Abbott	Clinical Investigation Plan Cover Page

NCT Number: NCT03650556
PERSIST-END Trial
Safety and Effectiveness of TactiCath™ Contact Force, Sensor Enabled™ (TactiCath SE) Catheter for Ablation of Drug Refractory, Symptomatic, Persistent Atrial Fibrillation
Study Document No: ABT-CIP-10239
Version D
Date: 14 JAN 2019

Sponsor

Abbott
5050 Nathan Lane N
Plymouth, MN 55442
USA

Clinical Investigation Plan

Safety and Effectiveness of TactiCath™ Contact Force, Sensor Enabled™ (TactiCath SE) Catheter for Ablation of Drug Refractory, Symptomatic, Persistent Atrial Fibrillation (PERSIST-END Trial)

January 14, 2019

[redacted]

ABT-CIP-10239

PERSIST-END

Safety and Effectiveness of TactiCath Contact Force, Sensor Enabled (TactiCath SE) Catheter for Ablation of Drug Refractory, Symptomatic, Persistent Atrial Fibrillation

Version Letter:	D
Date:	January 14, 2019
Planned Number of Sites and Region(s):	Up to 25 sites worldwide
Clinical Investigation Type:	Prospective, single arm, non-randomized, multi-center clinical trial compared to a performance goal
Sponsor:	Abbott 5050 Nathan Lane N. Plymouth, MN 55442 United States
Author of Current Version:	[redacted]

[redacted]

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:

TABLE OF CONTENTS

[redacted]

[redacted]

[redacted]

[redacted]

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.).

[redacted]

1 INTRODUCTION

This clinical investigation is intended to demonstrate the safety and effectiveness of the TactiCath™ Contact Force Ablation Catheter, Sensor Enabled™ (TactiCath SE) for use in cardiac electrophysiological mapping and for the treatment of drug-refractory, recurrent symptomatic persistent atrial fibrillation (AF) when used in conjunction with a compatible radiofrequency (RF) generator and three-dimensional mapping system. This clinical investigation will be conducted under an investigational device exemption (IDE) and is intended to support market approval of the TactiCath SE ablation catheter for the treatment of drug refractory, symptomatic persistent atrial fibrillation in the United States. Two hundred twenty-four (224) subjects will be enrolled at up to 25 investigational sites worldwide. This clinical investigation is sponsored by Abbott and will be conducted in accordance with this clinical investigation plan (CIP).

1.1 Background and Rationale

AF is a result of multiple diseases and mechanisms that are not completely understood and will often exacerbate an underlying heart condition. AF occurs when structural and/or electrophysiological abnormalities alter atrial tissue to promote abnormal impulse formation and/or propagation.[1] Symptoms associated with AF include fatigue, palpitations, dyspnea, hypotension, syncope, and heart failure. AF often progresses from paroxysmal to persistent over a variable period of time. Patients with persistent AF have worse outcomes than for patients with paroxysmal AF and are more likely to develop potentially life-threatening problems, such as stroke, tachycardia-induced cardiomyopathy and congestive heart failure, all of which may increase mortality.[2,3] Maintenance of sinus rhythm may confer a mortality benefit and is associated with improvements in symptoms and quality of life.

Management of patients with AF has traditionally consisted of three main components: (1) anticoagulation for stroke prevention; (2) rate control; and (3) rhythm control.[4] Persistent symptoms associated with AF remain the most compelling indication for a rhythm-control strategy. The efficacy of radiofrequency catheter ablation for maintaining sinus rhythm is superior to current antiarrhythmic drug therapy in select patient populations.[1] The decision whether to pursue catheter ablation depends on a large number of variables, including the type of AF, degree of symptoms, presence of structural heart disease, candidacy for alternative options such as rate control or antiarrhythmic drug therapy, likelihood of complications, and patient preference.[1] Catheter ablation is considered a reasonable indication for patients with symptomatic persistent AF refractory or intolerant to at least one Class I or III antiarrhythmic medication.[1,4] Catheter ablation may also be considered as first-line therapy in select patients before a trial of antiarrhythmic drug therapy when a rhythm-control strategy is desired.[1,4]

The method of catheter ablation for persistent AF remains controversial.[2,4] The strategy for ablation is often individualized based on patient characteristics, atrial fibrillation history and coexisting structural heart disease. Electrical isolation of the pulmonary veins by catheter ablation is the cornerstone for most AF ablation procedures as most triggers for AF originate from the pulmonary veins.[3] Pulmonary vein (PV) isolation involves creating circumferential lesions around the veins to electrically isolate them from the rest of the left atrium. Additional non-PV ablation strategies are also often employed in patients with persistent AF to improve outcome and may consist of the following: ablation of the posterior wall of the left atrium; creating linear ablation lesions in the right or left atrium; mapping and ablation of areas of abnormal myocardial tissue; ablation of complex fractionated atrial electrograms or rotational activity; and/or ablation of autonomic ganglia.[4] These additional non-pulmonary vein ablation strategies all have

a Class IIb recommendation (benefit of AF ablation is greater or equal to the risks and AF ablation may be considered) based on a moderate quality of evidence for these approaches.

Contact force sensing ablation catheter systems are a technology that is growing in adoption for AF ablation. Contact force sensing catheter systems provide feedback to operators regarding the force applied by the catheter tip on the cardiac wall. Recommendations for contact force catheters for atrial fibrillation ablation procedures are also defined in the 2017 HRS/EHRA/ECAS/APHRS/SOLAECE Expert Consensus on AF Ablation (Class IIa recommendation, Level of evidence C).[4]

The TactiCath family of contact force sensing catheters has been studied extensively. The early generation TactiCath catheters were investigated in the TOCCATA[5], EFFICAS I[6] and II[7], and TOCCASTAR[8] clinical trials. The next generation, TactiCath Quartz, implemented an updated contact force sensing mechanism, which was studied in the TOCCASTAR Supplemental Clinical Study. Long-term follow up data are currently being collected in the TactiCath Quartz Post Approval Study. These clinical trials have investigated the safety and effectiveness of the previous generations of the TactiCath ablation catheters for the treatment of drug refractory, symptomatic AF.[5-8]

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. Preclinical testing has demonstrated that the TactiCath SE ablation catheter has an acceptable safety profile. Refer to the Report of Prior Investigations that summarizes the preclinical testing, the on-going post-approval study, and the literature review demonstrating the safety of this device to date.

Currently, there are no ablation catheters with an indication for use in the persistent AF population available in the United States. The PERSIST-END clinical investigation will be used to obtain regulatory approval from the Food and Drug Administration (FDA) and will utilize the latest iteration of the TactiCath™ catheter (TactiCath™ Contact Force Ablation Catheter, Sensor Enabled). The PERSIST-END trial will be one of the first clinical trials within the United States to evaluate the safety and effectiveness of a radiofrequency ablation catheter for use in the persistent AF population.

2 CLINICAL INVESTIGATION OVERVIEW

2.1 Clinical Investigation Objective

The objective of this clinical trial is to demonstrate that ablation with the TactiCath™ Contact Force Ablation Catheter, Sensor Enabled™ (TactiCath SE) is safe and effective for the treatment of drug refractory, symptomatic persistent atrial fibrillation when following standard electrophysiology mapping and radiofrequency ablation procedures.

2.2 Devices to Be Used in this Clinical Investigation

2.2.1 Name of the Device Under Investigation

The investigational device to be used in this trial is the TactiCath™ Contact Force Ablation Catheter, Sensor Enabled™ and is manufactured by Abbott. The *Instructions for Use* document is available under separate cover and will be included with each shipped product whether it is market released (geographies outside of the United States) or labeled as investigational (within the United States).

United States only:
The system to be used for the ablation procedures in this clinical trial includes the TactiSys Quartz Equipment (PN-004 400) and Ampere Radiofrequency Generator (H700488), which, when used in combination with TactiCath SE for persistent atrial fibrillation ablation, are considered investigational. The Ampere generator and TactiSys Quartz Equipment will be obtained by U.S. study sites through their usual commercial channels. A label indicating each device is considered part of an investigational system will be affixed by Abbott personnel to the Ampere RF Generator and TactiSys Quartz Equipment at sites on those devices used for ablation in the PERSIST-END trial.

The list of investigational equipment for sites in the United States and their respective model numbers are listed in **Table 1**.

Table 1. Investigational Devices

Device name	Model/Type
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
TactiSys™ Quartz Equipment	PN-004 400
Ampere™ RF Generator	H700488 (US) H700489 (OUS)

All other geographies where TactiCath SE is commercially available:
In countries outside of the United States, the TactiCath SE is indicated for use in cardiac electrophysiological mapping (stimulation and recording), and, when used in conjunction with a radiofrequency generator for cardiac ablation of supraventricular arrhythmias in the right and left atrium, including atrial fibrillation. All devices to be used during the clinical trial are market released, and will be utilized according to approved labeling, *Instructions for Use*, and medical standard of care guidelines.

2.2.2 Ancillary Devices

The ancillary devices that will be used in this clinical investigation are listed in **Table 2**. The EnSite Precision Cardiac Mapping System, EnSite Velocity (v5.2 or equivalent) and Precision (v2.2 or equivalent) Software, Contact Force Module, and Cool Point™ Pump are not part of the investigational system and will be used as commercially indicated.

[redacted]

A restricted release of the commercial license entitlement kit for TactiCath SE will be provided only to sites participating in this clinical investigation under a Clinical Trial Authorization. This would allow recognition of the TactiCath SE catheter by the commercial EnSite systems at study centers and will appropriately limit use of the catheter to the clinical investigation prior to PMA approval.

Table 2. Ancillary Devices

Ancillary Device Name	Model Number
EnSite System (Amplifier and Display Workstation)	EE3000
EnSite Velocity Software v5.2 or equivalent	H702495
EnSite Precision Software v2.2 or equivalent	H702496
Ensite Precision Module, Sensor Enabled Kit	H702470
Contact Force Module	H702500
TactiCath Ablation Catheter, Sensor Enabled, Software Installation (License Entitlement)	H702517
Cool Point™ Pump, v24 or greater	IBI-89003 (US) 85784 (OUS)

2.2.3 Intended Indication for Use

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 persistent atrial fibrillation when used in conjunction with a compatible radiofrequency generator and three-dimensional mapping system.

2.2.4 Description of the Device Under Investigation

2.2.4.1 TactiCath Sensor Enabled Ablation Catheter

The TactiCath SE is designed to facilitate electrophysiological mapping of the heart chambers and to transmit RF current to the catheter tip electrode for intracardiac ablation purposes. The catheter is used in conjunction with a RF generator, an irrigation pump, and a dispersive pad (indifferent patch electrode) when ablating. 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.

TactiCath SE has novel contact force and magnetic sensors. It has a fluid lumen connected to open conduits within a 6-hole tip electrode for saline irrigation during the ablation procedure (**Figure 1**). For both uni-directional (**Figure 2**) and bi-directional catheters (**Figure 3**), 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.

Figure 1. Exposed View of the TactiCath SE Tip

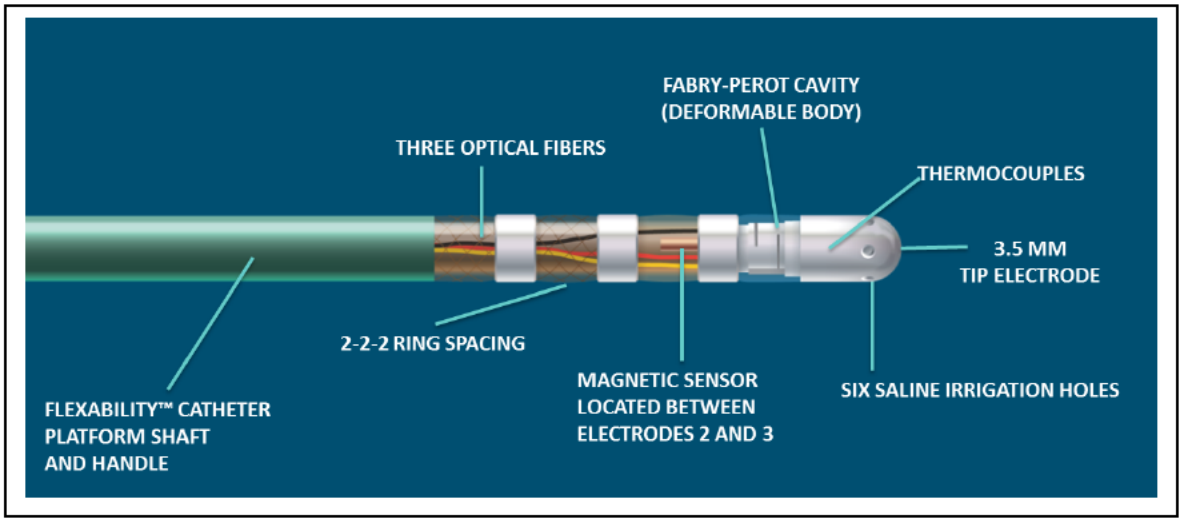


Figure 2. Uni-Directional TactiCath SE

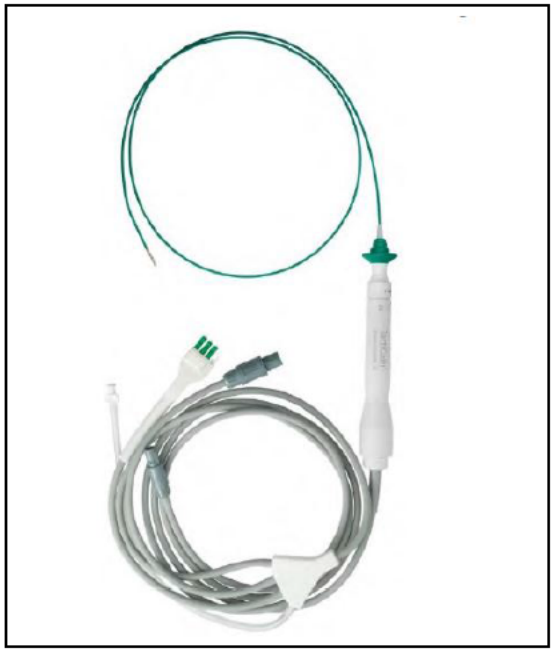
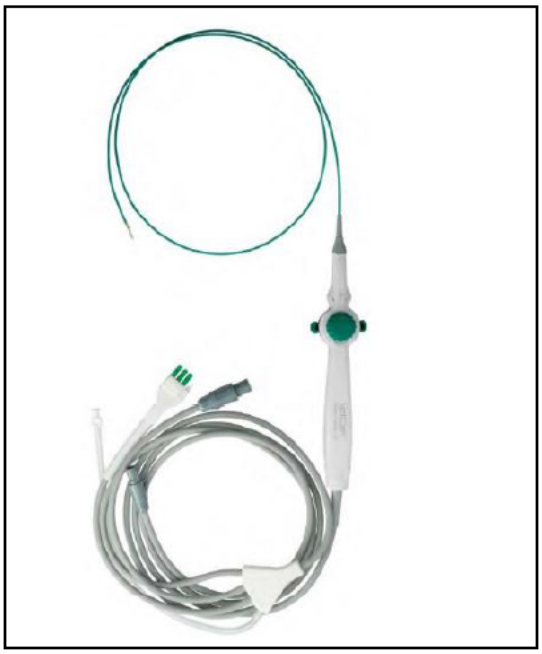


Figure 3. Bi-Directional TactiCath SE



2.2.5 Device Handling and Storage

The Sponsor requires all investigational products be stored according to the labeling and *Instructions for Use* in a secure area to prevent unauthorized access or use.

[redacted]

In the United States, the commercially available TactiSys Quartz Equipment and Ampere generator can be stored per standard practice at each hospital. The TactiCath SE Software license will be activated by Abbott personnel on commercially available EnSite Precision units (v2.2 or equivalent software) as part of site activation for sites participating in the trial that have not activated the license.

Outside the United States, all devices will be used according to approved labeling and published medical practice guidelines. Regulations for handling of investigational devices do not apply.

3 CLINICAL INVESTIGATION DESIGN

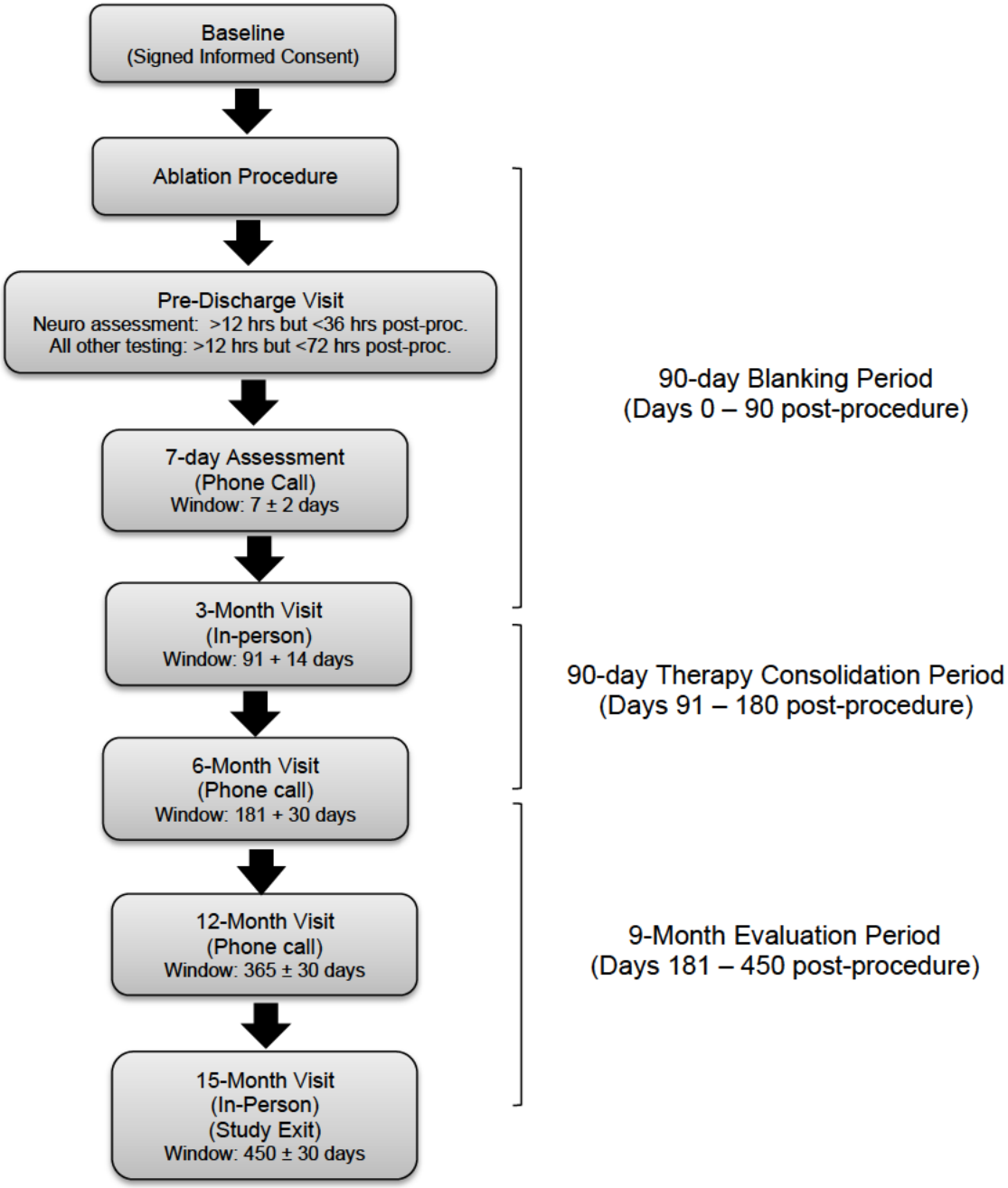
This is a prospective, single-arm, multi-center investigational device exemption (IDE) clinical trial to evaluate the safety and effectiveness of ablation with the TactiCath SE catheter for the treatment of drug refractory, symptomatic persistent AF compared to a predetermined performance goal. A total of 224 subjects will be enrolled at up to 25 investigational sites worldwide.

[redacted] Subjects will be followed for 15-months after their initial ablation procedure. The primary endpoints will be evaluated when all subjects have completed their 15-month follow-up visit. [redacted] The pre-market approval (PMA) clinical report will be prepared after the last subject has completed their final follow-up visit.

3.1 Clinical Investigation Procedures and Follow-up Schedule

The visit schedule for subjects is shown in **Figure 4**. Subjects will be consented for the trial at baseline as specified in **Section 5.2.2**. Once eligibility is confirmed, the subject will then undergo an ablation procedure for treatment of their persistent AF condition. A blanking period of 90-days will be employed after the initial ablation procedure, followed by a 90-day therapy consolidation period and then a 9-month evaluation period for a total of 15-months of follow-up. Medication adjustments, cardioversions, and one repeat ablation procedure may be performed in either the blanking or therapy consolidation periods. It is recommended that subjects are off antiarrhythmic drugs (AADs) after the blanking and/or therapy consolidation period. Follow-up assessments will occur either in-person at the clinic or via phone contact after the procedure. The scheduled follow-up visits will occur at 7-days post-procedure (phone call), and at 3-months (in-person visit), 6-months (phone call), 12-months (phone call), and 15-months (in-person visit). The subject will be exited from the trial after completing their 15-month follow-up visit.

Figure 4. Study Flow Diagram



3.2 Measures Taken to Avoid and Minimize Bias

Multiple measures will be taken to avoid and minimize bias in this clinical investigation. First, PERSIST-END is a prospective clinical investigation in which the outcome is unknown at the time of enrollment and

all subjects must meet the defined eligibility criteria to minimize selection bias. Next, guidance will be provided to sites regarding data collection for questionnaires and the post-procedure follow-up phone calls to be performed at 7-days, 6-months, and 12-months post-procedure. Additionally, case report forms for data collection will be provided to sites, which will minimize inter-observer variability.

Evaluation of primary endpoint data will be performed by an independent core laboratory and Clinical Events Committee (CEC). Collected electrocardiogram (ECG), trans-telephonic monitoring (TTM) data, and 24-hour Holter data from sites will be evaluated by a physician at a core laboratory to determine AF recurrence for subjects. Adverse events will be adjudicated by a CEC made up of physicians who are not investigators in the trial. Although the investigators at each site will perform their own adjudication regarding outcome data, only the core lab and the CEC's adjudication of the collected data will be used for analysis in order to minimize bias.

Protocols are also in place to minimize lost to follow-up subjects and for handling missing data. Sensitivity analyses will be performed demonstrating the impact missing data may have on the trial.

3.3 Suspension or Early Termination of the Clinical Investigation

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.

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

Should this occur, the investigator shall return all clinical investigation materials (including devices) to the Sponsor and provide a written statement to the IRB/EC (if applicable) as to why premature termination has taken place. All applicable clinical investigation documents shall be subject to the same retention policy as detailed in **Section 11.5** of this CIP.

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

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

4 ENDPOINTS

Two primary endpoints and three secondary endpoints will be evaluated in this clinical investigation. Additional data will also be collected for assessment in this trial.

4.1 Primary Endpoint

4.1.1 Primary Safety Endpoint

The primary safety endpoint is the rate of device and/or procedure-related serious adverse events with onset within 7-days of any ablation procedure that uses the TactiCath SE catheter (initial or repeat procedure performed ≤180 days of initial procedure) that are defined below:

- Atrioesophageal fistula[1]
- Cardiac tamponade/perforation[1]
- Death
- Heart block
- Myocardial infarction (MI)
- Pericarditis[2]
- Phrenic nerve injury resulting in diaphragmatic paralysis
- Pneumothorax
- Pulmonary edema (respiratory insufficiency)
- Pulmonary vein stenosis[1]
- Stroke/cerebrovascular accident (CVA)
- Thromboembolism
- Transient ischemic attack
- Vascular access complications (including major bleeding events[3])

1. Atrioesophageal fistula, cardiac tamponade/perforation and pulmonary vein stenosis will be evaluated through 15-months.
2. Pericarditis is a common occurrence for almost all procedures and will only be considered a primary safety endpoint event if the pericarditis pleuritic symptoms last longer than 7-days and/or requires hospitalization of greater than 24 hours for reasons other than for observational purposes only.
3. Bleeding is a major complication of AF ablation if it requires and/or is treated with transfusion or results in a 20% or greater fall in hematocrit.

Definitions regarding the primary safety events are provided in **Appendix III**.

Serious AF/atrial flutter (AFL)/atrial tachycardia (AT) recurrences without coexisting conditions (e.g. thromboembolism, worsening heart failure, etc.) will be counted as effectiveness failures but will not count against the primary safety endpoint.

The performance goal is set at [redacted] as determined by relevant studies for persistent AF that utilize radiofrequency ablation. Refer to the Statistical Analysis Plan for details regarding the rationale for the performance goal.

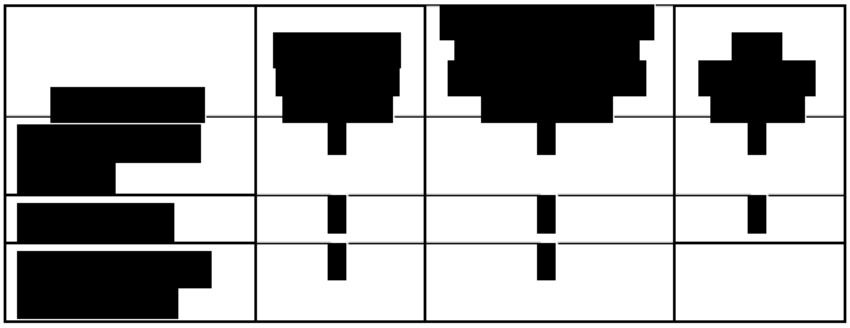
4.1.1.1 Rationale for Selection of the Primary Safety Endpoint

[redacted]

occur within the first 7-days following an ablation procedure. It has become industry standard to report

[redacted]

[redacted]



4.1.2 Primary Effectiveness Endpoint

The primary effectiveness endpoint for this clinical trial is freedom from AF/AFL/AT episodes of >30 seconds duration that is documented by an ECG (12-lead or TTM) or 24-hour Holter after the initial catheter ablation procedure through 15-months of follow-up (includes a 90-day blanking period followed by a 90-day therapy consolidation period). AF/AFL/AT recurrence during the blanking or therapy consolidation periods will not be considered a treatment failure. One repeat procedure is allowed for ablation of AF/AFL/AT recurrence during the blanking or therapy consolidation periods (≤180 days post-initial procedure) without being considered a treatment failure.

AF/AFL/AT recurrence will only be assessed by 12-lead ECG, TTM, and 24-hour Holter monitoring devices for assessment of this primary endpoint so that all subjects are monitored equally with devices of the same sensitivity and specificity. Collected ECG, TTM, and 24-hour Holter data from sites will be evaluated by a physician at a core laboratory for independent and unbiased assessment of AF recurrence for endpoint analysis.

There are multiple situations in which subjects will be considered primary effectiveness endpoint failures:

- If AF/AFL/AT recurrence (>30 second episode) occurs at any time after the therapy consolidation period (>180 days after the initial procedure), or
- If the subject requires a repeat procedure for the treatment of AF after the therapy consolidation period, the subject will be considered an effectiveness endpoint failure regardless of documentation of a >30 second AF/AFL/AT episode, or
- If the subject requires a second repeat procedure at any time after the initial procedure, or
- If the subject requires a new AAD or a previously failed AAD at a dose greater than the highest ineffective historical dose for AF after the therapy consolidation period, or
- If the subject requires a cardioversion (electrical or pharmacological) for the treatment of AF after the therapy consolidation period, or
- If the subject has a continuous atrial arrhythmia throughout a 12-lead ECG recording after the therapy consolidation period indicating arrhythmia recurrence, this will be considered sufficient documentation of recurrence unless there is evidence that the recorded arrhythmia is short-lived and less than 30 seconds.

As cavotricuspid isthmus-dependent atrial flutter is easily treated with cavotricuspid isthmus ablation and is not an iatrogenic arrhythmia following a left atrial ablation procedure for AF, occurrence of cavotricuspid isthmus-dependent atrial flutter confirmed by entrainment maneuvers that occurs at any time during the follow-up period and is ablated, will not be considered a primary effectiveness endpoint failure.

[redacted]

4.1.2.1 Rationale for Selection of the Primary Effectiveness Endpoint

[redacted]

4.2 Secondary Endpoints

Type I error among secondary endpoints will be controlled using appropriate statistical methodology as outlined in the Statistical Analysis Plan.

1) Proportion of subjects who achieve acute procedural success [redacted] for subjects who had the investigational catheter inserted into their vasculature, where acute procedural success is defined as confirmation of entrance block in all pulmonary veins.

2) Proportion of subjects off all AADs taken to treat AF/AFL/AT who achieve15-month success of [redacted], defined as freedom from documented AF/AFL/AT recurrence (episodes >30 seconds) during the 9-month period following the blanking and therapy consolidation periods.

3) Proportion of subjects who achieve 15-month single procedure success of [redacted], defined as freedom from documented AF/AFL/AT recurrence (episodes >30 seconds) during the 9-month period following the blanking and therapy consolidation periods after a single ablation procedure. Any repeat ablation procedure required by the subject at any time will be deemed an effectiveness failure in this analysis.

4.3 Additional Data

Additional data to be collected in this clinical investigation are described and will be reported using summary statistics. No hypothesis tests will be performed.

1) Procedure- and/or ablation catheter-related adverse events throughout the 15-month follow-up period
2) Success (defined as freedom from >30 second documented episodes of AF/AFL/AT recurrence) without Class I or III AAD dose increase from the historic maximum ineffective dose (prior to the ablation procedure) or initiation of a new Class I or III AAD for arrhythmia recurrence after the blanking and therapy consolidation periods.

[redacted]

3) Proportion of subjects who achieve 15-month symptomatic single procedure success (defined as freedom from >30 second documented symptomatic episodes of AF/AFL/AT recurrence after the blanking and therapy consolidation periods).
4) Cardiovascular-related health care utilization through 15-months after the initial procedure.
5) Procedure data, including but not limited to, ablation data, mapping data, and usage of Automark.
6) Proportion of cases achieving ≥ 90% lesions with ≥10g of contact force.
7) Evaluation of procedure data to determine target lesion index (LSI) value(s) as assessed by AF/AFL/AT recurrence.
8) Changes in EQ-5D-5L and AFEQT scores from baseline to follow up at 3, 6, 12, and 15-months after the initial procedure.

5 SUBJECT SELECTION AND WITHDRAWAL

5.1 Subject Population

This clinical investigation will enroll male and female subjects who have drug refractory, symptomatic, persistent AF. Subjects must 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

Members of the site's clinical investigation team (physician and/or research coordinator, or other delegated and qualified personnel) previously trained to this CIP must screen potential patients for clinical investigation eligibility and document the screening effort onto a site-specific Screening Log. Patients who meet the inclusion criteria and none of the exclusion criteria may participate in this clinical investigation.

Patients presenting at clinical sites as potential subjects will be fully informed about the clinical investigation. Once a duly dated and signed Informed Consent form is obtained, the clinical investigation-specific screening procedures may begin.

The following assessments may need to be performed after obtaining consent and prior to the procedure, as part of the screening process (further described in **Section 6**):

- Verification that a left atrial thrombus is not present on the day of or within one day of the ablation procedure
- Measurements for LVEF and LAD, if not documented prior to consent and/or is not standard of care at the site
- Administration of a 24-hour Holter, if not previously documented as part of standard of care within 90-days of the ablation procedure

Subject data will be collected following enrollment (consent) into the clinical investigation.

In the case in which a subject does not meet all inclusion criteria or meets one or more exclusion criteria that is discovered prior to insertion of the TactiCath SE catheter into their vasculature, the subject is considered a screen failure. The Principal Investigator or the delegated clinical investigation personnel will record the screen failure in the hospital records and on the Screening Log.

5.2.2 Informed Consent

A template informed consent form will be provided to each site by the Sponsor under separate cover for use in this clinical investigation. Site-specific language will be added to the template and approved by research personnel, the Sponsor, and governing IRB/EC prior for use in the trial.

The Investigator or his/her authorized designee will conduct the Informed Consent process, as required by applicable regulations and the center's IRB/EC. This process will include a verbal discussion with the subject on all aspects of the clinical 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. 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 every effort 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 hospital or research charts, and a copy will be provided to the subject.

Failure to obtain informed consent from a subject prior to undergoing study-specific procedure should be reported to the Sponsor within 5 working days and to the reviewing center's IRB/EC according to the IRB's/ EC's reporting requirements.

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

5.2.2.1 Special Circumstances for Informed Consent

The following individual populations will be excluded from participation in this clinical investigation:

- Individuals persons who are mentally ill, mentally handicapped, or individuals without legal authority, are excluded from the study population.
- Individuals under the age of 18 or age of legal consent are excluded from the study population.
- Individuals unable to read or write are excluded from the study population.
- Pregnant or breastfeeding women are excluded from the study population.

[redacted]

5.2.3 HIPAA Authorization Requirement (United States only)

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 or their legally authorized representative for sites located in the United States.

5.3 Eligibility Criteria

Assessment of eligibility criteria is based on review of candidate medical records at the site, an interview with a candidate patient, and determination by the investigator. The specific tests noted in **Section 5.2.1** (24-hour Holter, LVEF, LAD, and presence of thrombus) may not be able to be completed prior to obtaining consent if they were not performed as part of standard of care. In the case where these tests were not performed as part of standard of care and are only being performed for the purposes of this study, they must be assessed after obtaining consent, but before the subject has an ablation catheter inserted into their vasculature for an ablation procedure.

Patients must meet ALL of the inclusion criteria to be considered for this clinical investigation. If ANY of the exclusion criteria are met, the patient is excluded from the clinical investigation.

5.3.1 Inclusion Criteria

1) Patient must provide written informed consent prior to any clinical investigation related procedure.
2) Documented symptomatic persistent AF, which is defined as continuous AF sustained beyond 7-days and less than 1-year that is documented by (1) a physician's note AND (2) a 24-hour Holter within 90-days prior to the procedure, showing continuous AF, OR (3) two electrocardiograms (from any form of rhythm monitoring) showing continuous AF, with electrocardiograms taken at least 7 days apart
3) Refractory or intolerant to at least one Class I or III antiarrhythmic drug (AAD) as evidenced by recurrent symptomatic AF
4) Age 18 years or older
5) Able and willing to comply with all pre-, post-, and follow-up testing and requirements

5.3.2 Exclusion Criteria

1) Continuous AF > 12 months (longstanding persistent AF)
2) Previous left atrial surgical or catheter ablation for atrial fibrillation or a previous procedure that required an incision in the left atrium with resulting scar
3) Any cardiac procedure (surgical or percutaneous) within 90-days prior to the initial procedure
   NOTE: Diagnostic cardiac procedures in which no intervention, implant, or incision was made in the cardiac tissue are not considered a surgical or percutaneous cardiac procedure.
4) CABG surgery within the 6-months (180-days) prior to the initial procedure

[redacted]

5) Valvular cardiac surgical/percutaneous procedure (i.e. ventriculotomy, valve repair or replacement and/or presence of a prosthetic or mechanical valve)
6) Any carotid stenting or endarterectomy
7) Documented or known left atrial thrombus on imaging
8) Left atrial diameter > 50 mm (parasternal long axis view or by CT)
9) Left ventricular ejection fraction < 40%
10) Unable to take anticoagulation medication due to contraindication or intolerance
11) History of blood clotting or bleeding abnormalities
12) Myocardial infarction (MI), acute coronary syndrome, percutaneous coronary intervention (PCI) within the 3-months (90-days) prior to the initial procedure
13) Documented thromboembolic event (including TIA) within the 12-months (365 days) prior to the initial procedure
14) Rheumatic heart disease
15) Uncontrolled heart failure or NYHA functional class III or IV
16) Severe mitral regurgitation (regurgitant volume ≥ 60 mL/beat, regurgitant fraction ≥ 50%, and/or effective regurgitant orifice area ≥ 0.40cm^2)
17) Awaiting cardiac transplantation or other cardiac surgery within the 12-months (365 days) following the initial ablation procedure
18) Unstable angina at the time of the initial procedure
19) Acute illness or active systemic infection or sepsis
20) AF secondary to electrolyte imbalance, thyroid disease, acute alcohol intoxication, major surgical procedure in the preceding 3-months, or other reversible or non-cardiac cause
21) Diagnosed atrial myxoma
22) Presence of implanted implantable cardioverter defibrillator (ICD) or cardiac resynchronization therapy-defibrillator (CRT-D)
23) Significant pulmonary disease, (e.g., restrictive pulmonary disease, constrictive or chronic obstructive pulmonary disease) or any other disease or malfunction of the lungs or respiratory system that produces chronic symptoms
24) Significant congenital anomaly or other anatomic or comorbid medical problem that in the opinion of the investigator would preclude enrollment in this study or compliance with the follow-up requirements or impact the scientific soundness of the clinical trial results
25) Pregnant or nursing subjects and those who plan pregnancy during the clinical investigation follow-up period
26) Enrollment in an investigational study evaluating another device, biologic, or drug that may interfere with this clinical investigation at the time of the initial procedure or within 30 days prior to the initial procedure
27) Presence of any condition that precludes appropriate vascular access or manipulation of catheter
28) Life expectancy less than 12-months
29) Body mass index > 40 kg/m^2
30) Known sensitivity to contrast media (if needed during the procedure) that cannot be controlled with pre-medication

[redacted]

31) Renal failure requiring dialysis
32) Presence of 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
33) History of atriotomy or ventriotomy
34) Implanted endocardial left atrial appendage occlusion device

5.4 Subject Enrollment

A patient is considered enrolled in the clinical investigation from the moment the patient provides written informed consent and meets all eligibility criteria.

If a TactiCath SE device is used for ablation on an enrolled subject who does not meet eligibility criteria for the trial, they will not be withdrawn from the trial and will be counted in the analysis population and will complete all follow-up requirements.

5.4.1 Enrollment of Medicare Beneficiaries (United States only)

This clinical investigation will enroll Medicare beneficiaries that qualify based on the inclusion and exclusion criteria defined for this trial. This IDE clinical trial conforms to all standards of Medicare coverage requirements. The Risks and Benefits section (**Section 15**) describes how all enrolled subjects, including Medicare beneficiaries, may be affected by the device under investigation.

Subjects enrolled in this clinical investigation are expected to be consistent with the Medicare population based on demographic characteristics and cardiovascular risk factors and as such, the clinical investigation results are expected to be generalizable to the Medicare population.

5.4.2 Historically Under-Represented Demographic Subgroups

The Sponsor intends to implement FDA's guidance on sex-specific data in medical device clinical investigations to ensure adequate representation of women and other traditionally under-represented demographic subgroups in this clinical investigation. As noted in the FDA guidance, some barriers to participation of women and ethnic minorities in clinical investigations have traditionally been:

- Lack of understanding about main obstacles to participation of such subgroups in clinical research
- Inclusion/exclusion criteria potentially not needed to define the clinical investigation population may unintentionally exclude specific subgroups
- Under diagnosis of disease etiologies and pathophysiology leading to under referral of demographic subgroups
- Avoidance of specific subgroups by investigators and Sponsors due to the perception that it takes more time and resources to recruit them
- Fear of fetal consequences (for female participants)
- Family responsibilities limiting women's ability to commit time for follow-up requirements

The Sponsor will take the following steps to ensure adequate representation of women and racial or ethnic minorities in this clinical investigation:

[redacted]

- Abbott will provide training to investigational site personnel to ensure adequate representation of these demographic subgroups
- Abbott will approach sites without bias or consideration for specific demographic subgroups
- Abbott will have informed consent materials in alternative languages and will work with sites and IRBs/ECs on recruitment materials

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.

Abbott must be notified of the reason(s) for subject discontinuation. The site will provide this information to Abbott as documented on the appropriate CRF. 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 they are withdrawn from the clinical investigation. If a subject withdraws from the investigation due to problems related to the safety or performance of the device under investigation, they will be followed by their regular physician per their standard of care.

If for any reason, the subject has the TactiCath SE inserted into their vasculature, but no ablation is performed and the subject will not be rescheduled to receive another ablation procedure, the subject will be followed for 30-days to assess safety and then exited from the trial.

In the event that a subject does elect to withdraw from the trial, the site should make attempts to schedule the subject for a final visit. At this final follow-up visit, the subject will undergo assessments as outlined for an unscheduled visit (**Section 6.6.2**), if the visit does not coincide with a scheduled follow-up visit.

Withdrawn subjects count towards the total enrollment at the site and will not be replaced by enrolling additional subjects.

<u>Lost-to-Follow-up</u>

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 their efforts, including the following, for each time an attempt was made to contact the subject:

- 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 should be sent via registered mail to the subject.
- If a subject misses one or more non-consecutive follow-up contact time points, it will be considered a missed visit. The subject may then return for subsequent visits.

[redacted]

- If the subject misses two consecutive time points and the above-mentioned attempts at communicating with the subject are unsuccessful, the subject will be considered lost-to-follow-up.

Note: Telephone contact with the general practitioner, cardiologist not participating in this clinical investigation, or relative without the presence of the subject or indirect documentation obtained via discharge letters will not be considered as contact with the subject.

5.6 Total Expected Duration of the Clinical Investigation

[redacted] Subjects will be followed for 15-months after their initial ablation procedure [redacted]

5.7 Expected Duration of Each Subject's Participation

Scheduled visits and data collection for the trial will occur at baseline, procedure, and pre-discharge as well as at scheduled follow-up visits at 7-days (phone call), 3-months (in-person), 6-months (phone call), 12-months (phone call) and 15-months (in-person) post-procedure. Subjects will be exited from the trial at the conclusion of their 15-month follow-up visit.

5.8 Number of Subjects

Two hundred twenty-four (224) subjects will be enrolled in this clinical investigation at up to 25 sites worldwide for analysis of the primary endpoints. No center may contribute more than 20% of the total number of enrollments without Sponsor pre-approval and at least 50% of the subjects must be from the United States.

6 TREATMENT AND EVALUATION OF ENDPOINTS

The Principal Investigator is responsible for ensuring all clinical investigation data is collected as outlined in this CIP. However, other site personnel may obtain data to be used in the trial. Physical exams and adverse event assessment may be performed by an investigator, physician, or mid-level provider (i.e. nurse practitioners, physician assistants, or fellows). The neurological assessment needs to be performed by a qualified physician and the NIH Stroke Scale must be administered by a certified assessor.

6.1 Baseline Clinical Assessments

The assessments listed below will be collected from each subject at the Baseline Visit. Information gathered at this visit will be used to verify eligibility of the subject for the trial.

- Documentation of the informed consent process as defined in **Section 5.2.2**
- Demographics
- Medical history, cardiac arrhythmia history, and documentation for the diagnosis of persistent AF
- Healthcare utilization documentation for cardiovascular-related hospitalizations, emergency room and/or urgent care visits during the 12-month period prior to consent

[redacted]

- Administration of a 24-hour Holter that must demonstrate 100% continuous AF within 90-days of the procedure OR documentation of 2 ECGs (from any form of rhythm monitoring) taken at least 7 days apart showing continuous AF

  NOTE: Repeat Holter assessments are not allowed if 100% continuous AF was not demonstrated on the first 24-hour Holter assessment. If artifact is present in the tracing, it can be disregarded when assessing for 100% continuous AF. All readable portions of the tracing should demonstrate continuous AF (non-sinus rhythm).
- AAD history, including maximum ineffective dosages and dosages not tolerated
- Anticoagulation drug usage
- Complete physical exam including 12-lead ECG, NYHA assessment, and CHA_2DS_2VASc score assessment

  NOTE: If these assessments were performed as part of standard of care prior to consent, they may be used if they were completed within 30-days of the initial ablation procedure.
- Neurological assessment by a qualified physician and administration of the NIH Stroke Scale (NIHSS) by a certified assessor must be performed within 14-days of the ablation procedure.

  NOTE: Subjects with new findings on the neurologic assessment/NIHSS are required to have a formal neurological consult and follow-up diffusion-weighted magnetic resonance imaging (MRI) of the brain. If contra-indicated for MRI, then an alternate form of imaging may be performed.
- Echocardiography or CT results (LVEF and LAD assessments) obtained within 6-months of the ablation procedure may be used to meet eligibility criteria and documented at baseline, with the exception of thrombus assessment. Thrombus assessment must be performed as specified in **Section 6.2.6**.
- Administration of the AF Effect on Quality of Life Survey (AFEQT) and EuroQol Five Dimensions Questionnaire (EQ-5D-5L) quality of life questionnaires
- Documentation of adverse events and protocol deviations that occur after consent and prior to the procedure

6.2 Peri-procedural Considerations

6.2.1 Anticoagulation

The anticoagulation strategies from the 2017 Expert Consensus Statement on Catheter and Surgical Ablation for AF[4] for pre- and post-ablation are outlined below and are recommended to be followed for management of study subjects. However, **it is strongly recommended that a strategy of uninterrupted anti-coagulation be in place for peri-operative management**. All start and stop times of anticoagulants must be documented for the trial. Subjects who are taking coumadin or warfarin will have international normalized ratio (INR) values documented on the day of the procedure and after the drug is restarted after the ablation procedure.

Pre-ablation

- Patients who are therapeutically anticoagulated with warfarin, dabigatran or rivaroxaban prior to the ablation are recommended to have the ablation procedure performed without interruption of the anticoagulant.

[redacted]

- Patients anticoagulated with a novel oral anticoagulant (NOAC) prior to undergoing an AF ablation procedure may have one to two doses of the NOAC withheld prior to AF ablation with re-initiation of the NOAC post-ablation.

- Anticoagulation guidelines that pertain to cardioversion of AF should be adhered to in patients who present for an AF ablation procedure.

Post-ablation

- In patients who are not therapeutically anticoagulated prior to catheter ablation of AF and in whom warfarin will be used for anticoagulation post-ablation, low molecular weight heparin or intravenous heparin should be used as a bridge for initiation of systemic anticoagulation with warfarin following AF ablation.

- Systemic anticoagulation with warfarin or NOAC is recommended for at least 2-months post-ablation of AF. Systemic anticoagulation beyond 2-months post-ablation should be based on the patient's stroke risk profile (not on the perceived success or failure of the ablation procedure).

- In patients who have not been anticoagulated prior to catheter ablation of AF or in whom anticoagulation with a NOAC or warfarin has been interrupted prior to ablation, administration of a NOAC 3 to 5 hours after achievement of hemostasis is reasonable post-ablation.

6.2.2 Antiarrhythmic Drug Therapy

The 2017 Consensus Statement on Catheter and Surgical Ablation for Atrial Fibrillation[4] states that AADs need to be discontinued for at least five half-lives and beta-blockers withheld for at least 24-hours prior to the ablation procedure if a strategy searching for non-pulmonary vein triggers is employed. As the ablation strategy is left to the discretion of the investigator, other than the requirement for PV isolation, this clinical investigation will not require that all subjects discontinue AADs for at least five half-lives. However, AAD usage (start and stop date, time, frequency and dose information) will be documented for the trial prior to and after the subject's procedure(s).

During the blanking period after the ablation procedure, it is recommended that any current AAD medication be continued following the ablation procedure to aid with healing. Current AADs should be withdrawn 4-6 weeks after ablation, unless clinically contraindicated, to assess for recurrence of symptoms and for determination of the need for a repeat ablation during the blanking or therapy consolidation periods. It is recommended that sites phone subjects 4-6 weeks after ablation to remind them to discontinue their AAD medication.

It is recommended that subjects be taken off all Class I and III AADs prescribed for AF/AFL/AT after the blanking and therapy consolidation periods. If the investigator feels that the subject may benefit from a Class I or III AAD during the 9-month evaluation period (post-blanking and therapy consolidation periods), then the investigator should first prescribe a previously ineffective Class I or III AAD up to the historic maximum ineffective dose prior to the ablation procedure. If the historic maximum ineffective dose remains ineffective then a new Class I or III AAD may be initiated.

Subjects using AADs without documented AF/AFL/AT recurrence during the follow-up period will not be considered effectiveness endpoint failures. However, if the subject requires a new AAD or a previously

failed AAD at a dose greater than the highest ineffective historical dose for AF after the therapy consolidation period (>180 days post-procedure), they will be considered a primary effectiveness endpoint failure.

6.2.3 Vascular Access

It is strongly recommended that vascular access be obtained using ultrasound to minimize complications.

6.2.4 Esophageal Temperature Monitoring

It is strongly recommended that esophageal temperature be monitored using an esophageal temperature probe at the anatomical location nearest the site of energy delivery. Alternatively, esophageal deviation may be performed when ablating near the esophagus.

Termination of energy is strongly recommended if a >1°C rise in esophageal temperature is observed.

6.2.5 Pregnancy Testing

A urine pregnancy test should be performed for women of child-bearing potential, preferably on the day of the procedure.

6.2.6 Thrombus Assessment

Left atrial thrombus assessment by transesophageal echocardiography (TEE) (recommended method) must be performed within one day of the ablation procedure (the day before or the day of the ablation procedure). Alternatively, phased-array intracardiac echocardiography (ICE) or TEE assessment can be performed on the day of the procedure, if the presence of thrombus has not been ruled out prior to the procedure. Standard of care may be used for this assessment.

If a thrombus is discovered within a day of the procedure, the procedure should be postponed and the subject placed on anticoagulation until the thrombus is resolved and confirmed by imaging. Once confirmation is obtained demonstrating resolution of the thrombus, the inclusion/exclusion criteria should be re-reviewed for the subject to confirm continued eligibility for the trial. The neurological assessment and NIH Stroke Scale must be repeated within 2-weeks of the newly scheduled procedure and these assessments used to determine if the subject still meets eligibility for inclusion in the trial.

The subject will not need to be re-consented for the trial after the thrombus resolves, provided that the subject meets all eligibility criteria and will undergo an ablation procedure within 90-days of the original consent date unless otherwise indicated by the governing IRB/EC.

6.3 Ablation Procedure

Any subject who does not meet eligibility requirements will be a screen failure and will be excluded from this trial and will not have the TactiCath SE catheter inserted into their vasculature.

For those subjects meeting eligibility criteria and are enrolled in the trial, it is preferable that the ablation procedure be performed within 14-days of consent. Use of robotic systems or Stereotaxis to assist with the procedure is not allowed.

[redacted]

The subject's rhythm when they enter the EP lab will be documented for the trial. All cardioversions that occur from the time the subject enters the lab to the start of the procedure and during the procedure will be documented.

It is recommended that heparin be administered prior to trans-septal puncture during the AF catheter ablation procedure and adjusted to achieve and maintain an ACT of at least 300 seconds. Use of an ICE probe during the procedure to guide septal puncture and to monitor catheter position and manipulation is strongly recommended. Administration of protamine to reverse heparin is acceptable.

Following trans-septal access, a standard treatment scheme for mapping and ablation should be conducted. Physicians performing ablations must be qualified operators and trained on the study. Each physician who ablates during a particular case needs to be documented on the Procedure CRF. Fellows will not be allowed to perform ablations unless an exception is made by Abbott's Medical Director in writing prior to the fellow performing ablations for this trial.

The procedure should be performed according to the TactiCath SE *Instructions for Use* document using the recommended ablation parameters as noted in the document:

- Power (10 - 30W)
- Contact force (target 20 g, 10-30 g)
- Temperature (37 – 50 °C)
- Irrigation flow rate (17 - 30 ml/min)

When ablating near the left atrial posterior wall, it is recommended that a minimum targeted contact force of 5-10 grams be used as specified in the 2017 HRS Consensus Statement. Recommended maximum parameters for ablating the left atrial posterior wall near the esophagus are:

- Contact force: ≤15 g for ≤10 seconds
- Power: up to 40W

The following ablation strategy should be followed for all subjects:

1. Perform wide area circumferential ablation to electrically isolate the pulmonary veins.
2. Administer isoproterenol following initial pulmonary vein isolation if the subject is in sinus rhythm to identify gaps in ablation and to identify and ablate any additional AF triggers.
3. Cardiovert the subject before isoproterenol challenge if he/she is not in sinus rhythm after initial pulmonary vein isolation.
4. Ablation of additional cardiac substrate (e.g. ablation of complex fractionated atrial electrograms (CFAE) or linear ablations) should only be considered if sinus rhythm is not restored after isolation of the pulmonary veins and ablation of non-PV triggers.

All subjects will receive ablations to achieve electrical isolation of the PVs. A minimum 20-minute wait period following electrical isolation of all PVs is required. Achievement of electrical isolation of the PVs requires assessment and documentation of entrance block. It is recommended that exit block also be demonstrated.

If PV reconnection occurs during or after the 20-minute wait period following initial PV isolation of all veins, the vein(s) that reconnected and whether it was successfully isolated after administration of additional ablation lesions will be documented on the CRF. Another 20-minute waiting period is not required after performing touch-up ablation lesions for reconnected PVs.

Subjects with a history of AFL, AT or other SVT (spontaneous or induced) or if these arrhythmias are induced at the time of AF ablation, may undergo additional targeted ablation as clinically indicated. All subjects with a history of typical atrial flutter or induced cavotricuspid isthmus (CTI)-dependent atrial flutter need to undergo concomitant AFL ablation and are required to verify bi-directional block by mapping and pacing maneuvers after initial bi-directional block is achieved.

Additional non-pulmonary vein AF ablation targets (e.g. linear ablation, elimination of CFAEs, rotational activity, autonomic ganglia, isolation of the left atrial appendage, ablation of scar identified by voltage mapping or MRI, and non-PV triggers) are permitted per the investigator's discretion and will be documented for the trial if sinus rhythm is not restored after isolation of the pulmonary veins and ablation of non-PV triggers. If a linear ablation strategy is used, documentation of bidirectional block across the ablation line must be demonstrated and assessed in sinus rhythm and with differential pacing maneuvers. High-dose isoproterenol may be administered to screen for and ablate non-PV triggers. If CFAEs, rotational activity, or non-PV triggers are ablated, the acute goal is elimination of CFAEs, rotational activity, and non-PV triggers and AF termination.

The goal is that the subject is in sinus rhythm at the end of the procedure. If AF cannot be terminated by ablation at the conclusion of the procedure, it is recommended that the patient be cardioverted and PV isolation rechecked.

Verify that the subject has not experienced pericardial effusion by ICE or transthoracic echocardiogram (TTE) at the end of the procedure.

The data from the entire procedure recorded on the commercial EnSite system should be anonymized and labeled with the study information, Subject ID, backed up on a USB or external drive, and sent to Abbott within a reasonable time frame (within 10 days).

If for any reason, the subject has the TactiCath SE inserted into their vasculature, but no ablation is performed and the subject will not be rescheduled to receive another ablation procedure, the subject will be followed for 30-days to assess safety and then exited from the trial. Follow-up at 30-days will be conducted via a phone call to the subject (may also be an on-site visit). Subjects who will have their ablation procedure re-scheduled will not need to be re-consented for the trial provided they are rescreened (all eligibility criteria met prior to the procedure) within 90-days of the initial consent date.

6.3.1 Description of Study Activities Performed by Abbott Field Representatives

Trained Abbott personnel may provide technical expertise and technical guidance on the use of the device. However, the Principal Investigator remains responsible for ensuring all clinical investigation data is collected as required per the CIP. An Abbott field representative may assist with obtaining procedure data from the EnSite system for documentation for the trial and/or downloading procedure data to a USB or external drive and sending to Abbott.

6.4 Pre-Discharge Visit (In-hospital)

Same day discharge after the ablation procedure is not allowed for the study, even if it is considered standard of care at some institutions. It is strongly recommended that the investigator performing the ablation procedure personally evaluates the subject on the evening of the procedure and/or the morning

following the procedure and maintains active surveillance of the subject's postoperative care and condition for at least 72-hours or prior to discharge, whichever occurs first.

The following are required testing for the Pre-Discharge Visit:

- Complete physical exam and 12-lead ECG
- Neurological assessment by a qualified physician and administration of the NIHSS by a certified assessor must be performed >12 hours post-procedure prior to discharge, but no later than 36 hours after the procedure.

  NOTE: Subjects with new findings on the neurologic assessment/NIHSS are required to have a formal neurological consult and follow-up diffusion-weighted magnetic resonance imaging (MRI) of the brain. If contra-indicated for MRI, then an alternate form of imaging may be performed.
- Document AAD and anticoagulant drug usage
- Document adverse events and protocol deviations

If the subject requires an extended hospitalization due to a complication or other reason, the neurological exam and NIHSS assessment should be performed within 36-hours of the procedure. All other pre-discharge testing should be performed prior to discharge, but no later than 72 hours post-procedure.

6.5 Blanking and Therapy Consolidation Periods

A blanking period of 90-days will be employed after the initial ablation procedure, followed by a 90-day therapy consolidation period and then a 9-month evaluation period for a total of 15-months of follow-up. Early recurrence of AF, AFL, or AT within the blanking period or therapy consolidation period will not be considered treatment failures. During the blanking and therapy consolidation periods, adjustment of antiarrhythmic medications, cardioversions, and one repeat ablation procedure may be performed.

6.6 Follow-up Assessments

Subjects will undergo the following assessments described below at 7-days and at 3, 6, 12 and 15-months post-ablation.

7-Day (7 ± 2 days) Follow-up Visit

This visit constitutes a phone call to the subject after each ablation procedure (initial and if applicable, a repeat procedure) and requires documentation of the following:

- Document AAD and anticoagulant drug usage
- Document adverse events and protocol deviations
  - If the subject describes symptoms suggestive of pulmonary vein stenosis (e.g. shortness of breath, cough, and hemoptysis), have the subject schedule a visit with the investigator to determine if CT or MRI imaging of the pulmonary veins should be performed.
  - If the subject describes symptoms suggestive of atrioesophageal fistula such as chest pain, painful swallowing, fever, and/or describes symptoms of stroke, have the subject schedule a visit with the investigator immediately or go to the emergency room based on the severity of the symptoms.

[redacted]

- If the subject describes symptoms suggestive of cardiac tamponade (i.e., chest pain with hypotension) or if cardiac tamponade is suspected, the subject should be evaluated promptly by the investigator and a TTE performed.

- Document any cardiovascular healthcare utilization performed since the last scheduled study visit as defined in **Section 6.6.3**

3-Month (91 + 14 days) Follow-Up Visit

The 3-month follow-up visit is a scheduled in-person site visit.

- Provide the subject with a TTM device for monthly heart rhythm transmission and transmission of symptomatic episodes, if the subject does not have the device provided to them at the Baseline visit.
- When subjects are seen at the 3-month visit, it is recommended that they are weaned off AADs during the therapy consolidation period if they are doing well and have not discontinued these medications previous to this visit.
- 12-lead ECG
- Document AAD and anticoagulant usage
- Administer the AFEQT and EQ-5D-5L questionnaires
- Document any cardiovascular healthcare utilization performed since the last visit as defined in **Section 6.6.3**
- Document adverse events and protocol deviations
  - If the subject describes symptoms suggestive of pulmonary vein stenosis (e.g. shortness of breath, cough, and hemoptysis), complete CT or MRI imaging of pulmonary veins.
- Administer a 24-hour Holter monitor

6-Month (181 + 30 days) Follow-Up Visit

The 6-month follow-up visit is a phone call to the subject, but may also be performed in-person.

- Document AAD and anticoagulant usage
- Administer the AFEQT and EQ-5D-5L questionnaires
- Document any cardiovascular healthcare utilization performed since the last visit as defined in **Section 6.6.3**
- Document adverse events and protocol deviations
  - If the subject describes symptoms suggestive of pulmonary vein stenosis (e.g. shortness of breath, cough, and hemoptysis), have the subject schedule a visit with the investigator to determine if CT or MRI imaging of the pulmonary veins should be performed.
  - If the subject describes symptoms suggestive of atrioesophageal fistula such as chest pain, painful swallowing, fever, and/or describes symptoms of stroke, have the subject schedule a visit with the investigator immediately or go to the emergency room based on the severity of the symptoms.

[redacted]

- If the subject describes symptoms suggestive of cardiac tamponade (i.e., chest pain with hypotension) or if cardiac tamponade is suspected, the subject should be evaluated promptly by the investigator and a TTE performed.

- Administer a 24-hour Holter monitor
- Review TTM transmissions

12-Month (365 ± 30 days) Follow-Up Visit

The 12-month follow-up visit is a phone call to the subject, but may also be performed in-person.

- Document AAD and anticoagulant usage
- Administer the AFEQT and EQ-5D-5L questionnaires
- Document any cardiovascular healthcare utilization performed since the last visit as defined in **Section 6.6.3**
- Document adverse events and protocol deviations
  - If the subject describes symptoms suggestive of pulmonary vein stenosis (e.g. shortness of breath, cough, and hemoptysis), have the subject schedule a visit with the investigator to determine if CT or MRI imaging of the pulmonary veins should be performed.
  - If the subject describes symptoms suggestive of atrioesophageal fistula such as chest pain, painful swallowing, fever, and/or describes symptoms of stroke, have the subject schedule a visit with the investigator immediately or go to the emergency room based on the severity of the symptoms.
  - If the subject describes symptoms suggestive of cardiac tamponade (i.e., chest pain with hypotension) or if cardiac tamponade is suspected, the subject should be evaluated promptly by the investigator and a TTE performed.
- Administer a 24-hour Holter monitor
- Review TTM transmissions

15-Month (450 ± 30 days) Follow-Up Visit

The 15-month follow-up visit is a scheduled in-person site visit.

- 12-lead ECG
- Document AAD and anticoagulant usage
- Administer the AFEQT and EQ-5D-5L questionnaires
- Document any cardiovascular healthcare utilization performed since the last visit as defined in **Section 6.6.3**
- Document adverse events and protocol deviations
  - If the subject describes symptoms suggestive of pulmonary vein stenosis (e.g. shortness of breath, cough, and hemoptysis), complete CT or MRI imaging of pulmonary veins.
- Administer a 24-hour Holter monitor

[redacted]

- Review TTM transmissions

6.6.1 Repeat Ablation Procedures

One ablation procedure is allowed during the blanking and therapy consolidation periods (within 180 days post-initial procedure) due to AF/AFL/AT recurrence without being considered an effectiveness endpoint failure. The repeat procedure must be performed with the TactiCath SE catheter using the recommended parameters listed in the *Instructions for Use* document and in **Section 6.3**. The TactiCath SE catheter should not be used for repeat procedures that occur ≥181 days after the initial procedure or if the subject requires a third ablation procedure at any time during the follow-up period.

Certain assessments need to be performed if a repeat ablation is required. Neurological assessment and administration of the NIHSS by a certified assessor must be performed within 14-days of the repeat ablation procedure. Thrombus assessment must be performed as outlined in **Section 6.2.6** prior to ablating the subject. Verification of the exclusion of pericardial effusion by ICE or TTE must also be performed prior to the conclusion of the procedure.

A 7-day (± 2 days) follow-up phone call to the subject will need to be conducted after the repeat procedure. All other follow-up visits will occur as previously scheduled from the initial ablation procedure. Note that the 90-day blanking period followed by a 90-day therapy consolidation period are still in place from the initial procedure.

If AF/AFL/AT recurrence (>30 second episode) occurs at any time after this second ablation procedure or after the therapy consolidation period (≥181 days post-initial procedure), the subject will be considered an effectiveness endpoint failure. If the subject requires a repeat procedure for AF/AFL/AT recurrence after the therapy consolidation period or the subject requires a third ablation procedure, then the subject will be considered an effectiveness endpoint failure regardless of documentation of a >30 second AF/AFL/AT episode.

6.6.2 Unscheduled Visits

If a subject is seen by any physician for possible AF recurrence and/or arrhythmia associated symptoms outside of a regularly scheduled study visit and/or had an urgent care or emergency room visit regarding possible arrhythmia, these visits need to be documented as “Unscheduled Visits”. Minimally, the following information should be documented for an unscheduled visit.

- 12-lead ECG, if performed during the visit
- Document AAD and anticoagulant usage
- Document adverse events and protocol deviations

6.6.3 Healthcare Utilization Documentation

Healthcare utilization for cardiac-related hospitalizations (inpatient or outpatient), emergency room visits, and/or urgent care visits in the year previous to enrollment (consent) in this trial will be documented. Additionally, subjects will be interviewed at each scheduled visit to determine if they had any cardiac-related hospitalizations (inpatient or outpatient), emergency room visits, and/or urgent care visits since their last scheduled visit. Source documentation for these visits should be obtained and a Healthcare Utilization form completed.

6.6.4 Patient Reported Outcome Measures – AEFQT and EQ-5D-5L Questionnaires

The 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 coordinator or designee will review for completeness to verify that all questions have been answered according to the directions provided.

The following patient-reported outcome measures will be collected:

- AF Effect on Quality of Life Survey (AFEQT)
- EuroQol Five Dimensions Questionnaire (EQ-5D-5L)

The AFEQT questionnaire is an AF-specific health-related quality of life questionnaire designed to be used in different clinical settings including clinical research, survey studies, or clinical practice to assess the impact of AF on a patient's quality of life and possibly to assess changes with treatment. The AFEQT is a self-administered questionnaire that should take approximately 5-minutes to complete and consists of 20 questions. Four of the 20 questions target AF-related symptoms, 8 questions evaluate daily function, and 6 questions assess AF treatment concerns on a 7-point Likert scale (1= "Not at all…" to 7 "Extremely…"). Two of the questions are not scored and are to assess the subject's satisfaction with treatment. The AFEQT questionnaire should ideally be administered prior to the subject being seen by the physician to ensure the subject's responses are not influenced by the physician's evaluation. If other questionnaires are to be administered at the same time, the AFEQT should be completed first so that answers to other questionnaires do not influence the response to the AFEQT.

The EQ-5D-5L questionnaire is a standardized measure of health status that is applicable to a wide range of health conditions and treatments. It provides a simple descriptive profile and a single index value for health status that can be used in the clinical and economic evaluation of health as well as in population health surveys. EQ-5D-5L is designed for self-completion and is ideally suited for use in postal surveys, in clinics, and in face-to-face interviews and takes only a few minutes to complete. The questionnaire includes five dimensions assessing mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension is measured based on responses to 5 levels: no problems, slight problems, moderate problems, severe problems, and extreme problems. Respondents evaluate their overall health status using a visual analogue scale, which can easily be converted to quality-adjusted life years for cost utility analysis.

Note that it will not be a deviation for the 6-month and 12-month visits administered by phone to not have the visual analogue scale of the EQ-5D-5L questionnaire completed. Research personnel should use the EQ-5D-5L Script for Telephone Interview questionnaire for visits conducted over the phone.

6.6.5 Schedule of Events

The schedule of activities specific to this clinical investigation are described in the preceding sections and are summarized in **Table 4**.

Table 4. Schedule of Clinical Investigation Activities

Activity	Enrollment / Baseline	Procedure (~14-days of consent)	Pre-Discharge (>12 hrs and <72 hrs post-proc.)	7-Day Phone Call (± 2 days)	3-Month In-Person (91+14 days)	6-Month Phone Call[6] (181+30 days)	12-Month Phone Call[6] (365±30 days)	15-Month In-Person (450±30 days)
Informed Consent Process	X							
Demographics	X							
Medical History	X							
Cardiovascular History	X							
AAD & Anticoagulant Medications	X		X	X	X	X	X	X
Physical Examination	X		X					
Neurological Assessment & NIHSS	X		X[5]					
Diffusion-weighted MRI - Brain	(X)		(X)					
NYHA	X							
CHA_2DS_2VASc score	X							
12-Lead ECG	X[7]		X		X			X
AFEQT & EQ-5D-5L Questionnaires	X				X	X	X	X
24-Hour Holter	X[7]				X	X	X	X
Urine Pregnancy Test		(X)						
Confirm absence of thrombus		X[1]						
Ablation procedure		X						
TTE or ICE		X[2]	(X)[2]					
Trans-Telephonic Monitoring (TTM)					X[3]	X[3]	X[3]	X[3]
CT or MRI of pulmonary veins				(X)	(X)	(X)	(X)	(X)
Adverse Event Assessment	X	X	X	X	X	X	X	X
Document Deviations	X	X	X	X	X	X	X	X
Document Cardiovascular Healthcare Utilization	X[4]		X[4]	X[4]	X[4]	X[4]	X[4]	X[4]
Withdrawal	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)
Death	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)

(X) If applicable

1. Thrombus assessment must be performed the day prior to or on the day of the procedure. If a thrombus is discovered, the procedure should be postponed and the subject placed on anticoagulation until the thrombus is resolved as confirmed by imaging.
2. TTE or ICE imaging must be performed prior to the conclusion of the procedure to exclude pericardial effusion.

[redacted]

3. TTMs are collected monthly and whenever the subject is experiencing a symptomatic episode starting at 3-months post-procedure to 15-months.
4. At each scheduled visit, the subject will be interviewed to determine if they have had any cardiac-related hospitalizations (inpatient or outpatient), emergency room visits, and/or urgent care visits since the last scheduled study visit and a healthcare utilization form completed. Additionally, healthcare utilization in the year previous to enrollment in this trial will be assessed.
5. The neurological exam and NIHSS must be performed >12 hours, but no later than 36 hours after the procedure.
6. The 6 and 12-month visits are phone calls to the subject. However, these visits may be conducted in-person as well.
7. Either a 24-hr Holter or 2 ECGs obtained ≥7 days apart may be used to demonstrate continuous AF at Baseline.

6.7 Core Laboratory

A core lab will be used for the collection, interpretation, and collation of data collected from the following sources:

- TTM
- 24-hour Holter monitoring
- 12-lead ECGs

The core lab will provide independent review of this data by appropriately trained personnel using standardized procedures to interpret TTM, 24-hour Holter, and 12-lead ECG tracings for adjudication of atrial arrhythmias. Findings will be communicated to the investigator and to Abbott. The core lab's adjudication findings will be used for analysis.

7 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 Definitions

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.

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

7.1.3 Device Deficiency/Device Malfunction

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

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

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 AE is to be **determined by the Investigator** and recorded on the appropriate CRF form. Determination should be based on assessment of temporal relationships, evidence of alternative etiology, medical/biologic plausibility, and patient condition (pre-existing condition).

7.2.1 Adverse Device Effect (ADE)

The following definition will be used to categorize non-serious procedure or device-related AEs:

- 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.

7.2.2 Serious Adverse Device Effect (SADE)

The following definition will be used to categorize serious procedure or device-related AEs:

- Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.
- This definition includes events related to the investigational medical device or the comparator.

[redacted]

7.2.3 Unanticipated Device Effect (UADE) – United States only

Unanticipated serious adverse device effect (UADE) refers to any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

7.3 Adverse Event and Device Deficiency/Device Malfunction Reporting

7.3.1 Adverse Event Reporting

Safety surveillance and reporting starts as soon as the patient is enrolled in the clinical investigation. Adverse event data, including deaths, will be collected starting at the time of enrollment (after consent and eligibility criteria are met) and throughout the 15-month follow-up period and will be reported to the Sponsor on the Adverse Event CRF. 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.

For the purposes of this clinical investigation, the following adverse events will be reported:

- Adverse events that are assessed by the investigator as being related to either the ablation catheter or the ablation procedure will be reported in the database, preferably within 7-days of the site learning of the event
- Serious adverse events, regardless of relatedness to the procedure and/or the ablation catheter will be reported as described in **Section 7.3.2**.

Recurrence of AF, AFL, or AT are not considered reportable adverse events unless they occur in severity, frequency, or other manner that is significantly worse than the subject's baseline condition. Recurrence of AF, AFL, or AT will affect the primary effectiveness endpoint and should be reported on the Follow-Up Visit CRF.

Additionally, urinary tract infections (UTIs) that occur after a procedure and do not require a Foley catheter will not be considered adverse events. UTIs that require a Foley catheter will be reported as AEs if related to the procedure or meet serious criteria.

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

7.3.2 Serious Adverse Event (SAE) Reporting to Sponsor and IRB/EC

The investigator should report all SAEs to the Sponsor as soon as possible but no later than outlined below.

Clinical Sites	Reporting Timelines
All Sites	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.

[redacted]

The date the site staff became aware that 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.

7.3.3 Unanticipated Serious Adverse Device Effect Reporting to Sponsor and IRB

The Sponsor requires the Investigator to report any UADE to the Sponsor within 3 calendar days of the investigator's knowledge of the event, unless local requirements are more stringent, and to the IRB/EC per IRB/EC requirements.

7.3.4 Device Deficiency/Malfunction Reporting

All device deficiencies/malfunctions should be reported on the appropriate CRF form.

The investigator should report all device deficiencies/malfunctions to the Sponsor as soon as possible but no later than outlined below.

Clinical Sites	Reporting timelines
All Sites	Device deficiencies/malfunctions 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 device should be returned to the Sponsor.

Device deficiencies/malfunctions should be reported to the IRB/EC per the investigative site's local requirements.

7.3.5 Adverse Event Reporting to Country Regulatory Authorities by the Sponsor

The Sponsor will report SAEs to the country regulatory authority, per local requirements.

8 STATISTICAL CONSIDERATIONS

The following section describes the statistical methods for the clinical investigation. Additional details on statistical analyses, including justification of clinical investigation design, sensitivity analyses, poolability analyses, subgroup analyses and analysis of descriptive endpoints, will be maintained in a separate Statistical Analysis Plan (SAP).

8.1 [redacted]

[redacted]

8.2 Statistical Analyses

8.2.1 Primary Endpoint Analyses

8.2.1.1 Primary Safety Endpoint Analysis

The primary safety endpoint hypothesis is stated as follows:

H_0: P ≥ 16.8%

[redacted]

8.2.1.2 Primary Effectiveness Endpoint Analysis

The primary effectiveness endpoint hypothesis is stated as follows:

[redacted]

8.2.2 Secondary Endpoint Analyses

8.2.2.1 Secondary Endpoint – Acute Procedural Success

The hypothesis is stated as follows:

H_0: P ≤ 90%

[redacted]

8.2.2.2 Secondary Endpoint – Chronic Success Off Antiarrhythmic Drugs

The hypothesis is stated as follows:

[redacted]

[redacted]

8.2.2.3 Secondary Endpoint - Asymptomatic and Symptomatic Single Procedure Success

The hypothesis is stated as follows:

[redacted]

power to reject the null hypothesis with a performance goal of 16.8% and an attrition rate of 20%, is 224 [redacted]

8.4 Timing of Analysis

The primary endpoint analysis will be performed and the pre-market approval (PMA) clinical report submitted after the last subject has completed their 15-month follow-up visit or passed the end of the 15-month visit window.

8.5 Subgroup Analysis

Subgroup analyses will be performed to examine the consistency of results for the primary safety and effectiveness endpoints. [redacted]

[redacted]

8.6 Multiplicity

[redacted]

8.7 Procedures for Accounting for Missing Data

[redacted]

8.8 Planned Interim Analysis

No interim analyses are planned for this study.

8.9 Statistical Criteria for Termination

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

8.10 Success Criteria

[redacted]

8.11 Deviations from Statistical Plan

Any major changes to the statistical plan will be documented in an amendment to the statistical plan. Less significant changes to the planned analyses will be documented in the final report.

9 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 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.

[redacted]

10 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 Abbott 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 Abbott 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, investigational device usage, 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.

10.3.2 Training Required for the Use of the Device

All investigators involved in the conduct of this clinical investigation will be qualified by education, training, or experience to perform their tasks and this training will be documented appropriately. Each ablating physician must have contact force sensing experience and must have experience using EnSite Precision for AF treatment prior to site activation.

10.4 Monitoring

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

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

[redacted]

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

10.5 Deviations from the 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 Steering Committee

The Steering Committee is assigned by Abbott and consists of investigators. Abbott will also be represented on the committee. The Chairman of the core laboratories and other Sponsor personnel may also participate in the Committee meetings, if appropriate. Meeting minutes from this committee will be filed at Abbott.

The Steering Committee is responsible for overseeing the scientific and operational aspects of the clinical investigation. This committee will meet regularly to monitor subject enrollment, general data collection and non-compliance with the CIP at individual centers, to review operational issues that may arise and warrant a CIP amendment or other corrective action and to determine policy regarding any publications arising from data generated from the performance of the clinical investigation.

10.7.2 Clinical Events Committee (CEC)

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

11 DATA HANDLING AND RECORD KEEPING

The 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, if requested.

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.

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

[redacted]

- Dated and signed notes from each subject visit (for specific results of procedures and exams)
- Adverse events reported and their resolution, including supporting documents, such as discharge summaries, catheterization laboratory reports, ECGs, and lab results including documentation of site awareness of SAEs and of investigator assessment of device relationship for SAEs.
- CIP-required laboratory reports and 12-lead ECGs, reviewed and annotated for clinical significance of out-of-range results. It is acceptable to have labs and/or ECGs reviewed and annotated in the electronic medical record system for site's that have these capabilities. For those sites that do not have such capability, the labs and ECGs should be printed and signed by the investigator.
- Notes regarding CIP-required and prescription medications taken during the clinical investigation (including start and stop dates)
- Subject's condition upon completion of or withdrawal from the clinical investigation
- Cardiac-related hospitalizations (inpatient or outpatient), emergency room visits, and/or urgent care visits that occurred one year prior to consent and for the remainder of the trial
- Any other data required to substantiate data entered into CRFs

11.4 Case Report Form Completion

Worksheets will be provided to sites under separate cover for review of the required data collection for the trial. Sites may also create their own worksheets for data collection.

Primary data collection based on source-documented hospital and/or clinic chart reviews will be clearly and accurately documented 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 will be collected on CRFs for all subjects that are enrolled in the clinical investigation.

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 the Sponsor in writing before destroying or transferring control of any clinical investigation records.

11.6 Investigational Device Accountability (United States only)

The Sponsor will ship investigational TactiCath SE catheters only to activated sites. The Principal Investigator or an authorized designee will maintain records of the date of receipt and disposition of each investigational catheter. Abbott will also maintain device accountability by documenting all shipments and return of investigational catheters.

Serial numbers of Ampere Generator and TactiSys Quartz Equipment used in this IDE clinical investigation will be recorded on each Procedure CRF.

All investigational devices that are associated with a device failure must be returned immediately to the Sponsor.

12 ETHICAL CONSIDERATION

12.1 Institutional Review Board/Medical Ethics Committee Review and Approval

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

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 regulatory agencies (if applicable). 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.

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

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

13 CLINICAL INVESTIGATION CONCLUSION

The clinical investigation will be concluded when:

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

14 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.

Upon receiving IDE approval from the FDA, this clinical trial will be registered on ClinicalTrials.gov. A full report of the pre-specified outcomes, including any negative outcomes, will be made public through the ClinicalTrials.gov website no later than 12-months after clinical trial completion, as required by section 801 of the FDA Amendments Act. If this clinical trial is terminated early for safety, the Sponsor will make every effort to hasten the release of the pre-specified outcomes through the ClinicalTrials.gov website.

15 RISK ANALYSIS

Risks associated with the device are managed in accordance with ISO 14971. The risk analysis included an objective review of published and available unpublished medical and scientific data. The sections below provide an overview of residual risks identified in the risk management report and anticipated benefits of the medical device. The additional tests and assessments required by the clinical investigation were analyzed for additional risks and are incorporated in the sections below.

15.1 Risks Associated with the Device Under Investigation

The following sections outline the risks and control measures related to the TactiCath SE.

15.1.1 Anticipated Adverse Device Effects

The following is a list of anticipated adverse device effects:

- Air embolism
- Anesthesia reaction
- Aorto-right atrial fistula
- Arrhythmias, bradycardia, and tachycardia
- Arteriovenous fistula
- Cardiac perforation/tamponade
- Cardiac thromboembolism
- Cerebrovascular incident or Attack / Stroke
- Chest pain/discomfort
- Coronary artery dissection
- Coronary artery spasm
- Coronary artery thrombosis / occlusion
- Death
- Diaphragmatic paralysis
- Dislodgement of implantable cardioverter defibrillator or permanent pacing leads
- Endocarditis
- Gastroparesis
- Heart failure / pump failure
- Hemothorax
- Hospitalization (initial and prolonged)
- Increased creatinine phosphokinase (CPK) level
- Infections
- Laceration
- Leakage of air or blood into the lungs or other organs due to perforation
- Left atrial-esophageal fistula

- Major bleeding, requiring surgery or transfusion
- Myocardial infarction
- Obstruction or perforation or damage to the vascular system
- Pericarditis
- Pericardial effusion
- Phrenic nerve damage including diaphragmatic paralysis
- Pleural effusion
- Pneumonia
- Pneumothorax
- Pseudoaneurysm
- Pulmonary edema
- Pulmonary embolism
- Pulmonary vein dissection
- Pulmonary vein thrombus
- Pulmonary hypertension
- Respiratory depression
- Skin burns
- Severe PV stenosis (>70%), or complete occlusion of a PV, even in the absence of symptoms
- Tamponade, potentially requiring surgery
- Temperature elevation or fever
- Transient ischemic attack (TIA)
- Thromboembolism
- Thrombosis
- Unintended complete or incomplete AV, sinus node, or other heart block or damage
- Valvular damage
- Vascular bleeding/local hematomas/ecchymosis
- Vasovagal reactions
- Ventricular tachyarrhythmia
- Volume overload

15.1.2 Risks Associated with Clinical Investigation Assessments

The study does not require additional procedures or assessments beyond the standard of care for an atrial fibrillation ablation procedure. Study subjects are not exposed to additional medical risks due to their study participation.

15.1.3 Risk Control Measures

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

- Careful selection of experienced Investigators for the clinical investigation
- Adequate monitoring for each clinical investigation site
- Conducting the clinical investigation 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 investigation is performed
- Preparation of the device in accordance with the device IFU
- Training of Investigators and other applicable site personnel on the CIP
- Selection of investigators trained on the device

[redacted]

- Assessment of continuing safety of subjects in the clinical investigation by internal Abbott safety personnel

15.2 Possible Interactions with Concomitant Treatments

There are no known interactions with concomitant treatments.

15.3 Anticipated Benefits

It is possible the subject may have a more effective ablation procedure than they would have otherwise had with a different ablation catheter due to the improved visualization from the sensor, and improved maneuverability of the catheter with a bidirectional tip. The information gathered from the study will also add to the understanding of the treatment options for subjects with paroxysmal atrial fibrillation. This knowledge may advance medical science and have a benefit on other subjects with a similar arrhythmia.

15.4 Risk-to-Benefit Rationale

An extensive risk analysis and risk mitigation plan has been implemented to minimize any residual risk of the TactiCath SE to the subject. The improved maneuverability and visualization during the procedure may convey a benefit to the subject and outweigh any potential residual risk.

15.5 History of Device Modifications or Recall

There have been no modifications or recalls in relation to safety and clinical performance of the TactiCath SE device under investigation.

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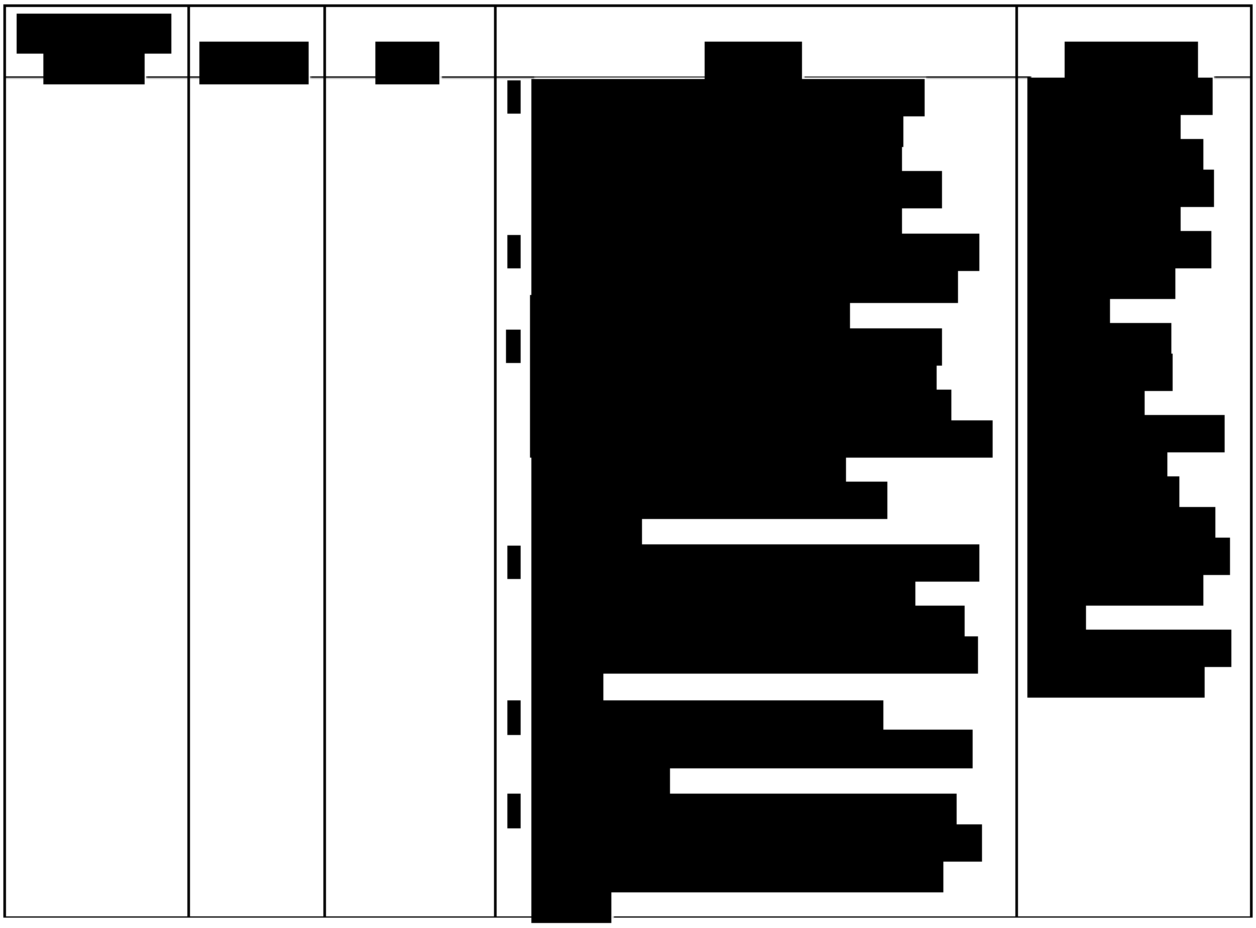

APPENDIX II. ABBREVIATIONS AND ACRONYMS

All relevant abbreviations and acronyms specific to this clinical investigation are outlined in the table below.

Acronym/Abbreviation	Description
AAD	Antiarrhythmic drug
AE	Adverse event
AF	Atrial fibrillation
AFEQT	Atrial Fibrillation Effect on QualiTy of Life
AFL	Atrial flutter
APHRS	Asia Pacific Heart Rhythm Society
AT	Atrial tachycardia
CEC	Clinical Events Committee
CFAE	Complex fractionated atrial electrograms
CIP	Clinical investigation plan
CRF	Case report form
CRT-D	Cardiac resynchronization therapy defibrillator
CTI	Cavotricuspid isthmus
CVA	Cerebrovascular accident
DMP	Data Management Plan
EC	Ethics Committee
ECAS	European Cardiac Arrhythmia Society
ECG	Electrocardiogram
EDC	Electronic data capture
EHRA	European Heart Rhythm Association
EQ	EuroQol Group
FDA	Food and Drug Administration
GCP	Good Clinical Practice
HIPAA	Health Insurance and Portability and Accountability Act
HRS	Heart Rhythm Society
ICE	Intracardiac echocardiography
ICD	Implantable cardioverter defibrillator
ICF	Informed Consent form
IDE	Investigational device exemption
IFU	Instructions for Use
INR	International normalized ratio
IRB	Institutional Review Board
LAD	Left atrial diameter
LCD	Liquid crystal display
LVEF	Left ventricular ejection fraction
MI	Myocardial infarction
NIHSS	National Institutes of Health Stroke Scale
NOAC	Novel oral anticoagulant
NYHA	New York Heart Association

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Acronym/Abbreviation	Description
OPC	Objective performance criterion
PCI	Percutaneous coronary intervention
PMA	Pre-market approval
PTE	Per treatment evaluable
PV	Pulmonary vein
RF	Radiofrequency
SAE	Serious adverse event
SE	Sensor enabled
SOLAECE	Latin America Society of Electrophysiology and Cardiac Stimulation
SVT	Supraventricular tachycardia
TEE	Transesophageal echocardiogram
TIA	Transient ischemic attack
TTE	Transthoracic echocardiogram
TTM	Transtelephonic monitoring
UADE	Unanticipated adverse device effect
UTI	Urinary tract infection

APPENDIX III. DEFINITIONS

The following definitions will be used by the CEC to determine whether the events listed below constitute a device or procedure related serious adverse event included in the primary endpoint. Most of the definitions have been adapted from the 2017 HRS/EHRA/ECAS/APHRS/SOLAECE Expert Consensus on AF Ablation.[4]

Primary Safety Event	Description
Atrioesophageal fistula	A connection between the atrium and the lumen of the esophagus. Evidence supporting this diagnosis includes documentation of esophageal erosion combined with evidence of a fistulous connection to the atrium, such as air emboli, an embolic event, or direct observation at the time of surgical repair. A CT scan or MRI scan is the most common method of documentation of an atrioesophageal fistula.
Bleeding	Bleeding is a major complication of AF ablation if it requires and/or is treated with transfusion or results in a 20% or greater fall in hematocrit.
Cardiac tamponade/perforation	The development of a significant pericardial effusion during or within 30 days of undergoing an AF ablation procedure. A significant pericardial effusion is one that results in hemodynamic compromise, requires elective or urgent pericardiocentesis, or results in a 1-cm or more pericardial effusion as documented by echocardiography. Cardiac tamponade/perforation should also be classified as "early" or "late" depending on whether it is diagnosed during or following initial discharge from the hospital.
Death	Adverse event resulting in the patient's death.
Heart block (AV block)	New, persistent 2nd or 3rd degree AV block not attributable to a vasovagal reaction or medication effect and requiring permanent pacing.
Myocardial infarction	Irreversible necrosis of heart muscle secondary to prolonged ischemia with at least one of the following three criteria: (2) Detection of ECG changes indicative of new ischemia (new ST-T wave changes or new LBBB) that persist for more than 1 hour; (3) Development of new pathological Q waves on an ECG; (4) Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.
Pericarditis	Pericarditis should be considered a major complication following ablation if it results in an effusion that leads to hemodynamic compromise or requires pericardiocentesis, prolongs hospitalization by more than 48 hours, requires hospitalization, or persists for more than 30 days following the ablation procedure.
Phrenic nerve injury resulting in diaphragmatic paralysis	Phrenic nerve paralysis is defined as absent phrenic nerve function as assessed by a sniff test. A phrenic nerve paralysis is considered to be permanent when it is documented to be present 12 months or longer following ablation.
Pneumothorax	Abnormal collection of air in the pleural space between the lung and the chest wall that prolongs the hospital stay (for observation) or requires surgical intervention or chest tube placement.
Pulmonary edema	Excess fluid in the lungs that includes all of the following: • Symptoms (e.g. dyspnea) • Physical findings (e.g. rales, hypoxemia) • Radiologic findings • Response to diuretic therapy • Requires hospitalization
Pulmonary vein stenosis	Reduction of the diameter of a pulmonary vein or a pulmonary vein branch of ≥70% confirmed via imaging (CT or MRI).
Stroke / cerebrovascular accident	Stroke diagnostic criteria:

Primary Safety Event	Description
	• Rapid onset of a focal or global neurological deficit with at least one of the following: change in level of consciousness, hemiplegia, numbness or sensory loss affecting one side of the body, dysphasia or aphasia, hemianopia, amaurosis fugax, or other neurological signs or symptoms consistent with stroke • Duration of a focal or global neurological deficit ≥24 hours; OR <24 hours if therapeutic intervention(s) were performed (e.g. thrombolytic therapy or intracranial angioplasty); OR available neuroimaging documents a new hemorrhage or infarct; OR the neurological deficit results in death. • No other readily identifiable nonstroke cause for the clinical presentation (e.g. brain tumor, trauma, infection, hypoglycemia, peripheral lesion, pharmacological influences). • Confirmation of the diagnosis by at least one of the following: neurology or neurosurgical specialist; neuroimaging procedure (MRI or CT scan or cerebral angiography); lumbar puncture (i.e. spinal fluid analysis diagnostic of intracranial hemorrhage)
Thromboembolism	An arterial or venous thrombus that results in deep vein thrombosis, pulmonary embolism, or peripheral arterial embolism.
Transient ischemic attack	New focal neurological deficit of vascular (occlusive) origin with rapid symptom resolution (usually 1 to 2 hours), always within 24 hours determined by the consulting neurologist; neuroimaging without tissue injury.
Vascular access complication	Vascular access complications include development of a hematoma, an AV fistula, or a pseudoaneurysm. A major vascular complication is defined as one that requires intervention, such as surgical repair or transition, prolongs the hospital stay, or requires hospital admission.

APPENDIX IV. CIP SUMMARY

Clinical Investigation	PERSIST-END (CRD-901)
Title	Safety and Effectiveness of TactiCath Contact Force, Sensor Enabled (TactiCath SE) Catheter for Ablation of Drug Refractory, Symptomatic, Persistent Atrial Fibrillation
Objective	The objective of this clinical trial is to demonstrate that ablation with the TactiCath™ Contact Force Ablation Catheter, Sensor Enabled™ (TactiCath SE) is safe and effective for the treatment of drug refractory, symptomatic persistent atrial fibrillation when following standard electrophysiology mapping and radiofrequency ablation procedures.
Device Under Investigation	TactiCath™ Contact Force Ablation Catheter, Sensor Enabled™ (TactiCath SE)
Number of Subjects	224 subjects
Clinical Investigation Design	Prospective, single-arm, multi-center IDE clinical trial
Primary Endpoints	1. The **primary safety endpoint** is the rate of device and/or procedure-related serious adverse events with onset within 7-days of any y ablation procedure that uses the TactiCath SE catheter (initial or repeat procedure performed ≤180 days of initial procedure) that are defined below: • Atrioesophageal fistula[1] • Cardiac tamponade/perforation[1] • Death • Heart block • Myocardial infarction (MI) • Pericarditis[2] • Phrenic nerve injury resulting in diaphragmatic paralysis • Pneumothorax • Pulmonary edema (respiratory insufficiency) • Pulmonary vein stenosis[1] • Stroke/cerebrovascular accident (CVA) • Thromboembolism • Transient ischemic attack • Vascular access complications (including major bleeding events[3]) 1. Atrioesophageal fistula, cardiac tamponade/perforation and pulmonary vein stenosis will be evaluated through 15-months. 2. Pericarditis is a common occurrence for almost all procedures and will only be considered a primary safety endpoint event if the pericarditis pleuritic symptoms last longer than 7-days and/or requires hospitalization of greater than 24 hours for reasons other than for observational purposes only. 3. Bleeding is a major complication of AF ablation if it requires and/or is treated with transfusion or results in a 20% or greater fall in hematocrit. Serious AF/atrial flutter (AFL)/atrial tachycardia (AT) recurrences without coexisting conditions (e.g. thromboembolism, worsening heart failure, etc.) will be counted as effectiveness failures but will not count against the primary safety endpoint.

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	2. The **primary effectiveness endpoint** for this clinical trial is freedom from AF/AFL/AT episodes of >30 seconds duration that is documented by an ECG (12-lead or TTM) or 24-hour Holter after the initial catheter ablation procedure through 15-months of follow-up (includes a 90-day blanking period followed by a 90-day therapy consolidation period). AF/AFL/AT recurrence during the blanking or therapy consolidation periods will not be considered a treatment failure. AF/AFL/AT recurrence will only be assessed by 12-lead ECG, TTM, and 24-hour Holter monitoring devices for assessment of this primary endpoint so that all subjects are monitored equally with devices of the same sensitivity and specificity. Collected ECG, TTM, and 24-hour Holter data from sites will be evaluated by a physician at a core laboratory for independent and unbiased assessment of AF recurrence for endpoint analysis. There are multiple situations in which subjects will be considered primary effectiveness endpoint failures: • If AF/AFL/AT recurrence (>30 second episode) occurs at any time after the therapy consolidation period (>180 days after the initial procedure), or • If the subject requires a repeat procedure for the treatment of AF after the therapy consolidation period, the subject will be considered an effectiveness endpoint failure regardless of documentation of a >30 second AF/AFL/AT episode, or • If the subject requires a second repeat procedure at any time after the initial procedure, or • If the subject requires a new AAD or a previously failed AAD at a dose greater than the highest ineffective historical dose for AF after the therapy consolidation period, or • If the subject requires a cardioversion (electrical or pharmacological) for the treatment of AF after the therapy consolidation period, or • If the subject has a continuous atrial arrhythmia throughout a 12-lead ECG recording after the therapy consolidation period indicating arrhythmia recurrence, this will be considered sufficient documentation of recurrence unless there is evidence that the recorded arrhythmia is short-lived and less than 30 seconds.
Secondary Endpoints	• Proportion of subjects who achieve acute procedural success of >90% for subjects who had the investigational catheter inserted into their vasculature, where acute procedural success is defined as confirmation of entrance block in all pulmonary veins. • Proportion of subjects off all AADs taken to treat AF/AFL/AT who achieve15-month success of >40%, defined as freedom from documented AF/AFL/AT recurrence (episodes >30 seconds) during the 9-month period following the blanking and therapy consolidation periods. • Proportion of subjects who achieve 15-month single procedure success of >40%, defined as freedom from documented AF/AFL/AT recurrence (episodes >30 seconds) during the 9-month period following the blanking and therapy consolidation periods after a single ablation procedure. Any repeat ablation procedure required by the subject at any time will be deemed an effectiveness failure in this analysis.

Subject Follow-up	• Baseline, Procedure, Pre-Discharge, 7-days, 3-months, 6-months, 12-months, 15-months
	  • The 7-day, 6-month, and 12-month visits are phone calls to the subject
	  • Baseline, Procedure, Pre-Discharge, 3-month, and 15-month visits are in-person

Inclusion Criteria	1) Subject must provide written informed consent prior to any clinical investigation related procedure.

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	2) Documented symptomatic persistent AF, which is defined as continuous AF sustained beyond 7-days and less than 1-year that is documented by (1) a physician's note AND (2) a 24-hour Holter within 90-days prior to the procedure, showing continuous AF, OR (3) two electrocardiograms (from any form of rhythm monitoring) showing continuous AF, taken at least 7 days apart 3) Refractory or intolerant to at least one Class I or III antiarrhythmic drug (AAD) as evidenced by recurrent symptomatic AF 4) Age 18 years or older 5) Able and willing to comply with all pre-, post-, and follow-up testing and requirements
Exclusion Criteria	1) Continuous AF > 12 months (longstanding persistent AF) 2) Previous left atrial surgical or catheter ablation for atrial fibrillation or a previous procedure that required an incision in the left atrium with resulting scar 3) Any cardiac procedure (surgical or percutaneous) within 90-days prior to the initial procedure NOTE: Diagnostic cardiac procedures in which no intervention, implant, or incision was made in the cardiac tissue are not considered a surgical or percutaneous cardiac procedure. 4) CABG surgery within the 6-months (180-days) prior to the initial procedure 5) Valvular cardiac surgical/percutaneous procedure (i.e. ventriculotomy, valve repair or replacement and/or presence of a prosthetic or mechanical valve) 6) Any carotid stenting or endarterectomy 7) Documented or known left atrial thrombus on imaging 8) Left atrial diameter > 50 mm (parasternal long axis view or by CT) 9) Left ventricular ejection fraction < 40% 10) Unable to take anticoagulation medication due to contraindication or intolerance 11) History of blood clotting or bleeding abnormalities 12) Myocardial infarction (MI), acute coronary syndrome, percutaneous coronary intervention (PCI) within the 3-months (90-days) prior to the initial procedure 13) Documented thromboembolic event (including TIA) within the 12-months (365 days) prior to the initial procedure 14) Rheumatic heart disease 15) Uncontrolled heart failure or NYHA functional class III or IV 16) Severe mitral regurgitation (regurgitant volume ≥ 60 mL/beat, regurgitant fraction ≥ 50%, and/or effective regurgitant orifice area ≥ 0.40cm^2) 17) Awaiting cardiac transplantation or other cardiac surgery within the 12-months (365 days) following the initial ablation procedure 18) Unstable angina at the time of the initial procedure 19) Acute illness or active systemic infection or sepsis 20) AF secondary to electrolyte imbalance, thyroid disease, acute alcohol intoxication, major surgical procedure in the preceding 3-months, or other reversible or non-cardiac cause 21) Diagnosed atrial myxoma 22) Presence of implanted implantable cardioverter defibrillator (ICD) or cardiac resynchronization therapy-defibrillator (CRT-D)

	23) Significant pulmonary disease, (e.g., restrictive pulmonary disease, constrictive or chronic obstructive pulmonary disease) or any other disease or malfunction of the lungs or respiratory system that produces chronic symptoms 24) Significant congenital anomaly or other anatomic or comorbid medical problem that in the opinion of the investigator would preclude enrollment in this study or compliance with the follow-up requirements or impact the scientific soundness of the clinical trial results 25) Pregnant or nursing subjects and those who plan pregnancy during the clinical investigation follow-up period 26) Enrollment in an investigational study evaluating another device, biologic, or drug that may interfere with this clinical investigation at the time of the initial procedure or within 30 days prior to the initial procedure 27) Presence of any condition that precludes appropriate vascular access or manipulation of catheter 28) Life expectancy less than 12-months 29) Body mass index > 40 kg/m^2 30) Known sensitivity to contrast media (if needed during the procedure) that cannot be controlled with pre-medication 31) Renal failure requiring dialysis 32) Presence of 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. 33) History of atriotomy or ventriotomy 34) Implanted endocardial left atrial appendage occlusion device