Abbott	Clinical Investigation Plan Cover Page

NCT Number: NCT03906461
LSI Workflow
LSI (Lesion Index) Workflow Observational Study
Study Document No: ABT-CIP-10276
Version B
Date: 04-MAR-2019

Sponsor	Abbott 5050 Nathan Lane North Plymouth, MN 55442 USA

Clinical Investigation Plan

ABT-CIP-10276
LSI Workflow

Version Number	B
Date	March 4, 2019
Planned Number of Sites	10 sites
Clinical Investigation Type	Prospective, multicenter, post-market, single-arm, observational study
Abbott Medical Expert	[redacted]
Sponsor	Abbott 5050 Nathan Lane North Plymouth, MN 55442 USA
Electronic Data Capture Software	Oracle Clinical, Remote Data Capture
CIP Author of Current Version	[redacted]

[redacted]

Clinical Investigation Plan

SITE PRINCIPAL INVESTIGATOR SIGNATURE PAGE

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

Site Principal Investigator

Printed name:
Signature:
Date:

Clinical Investigation Plan

TABLE OF CONTENTS

Clinical Investigation Plan

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Clinical Investigation Plan

Clinical Investigation Plan

COMPLIANCE STATEMENT:

This clinical investigation will be conducted in accordance with this Clinical Investigation Plan, the Declaration of Helsinki, applicable Good Clinical Practices and regulations (e.g., US 21 CFR Part 50, 21 CFR Part 56, 21 CFR Part 812 and OUS ISO14155:2011) and the appropriate local legislation(s). The most stringent requirements, guidelines or regulations must always be followed. The conduct of the clinical investigation will be approved by the appropriate Institutional Review Board (IRB)/Ethics Committee (EC) of the respective investigational site and by the applicable regulatory authorities (e.g., FDA, PMDA, MHRA, etc.).

Clinical Investigation Plan

1.0 INTRODUCTION

This document is the clinical investigation plan (CIP) for the LSI Workflow Study. This clinical study is a prospective, multicenter, post-market, single-arm, observational study designed to characterize the usage of the Lesion Index (LSI™) with the market-released TactiCath™ Contact Force Ablation Catheter, Sensor Enabled™ (TactiCath SE) in subjects with Paroxysmal Atrial Fibrillation (PAF) in a real-world environment. This clinical study is sponsored by Abbott.

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

1.1 Background and Rationale

1.1.1 Background

Atrial Fibrillation (AF) is an irregular and often rapid heart rhythm where the different chambers of the heart are not working together in a normal coordinated pattern, resulting in decreased blood flow. AF is a major cause of stroke, heart failure, sudden death, and cardiovascular morbidity. AF is also associated with high rates of hospitalization due to AF management, heart failure, myocardial infarction, and treatment associated complications.[7-9] It has been estimated that 20.9 million men and 12.6 million women have AF worldwide and that one in four middle-aged adults in the US and Europe will develop AF in their lifetime.[10-13]

Treatment for AF includes thromboembolic risk management, heart rate control, and heart rhythm control, which includes cardioversion and catheter ablation. The 2016 ESC AF Guideline indicates that catheter ablation of AF is effective in restoring and maintaining sinus rhythm in patients with symptomatic paroxysmal, persistent, and probably long-standing persistent AF in general as a second-line treatment after failure of or intolerance to antiarrhythmic drug therapy.[1] The 2017 HRS/EHRA/ECAS/APHRS/SOLAECE Expert Consensus on AF Ablation provided targeted contact force (CF) recommendations during ablation.[2] Contact force sensing catheter system provide operators with information on how much force is being applied by the catheter tip on the cardiac wall – a key factor in effective lesion formation.

The TactiCath™ Quartz and the TactiCath™ Sensor Enabled (SE) ablation catheters are ablation catheters with CF measuring capability. Measurement of CF between the catheter tip and the target tissue can help guide physicians during mapping and ablation procedures. The first recommendations for CF sensing during pulmonary vein isolation (PVI) procedures was provided for TactiCath Quartz. Data from several studies such as TOCCATA, EFFICAS I and EFFICAS II show that CF sensing is not only safe for use in PVI but also associated with lower rates of gap and atrial fibrillation (AF) recurrence.[14-18] The Force Time Integral (FTI™) is a linear calculation that combines CF and radiofrequency (RF) ablation time. The EFFICAS I and II studies established a minimum FTI threshold of 400 gram-seconds (gs) that was associated with significantly higher PVI success rates at 3-months.[14,16] The TOCCASTAR investigational device exemption (IDE) study provided evidence proving the safety and effectiveness of the TactiCath Quartz ablation catheter for the treatment of paroxysmal AF.[19] The TactiCath SE ablation catheter is the latest TactiCath contact force sensing catheter from Abbott, which incorporates a magnetic sensor for tracking with the EnSite Precision Mapping System and utilizes a new handle and shaft to improve catheter handling. The TactiSense IDE study showed that TactiCath SE has a similar safety profile as TactiCath Quartz – 12-month effectiveness data is pending. The TactiCath Post Approval Study is underway and currently has 2 years of data for all subjects showing the TactiCath Quartz catheter is safe and effective.

Clinical Investigation Plan

The TactiCath Quartz Ablation Catheter Clinical Compendium (available from Abbott) provides a thorough review of clinical outcomes for AF Ablation with Contact Force and the Force Time Integral. Current recommendations are to target a CF of 20g (range 10-30g) with a minimum CF value of 10g and a minimum FTI value of 400gs for any ablation points.[14,16]

The relationship between Power (P, Watts), Voltage (V, Volts), and Current (I, Amps) is expressed as P = I*V. Building on the concept of CF and FTI, the Lesion index (LSI™) is a proprietary index that combines CF, RF duration (S), and RF current into a single value: LSI = CF x S (RF Time) x I (Current). The LSI value expresses the gradual growth of lesion formation. All three sub-components are proportional to ~$(1 - e^{-t/\tau})$. Factors under an operator's control during an ablation procedure include CF, duration of ablation, and the power (Watts) setting of the RF generator. LSI combines these variables into a single value that is displayed in the EnSite™ contact force module on the EnSite Velocity™ or EnSite Precision™ Cardiac Mapping Systems and can be used (outside of the US), along with FTI, as the AutoMark lesion color or size metric. Additional evaluations of data generated in the EFFICAS I, EFFICAS II, and TOCCASTAR studies, suggest that use of LSI provides a more uniform lesion delivery and that the addition of LSI to the CF recommendations may lead to a higher rate of durable PVI[3,4], and long-term clinical success.[5,6]

1.1.2 Rationale for Conducting this Clinical Investigation

To date, there have been no Abbott-sponsored prospective clinical studies focused on LSI. However, data from three previous studies was retrospectively analyzed. Two additional non-Abbott-sponsored studies have presented results via meeting abstracts. Results are summarized in Appendix V. These studies agree that LSI correlates with successful acute (intra-procedural) and longer-term PVI – which in turn is considered strongly correlated with freedom from AF recurrence. The purpose of this study is to systematically gather data on the use of LSI in real-world clinical settings with the new TactiCath SE catheter.

2.0 CLINICAL INVESTIGATION OVERVIEW

2.1 Clinical Investigation Objective

2.1.1 Primary objective

The primary objective of this study is to characterize LSI achieved values for durable lesion formation using the TactiCath SE catheter in the different anatomical regions around the pulmonary veins (PVs) of the heart during RF ablation for the treatment of drug-refractory paroxysmal atrial fibrillation (PAF).

2.1.2 Secondary objective

Secondary objectives of this study are as follows:

- To characterize the use of EnSite Automap and AutoMark module software settings, including LSI threshold (OUS), contact force, time, power, flow, and AutoMark spacing using the TactiCath SE catheter for RF ablation for the treatment of drug-refractory PAF.
- To characterize LSI achieved values for lesions that reconnected versus those that were durable, both in an acute procedural setting as well as in patients who undergo additional ablations during the 12-month follow-up period after an index RF ablation procedure for the treatment of drug-refractory PAF.

Clinical Investigation Plan

2.2 Device(s) To Be Used in the Clinical Investigation

2.2.1 Name of the Device(s) Under Investigation

All devices used during this study must have regulatory clearance and will be used according to their Instructions for Use (IFU).

The following devices, listed in Table 1 and manufactured by St. Jude Medical (SJM), will be used in this clinical study:

Table 1. Devices to be used in the study

Device name	Model/Type
EnSite Precision™ Cardiac Mapping System	EE3000
EnSite Precision Software, v2.2 or greater	H702496
EnSite Precision Module, Sensor Enabled	H702473
EnSite Precision Module, Contact Force	H702500
EnSite Precision Surface Electrode Kit	EN0020-P
EnSite AutoMap Module	H702498
AutoMark Module	V1.0
Cool Point™ Pump v24 or greater	IBI-89003 (US) 85784 (OUS)
TactiSys™ Quartz Equipment	PN-004 400
TactiCath™ Contact Force Ablation Catheter, Sensor Enabled™	A-TCSE-D A-TCSE-F A-TCSE-J A-TCSE-DD A-TCSE-FF A-TCSE-JJ A-TCSE-DF A-TCSE-FJ

2.2.2 Indication for Use

Indications for use may be found in the appropriate device IFU. Indications for the use of TactiCath SE are described below.

United States:

The TactiCath™ Contact Force Ablation Catheter, Sensor Enabled™ is indicated for use in cardiac electrophysiological mapping and for the treatment of drug refractory recurrent symptomatic paroxysmal atrial fibrillation, when used in conjunction with a compatible radiofrequency (RF) generator and three-dimensional mapping system.

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Clinical Investigation Plan

Outside of the United States:

The TactiCath™ Contact Force Ablation Catheter, Sensor Enabled™ is indicated for use in cardiac electrophysiological mapping (stimulation and recording), and, when used in conjunction with a RF generator, for cardiac ablation of supraventricular arrhythmias in the right and left atrium, including atrial fibrillation.

2.2.3 Device Description and Intended Purpose

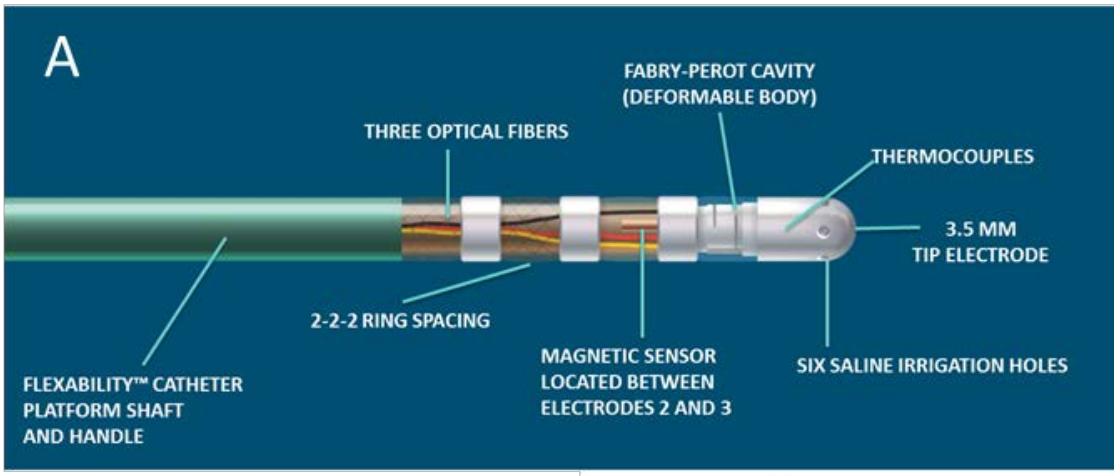
Please refer to the relevant IFUs for additional information regarding all devices used in this clinical investigation.

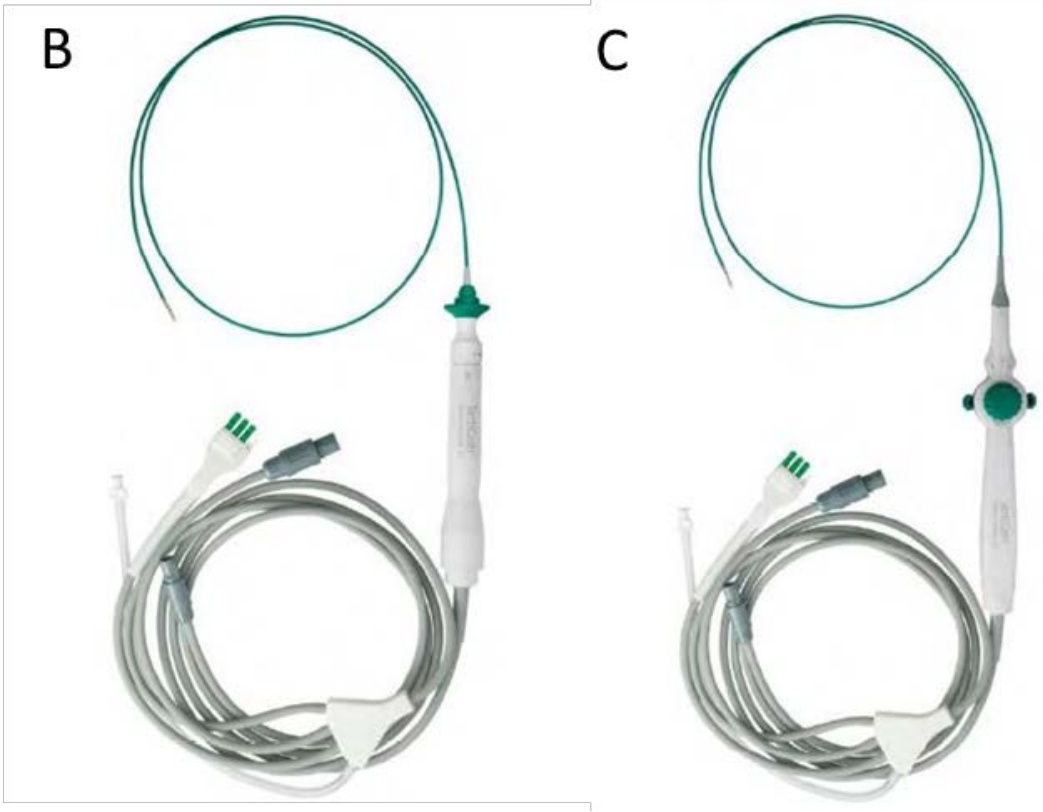
The TactiCath™ Contact Force Ablation Catheter, Sensor Enabled™ (TactiCath SE) is designed to facilitate electrophysiological mapping of the heart chambers and to transmit radiofrequency (RF) current to the catheter tip electrode for intracardiac ablation purposes. For ablation, the catheter is used in conjunction with a RF generator, an irrigation pump, and a dispersive pad (indifferent patch electrode). TactiCath SE is compatible with introducers or sheaths with a minimum diameter of 8.5 F. TactiCath SE is a sterile, single use catheter with a 7.5 F shaft and an 8 F distal section. It is constructed of thermoplastic elastomer material and noble metal electrodes.

The catheter has novel force and magnetic sensors (Figure 1A). It has a fluid lumen connected to open conduits within a 6-hole tip electrode for saline irrigation during the ablation procedure. For both uni-directional (Figure 1B) and bi-directional catheters (Figure 1C), the tip curvature is manipulated by the control mechanism located on the handle at the catheter's proximal end. To adjust the curve of the distal tip on the uni-directional catheter, the thumb control located on the handle may be pushed or pulled. To adjust the curve of the distal tip on the bi-directional catheter, the actuator may be used to deflect the catheter in either direction. The catheter interfaces with standard recording equipment and a compatible RF generator via the TactiSys Quartz Equipment using the optical connector and 19-pin electrical connector on the catheter. The catheters are available in eight distal curve shapes.

Clinical Investigation Plan

Figure 1. (A) Exposed View of TactiCath SE Tip. (B) Uni-Directional and (C) Bi-Directional TactiCath SE Catheter





Clinical Investigation Plan

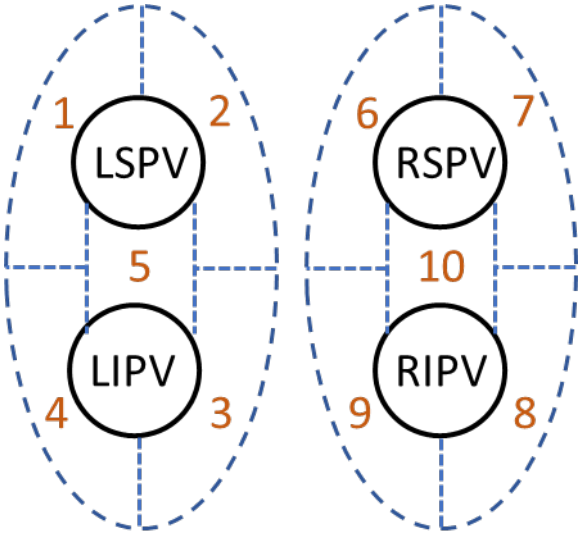
3.0 CLINICAL INVESTIGATION DESIGN

This is a prospective, multicenter, post-market, single-arm, observational study designed to quantify and characterize the usage of LSI with the TactiCath SE catheter in a real-world environment. This study will enroll approximately 150 patients at approximately 10 sites. Since endpoint evaluations will be descriptive, there are no statistical power considerations for this sample size.

Primary Endpoint

The primary endpoint is a summary of LSI achieved values for RF lesion formation in different anatomical regions of the heart around the pulmonary veins (PVs, see Figure 2). The areas around the left and right pairs of PVs will be each divided into 5 zones, with 4 zones representing four circumferential quadrants and the fifth zone representing the region between the pair of veins.

Figure 2. Numbered anatomical zones around the pulmonary veins (PVs). LSPV = Left Superior Pulmonary Vein; LIPV = Left Inferior Pulmonary Vein; RSPV = Right Superior Pulmonary Vein; RIPV = Right Inferior Pulmonary Vein.



Additional evaluations

- A summary of EnSite AutoMap and AutoMark module software settings, including LSI threshold (in OUS), contact force, time, power, flow, and AutoMark spacing
- Acute electrical isolation of PVs, 20 minutes after last RF ablation in PV region
- Device- or procedure-related SAEs within 7-days and 12-months of index procedure
- Freedom from documented AF/AFL/AT recurrence at 12-months post-index ablation, excluding a 90-day blanking period.
    - Freedom from AF/AFL/AT recurrence is defined as no documented episodes greater than 30 seconds with a 24-Holter.
- Proportion of patients with a repeat ablation up to 12-months post index procedure (excluding 90-day blanking period)
- Proportion of lesions generated during first-pass PVI that required touch-up* ablation

Clinical Investigation Plan

  - *In this CIP, a “touch-up” ablation is defined as an ablation occurring during the same procedure that is performed to close an identified gap in the first-pass ablations

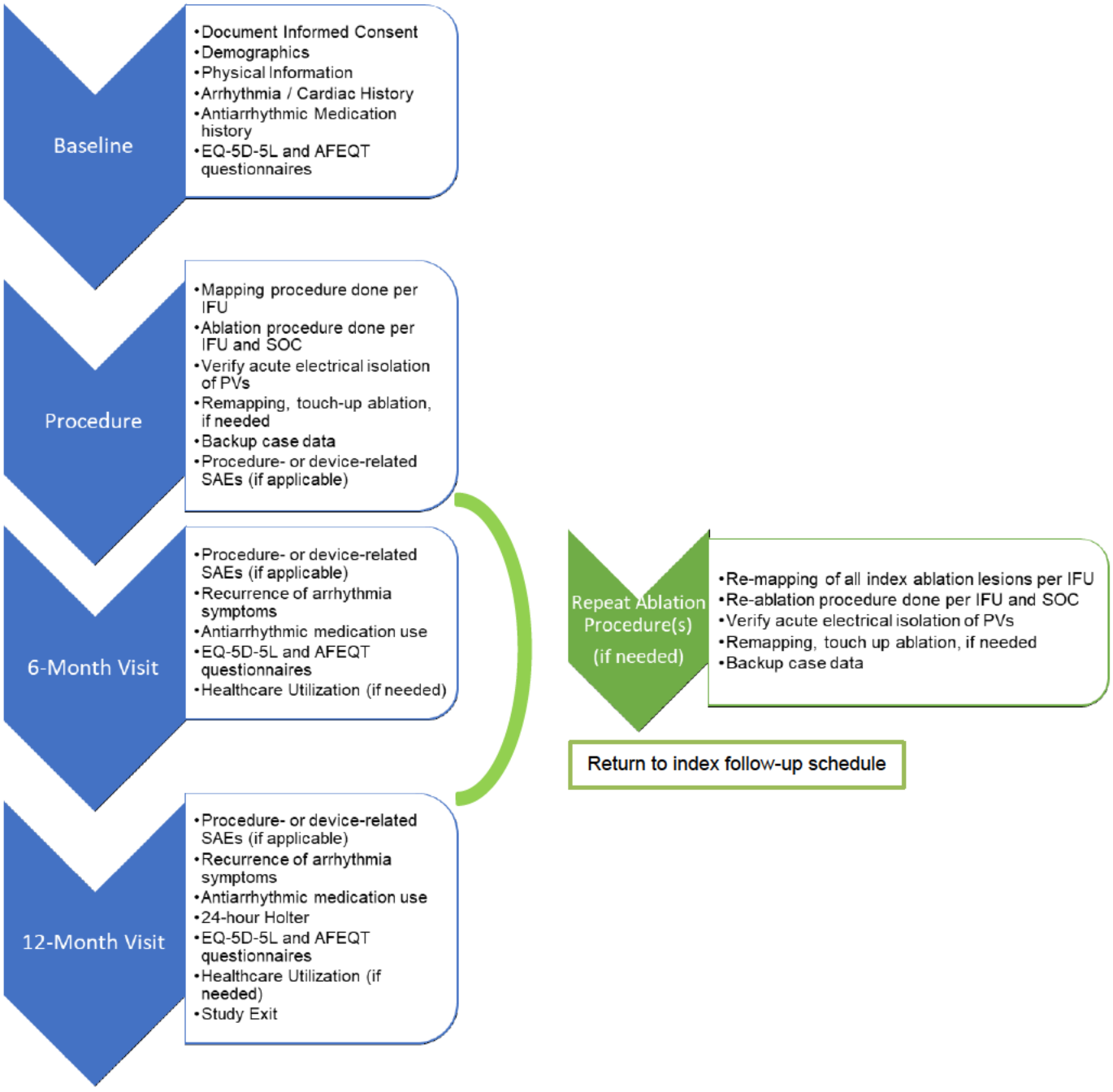
- Proportion of pulmonary veins (PVs) requiring touch-up ablation
- Proportion of patients who required at least one touch-up ablation during the index procedure
- In patients who undergo any repeat RF ablation procedures up to 12-months post index procedure, characterization of LSI achieved values for lesions that resulted in electrically conducting gaps versus those that were durable
- Overall procedure time and the subset of time elapsed for: first-pass PVI, any other ablations, and any touch-up ablations
- Overall RF ablation time and the subset of RF ablation time for: first-pass PVI, any other ablations, and any touch-up ablations
- Overall fluoroscopy time
- Changes in EQ-5D-5L and AFEQT quality of life scores at 6- and 12-months post index ablation, compared to baseline scores
- AAD use at 12-months
- Health care utilization (including number of unscheduled hospital outpatient/ER visits and inpatient hospitalizations due to arrhythmias) collected throughout the 12-month follow-up period

Clinical Investigation Plan

3.1 Clinical Investigation Procedures and Follow-up Schedule

Once eligibility is confirmed and a subject is consented, baseline information will be collected, and the subject will undergo the RF ablation procedure per physician discretion. Subjects will be followed for 12-months post procedure. The study visits will occur at baseline, procedure, 3-to-6-months post-ablation (referred to as "6 Months" in Figure 3), and 12-months post-ablation procedure. The subject will be exited from the study after completion of the 12-month follow-up visit. The visit schedule and related study assessments are summarized in Figure 3 and further detail provided in Section 6.

Figure 3: Clinical Investigation Flow Chart



Clinical Investigation Plan

Study visit windows:

- Baseline Visit, after Informed Consent
- Procedure Visit, preferably within 14 days but not more than 30 days of Informed Consent
- 3- to 6-Month* Follow-Up Visit, 90 to 183 ± 21 days after Procedure
- 12-Month Follow-Up Visit, 365 ± 21 days after Procedure
- Repeat Ablation**, any time after Procedure during follow-up period, at physician's discretion

*A follow-up visit must occur between 3- and 6-months post-index procedure (with a 21-day window). For readability, this follow-up visit will be referred to as the "6-Month" follow-up visit.

**Repeat ablations that occur within the 90-day blanking period will not be considered an effectiveness failure and will follow the repeat ablation procedure

3.2 Suspension or Early Termination of the Clinical Investigation

While no formal statistical rule for early termination of the clinical investigation for insufficient effectiveness of the device under investigation is defined, the Sponsor reserves the right to discontinue the clinical investigation 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:

- An oversight committee makes a recommendation to stop or terminate the clinical investigation (such as higher frequency of anticipated adverse device effects)
- Further product development is cancelled.

Should the clinical investigation be discontinued by the Sponsor, subjects will be followed per routine hospital practice with device-related SAEs reported to the Sponsor as per vigilance/commercial reporting requirements. The investigator shall return all clinical investigation materials to the Sponsor and provide a written statement to the IRB/EC (if applicable). All applicable clinical investigation documents shall be subject to the same retention policy as detailed in Section 11.5 of the CIP.

A Principal Investigator, IRB/EC or regulatory authority may suspend or prematurely terminate participation in the clinical investigation at the investigational site(s) 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 investigation at an individual site in the interest of safety, the Sponsor will inform all other Principal Investigators.

If suspension or premature termination occurs, the Principal Investigator or authorized designee will promptly inform the enrolled subjects at his/her site, if appropriate, and return patients to their standard medical treatment.

Clinical Investigation Plan

4.0 ENDPOINTS

Outcomes were selected, when possible, following the recommendations published in "Harmonized Outcome Measures for Use in Atrial Fibrillation Patient Registries and Clinical Practice"[24], which were endorsed by the Heart Rhythm Society Board of Trustees.

All endpoints and additional evaluations will be descriptive, there will be no hypothesis testing, and there are no statistical power considerations.

4.1 Primary Endpoint and Rationale

The primary endpoint is a summary of LSI values achieved for RF lesion formation in different anatomical regions of the heart around the pulmonary veins (PVs, see Figure 2).

4.2 Additional Evaluations

- A summary of EnSite AutoMap and AutoMark module software settings, including LSI threshold settings (in OUS), contact force, time, power, flow settings, and AutoMark spacing
- Acute electrical isolation of PVs, 20 minutes after last RF ablation in PV region
- Device- or procedure-related SAEs within 7-days and 12-months of index procedure
- Freedom from documented AF/AFL/AT recurrence at 12-months post-index ablation, excluding a 90-day blanking period.
    - Freedom from AF/AFL/AT recurrence is defined as no documented episodes greater than 30 seconds with a 24-Holter.
- Proportion of patients with a repeat ablation up to 12-months post index procedure (excluding 90-day blanking period)
- Proportion of lesions generated during first-pass PVI that required touch-up ablation
- Proportion of pulmonary veins (PVs) requiring touch-up ablation
- Proportion of patients who required at least one touch-up ablation during the index procedure
- In patients who undergo any repeat RF ablation procedures up to 12-months post index procedure, characterization of LSI achieved values for lesions that resulted in electrically conducting gaps versus those that were durable
- Overall procedure time and the subset of time elapsed for: first-pass PVI, any other ablations, and any touch-up ablations
- Overall RF ablation time and the subset of RF ablation time for: first-pass PVI, any other ablations, and any touch-up ablations
- Overall fluoroscopy time
- Changes in EQ-5D-5L and AFEQT quality of life scores at 6- and 12-months post index ablation, compared to baseline scores
- AAD use at 12-months
- Health care utilization (including number of unscheduled hospital outpatient/ER visits and inpatient hospitalizations due to arrhythmias) collected throughout the 12-month follow-up period

Clinical Investigation Plan

5.0 SUBJECT SELECTION AND WITHDRAWAL

5.1 Subject Population

This clinical investigation will enroll male and female subjects undergoing their first ablation procedure from the documented drug-refractory, paroxysmal atrial fibrillation (PAF) population. Subjects must meet all eligibility criteria and provide written informed consent prior to conducting any investigation-specific procedures not considered standard of care.

5.2 Subject Screening and Informed Consent

5.2.1 Subject Screening

Potential patients presenting at the clinical sites will be fully informed about the clinical investigation, following the established Informed Consent process (described in Section 5.2.2). Once a duly dated and signed Informed Consent form is obtained, the clinical investigation-specific screening procedures may begin.

Subjects must be screened for clinical investigation eligibility by a member of the site's clinical investigation team previously trained to the CIP and will be entered into a site-specific screening log.

In case the subject does not meet all inclusion criteria or meets any of the exclusion criteria, the subject is considered a screening point failure. The Principal Investigator or the delegated clinical investigation personnel will record the screening failure on a screening log as required.

Patients meeting general inclusion criteria and no exclusion criteria will be asked to sign an Informed Consent form if they wish to participate in the clinical investigation.

Subject data will be collected following informed consent into the clinical investigation.

5.2.2 Informed Consent

The Investigator or his/her authorized designee (if applicable) will conduct the Informed Consent process, as required by applicable regulations and the center's IRB/EC. This process will include a verbal discussion with the subject on all aspects of the clinical investigation that are relevant to the subject's decision to participate, such as details of clinical investigation procedures, anticipated benefits, and potential risks of clinical investigation participation. Subjects must be informed about their right to withdraw from the clinical investigation at any time and for any reason without sanction, penalty or loss of benefits to which the subject is otherwise entitled. Withdrawal from the clinical investigation will not jeopardize their future medical care or relationship with the investigator.

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. Financial incentives will not be given to the subject. 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 investigation-specific procedures. The signed original will be filed in the subject's medical record, 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 may significantly affect a subject's future health and medical care, the Principal Investigator or his/her authorized designee (if applicable) will provide this information to the subject. If relevant, the subject will be asked to confirm their continuing participation in the study by signing another informed consent.

For US sites:

In addition, an authorization for use and disclosure of the subject's protected health information, in accordance with the Health Insurance Portability and Accountability Act (HIPAA), must be obtained from the subject.

5.3 Eligibility Criteria

5.3.1 General Eligibility 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 of the inclusion criteria to be considered for the clinical investigation. If any of the exclusion criteria are met, the patient is excluded from the clinical investigation and cannot be enrolled.

5.3.2 Inclusion Criteria

5.3.2.1 General Inclusion Criteria

1. Subject must provide written informed consent prior to any clinical investigation related procedure.
2. Subject is at least 18 years of age.
3. Subject is willing and able to comply with the protocol-described evaluations and follow-up schedule.
4. Subject plans to undergo a pulmonary vein isolation (PVI) procedure due to symptomatic paroxysmal AF using RF ablation.
5. Subject is refractory or intolerant to at least one class I or class III anti-arrhythmic drug.
    - For the purposes of this study, "intolerant" includes either:
        i. Subject attempted the drug at any dose and either the subject or their physician chose to discontinue for any reason
        ii. Subject was offered the drug and refused to take for any reason

5.3.3 Exclusion Criteria

5.3.3.1 General Exclusion Criteria

1. Previous ablation or surgery in the left atria.

2. Has an implantable cardiac defibrillator (ICD), pacemakers without defibrillation capacity are allowable).
3. Participation in another clinical investigation that may confound the results of this study.
4. Pregnant or nursing.
5. Presence of other anatomic or comorbid conditions, or other medical, social, or psychological conditions that, in the investigator's opinion, could limit the subject's ability to participate in the clinical investigation or to comply with follow-up requirements, or impact the scientific soundness of the clinical investigation results.
6. Life expectancy less than 12 months.

5.4 Subject Enrollment

A patient is considered enrolled in the study after they have provided written informed consent, have been confirmed that they meet all the inclusion criteria and none of the exclusion criteria, and the mapping catheter has been inserted into their vasculature.

If a subject that is enrolled into the study is later found to have met exclusion criteria or not all inclusion criteria, they will continue follow-up in the study and their data will be included in the analysis population.

5.5 Subject Withdrawal

Each enrolled subject shall remain in the clinical investigation until completion of the required follow-up period; however, a subject's participation in any clinical investigation 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 3.2 (Suspension or Early Termination of the Study)

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 investigation. The subject's status (deceased/alive) must be reported at the time of withdrawal.

In case of subject withdrawal of consent, the site should make attempts to schedule the subject for a final clinical investigation visit. At this final follow-up visit the subject will undergo the assessments specified for the 12-month follow-up visit.

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.

Note: Telephone contact with a 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.

5.6 [redacted]

[redacted]

5.7 [redacted]

[redacted]

6.0 TREATMENT AND EVALUATION OF ENDPOINTS

6.1 Baseline Clinical Assessments

The following assessments and information will be collected at the baseline visit.

- Documentation of the informed consent process
- Confirmation of enrollment criteria
- Subject demographics

[redacted]

- Cardiovascular disease history (most recent value prior to baseline visit)
- Arrhythmia history including documentation of PAF diagnosis (as described in the inclusion criteria)
- Complete physical exam (if the requested physical exam data are available from a standard of care visit prior to consent, they may be used if they were done within 30 days prior to consent)
- Anti-arrhythmic drug (AAD) usage
- Presence of a left atrial appendage occluder
- Completion of the EQ-5D-5L and AFEQT questionnaires

It is recommended to follow pre-ablation anticoagulation guidelines from the 2017 HRS/EHRA/ECAS/APHRS/SOLAECE Expert Consensus Statement on Catheter and Surgical Ablation for Atrial Fibrillation.[2]

6.2 Index Procedure

The procedure will be performed according to the IFU of the EnSite Precision Cardiac Mapping System, the IFUs of the AutoMark and EnSite AutoMap modules, the IFU of the TactiCath SE catheter, and the respective IFUs of any other medical devices used during the procedure. The subject should be prepped for an electrophysiology study per the site's standard of care. If there is a thrombus noted, the procedure must be delayed until the thrombus has been resolved, or the subject must be withdrawn from the investigation no later than 30 days after the first index procedure attempt.

- A standard mapping procedure should be performed using a mapping catheter(s) of the operator's choice, as long as it follows the respective IFU(s) and is compatible with the EnSite system and AutoMap module.
- Ablation to achieve pulmonary vein isolation (PVI) must be conducted using the TactiCath SE catheter and the EnSite AutoMark module.
    - US only: Operators should choose their standard metrics for use with AutoMark. These settings will be collected.
    - OUS: Operators should use LSI as the color metric for AutoMark.
- The start and finish procedure times and the RF time of the first-pass PVI should be noted.
- PVI should be completed first. Then, subjects with documented atrial flutter, AT, or other SVT (spontaneous or induced) should undergo additional targeted ablation as clinically indicated following standard practice at the site. Additional ablations will be documented along with their additional procedure and RF ablation times.
- PVI must be verified via entrance block with a multipolar catheter at or beyond 20 minutes from the last ablation lesion for each vein. Isolation of PVs must be documented.
- Use of adenosine and/or isoproterenol is acceptable to assist in finding gaps.
- Cardioversion after PVI is allowed to assist with checking for isolation.
- If acute success of PVI is not achieved, a new map of the pulmonary vein region must be captured using the AutoMap module, if possible. The number and location of any reconnections or gaps should be noted.
- Touch-up ablations to close identified gaps should be performed if possible, unless the operator decides that it would be better medically not to do so. AutoMark should be used, if possible, following the same guidelines as for the initial lesion set.
- Re-mapping and touch-up ablation procedure and RF-ablation times should be noted.
- Data on total RF ablation time, total fluoroscopy time, and total procedure time will also be collected.

[redacted]

- The recorded procedure data from the EnSite system should be anonymized and backed up.

Trained Sponsor personnel may provide technical expertise and technical guidance on the use of the EnSite system and the TactiCath SE catheter. While Sponsor representatives may perform these activities, the Principal Investigator remains responsible for ensuring all clinical investigation data is collected as required per the CIP.

If for any reason the enrolled subject has the TactiCath SE inserted into their vasculature, but no ablation is performed, the subject will be followed for up to 30 days to assess safety, then exit the trial.

6.2.1 Re-ablation Treatment Procedures

Subjects experiencing a recurrence of arrhythmia symptoms* may undergo additional ablations procedures at the discretion of their treating physician, following standard practice at the site. Re-ablations that occur during the 90-day "blanking" period post-index procedure will not be considered treatment failures in outcome analyses. Any re-ablation procedures must be conducted following the same device guidelines as the index procedure (i.e. EnSite Precision AutoMap and AutoMark, TactiCath SE, etc.).

*Repeat procedures that only ablate CTI-dependent typical atrial flutter will be excluded from the re-ablation treatment procedures and requirements listed in this section but should be archived to the local EnSite system at the study site until the study is complete.

In general, any re-ablation procedure should follow the standard practice of the site, with the following additions:

- A standard mapping procedure that covers all areas ablated in a previous procedure will be performed using a mapping catheter(s) of the operator's choice, as long as it follows the respective IFU(s) and is compatible with the EnSite system and AutoMap module. AutoMap settings will be collected.
- The number and location of any reconnections or gaps will be noted by annotating the locations on the EnSite map and the CRF.
- Ablations to close identified gaps should be performed if possible, unless the operator decides that it would be better medically not to do so. AutoMark should be used, if possible, following the same guidelines as for the initial procedure.
- Any additional lesions deemed medically warranted, following standard practice at the site, can be created.
- PVI must be verified via entrance block with a multipolar catheter at or beyond 20 minutes from the last ablation lesion for each vein. Additional "touch-up" ablations to complete the PVI should be performed if needed. Isolation of PVs must be documented.
- Data on total RF ablation time, total fluoroscopy time, and total procedure time will be collected. Data will also be collected on the time (procedure and RF) required for the initial ablation set to isolate PVs (in this procedure), any additional ablations, and any "touch-up" ablations required due to incomplete PVI.
- The recorded procedure data from the EnSite system should be anonymized and backed up.

6.3 Post–procedure

It is recommended that sites follow the post ablation anticoagulation strategy recommendations from the 2017 HRS/EHRA/ECAS/APHRS/SOLAECE Expert Consensus Statement on Catheter and Surgical Ablation for Atrial Fibrillation[2].

Antiarrhythmic drug usage, SAEs, and protocol deviations will be documented prior to hospital discharge.

6.4 Follow-up Assessments

6.4.1 Follow-up for All Subjects (Clinic Visit)

In the clinic, subjects will undergo the following assessments described below at 6- and 12-months post-ablation procedure.

6-Month* (90 to 183 ± 21 days) and 12-Month (365 ± 21 days) Follow-up

- 24-hour Holter monitor (12-month follow-up only)
- Document device- and procedure-related SAEs and protocol deviations
- Document AAD usage
- Complete EQ-5D-5L and AFEQT questionnaires
- Healthcare utilization data, if needed

*A follow-up visit must occur between 3- and 6-months post-index procedure (with a 21-day window). For readability, this follow-up visit will be referred to as the "6-Month" follow-up visit.

Trained Sponsor personnel may provide technical expertise and technical guidance on the use of the Holter device. While Sponsor representatives may perform these activities, the Principal Investigator remains responsible for ensuring all clinical investigation data is collected as required per the CIP.

6.4.2 Patient Reported Outcome (PRO) Measures

The Site Coordinator or designee will administer patient-reported outcome questionnaires. It is important the subject understands the meaning of all words and instructions in the questionnaires. The subject should be instructed to ask any questions about the questionnaires if further explanation is needed. Once the questionnaires are completed, the Site Coordinator or designee will review for completeness to verify that all questions have been answered according to the directions provided.

The following PRO measures will be collected according to the CIP requirements.

- EQ-5D-5L
- AFEQT

The EQ-5D-5L[27] Questionnaire is a widely used validated questionnaire used to measure quality of life consisting of 6 questions. The subject is instructed to choose the option that best describes their health on the day of the assessment. The questionnaire takes approximately 5 minutes to complete.

The AF Effect on Quality of life survey, or AFEQT[28] questionnaire, is a reliable and responsive measure of quality of life, specifically for atrial fibrillation. It evaluates health related quality of life across three domains: symptoms, daily activities, and treatment concerns. It has an easy to use format with 20 questions on a seven-point Likert scale. It takes approximately 5 minutes to complete.

6.4.3 Schedule of Events

The Informed Consent process can take place at or before the baseline visit. The schedule of activities specific to this clinical study are described in the preceding sections and are summarized in Table 2.

Clinical Investigation Plan

Repeat ablation activities would only occur if a repeat procedure was necessary, as determined by treating physician. (X) indicates ‘if applicable’. All study visits must occur in-person.

Clinical Investigation Plan

Table 2. Schedule of Events

Study Activity	Time of Consent*	Baseline	Procedure	6-Month Visit **	12-Month Visit	Repeat Ablation
Eligibility check	X	(X)	(X)			
Informed Consent	X					
Demographics		X				
Physical information		X				
Cardiac history		X				
Arrhythmia history		X				
AAD medication		X	X	X	X	X
QOL questionnaires		X		X	X	
Mapping			X			X
RF Ablation			X			X
Anonymize and backup EnSite data			X			X
Procedure- or device-related SAEs (if needed)	(X)		(X)	(X)	(X)	(X)
Arrhythmia recurrence				X	X	
24-Holter monitoring (in clinic)					X	
Healthcare Utilization				(X)	(X)	
Deviation	(X)	(X)	(X)	(X)	(X)	
Withdrawal	(X)	(X)	(X)	(X)	(X)	
Re-mapping			(X)			(X)
Touch-up ablation			(X)			(X)
Study Exit					X	

*Time of consent may be at the time of baseline visit.

**A follow-up visit must occur between 3- and 6-months post-index procedure (with a 21-day window). For readability, this follow-up visit will be referred to as the "6-Month" follow-up visit.

Clinical Investigation Plan

7.0 Adverse Events

To comply with worldwide standards and guidelines on clinical investigation 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.

7.1 Definition

7.1.1 Adverse Event

An adverse event (AE) is 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 medical device under investigation.

Abnormal laboratory values will not be considered AEs unless:

1) the investigator determined that the value is clinically significant,
2) the abnormal lab value required intervention, or
3) the abnormal lab value required subject withdrawal from the clinical investigation.

Note 1: This definition includes events related to the medical device under investigation.

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.

7.1.2 Serious Adverse Event

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.

7.2 Device Relationship

Determination of whether there is a reasonable possibility that an investigational product or device under investigation caused or contributed to an SAE 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).

7.3 Serious Adverse Event Reporting

Safety surveillance and reporting starts as soon as the patient is enrolled in the clinical investigation. Safety surveillance and reporting will continue until the last follow-up visit has been performed, the subject is deceased, the subject concludes participation in the clinical investigation or the subject withdraws from the clinical investigation. Device- and procedure-related SAE data will be collected throughout the time period defined above and will be reported to the Sponsor on a CRF. Additional information with regard to a previously-reported SAE should be updated within the appropriate CRF.

SAE Reporting

Clinical Site	Reporting timelines
All Sites	Device- and procedure-related SAEs must be reported to the Sponsor no later than 3 calendar days 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.

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.

An offline form will be made available to allow the investigator to report SAEs in the event the entry cannot be made in the EDC. This does not replace the EDC reporting system. All information must still be entered in the EDC system as soon as feasible.

7.3.1 Device Complaint Reporting

The investigator is responsible for reporting all complaints to the manufacturer of a device that meets the definition of a complaint. 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.

For Abbott products, the investigator must notify Abbott's Product Performance Group (PPG) by submitting the information on the device via email to AF_ProductSurveillance@abbott.com or by phone +1-651-756-5400 as soon as possible after becoming aware of the complaint. For non-Abbott products, the investigator must notify the manufacturer of the device per that manufacturer's complaint reporting mechanisms or per the investigator's user facility procedures. This information is not collected on a CRF for the study.

8.0 STATISTICAL CONSIDERATIONS

The following section describes the statistical methods for the clinical investigation.

8.1 Analysis Populations

The primary analysis population for this study is the enrolled population. The enrollment criteria for this trial are as follows:

[redacted]

- Subject has provided written informed consent, and
- Subject has confirmed that they meet all the inclusion criteria and none of the exclusion criteria, and
- The mapping catheter has been inserted into the subject's vasculature.

8.2 Statistical Analyses

The primary endpoint and additional evaluation analyses will be summarized descriptively based on available data or measurements in the analysis population. No formal hypothesis testing will be performed.

In general, continuous (CONT) variables will be summarized with the numbers of observations, means with standard deviations, quartiles, minimums, maximums, and 95% confidence intervals for the means as per the table mockups.

Categorical (CAT) variables will be summarized with subject counts and percentages/rates, and where specified in the table mockups, with exact 95% Clopper-Pearson confidence intervals.

Survival (SURV) analysis will be conducted to analyze time-to-event variables. Subjects without events will be censored at their last known event-free time point. Subjects withdrawn or otherwise lost-to-follow-up during the follow-up period will be censored at their last known visit. Survival data will be presented using the Kaplan-Meier product limit method.

The following list of analyses describes how the primary endpoint and additional evaluations will be analyzed:

- Primary Endpoint: LSI values achieved for RF lesion formation in different anatomical regions of the heart around the pulmonary veins (CONT)
- A summary of EnSite AutoMap and AutoMark module software settings, including LSI threshold (in OUS), contact force, time, power, flow, and AutoMark spacing (CONT)
- Acute electrical isolation of PVs, 20 minutes after last RF ablation in PV region (CAT)
- Device- or procedure-related SAEs within 7-days (CONT) and 12-months of index procedure (SURV)
- Freedom from documented AF/AFL/AT recurrence at 12-months post-index ablation, excluding a 90-day blanking period (SURV)
    - Freedom from AF/AFL/AT recurrence is defined as no documented episodes greater than 30 seconds with a 24-Holter. (SURV)
- Proportion of patients with a repeat ablation up to 12-months post index procedure (excluding 90-day blanking period) (SURV)
- Proportion of lesions generated during first-pass PVI that required touch-up ablation (CONT)
- Proportion of pulmonary veins requiring touch-up ablation (CONT)
- Proportion of patients who required at least one touch-up ablation during the index procedure (CONT)
- In patients who undergo any repeat RF ablation procedures up to 12-months post index procedure, characterization of LSI achieved values for lesions that resulted in electrically conducting gaps versus those that were durable (CONT)
- Overall procedure time and the subset of time elapsed for: first-pass PVI, any other ablations, and any touch-up ablations (CONT)

[redacted]

- Overall RF ablation time and the subset of RF ablation time for: first-pass PVI, any other ablations, and any touch-up ablations (CONT)
- Overall fluoroscopy time (CONT)
- AAD use at 12-months (CONT)
- Changes in EQ-5D-5L and AFEQT quality of life scores at 6- and 12-months post index ablation, compared to baseline scores (CONT)
- Health care utilization (including number of unscheduled hospital outpatient/ER visits and inpatient hospitalizations due to arrhythmias) collected throughout the 12-month follow-up period (CONT, CAT)

8.3 [redacted]

[redacted]

[redacted]

8.4 Timing of Analysis

Data analyses will be performed at the completion of the 12-month follow-up period for all subjects or as desired by Sponsor. In addition, study progress and data may be summarized and reported as needed.

8.5 Subgroup Analysis

No subgroup analyses are planned for this clinical investigation.

8.6 Multiplicity

No hypothesis testing will be performed; therefore, no adjustments will be made for multiplicity in the endpoint analyses.

8.7 Procedures for Accounting for Missing Data

Every effort will be made to collect all required data. All data available for the endpoints specified among the analysis population will be used. Missing data will not be imputed. Kaplan-Meier analysis will censor subjects withdrawn or otherwise lost-to-follow-up at last known visit.

[redacted]

8.8 Planned Interim Analysis

No interim analyses are planned for this study.

Since there are no formal hypotheses being tested, the Sponsor may analyze study procedure data after all procedures have been completed and 12-month outcome data after all subject have been followed up through 12-months post-procedure.

8.9 Statistical Criteria for Termination

There are no statistical criteria for termination of this clinical investigation.

8.10 Success Criteria

Pass/Fail criteria do not apply to this study.

8.11 Deviations from Statistical Plan

Any major changes or less significant changes to the planned statistical analyses will be documented in the final report.

9.0 DIRECT ACCESS TO SOURCE DATA/DOCUMENTS

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

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

10.0 QUALITY CONTROL AND QUALITY ASSURANCE

10.1 Selection of Clinical Sites and Investigators

The Sponsor will select investigators qualified by training and experience to participate in the clinical investigation. 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 investigation.

10.2 CIP Amendments

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.

10.3 Training

10.3.1 Site Training

All Investigators and clinical investigation personnel are required to attend Sponsor training sessions, which may be conducted at an Investigator's meeting, a site initiation visit, or other appropriate training sessions. Over-the-phone or self-training may take place as required. Training of Investigators and clinical investigation personnel will include, but is not limited to, the CIP requirements, electronic case report form completion and clinical investigation personnel responsibilities. All Investigators and clinical investigation personnel that are trained must sign a training log (or an equivalent) upon completion of the training. Prior to signing the training log, Investigators and clinical investigation personnel must not perform any CIP-related activities that are not considered standard of care at the site.

10.4 Monitoring

It is the responsibility of the Sponsor to ensure the clinical study is conducted, recorded and reported according to the approved CIP, subsequent amendment(s), applicable regulations and guidance documents.

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

10.5 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.

10.6 Quality Assurance Audit

A Sponsor representative or designee may request access to all clinical investigation records, including source documentation, for inspection during a Quality Assurance audit.

In the event that an investigator is contacted by a Regulatory Agency in relation to this clinical investigation, the Investigator will notify Sponsor immediately. The Investigator and Research Coordinator must be available to respond to reasonable requests and audit queries made during the audit process. The Investigator must provide Sponsor with copies of all correspondence that may affect the review of the current clinical investigation (e.g., Form FDA 483, Inspectional Observations, Warning Letters, Inspection Reports, etc.). Sponsor may provide any needed assistance in responding to regulatory audits.

10.7 Committees

10.7.1 Publications Committee

A Publication Committee may be established to oversee clinical investigations publications, including publication planning and authorship determinations, at the discretion of the Sponsor. Publication Committee membership may include Principal Investigators, a representative of the Sponsor and a statistician. The Publication Committee will determine policy and strategies regarding individual presentations and/or publications arising from clinical investigation generated data. The committee will also review all external requests for accessing clinical investigation-related data and strategies aligning with the Sponsor's presentation and publication team expectations. The committee will also follow the Sponsor's applicable policies and Standard Operating Procedures.

11.0 DATA HANDLING AND RECORD KEEPING

Sponsor and/or its affiliates will maintain documentation of the systems and procedures used in data collection for the duration of the clinical investigation.

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.

At the conclusion of the clinical investigation, 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 investigational sites.

For the duration of the clinical investigation, the Investigator will maintain complete and accurate documentation including, but not limited to, medical records, clinical investigation progress records, laboratory reports, CRFs, signed ICFs, device accountability records (if applicable), correspondence with

the IRB/EC and clinical investigation monitor/Sponsor, adverse event reports, and information regarding subject discontinuation or completion of the clinical investigation.

11.1 Protection of Personally Identifiable Information

The Sponsor respects and protects personally identifiable information collected or maintained for this clinical investigation.

The Sponsor implements technical and physical access controls to ensure that Personal Information is accessible only to and processed only on a 'need to know' basis, including periodic review of access rights, and revocation of access when an individual's employment is terminated or the individual transitions to a role that does not require access to Personal Information, and appropriate restrictions on physical access to premises, facilities, equipment, and records containing Personal Information.

The Sponsor requires the investigational sites to transfer into Sponsor's data management systems only pseudonymous Personal Information (key-coded) necessary to conduct the Clinical Investigation, such as the patient's medical condition, treatment, dates of treatment, etc. The Sponsor discloses as part of the clinical investigation informed consent process that some Sponsor representatives still may see Personal Information at the participating sites for technical support of the participating physicians on the device implant or procedures, monitoring and quality control purposes. Confidentiality of Personal Information will be observed by all parties involved at all times throughout the clinical investigation. The privacy of each subject and confidentiality of his/her information will be preserved in reports and when publishing any data.

The Sponsor data management systems and processes were designed, developed, and tested according to industry standards to appropriately safeguard Confidential Information (including any Personal Information) against unauthorized access and/or interference by third parties, intrusion, theft, destruction, loss or alteration. Clinical Investigation data are encrypted in transit and at rest.

The Sponsor maintains a Privacy Incident procedure that complies in all respects with Applicable Law and industry best practices.

11.2 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 investigation. All revisions will be tracked and document controlled.

11.3 Source Documentation

Regulations and GCP require the Investigator to maintain information in the subject's original medical records that corroborates data collected on the CRFs. In order 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 investigation:

- Medical history/physical condition of the subject before involvement in the clinical investigation sufficient to verify CIP entry criteria
- Dated and signed notes on the day of entry into the clinical investigation 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)
- Serious Adverse Events reported and their resolution including documentation of site awareness of SAEs and of investigator assessment of device relationship for SAEs.
- Subject's condition upon completion of or withdrawal from the clinical investigation
- Any other data required to substantiate data entered into the CRF
- Patient reported outcome measures may be completed using CRF worksheets. These serve as the source documentation.

11.4 Case Report Form Completion

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.

Data on CRFs will be collected for all subjects that are enrolled into the clinical investigation and submitted to the Sponsor, preferably within 10 days.

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.

11.5 Record Retention

The Sponsor and Investigator/Site will archive and retain all documents pertaining to the clinical investigation 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 investigation records.

12.0 ETHICAL CONSIDERATION

12.1 Institutional Review Board/Medical Ethics Committee Review and Approval

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 investigational site prior to consenting and enrolling patients in this clinical investigation. The approval letter must be received prior to the start of this clinical investigation 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 investigation is completed, the Investigator will advise his/her IRB/EC of the progress of this clinical investigation, per IRB/EC requirements. Written approval must be obtained from the IRB/EC yearly to continue the clinical investigation, or according to each institution's IRB/EC requirements.

Clinical Investigation Plan

No investigative 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.

13.0 CLINICAL INVESTIGATION CONCLUSION

The clinical investigation report will be submitted within one year of the end of the investigation (defined as the last visit of the last subject).

The clinical investigation will be concluded when:

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

14.0 PUBLICATION POLICY

The data and results from the clinical investigation 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 investigation. The Investigators will not use this clinical investigation-related data without the written consent of the Sponsor for any purpose other than for clinical investigation 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 investigation on www.clinicaltrials.gov or any other clinical trials, in accordance with the International Committee of Medical Journal Editors guidelines, or any other applicable guidelines. In the event Sponsor determines that the clinical investigation 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 investigation.

15.0 RISK ANALYSIS

The risks associated with the TactiCath SE catheter and other devices used in the clinical study can be found in the appropriate Instructions for Use. The clinical study does not require additional procedures or assessments beyond what could be considered standard of care. There are no additional risks introduced to subjects due to participation in this study.

15.1 Anticipated Clinical Benefits

The primary objective of this study is to characterize LSI achieved values for durable lesion formation using the TactiCath SE catheter in the different anatomical regions around the pulmonary veins (PVs) of the heart during RF ablation for the treatment of drug-refractory paroxysmal atrial fibrillation (PAF).

The information collected in this clinical study will be added to the current knowledge and understanding of treatment options for patients with arrhythmias. Subjects participating in this clinical study are not expected to experience any additional benefit or harm compared to patients who are not participating in this clinical study as the clinical study will follow local standard practice.

15.2 Foreseeable Adverse Events and Anticipated Adverse Device Effects

Risks associated with the specified devices and procedure, together with their likely incidence, are described in their respective IFUs. There may be risks related to the device under investigation that are unknown at present. Likewise, the exact frequency of the risk may be unknown.

15.3 Risks Associated with Participation in this Clinical Investigation

Risks to subjects enrolled in this clinical study include those risks currently associated with other commercially available electrophysiology diagnostic procedures and RF catheter ablation procedures. The risks of the procedure are related primarily to mechanical injury to the heart and vessels from catheter manipulation and thermal injury due to RF current delivery, including the risk of thromboembolism and myocardial perforation, especially for ablations in the left atrium.

For those procedures where the physician applies sedation or anesthesia, the standard risks of anesthesia also exist and include allergic reactions, pneumonia, aspiration pneumonitis, atelectasis, prolonged sedation, other medical complications and in very rare cases, death.

15.4 Steps Taken to Control or Mitigate Risks

Every possible effort will be taken to minimize the risks, including:

- Careful selection of experienced Investigators for the study
- Training of Investigators and other applicable site personnel on the CIP
- Conducting the clinical study in accordance with the CIP, all applicable laws and regulations and any conditions of approval imposed by the appropriate IRB/EC or applicable regulatory authorities where the clinical study is performed
- Preparation of the all devices in accordance with device IFU, and conducting the ablation procedures in accordance with the IFU of corresponding devices

In-depth recommendations, special precautions and instructions regarding patient selection and device handling are included in the IFU.

It is also stated in the IFU that the devices can only be used by physicians who have received appropriate training on how to use the device. This statement is interpreted to mean that the physician users are expected to be aware of the known and foreseeable safety risks associated with the use of the devices including the surgical and/or non-surgical treatment of these conditions.

Risks associated with the use of the device under investigation are minimized through device design, investigator selection and training, pre-specified patient eligibility requirements, and study monitoring to ensure adherence to the protocol. All adverse events and device deficiencies will be reported to the Sponsor and will be monitored internally for safety surveillance purposes.

15.5 Risk to Benefit Rationale

Catheter ablation is a recognized safe and effective treatment of cardiac arrhythmias. As this study follows the standard of care, it is not believed that any additional unanticipated risks will be introduced compared to current practice.

Clinical Investigation Plan

APPENDIX I: ABBREVIATIONS AND ACRONYMS

AAD	Anti-arrhythmic drug
AE	Adverse Event
AF	Atrial fibrillation
AFL	Atrial flutter
AT	Atrial tachycardia
BMI	Body Mass Index
CIED	Cardiac implanted electronic device
CRF	Case Report Form
CTI	Cavotriscuspid isthmus
EC	Ethics Committee
ECG	Electrocardiogram
EDC	Electronic Data Capture
FTI	Force time integral
GCP	Good Clinical Practice
ICF	Informed consent form
ICH	International Conference on Harmonization
IFU	Instructions for use
LAA	Left atrial appendage
LIPV	Left inferior pulmonary vein
LSPV	Left superior pulmonary vein
LA	Left atrium
LSI	Lesion Index
LV	Left ventricle
NYHA	New York Heart Association
OUS	Outside of the United States
PAF	Paroxysmal atrial fibrillation
PV	Pulmonary vein
PVI	Pulmonary vein isolation
RF	Radiofrequency
RIPV	Right inferior pulmonary vein
RSPV	Right superior pulmonary vein
SAE	Serious Adverse Event
SD	Standard deviation
SJM	Saint Jude Medical
TEE	Transesophageal echocardiography
TIA	Transient ischemic attack

Clinical Investigation Plan

APPENDIX II: SITE CONTACT INFORMATION

Contact information for each participating clinical site is available under separate cover by contacting the Sponsor.

APPENDIX III: INFORMED CONSENT

A template informed consent form will be provided under a separate cover.

Clinical Investigation Plan

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Clinical Investigation Plan

Clinical Investigation Plan

APPENDIX VI: CIP SUMMARY

Clinical Investigation Name and Number	LSI Workflow CRD 970
Title	LSI Workflow
Objective(s)	The primary objective of this study is to characterize LSI achieved values for durable lesion formation using the TactiCath SE catheter in the different anatomical regions around the pulmonary veins (PVs) of the heart during RF ablation for the treatment of drug-refractory paroxysmal atrial fibrillation (PAF). Secondary objectives of this study are as follows: • To characterize the use of EnSite Automap and AutoMark module software settings, including LSI threshold settings (in OUS), power, flow settings, and AutoMark spacing using the TactiCath SE catheter for RF ablation for the treatment of drug-refractory PAF. • To characterize LSI values for lesions that reconnected versus those that were durable, both in an acute procedural setting as well as in patients who undergo additional ablations during the 12-month follow-up period after an index RF ablation procedure for the treatment of drug-refractory PAF.
Device Under Investigation	EnSite Precision™ Cardiac Mapping System with the AutoMap, AutoMark, and Contact Force modules TactiCath™ Contact Force Ablation Catheter, Sensor Enabled™
Number of Subjects Required for Inclusion in Clinical Investigation	Approximately 150 patients at approximately 10 sites
Clinical Investigation Design	Prospective, multicenter, post-market, single-arm, observational study
Primary Endpoint(s)	The primary endpoint is a summary of LSI achieved values for RF lesion formation in different anatomical regions of the heart around the pulmonary veins
Additional Evaluations	• A summary of EnSite AutoMap and AutoMark module software settings, including LSI threshold settings (in OUS), contact force, time, power, flow settings, and AutoMark spacing • Acute electrical isolation of PVs, 20 minutes after last RF ablation in PV region

Clinical Investigation Plan

	• Device- or procedure-related SAEs within 7-days and 12-months of index procedure • Freedom from documented AF/AFL/AT recurrence at 12-months post-index ablation, excluding a 90-day blanking period. ○ Freedom from AF/AFL/AT recurrence is defined as no documented episodes greater than 30 seconds with a 24-Holter. • Proportion of patients with a repeat ablation up to 12-months post index procedure (excluding 90-day blanking period) • Proportion of lesions generated during first-pass PVI that required touch-up ablation • Proportion of pulmonary veins (PVs) requiring a touch-up ablation • Proportion of patients who required at least one touch-up ablation during the index procedure • In patients who undergo any repeat RF ablation procedures up to 12-months post index procedure, characterization of LSI achieved values for lesions that resulted in electrically conducting gaps versus those that were durable • Overall procedure time and the subset of time elapsed for: first-pass PVI, any other ablations, and any touch-up ablations • Overall RF ablation time and the subset of RF ablation time for: first-pass PVI, any other ablations, and any touch-up ablations • Overall fluoroscopy time • AAD use at 12-months • Changes in EQ-5D-5L and AFEQT quality of life scores at 6- and 12-months post index ablation, compared to baseline scores • Health care utilization (including number of unscheduled hospital outpatient/ER visits and inpatient hospitalizations due to arrhythmias) collected throughout the 12-month follow-up period
Subject Follow-up	• Baseline Visit, after Informed Consent • Procedure Visit, preferably within 14 days of Informed Consent • 3- to 6-Month Follow-Up Visit, 90 to 183 ± 21 days after Procedure • 12-Month Follow-Up Visit, 365 ± 21 days after Procedure • Repeat Ablation, any time after Procedure during follow-up period, at physician's discretion
Inclusion Criteria	1. Subject must provide written informed consent prior to any clinical investigation related procedure. 2. Subject is at least 18 years of age.

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Clinical Investigation Plan

	3. Subject is willing and able to comply with the CIP-described evaluations and follow-up schedule. 4. Subject plans to undergo a pulmonary vein isolation (PVI) procedure due to symptomatic paroxysmal AF using RF ablation. 5. Subject is refractory or intolerant to at least one class I or class III anti-arrhythmic drug. a. For the purposes of this study, "intolerant" includes either: i. Subject attempted the drug at any dose and either the subject or their physician chose to discontinue for any reason ii. Subject was offered the drug and refused to take for any reason
Exclusion Criteria	1. Previous ablation or surgery in the left atria. 2. Has an implantable cardiac defibrillator (ICD, pacemakers without defibrillation capacity are allowable). 3. Participation in another clinical investigation that may confound the results of this study. 4. Pregnant or nursing. 5. Presence of other anatomic or comorbid conditions, or other medical, social, or psychological conditions that, in the investigator's opinion, could limit the subject's ability to participate in the clinical investigation or to comply with follow-up requirements, or impact the scientific soundness of the clinical investigation results. 6. Life expectancy less than 12 months.

Clinical Investigation Plan

APPENDIX VII: REFERENCES

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