Cover Page

Title of the study: Usefulness of Unipolar and Bipolar Electrograms in Predicting Successful Ablation Site During Idiopathic Outflow Tract Ventricular Arrhythmia Ablation

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CRD_801

EGM Analysis in Idiopathic OTVA

"Usefulness of Unipolar and Bipolar Electrograms in Predicting Successful Ablation Site during Idiopathic Outflow Tract Ventricular Arrhythmia Ablation"

Clinical Investigation Plan (CIP)

Sponsor

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PRINICPAL INVESTIGATOR SIGNATURE PAGE

EGM Analysis in Idiopathic OTVA

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Version A

Reference #: CRD_801

I have read and agree to adhere to the clinical investigational plan and all regulatory requirements applicable in conducting this clinical study.

Principal Investigator

Printed name: _____

Signature: _____

Date: _____

Coordinating Investigator/ National Investigator/ Medical Advisor

SIGNATURE PAGE

EGM Analysis in Idiopathic OTVA

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Coordinating Investigator/Medical Advisor, PI

Printed name: _____

Signature: _____

Date: _____

Table of Contents

1.0 SYNOPSIS

Title:	Usefulness of Unipolar and Bipolar Electrograms in Predicting Successful Ablation Site during Idiopathic Outflow Tract Ventricular Arrhythmia Ablation
Acronym:	EGM Analysis in Idiopathic OTVA
Purpose:	Investigate the value of unipolar and bipolar electrograms (EGM) for predicting the successful ablation site for idiopathic outflow tract ventricular arrhythmia (OTVA)
Objectives:	Primary Objective: Evaluate the predictive value of using reversed polarity in adjacent bipolar EGMs (bi-RP method) and unipolar EGM with QS morphology (uni-QS method) for identifying successful ablation site
	Secondary Objective: Evaluate the feasibility of enhancing uni-QS method's performance by using its morphology characteristics such as descending slope and symmetry
Endpoints:	Primary Endpoint: Predictive values of the bi-RP method and uni-QS method for successful ablation Secondary Endpoint: Predictive value of a new method by combining bi-RP and uni-QS for successful ablation.
Design:	The study is an acute, non-randomized, feasibility study in Fuwai Hospital, China.
Devices used:	Any commercially available SJM quadripolar RF ablation catheters in China.
Study Population	Approximately 20 patients meeting the specific criteria.
Inclusion/Exclusion Criteria	Inclusion Criteria: - Patients scheduled to undergo ablation for idiopathic OTVA - Have the ability to provide informed consent for study participation. Exclusion Criteria - Be currently participating in any other investigational study - Be less than 18 years of age - Be pregnant - Has any other conditions that are not suitable for catheter ablation (including but are not limited to active whole-body infection or sepsis, coagulation or hemorrhage disorder history)
Data Collection	Data will be collected at: Enrollment and OTVA ablation visit.

1.1 Study Flow Chart

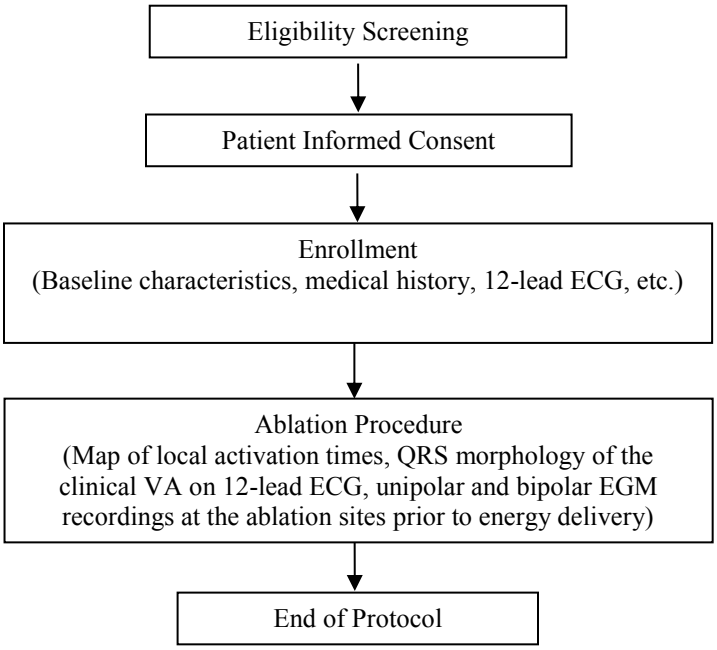

Figure 1: Study flow from enrollment to end of protocol

1.2 Study Contacts

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2.0 BACKGROUND AND JUSTIFICATION FOR CLINICAL STUDY

Currently, the first-line therapy for symptomatic Ventricular Arrhythmia (VA) patients is still antiarrhythmic drugs[1]. Unfortunately, drug therapy is not always effective and can be hindered by side effects[1-3]. As an alternative, Radiofrequency Catheter Ablation (RFCA) has been shown to be highly effective in treating focal idiopathic VAs in the outflow tract (OT), with acute success rates greater than 80%[1,4-6]. Although RFCA is generally considered a safe procedure, serious complications may still occur[1,7-8]. Therefore, it is important to minimize the number of lesions while achieving an effective treatment.

The classic strategy to guide RFCA is based on local activation time (LAT) map and the presence of a QS morphology in the unipolar electrograms (uni-QS)[9-12]. However, the actual LAT at the successful ablation site may vary a lot among patients, and the area demonstrating a unipolar QS morphology may be larger than the focal source[9-12]. In practice, these factors may greatly affect the efficiency of the physicians to locate the focal source and cause unnecessary ablation lesions. Thus, more specific criteria are needed to help guide the search for successful ablation site.

The presence of reverse polarity in adjacent bipolar electrograms (bi-RP) has been demonstrated in pulmonary vein isolation procedure using circular catheter based on the hypothesis that the excitation wavefront propagates radially from the breakthrough site in the pulmonary vein[14]. A similar approach using the reversal initial deflection of adjacent bipolar electrograms has been demonstrated in patients with accessory pathways and focal atrial tachycardia[15]. Lately, Carine et al., in a retrospective analysis, showed that a method combining the use of LAT and bi-RP phenomenon in focal right ventricular outflow tract (RVOT) arrhythmias could yield a higher specificity for identifying successful ablation sites than the conventional LAT plus unipolar QS morphology method[16].

The proposed study aims to evaluate the predictive value of bi-RP and uni-QS for identifying successful ablation site. It will also evaluate the feasibility to enhance uni-QS method's performance by using uni-QS and its morphology characteristics such as descending slope and symmetry.

3.0 RISKS AND BENEFITS OF THE CLINICAL STUDY

3.1 Description of subject population

The inclusion/exclusion criteria for participation in this study is specified in section 4.5. This study will attempt to recruit consecutive subjects who meet all inclusion criteria and does not meet any exclusion criteria for study enrollment. A signed Informed Consent Form (ICF) for study participation must be obtained by the principal investigator (PI) or designated personnel prior to subject enrollment.

3.2 Anticipated clinical benefits

There is no direct benefit to the studied patient because we simply collect electrograms during the ablation procedure. However, findings from this study may help physicians to develop more efficient ablation strategy and potentially benefit future patients.

3.3 Anticipated adverse events and adverse device effects

There are no adverse events associated with the additional data collection for this study. Possible adverse events (in alphabetical order) associated with the standard RFCA include but are not limited to the following:

- Allergic reactions to contrast media (agents)
- Arrest (cardio)
- Arrest (respiratory)
- Arrhythmias
- Air embolism
- Bleeding (non-hematoma)
- Cardiac perforation
- Cardiac tamponade
- Damage to the conduction system
- Damage to the coronary arteries
- Death
- Endocarditis
- Groin hematoma
- Heart failure
- Hemothorax
- Myocardial ischemia
- Myocardial Infarction
- Phrenic nerve injury
- Periprocedural death
- Stroke or transient ischemic attack
- Thromboembolism
- Valve injury
- Vascular injury

3.4 Residual risks associated with the study, as identified in the risk analysis report

The risks in this study are similar to the risks associated with standard RF ablation procedure for OTVA.

3.5 Risks associated with participation in the clinical study

Participation in this study does not provide additional risk to the subjects who will nevertheless undergo RF ablation for OTVA. No additional device or catheter will be inserted during the procedure, nor should the procedure time be lengthened due to participation in this study. As with any interventional procedure, participation in this study has risks and complications that are associated or anticipated with percutaneous vascular access and catheter ablation.

3.6 Risk-to-benefit rationale

There is no additional risk more than the risks associated with standard RF ablation procedure for OTVA. Findings from this study may help physicians to develop more efficient ablation strategy and potentially benefit future patients.

4.0 STUDY DESIGN

4.1 Purpose

The purpose of this clinical study is to investigate the value of unipolar and bipolar EGM for predicting the successful ablation site for idiopathic OTVA.

4.2 Study Design and Scope

The study is an acute, non-randomized, feasibility study.

- Approximately 20 subjects meeting the inclusion criteria will be enrolled in this study
- The estimated time to enroll the required patients is 6 months
- The study will be conducted in one medical center, the Fuwai Hospital in Beijing, China.

Number of subjects required to be included in the study

Approximately 20 subjects meeting the inclusion criteria will be enrolled in this study.

Estimated time needed to enroll this subject population

The estimated time to enroll this subject population is 6 months. The study may continue up to 12 months, dependent on the rate of enrollment and the regulatory timeline.

4.3 Objectives

Primary Objective

Evaluate the predictive value of using reversed polarity in adjacent bipolar EGMs (bi-RP method) and unipolar EGM with QS morphology (uni-QS method) for identifying successful ablation site

Secondary Objective

Evaluate the feasibility of enhancing uni-QS method's performance by using its morphology characteristics such as descending slope and symmetry.

4.4 Endpoints

Primary Endpoint

Predictive values of the bi-RP method and uni-QS method for successful ablation

Secondary Endpoint

Predictive value of a new method by combining bi-RP and uni-QS for successful ablation.

4.5 Inclusion and Exclusion Criteria

A subject, who meets all of the inclusion criteria, and none of the exclusion criteria, is eligible to participate in this study.

All subjects enrolled in the clinical study (including those withdrawn from the clinical study or lost to follow-up) will be accounted for and documented, assigning an identification code linked to their names, alternative identification or contact information.

This log will be kept up to date throughout the clinical study by the principal investigator or his/her authorized designee. To ensure subject privacy and confidentiality of data this log must be maintained throughout the clinical study at the clinical site.

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

Inclusion Criteria

Subjects are eligible for clinical study participation if they meet all of the following inclusion criteria:

- Patients scheduled to undergo ablation for idiopathic OTVA
- Have the ability to provide informed consent for study participation.

Exclusion Criteria

Patients will be excluded from the study if they meet any of the following exclusion criteria:

- Be currently participating in any other investigational studies
- Be less than 18 years of age
- Be pregnant
- Has any other conditions that are not suitable for catheter ablation (including but are not limited to active whole-body infection or sepsis, coagulation or hemorrhage disorder history)

4.6 Subject Population

Subject Screening

All subjects presenting at the investigational site can be screened by a member of the investigational team previously trained on the CIP and delegated to do so.

Subjects who do not meet the inclusion/exclusion criteria will not be eligible to participate in this study.

Subjects meeting the inclusion/exclusion criteria will be fully informed about the study and asked to participate in the study. In case the subject agrees, a duly signed and dated ICF will be obtained.

Point of Enrollment

Subjects are considered enrolled in the study from the moment the subject has provided written ICF. (Refer to section 4.7 for the Informed Consent Process).

4.7 Informed Consent Process

General process

Prior to enrolling in the clinical study and conducting study-specific procedures, all subjects will be consented, as required by applicable regulations and the center's IRB/EC. Informed consent must be obtained from each subject prior to any study related procedures. The consent form must be signed and dated by the subject and by the person obtaining the consent.

The principal investigator or his/her authorized designee will conduct the Informed Consent Process. 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 in the clinical study.

The subject shall be provided with the informed consent form that is written in a language that is understandable to the subject and has been approved by the center's IRB/EC. Failure to obtain informed consent from a subject prior to study enrollment should be reported to St. Jude Medical within 5 working days and to the reviewing center's IRB/EC consistent with the center's IRB/EC reporting requirements.

5.0 DEVICE UNDER INVESTIGATION

5.1 Device Description

All the devices and systems (including software) used in this study are commercially approved in China. Including the following items:

- Any standard fluoroscopy equipment used in the Fuwai Hospital
- Any standard EP recording systems used in the Fuwai Hospital
- Any SJM quadripolar ablation catheters (e.g. the Safire Ablation Catheter)
- Any SJM ablation therapy hardware (e.g. the 1500T series Cardiac Ablation Generator, Cool Point Irrigation Pump)
- The SJM Ensite Velocity Cardiac Mapping System

5.2 Device Accountability (if applicable)

Device accountability is not required.

5.3 Device Handling & Storage

All products used in this study are commercially approved.

6.0 PROCEDURES

6.1 Study Flow Chart

Refer to section 1.1 for the study flow chart

6.2 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 St. Jude Medical receives written approval from the IRB/EC and relevant regulatory authorities and all required documents have been collected from the Fuwai Hospital.

Table 1: List of all study specific activities/procedures

Visit / Study Activity	Enrollment	Ablation Procedure
Informed Consent Process	X	
Verification of Inclusion and Exclusion Criteria	X	
Demographics and Medical History	X	
12-lead ECG	X	
Record Unipolar EGM during mapping		X
Record Bipolar EGM during mapping		X
Record successful/unsuccessful ablation sites		X
Adverse Event	(X)	(X)
Withdrawal	(X)	(X)
Deviation	(X)	(X)
Death	(X)	(X)

X: Mandatory CRFs
(X) : CRF will be completed if applicable

The following table lists all Case Report Forms (CRFs) that are to be completed during the respective visits. Mandatory CRFs are identified with an "X". CRFs that are optional or have to be completed only in case of a certain event (i.e. Death) are marked with an "(X)"

Table 2: Case report forms

Visit / CRFs	Enrollment	Ablation Procedure
Enrollment	X	
Baseline	X	
Ablation Procedure		X
Adverse Event	(X)	(X)
Withdrawal	(X)	(X)

Visit / CRFs	Enrollment	Ablation Procedure
Deviation	(X)	(X)
Death	(X)	(X)

X: Mandatory CRFs
(X) : CRF will be completed if applicable

6.3 Enrollment Visit

Patient Informed Consent Process

The following enrollment activities are performed after the subject has been screened and must occur before any study procedure/visit.

- The principal or delegated study personnel are responsible for screening all potential subjects to determine subject eligibility for the study
  - Inform the eligible patient verbally about the investigation and provide the information sheet and consent to the patient.
  - Provide ample time to the patient to read and understand the information sheet and PIC and to consider participation in the clinical investigation.
  - Obtain the signature and date from the eligible patient on the Ethics Committee (EC) approved PIC.
  - If an eligible patient does not sign and date the PIC, he cannot participate in the investigation. No further protocol required activities are performed.
  - Obtain the signature and date from the PI or delegated investigator on the EC approved PIC.
  - The subject is enrolled in the investigation when the patient signed the EC approved PIC.
  - Provide one original signed version of the PIC to the subject (signed by both subject and investigator).
  - File second original signed version of the PIC in the Investigator Site Binder (ISB).

- Record enrollment information (name of the study, date of consent and Inclusion/exclusion information) in the hospital records and complete and submit the Enrollment CRF in a timely manner (recommended within 5 days)
- Notification of enrollment to the sponsor will take place only when the sponsor receives the enrollment form

NOTE: As soon as the subject signs the ICF, adverse events need to be reported according to the guidelines mentioned in section 8.2.

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 does not meet inclusion/exclusion criteria, the following actions will be taken.

If study procedure has not occurred:

- Document enrollment information (name of the study, date of consent and inclusion/exclusion) in the hospital records; complete the Enrollment and Withdrawal Forms. The form must be authorized / approved by the principal or delegated investigator.
  - Inform the subject about the withdrawal.
  - The EC/IRB and CA should be notified appropriately about any deviations with regards to obtaining the informed consent.

If study procedure has occurred:

- Document enrollment information (name of the study, date of consent and inclusion/exclusion) in the hospital records; complete the Enrollment and Withdrawal Forms. The form must be authorized / approved by the principal or delegated investigator.
  - Complete study deviation for inclusion/exclusion not met
  - Inform the subject about the withdrawal.
  - The EC/IRB and CA should be notified appropriately about any deviations with regards to obtaining the informed consent.

Demographics and Medical History

- Demographics - include subject's Age and Gender
- Medical History - include subject's height, weight, blood pressure (measurements taken during visit), cardiovascular history (most recent value closest to baseline visit), risk factors, relevant co-morbidities, previous cardiac procedures, VA diagnosis, and medication (only chronic cardiac related medication).

12-lead ECG

Standard 12-lead ECG will be collected. In addition, prior documentation of 12-lead ECG with VAs will be collected if available.

6.4 Ablation Procedure Visit

In case the patient's VA is not present and cannot be induced before the ablation procedure, the ablation should not be performed according to the 2009 EHRA/HRS Expert Consensus on Catheter Ablation of Ventricular Arrhythmias[1]. The following actions will be taken:

- Inform the subject about the withdrawal.
- Complete the Withdrawal CRF. The form must be authorized / approved by the principal or delegated investigator

The ablation procedure will be performed according to the Fuwai hospital's standard practice. During the ablation procedure, any clinical adverse events or protocol deviations are to be noted on the appropriate forms. The following information will be collected at the ablation procedure visit:

- Date of procedure

- The unipolar EGM, the bipolar EGM pairs as defined below, and the 12-lead surface ECG.
- Nonsuccessful and successful ablation sites tagged on the map.
- Acute success rate
- Indicate model and number of mapping and ablation catheters used in the procedure
- Adverse Events, Death, and/or Protocol Deviation notification (if applicable)

Mapping and EGM Recording

A quadripolar ablation catheter will be used to map the target site. Specifically, the unipolar EGM is recorded from the distal electrode (M1) of the mapping catheter and filtered at 0.5~100Hz. The bipolar EGMs are recorded from the distal (M1-M2), mid (M2-M3), and proximal (M3-M4) electrode pairs of the mapping catheter, respectively, and filtered at 30~500Hz. LAT is measured using the distal electrode pair and is defined as the interval between the initial sharp peak of the EGM and the onset of the VA QRS. The presence of the bi-RP is evaluated between the distal and mid electrode pairs and is defined as a rapid simultaneous deflection in the opposite direction of the initial part of the bipolar EGM occurring before the onset of the VA QRS. All the unipolar EGM, bipolar EGMs, and the 12-lead surface ECG will be displayed on the monitor for the physician's reference and stored on the electrophysiology recording system and on the Ensite Velocity mapping system for off-line analysis. To guarantee accurate electroanatomic activation mapping and to avoid annotation of catheter-induced premature ventricular contractions (PVCs), the VA QRS morphology of each acquired mapping point will be compared to a 12-lead QRS template of the clinical arrhythmia.

Ablation

Radiofrequency energy will be applied at 30W with a maximum temperature of 55 ^{o}C for regular ablation catheter, and 35 to 40W with a maximum temperature of 43 ^{o}C for irrigated ablation catheter. If the VA is not abolished within 10 seconds of RF ablation, the energy application will be terminated and the ablation site will be tagged as a nonsuccessful site on the map. If the VA is abolished within 10 seconds, the energy application will be continued for a total of 90 seconds and the site will be tagged as a successful site on the map. The procedure endpoint is reached when the targeted VA did not occur spontaneously after a waiting period of 30 minutes and could not be induced by electrical programmed stimulation before and after isoproterenol infusion and Valsalva maneuver.

6.5 Scheduled Follow-ups

No follow-up visits or records are required for this study.

6.6 Description of activities performed by Sponsor Representatives

Trained sponsor personnel may perform certain activities to ensure compliance to the clinical investigational plan and may provide technical expertise.

Sponsor personnel will not:
- Perform the informed consent process
- Practice medicine

- Provide medical diagnosis or treatment to subject
- Discuss a subject's condition or treatment with a subject without the approval and presence of a health care practitioner
- Independently collect clinical study data
- Complete or sign study's Case report Forms

6.7 Subject study completion

When the subject's participation in the clinical study has been completed, the subject will return to the medical care as per physician's recommendation.

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

All foreseeable factors that may compromise the outcome have been taken into account by clinical study design and well-defined subject selection criteria.

6.9 Criteria and Procedures for Subject Withdrawal or Discontinuation

Subjects must be informed about their right to withdraw from the study at any time and for any reason without sanction, penalty or loss of benefits to which the subject is otherwise entitled and withdrawal from the study will not jeopardize their future medical care or relationship with the investigator. Subjects will be asked to specify the reason for the withdrawal, but have the right not to answer.

The investigator may decide to withdraw a subject from the study at any time with reasonable rationale. The subject's future care will not be influenced by a decision, voluntary or otherwise, to withdraw from the study. All reasonable efforts should be made to retain the subject in the clinical study until completion of the study.

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

- Subject refuses to continue participating in the study
- Subject does not meet the inclusion/exclusion criteria and does not require additional follow-up for safety reasons.
- Subject is deceased (cause must be documented)
- Subject's non-compliance
- Subject's participation is terminated by the PI or investigator, although the subject consented, since participation is no longer medically appropriate
- Subject's VA is not present or inducible before the ablation procedure

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

When subject withdrawal from the clinical study is due to an adverse event the subject will be followed until resolution of that adverse event or determination that the subject's condition is stable. The status of the subject's condition should be documented at the time of withdrawal.

7.0 COMPLIANCE TO CIP

7.1 Statements of Compliance

The study will be performed in accordance with the most current versions of the World Medical Association (WMA) Declaration of Helsinki, ISO14155 and any regional and/or national regulations and will be compliant to this International Standard and any regional and national regulations, as appropriate.

The investigator will not start enrolling subjects or requesting informed consent from any subject prior to obtaining IRB/EC approval and Competent Authority approval, if applicable, and authorization from the sponsor in writing for the study.

In case additional requirements are imposed by the IRB/EC or Competent Authority, those requirements will be followed, if appropriate. If any action is taken by an IRB/EC, and regulatory requirements with respect to the study, that information will be forwarded to St. Jude Medical.

As sponsor, St. Jude Medical has taken up general liability insurance in accordance with the requirements of the applicable local laws. Appropriate country representative will be utilized to understand the requirements for the type of insurance that will be provided for subjects, such information will be incorporated into the informed consent, as applicable.

If required, additional subject coverage or a study specific insurance will be provided by the Sponsor as well.

7.2 Adherence to the Clinical Investigation Plan

A deviation is defined as an event where the clinical investigator, site personnel, sponsor or sponsor representative did not conduct the clinical study according to the Clinical Investigational Plan, IRB/EC requirements or the Investigator Agreement. The investigator is not allowed to deviate from the CIP, except as specified under emergency circumstances.

In some cases, failure to comply with the CIP may be considered failure to protect the rights, safety and well-being of subjects, since the non-compliance exposes subjects to unreasonable risks. For example, failure to adhere to the inclusion/exclusion criteria: these criteria are specifically defined by the Sponsor to exclude subjects for whom the device is not beneficial and the use involves unreasonable risks. This may be considered failure to protect the rights, safety and well-being of the enrolled subject. Similarly, failure to perform safety assessments intended to detect adverse events may be considered failure to protect the rights, safety and well-being of the enrolled subject. Investigators should seek minimization of such risks by adhering to the CIP.

Simultaneously, in the event that adhering to the CIP might expose the subject to unreasonable risks, the investigator is also required to protect the rights, safety and well-being of the subject by intentionally deviating from the requirements of the CIP, so that subjects are not exposed to unreasonable risks.

It is the responsibility of the investigator to provide adequate medical care to a subject enrolled in a study.

Regulations require that the PI maintain accurate, complete, and current records, including documents showing the date of and reason for every deviation from the Clinical Investigational Plan. Relevant information for each deviation will be documented on a Deviation Case Report Form. The site will submit the CRF to St. Jude Medical.

Regulations require Investigators obtain approval from St. Jude Medical and the IRB/EC [as required] before initiating changes in or deviations from the protocol, except when necessary to protect the life or physical well-being of a subject in an emergency.

Prior approval must be requested when the PI anticipates, contemplates, or makes a conscious decision to depart from the CIP, except when unforeseen circumstances are beyond the investigator's control (e.g. a subject who fails to attend a scheduled follow-up visit, a subject is too ill to perform a CIP-required test, etc.). All deviations, including those beyond the investigator's control, must be reported on a CRF.

To obtain approval, the Principal Investigator may call or email and discuss the potential deviation with St. Jude Medical or designee prior to initiating any changes.

All deviations must be reported to appropriate regulatory authorities in specified timelines (if appropriate).

7.3 Repeated and serious non-compliance

In the event of repeated non-compliance or a one-time serious non-compliance, as determined by the Sponsor, a Clinical Research Associate or clinical representative 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.

8.0 ADVERSE EVENT

8.1 Definitions

Medical device

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

- 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
- 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

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 study.

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

Serious Adverse Event (SAE)

An adverse event that led to:

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

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

Adverse Device Effect (ADE)

An adverse event related to the use of an investigational medical device.

This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device.

This definition includes any event resulting from the use error or from intentional misuse of the investigational medical device.

Serious Adverse Device Effect (SADE)

Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.

8.2 Procedure for assessing, recording and reporting adverse events

Safety surveillance within this study and the safety reporting both performed by the investigator, starts as soon as the subject is enrolled in this study (date of signature of the informed consent). The safety surveillance and the safety reporting will continue until the last investigational visit has been performed, the subject is deceased, the subject/investigator concludes his participation into the study or the subject/investigator withdraws the subject from the study, except as otherwise specified in the CIP.

All adverse event data including deaths will be collected throughout the clinical study by the investigator and reported to the Sponsor on a dedicated CRF.

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:

- All Serious Adverse Events whether or not device/procedure related (SAEs and SADEs)
- Adverse Device Effects (ADE) Note: ADEs include procedure related events as well.
- Death events

All above events will be reported to the Sponsor, as soon as possible, but no later than 72 hours of first learning of the event.

The Sponsor will ensure that all events are reported to the relevant authorities as per regulations.

Should an AE occur, the investigator is requested to record AE information in the hospital records, document the information into the Adverse Event CRF according to the timelines mentioned above. Refer to Table 2 "Case Report Forms".

Additional information such as clinic notes or other forms of medical records may be requested, when required, by the Sponsor in order to support the appropriate classification of the AEs and 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 adverse events will be reported as per applicable regulatory requirements.

8.3 Subject Death

Procedure for recording and reporting subject death

All subject deaths are to be documented and reported to the sponsor within 72 hours after becoming aware of the event.

Should a death event occur, the investigator is requested to record death information in the hospital records, immediately document the information on the Death CRF and submit it to SJM. All subject deaths are to be documented and reported to the sponsor within 3 days after becoming aware of the event.

In order for the data related to deaths to be appropriately analyzed and adjudicated, the investigator is required to provide SJM with the appropriate source documentation of the death such as clinic notes or other forms of medical records.

A pre-procedure death is defined as death occurrs before the start of the ablation procedure. A peri-procedure death is defined as death occurs after the start but on the day of the ablation procedure. A post-procedure death is defined as death occurs after the day of the ablation procedure.

An Adverse Event CRF should be completed in addition to the Patient Death CRF only if the patient death is associated with an adverse event. Otherwise, if there are no AEs associated with death, the completion of Patient Death CRF is sufficient.

The patient's death is an Early Conclusion of the subject's participation in the study. Therefore, beside completion of a Death CRF, the investigator is required to complete the Withdrawal form.

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

8.4 COMPLAINT

Complaints are defined as an inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance. These include malfunctions, use errors and inadequate labeling.

Complaint reporting to sponsor: As this is a trial utilizing a market-released product, the investigator should notify the SJM Postmarket Surveillance Department by emailing the information about the complaint to the local country office or to: complaints_amplatzer@sjm.com or calling 1 6517565400. Please contact the local SJM representative for any questions regarding the complaint reporting.

9.0 DATA MANAGEMENT

Overall, the Sponsor will be responsible for the data handling.

The sponsor and/or its affiliates will be responsible for compiling and submitting all required reports to governmental agencies.

Data will be analyzed by the Sponsor and may be transferred to the Sponsor's locations outside of China and/or any other worldwide regulatory authority in support of a market-approval application.

St. Jude Medical respects and protects personally identifiable information that we collect or maintain. As part of our commitment, St. Jude Medical is certified to the U.S. - European Union Framework and U.S. – Swiss Safe Harbor Framework Agreements regarding human resources and subject clinical trial personal information. The privacy of each subject and confidentiality of his/her information will be preserved in reports and when publishing any data. Confidentiality of data will be observed by all parties involved at all times throughout the clinical study. All data will be secured against unauthorized access.

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

9.1 Data Management Plan

CRF data will be captured in a validated electronic database management Oracle Clinical system hosted by St. Jude Medical. All received data for the study will be entered by trained and qualified St. Jude Medical personnel. An electronic audit trail will be used to track any subsequent changes of the entered data.

9.2 Document and data control

Traceability of documents and data

The investigator shall ensure accuracy, completeness, legibility and timeliness of the data reported to the sponsor on the CRFs and in all required reports. Where copies of the original source document as well as print outs of original electronic source documents are retained, these shall be signed and dated by a member of the investigation site team with a statement that it is a true reproduction of the original source document.

Recording data

Source documents will be created and maintained by the investigational site team throughout the clinical study.The data reported on the CRFs will be derived from, and be consistent with, these source documents, and any discrepancies will be explained in writing.

The CRFs will be signed and dated by the authorized site personnel. Any change or correction to data reported on a paper CRF will be dated, initialed and explained if necessary, and will not obscure the original entry.

Review of data
The clinical investigation will be monitored by reviewing the CRFs approved by the investigators. The following activities will occur:

- All CRFs will be reviewed for completeness and accuracy after uploading into the database.
- The investigator (co-investigator) and/or delegate is notified regarding any missing or unclear/inconsistent data.

10.0 REGULATORY INSPECTIONS

The investigator and/or delegate should contact St. Jude Medical immediately upon notification of a governmental agency inspection at the site. A clinical monitor or designee will assist the investigator and/or delegate in preparing for the audit.

An investigator who has authority to grant access will permit authorized governmental agency employees, at reasonable times and in reasonable manner, to enter and inspect any establishment where devices are held (including any establishment where devices are used or where records or results are kept).

An investigator, or any person acting on behalf of such a person with respect to the study, will permit authorized governmental agency employees, at reasonable times and in reasonable manner, to inspect and copy all records relating to the study.

An investigator will permit authorized governmental agency employees to inspect and copy records that identify subjects, upon notice that governmental agency has reason to suspect that adequate informed consent was not obtained, or that reports required to be submitted by the investigator, to the Sponsor or IRB/EC have not been submitted or are incomplete, inaccurate, false or misleading.

11.0 STATISTICAL CONSIDERATIONS

11.1 Statistical design, hypotheses, method and analytical procedures

This study is an acute, prospective, non-randomized, feasibility study.

11.2 Sample size

This feasibility study is expected to be conducted in the Fuwai Hospital, Beijing, China. It is designed to investigate 20 subjects meeting the inclusion criteria. As a feasibility study, there is no statistical-based sample size. Because this study does not require follow-up visits, attrition (i.e. incomplete data set due to deviation from protocol) is anticipated to be low - in approximately 5% of patients. In case of substantial drop-out rate (more than 10%), an increase in population will be conducted by amendment.

11.3 The provision for an interim analysis, when applicable

An interim analysis may be conducted when the enrollment total count is greater than 10.

11.4 The treatment of missing, unused or spurious data, including drop-outs and withdrawals

In case when a drop-out or withdrawals occurs, the subject's data will not be included in the study result analysis.

12.0 DOCUMENT RETENTION

The principal investigator (PI) will maintain all clinical study documents from prior, during and (as specified) after the clinical study on file at the site for a minimum of 2 years after the termination of this study, or longer as per local laws, or when it is no longer needed to support a marketing application, whichever is later.

The PI must contact the sponsor prior to destroying or archiving off-site any records and reports pertaining to this study to ensure that they no longer need to be retained on-site.

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

All data and documents will be made available on request of the relevant authorities in case of an audit.

The sponsor will archive and retain all essential clinical study documents from prior, during and (as specified) after the clinical study as per requirements.

13.0 AMENDMENTS TO CLINICAL INVESTIGATIONAL PLAN

Study related documents such as, the CIP, CRFs, ICFs and other subject information, or other clinical study documents will be amended as needed throughout the clinical study, and a justification statement will be included with each amended section of a document. Proposed amendments to the CIP will be agreed upon between the Sponsor and the coordinating investigator (if applicable).

The amendments to the CIP and the subject's ICF will be notified to, or approved by, the IRB/EC and regulatory authorities, if required. The version number and date of amendments will be documented.

The amendment will identify the changes made, the reason for the changes and if it is mandatory or optional to implement the amendment.

Any amendment affecting the subject requires that the subject be informed of the changes and a new consent be signed and dated by the investigator at the subject's next follow up.

Changes to, or formal clarifications of, the CIP will be documented in writing and provided to the investigators. This information will be incorporated when an amendment occurs.

14.0 INVESTIGATION SUSPENSION OR TERMINATION

14.1 Premature termination of the whole clinical study or of the clinical study in one or more investigational sites.

The Sponsor reserves the right to stop the study at any stage, with appropriate written notice to the investigator.

Possible reasons for early termination of the study by the sponsor, either at local, national or international level, may include, but are not limited to:

- The device / therapy fails to perform as intended
- Occurrence of USADE which cannot be prevented in future cases
- Sponsor's decision
- Recommendation from DSMB to Steering committee and Sponsor
- Request from Regulatory bodies
- Request of Ethics Committee(s)
- Concern for subject safety and welfare
- Failure to secure subject Informed Consent prior to any investigational activity
- Failure to report unanticipated adverse device effects within 72 hours to St. Jude Medical and the EC
- Repeated non-compliance with this CIP or the Clinical Trial Agreement
- Inability to successfully implement this CIP
- Violation of the Declaration of Helsinki 2008
- Violation of applicable national or local laws and regulations
- Falsification of data, or any other breach of ethics or scientific principles
- Loss of or unaccounted use of investigational device inventory

The study will be terminated according to applicable regulations.

The investigator may also discontinue participation in the clinical study with appropriate written notice to the Sponsor.

Should either of these events occur, the investigator will return all documents to the sponsor; provide a written statement as to why the premature termination has taken place and notify the IRB/EC and/or the Competent Authority (if applicable). Follow-up for all enrolled subjects will be as per CIP requirements.

A Principal Investigator, IRB/EC or regulatory authority may suspend or prematurely terminate participation in a clinical study at the investigational sites for which they are responsible.

If suspicion of an unacceptable risk to subjects arises during the clinical study or when so instructed by the IRB/EC or regulatory authority, St. Jude Medical may suspend the clinical study as appropriate while the risk is assessed. St. Jude Medical will terminate the clinical study if an unacceptable risk is confirmed.

St. Jude Medical will consider terminating or suspending the participation of a particular investigational site or investigator in the clinical study if monitoring or auditing identifies serious or repeated deviations on the part of an investigator.

If suspension or premature termination occurs, the terminating party will justify its decision in writing and promptly inform the other parties with whom they are in direct communication. The Principal Investigator and St. Jude Medical will keep each other informed of any communication received from IRB/EC or regulatory authority.

If for any reason St. Jude Medical suspends or prematurely terminates the study at an individual investigational site, St. Jude Medical will inform the responsible regulatory authority, as appropriate, and ensure that the IRB/EC are notified, either by the Principal Investigator or by St. Jude Medical. If the suspension or premature termination was in the interest of safety, St. Jude Medical will inform all other Principal Investigators.

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

14.2 Resuming the study after temporary suspension

When St. Jude Medical concludes an analysis of the reasons for the suspension, implements the necessary corrective actions, and decides to lift the temporary suspension, St. Jude Medical will inform the Principal Investigators, IRB/EC, or regulatory authority, where appropriate, of the rationale, providing them with the relevant data supporting this decision.

Concurrence will be obtained before the clinical study resumes from the IRB/EC or regulatory authority where appropriate.

If subjects have been informed of the suspension, the Principal Investigator or authorized designee will inform them of the reasons for resumption.

14.3 Study conclusion

The study will be concluded when:

- All sites are closed AND
- The Final report generated by St. Jude Medical has been provided to sites or St. Jude Medical has provided formal documentation of study closure

15.0 PUBLICATION POLICY

The results of the clinical study will be submitted, whether positive or negative for publication.
A 'Publication Agreement' will be signed between the Principal Investigator and the Sponsor either as a separate Publication Agreement or within the Clinical Trial Agreement.

This study will be posted on ClinicalTrials.gov and results will be posted on ClinicalTrials.gov as required.

16.0 BIBLIOGRAPHY

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APPENDIX A: ABBREVIATIONS

Select or add abbreviations used

Abbreviation	Term
ADE	Adverse Device Effect
AE	Adverse Event
AF	Atrial Fibrillation
ASADE	Anticipated Serious Adverse Device Effect
CA	Competent Authority
CCI	Clinical Coordination Investigator
CIP	Clinical Investigational Plan
CRF	Case Report Form
CPRB	Clinical Project Review Board
DMP	Data Management Plan
EC	Ethics Committee
ECG	Electrocardiogram
EGM	Electrogram
EMEA	Europe, Middle East, Africa
GP	General Practitioner
ICF	Informed Consent Form
ICMJE	International Committee of Medical Journal Editors
IRB	Institutional Review Board
ISB	Investigator Site Binder
ISO	International Organization for Standardization
LAT	Local Activation Time
NA	Not Applicable
OTVA	Outflow Tract Ventricular Arrhythmia
PI	Principal Investigator
PVI	Pulmonary Vein Isolation
RF	Radiofrequency
RFCA	Radiofrequency Catheter Ablation
RP	Reversed Polarity
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SC	Steering Committee
SJM	St. Jude Medical
USADE	Unanticipated Serious Adverse Device Effect
WMA	World Medical Association

APPENDIX B: CIP REVISION HISTORY

Revision History				
Amendment Number	Version	Date	Rationale	Details
Not Applicable	VerA	14AUG2015	First release of CIP	NA

Appendix C: List of Clinical Investigation Sites and IRB/EC

Site Name: Fuwai Hospital
Address: No. 167 Beilishi Road,
Xicheng District, Beijing
China

Appendix D: Sample Informed Consent

A sample Patient Informed Consent Form will be provided under separate cover.

Appendix E: Case Report Forms

The final Case Report Forms will be provided under separate cover.