor and Investigator/Site will archive and retain all documents pertaining to the clinical study as per the applicable regulatory record retention requirements. The Investigator must obtain permission from Sponsor in writing before destroying or transferring control of any clinical study records.

18.2. Data management plan

A Data Management Plan (DMP) will describe procedures used for data review, data cleaning, and issuing and resolving data discrepancies. If appropriate, the DMP may be updated throughout the duration of the clinical study. All revisions will be tracked, and document controlled.

18.3. Document and data control

18.3.1. Traceability of documents and data

Primary data collection based on source-documented hospital and/or clinic chart reviews will be performed clearly and accurately by site personnel trained on the CIP and CRF

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

Only authorized site personnel will be permitted to enter the CRF data through the EDC system deployed by the Sponsor. An electronic audit trail will be used to track any subsequent changes of the entered data.

18.3.2. Recording data

Electronic CRFs will be used in this study, as noted below and in the data management plan. Informed consent documents will be provided in Chinese, according to China regulations. If additional documentation is required for any reason (e.g. procedural notes for an adverse event), it is to be appropriately redacted/de-identified prior to being sent to data management. Source documents will be collected and translated, as needed, for reporting, etc.

CRF data collection will be performed through a secure web portal and only authorized personnel will access the Electronic Data Capture (EDC) system using a unique username and password to enter, review or correct data. Passwords and electronic signatures will be strictly confidential.

The data will be subjected to consistency and validation checks within the EDC system and supplemental review by the Sponsor.

After the clinical study, completed CRF images with the date-and-time stamped electronic audit trail indicating the user, the data entered, and any reason for change (if applicable) will be provided to the study sites, if requested.

For the duration of the clinical study, the Investigator will maintain complete and accurate documentation including, but not limited to, medical records, clinical study progress records, laboratory reports, CRFs, signed ICFs, device accountability records (if applicable), correspondence with the IRB/EC and clinical study monitor/Sponsor, adverse event reports, and information regarding subject discontinuation or completion of the clinical study.

19. Finance and insurance

The Sponsor has taken up general liability insurance in accordance with the requirements of the applicable local laws. An appropriate Sponsor's country representative will be utilized to understand the requirements for the type of insurance that will be provided for subjects, and such information will be incorporated into the site informed consent, as applicable. If required, additional subject coverage or a clinical study specific insurance will be provided by the Sponsor.

20. Study report

Clinical study reports will be completed as each arm of the study finishes enrollment and all study procedures. Each separate clinical study report will include:

- Description of the devices under investigation
- Study design information
- Subject disposition
- Subject demographics
- Primary safety endpoint observed throughout the study
- Primary effectiveness endpoints observed throughout the study
- Adverse event observations
- Mortality reported
- Study withdrawals
- Device accountability
- Protocol deviations
- Summary of the study
- Study conclusions

21. Confidentiality principle

The Sponsor respects and protects personally identifiable information collected or maintained for this clinical study. 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 always throughout the clinical study. All data will be secured against unauthorized access.

22. Agreement on study results publication

The data and results from the clinical study are the sole property of the Sponsor. The Sponsor shall have the right to access and use all data and results generated during the clinical study. The Investigators will not use this clinical study-related data without the written consent of the Sponsor for any purpose other than for clinical study completion or for generation of publication materials, as referenced in the Clinical Trial Agreement.

Single-center results are not allowed to be published or presented before the multi-center results. Any proposals for publications or presentations by the investigators must be reviewed and approved by the Sponsor in a timely manner to enable Sponsor review in compliance with the Sponsor's publication policy set forth in the Clinical Trial Agreement.

The Sponsor will be responsible for determining whether to register the clinical study on www.clinicaltrials.gov or any other clinical studies, in accordance with the International

Committee of Medical Journal Editors guidelines, or any other applicable guidelines. In the event Sponsor determines that the clinical study should be registered, Sponsor shall be responsible for any such registration and results posting as required by the ClinicalTrials.gov website. Institution and/or Principal Investigator(s) shall not take any action to register the clinical study.

For live cases at congresses, the patients need to sign a specific Live Case ICF, approved by the IRB/EC. The investigator must notify the Sponsor prior to performing a live case.

23. Responsibilities assumed by each party

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

The Sponsor will select investigators qualified by training and experience to participate in the clinical study. Sites will be selected based upon review of a recent site assessment, if applicable, and the qualifications of the investigators who will participate in the clinical study.

Institutional Review Board (IRB)/ Ethics Committee (EC) approval for the CIP and ICF/other written information provided to the patient will be obtained by the Principal Investigator at each study site prior to consenting and enrolling patients in this clinical study. The approval letter must be received prior to the start of this clinical study and a copy must be provided to the Sponsor.

Any amendments to the CIP as well as associated ICF changes will be submitted to the IRB/EC and written approval obtained prior to implementation, according to each institution's IRB/EC requirements.

No changes will be made to the CIP or ICF or other written information provided to the patient without appropriate approvals, including IRB/EC, the Sponsor, and the regulatory agencies (if applicable).

Until the clinical study is completed, the Investigator will advise his/her IRB/EC of the progress of this clinical study, per IRB/EC requirements. Written approval must be obtained from the IRB/EC yearly to continue the clinical study, or according to each institution's IRB/EC requirements.

No study procedures other than those defined in this CIP will be undertaken on the enrolled subjects without the written agreement of the IRB/EC and the Sponsor.

23.1. 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.

23.2. Description of Activities Performed by Sponsor Representatives

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

- Interrogation of and testing the implanted ICD/ CRT-D system at any study visit (scheduled or unscheduled): capture, sense, pacing and HVLI measurements,
- Verifying MRI scan parameters on the programmer at the MRI Scan Visit or Non-Study MRI visit,
- Programming of the ICD/ CRT-D 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.

Investigator’s statement

I agree:

1. To conduct this clinical study in strict compliance with *Declaration of Helsinki*, current laws and regulations of China, and the requirements of the clinical trial protocol
2. To accurately record all data required into the Case Report Form (CRF) and complete the final report of the clinical study on time.
3. The medical devices are only used in this clinical trial. The receipt and use of the medical devices will be completely and accurately recorded and the records will be kept during the clinical study.
4. To allow the Clinical Research Associate and inspector authorized or designated by the Sponsor and supervision department to conduct inspection, verification and examination on the clinical study.
5. To strictly perform the clinical study contract and articles of agreement signed by all parties.

I have already read the clinical study protocol, including above Statement and fully agree all requirements above.

Comments of the Sponsor Signature (stamp) Date: MM DD YYYY

Comments of the Investigator: Signature: Date: MM DD YYYY

Comments of medical device clinical trial institution Signature (stamp) Date: MM DD YYYY

Appendix A: Definitions

Non-study Specific Definitions

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.
Note 1: This definition includes events related to the medical device under investigation or the comparator.
Note 2: This definition includes events related to the procedures involved.
Note 3: For users or other persons, this definition is restricted to events related to medical devices under investigation

Serious Adverse Event (SAE)
If the AE meets any of the criteria below, it is regarded as a serious adverse event (SAE).

a) Led to a death,
b) Led to a serious deterioration in health of the subject, that either resulted in
    1. a life-threatening illness or injury, or
    2. a permanent impairment of a body structure or a body function, or
    3. in-patient hospitalization or prolongation of existing hospitalization, or
    4. medical or surgical intervention to prevent life threatening illness or injury or permanent impairment to a body structure or a body function.
    5. chronic disease
c) Led to fetal distress, fetal death or a congenital abnormality or birth defect.

Note: A planned hospitalization for pre-existing condition, or a procedure required by the CIP, without a serious deterioration in health, is not considered to be an SAE.

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.

Unanticipated Adverse Device Effect (UADE)
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 CIP 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 subjects.

Anticipated Serious Adverse Device Effect (ASADE)
A serious adverse device effect which by its nature, incidence, severity or outcome has been previously identified in the risk analysis report.

Unanticipated Serious Adverse Device Effect (USADE)
A serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis report.

Complication
A complication is defined as an SADE that requires an invasive intervention or leads to death.

Device Deficiency (DD)
Device deficiency is defined as an inadequacy of a medical device related to its identity, quality, durability, reliability, safety or performance, such as malfunction, misuse or use error and inadequate labeling. This includes the failure of the device to meet its performance specifications or otherwise perform as intended. Note: Performance specifications include all claims made in the labeling of the device.

Device Malfunction
A failure of a device to meet its performance specifications or otherwise perform as intended, when used in accordance with the instructions for use or CIP.

Device Relationship
Determination of whether there is a reasonable possibility that an investigational product or device under investigation caused or contributed to an AE is to be determined by the Investigator and recorded on the appropriate CRF form. Determination should be based on assessment of temporal relationships, evidence of alternative etiology, medical/biologic plausibility, and patient condition (pre-existing condition).

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.

The definition shall be applied by the investigator judgement to exclude individuals who are unable to fully understand all aspects of the investigation that are relevant to the decision to participate, or who could be manipulated or unduly influenced as a result of a compromised position, expectation of benefits or fear of retaliatory response.

Study Specific Definitions

Medical Device
Any instrument, apparatus, implement, machine, appliance, implant, software, material or other similar or related article

(a) Intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the specific purpose(s) of

- Diagnosis, prevention, monitoring, treatments or alleviation of disease,
- Diagnosis, monitoring, treatment, alleviation of, or compensation for, an injury,
- Investigation, replacement, modification, or support of the anatomy or of a physiological process,
- Supporting or sustaining life,
- Control of conception,
- Disinfection of medical devices and

(b) Which does not achieve its primary intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its intended function by such means

MRI Scan Related Complication
A complication is deemed to be MRI related if it is caused by or related to the interaction between the ICD/ CRT-D system and the MRI system that occurs during the MRI scan and includes the time the subject is within the 5 Gauss line of the MRI system, or up through the subject's 1-month post MRI scan follow up visit. The MRI scan related complications will be based on the CEC adjudication data.

Appendix B: Case Report Form

The case report forms for the study are kept under a separate cover and are available upon request.

Appendix C: Bibliography

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Statistical Analysis Plan

Protocol No.: CRD_930 ABT-CIP-10238

Clinical Study Protocol for the Evaluation of ICD Defibrillation Systems in a 1.5T Magnetic Resonance Imaging (MRI) Environment in China

Statistical Analysis Plan (SAP)

Version C

11 May 2020

[redacted]

Statistical Analysis Plan

TABLE OF CONTENTS

1.0 SYNOPSIS OF STUDY DESIGN

1.1 Purpose of the Statistical Analysis Plan

This statistical analysis plan (SAP) is intended to provide a detailed and comprehensive description of the planned methodology and analysis to be used for Clinical Study Protocol for the Evaluation of ICD Defibrillation Systems in a 1.5T Magnetic Resonance Imaging (MRI) Environment in China, the CRD-930 (ABT-CIP-10238) clinical investigation. This plan is based on the ABT-CIP-10238 Ver. D, 30SEP2019 Clinical Investigation Plan (CIP).

1.2 Clinical Investigation Objectives

The objective of this clinical study is to evaluate the safety and effectiveness of the Ellipse VR/DR implantable cardiac defibrillators (ICDs) and the Quadra Assura MP cardiac resynchronization therapy defibrillators (CRT-Ds), with Durata or Optisure defibrillation leads, Tendril STS or Isoflex pacing leads, and the Quartet quadripolar leads in a 1.5T MRI environment for MR-conditional labeling expansion of these market-approved ICD/CRT-D systems in China.

1.3 Clinical Investigation Design

This is a prospective, multi-center, single-arm study to evaluate the safety and effectiveness of the Ellipse VR/DR ICDs, and the Quadra Assura MP CRT-D, with Durata or Optisure defibrillation leads, Tendril STS or Isoflex pacing leads, and the Quartet quadripolar LV lead in a 1.5T MRI environment for MR-conditional labeling expansion in China.

This study will be conducted in at least 6 centers in China and at least 60 subjects who provide consent for participation will be enrolled. Subjects will be considered enrolled after providing consent. Subjects will be implanted with any one of the device/lead combination groups outlined as following**,** depending on their clinical need as determined by the Investigators. At least 15 subjects will be enrolled in each group.

- **Group 1** will have at least 15 enrolled subjects with the Ellipse VR single-chamber ICD with a Durata lead in the right ventricle (RV).
- **Group 2** will have at least 15 enrolled subjects with the Ellipse DR dual-chamber ICD with a Durata lead in the RV and a Tendril STS lead in the right atrium (RA).
- **Group 3** will have at least 15 enrolled subjects with the Ellipse DR dual-chamber ICD with a Optisure lead in the RV and a Isoflex lead in the RA.
- **Group 4** will have at least 15 enrolled subjects with a Quadra Assura MP CRT-D and an Optisure or Durata lead in the RV, an Isoflex or Tendril STS lead in the RA, and a Quartet lead in the left ventricle (LV).

A prospective, multi-center, non-randomized, open-label, single arm clinical study design was chosen to generalize the study results [redacted]. This study intends to provide clinical data from a local Chinese population to supplement IDE clinical data from a population in the United States and Europe for submission to the

NMPA in support of a marketing application of MRI labeling expansion for these ICD/CRT-D systems in China.

1.4 Endpoints

1.4.1 Primary Safety Endpoint

Freedom from MRI-scan related complications related to the ICD/CRT-D device and/or leads from the time of the MRI scan to 1-month post-MRI scan testing.

1.4.2 Primary Effectiveness Endpoints

• #1: Proportion of leads with a capture threshold increase of ≤ 0.5V at 0.5ms for RA and RV leads and ≤1.0V at 0.5ms for LV leads from pre-MRI scan to 1-month post-MRI scan testing.

• #2: Proportion of leads with a sensing amplitude decrease of ≤ 50% from pre-MRI scan to 1-month post-MRI scan testing.

1.4.3 Descriptive Endpoints

Descriptive endpoints are reported using only summary statistics and no hypothesis tests will be performed.

The following data will be collected:

1. Demographics: gender, age, ethnicity, race, cardiac disease history, arrhythmia history, indication for ICD/CRT-D implant, history of smoking, etc.
2. Device electrical measurements at the MRI Scan Visit (pre- and post-scan) and at the 1-Month Post Scan Visit
3. ADE, SADE, USADE
4. Mortality
5. Number of non-study MRI scans
6. Summarize number of subjects that returned to usual programming after the MRI scan and number of subjects, if any, experiencing delays in reprogramming

1.5 Randomization

Not applicable.

1.6 Blinding

Not applicable.

2.0 ANALYSIS CONSIDERATIONS

2.1 Analysis Populations

[redacted]

2.2 Statistical Methods

This study is an observational study to meet the requirements for device approval by the NMPA. There is no endpoint hypotheses testing planned in this study. The endpoints, demographics, safety and device data will be summarized using descriptive statistics.

2.2.1 Descriptive Statistics for Continuous Variables

For continuous variables (e.g., age), results will be summarized with the numbers of observations, means, and standard deviations, with minimums and maximums. Two-sided 95% confidence intervals for the means may be presented, or otherwise will be specified.

2.2.2 Descriptive Statistics for Categorical Variables

For categorical variables (e.g. gender, cardiac disease history), results will be summarized with subject (or device/lead) counts and percentages/rates. Two-sided exact 95% Clopper-Pearson confidence intervals may be presented, or otherwise will be specified.

2.3 Endpoint Analysis

2.3.1 Primary Safety Endpoint

The primary safety endpoint is freedom from MRI-scan related complications related to the ICD/CRT-D device and/or leads from the time of the MRI scan to 1-month post-MRI scan testing. The CEC adjudicated data will be used for the primary safety endpoint analysis.

[redacted]

[redacted]

2.3.2 Primary Effectiveness Endpoints

Effectiveness endpoint #1:

Effectiveness endpoint #1 is the proportion of leads with a capture threshold increase of ≤ 0.5V at 0.5ms for RA and RV leads and ≤1.0V at 0.5ms for LV leads from pre-MRI scan to 1-month post-MRI scan testing.

[redacted]

Effectiveness endpoint #2:

Effectiveness endpoint #2 is the proportion of leads with a sensing amplitude decrease of ≤ 50% from pre-MRI scan testing to 1-month post-MRI scan.

[redacted]

[redacted]

[redacted]

2.4 Sample Size Calculations

There is no hypothesis testing is planned in this study, and no sample size calculation or power analysis has been performed.

[redacted]

2.5 Interim Analysis

No formal interim analyses are planned for this study. As such, no formal statistical rule for early termination of the trial is defined. Interim study reports with descriptive analysis may be produced for regulatory or reimbursement purposes as needed.

2.6 Timing of Analysis

Analysis will be performed after all subjects in each device Group complete their 1-month post-MRI scan visit or pass their 1-month post-MRI scan follow-up visit window, and when data are available for the analysis for the respective device Group(s).

2.7 Study/Trial Success

There is no hypothesis testing planned in this study, therefore no statistical criteria are specified for success. Data will be summarized and presented descriptively.

2.8 Subgroups for Analysis

No subgroup analysis is planned.

2.9 Handling of Missing Data

A subject may discontinue from the study prior to the 1-month visit. If this situation occurs, reasons for missing primary endpoint data will be summarized to assess the plausibility if the missing data could affect subject's endpoint results.

2.10 Poolability Analysis

No poolability analysis is planned for the study.

2.11 Multiplicity Issues

Not applicable.

2.12 Adjustments for Covariates

Unless otherwise specified, no adjustments for covariates will be made for any of the variables in the analyses.

2.13 Exploratory Analysis

No exploratory analysis is planned.

3.0 DESCRIPTIVE ENDPOINTS AND ADDITIONAL DATA

The following data will be summarized descriptively as outlined in Section 2.2 Statistical Methods in the SAP, based on Analysis Cohort, or otherwise as specified.

3.1 Baseline and Demographic Characteristics

The baseline and demographic variables such as gender, age, ethnicity, race, key cardiovascular history, prior cardiac interventions, arrhythmia history, primary indication for ICD/CRT-D implant, and history of smoking, will be summarized descriptively.

3.2 Adverse Events

CEC adjudicated ADE, SADE, USADE data will be summarized in terms of the number of events, the number of subjects with event(s), and the percentage of subjects with event(s). Subjects who die or withdraw before 1-month post-MRI scan will be included in the denominator, and their last know status of event will be included in the numerator.

3.3 Subject Early Termination

Subject early termination reasons such as deaths, withdrawals, lost-to-follow-up. will be summarized at scheduled visits.

3.4 Protocol Deviation

Protocol deviations will be summarized descriptively by category.

3.5 Descriptive Endpoints or Additional Data

Following Descriptive Endpoints will be reported using only summary statistics and no hypothesis tests will be performed.

1) Demographics: gender, age, ethnicity, race, cardiac disease history, arrhythmia history, indication for ICD/CRT-D implant, history of smoking, etc. Refer to Section 3.1 for the detail.

2) Device electrical measurements: device electrical measurements at the MRI Scan Visit (pre- and post-scan) and at the 1-Month Post Scan Visit will be summarized based on Analysis Cohort subjects who undergo the 1-month post-MRI scan testing, and with evaluable device data available for analysis to be performed.

3) ADE, SADE, USADE: Refer to Section 3.2 for the detail.

4) Mortality: The number of subjects who die and the primary cause of death will be presented based on the CEC adjudicated data.

5) Non-study MRI scan data: The number, type, available adverse event(s), and key electrical measurements will be summarized for non-study MRI scans performed.

6) Summarize number of subjects that returned to usual programming after the MRI scan and number of subjects, if any, experiencing delays in reprogramming: Data will be summarized descriptively based on available information from MRI Scan form. A subject with 'Yes' to question of 'Were the MRI settings disabled after MRI scan' in MRI Scan form is considered as 'returned to usual programming after the MRI scan'.

In addition, the adverse events and mortality that are reported prior to the completion of the study pre-MRI scan visit on the All Consented subjects will be summarized separately using descriptive statistics. Listings of the adverse events and mortality with an event description will be provided as appropriate.

4.0 DOCUMENTATION AND OHER CONSIDERATIONS

All analyses will be performed using SAS® for Windows, version 9.3 or higher.

5.0 ACRONYMS AND ABBREVIATIONS

Acronym or Abbreviation	Complete Phrase or Definition
CEC	Clinical Events Committee
CIP	Clinical Investigation Plan
CRF	Case Report Form

Acronym or Abbreviation	Complete Phrase or Definition
SAE	Serious Adverse Event
ADE	Adverse Device Effect
SADE	Serious Adverse Device Effect
USADE	Unanticipated Serious Adverse Device Effect
SAP	Statistical Analysis Plan
NMPA	China National Medical Products Administration
MRI	Magnetic Resonance Imaging
ICD	Implantable Cardiac Defibrillator
CRT-D	Cardiac Resynchronization Therapy Defibrillator

6.0 REFERENCES

CRD_930 CIP ABT-CIP-10238 Ver. D, 30SEP2019
CRD_930 CHINA MRI ICD Case Report Form (CL1005575)
CRD_930 CHINA MRI ICD AE Adjudication From (CL1008482)