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TactiSense IDE
Multi-Center Acute Safety Trial of TactiCath™ Contact Force Ablation Catheter, Sensor Enabled™ (TactiCath SE) for the Treatment of Drug Refractory Recurrent Symptomatic Paroxysmal Atrial Fibrillation
Study Document No: SJM-CIP-10216
Version E
Date: 06-MAR-2018

Sponsor

Abbott  
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Plymouth, MN 55442  
United States

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<b>Clinical Investigation Plan (CIP)</b>
<b>G170245</b>

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## 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.

Principal Investigator

Printed name:

Signature:

Date:

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## 1 Introduction

This document is a clinical investigation plan (CIP) for the TactiSense IDE Clinical investigation. This clinical investigation is intended to demonstrate the acute safety and effectiveness of ablation with the TactiCath™ Contact Force Ablation Catheter, Sensor Enabled™ (TactiCath SE) for the treatment of drug refractory recurrent symptomatic paroxysmal atrial fibrillation (PAF). 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 in the United States. One hundred fifty six (156) subjects will be enrolled at up to 35 investigational sites in the US, Europe, and Australia. This clinical investigation is sponsored by Abbott.

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

## 2 Background and Justification for Clinical Investigation

It has been estimated that 20.9 million men and 12.6 million women have AF worldwide.<sup>1, 2</sup> AF has a prevalence of approximately 3% in adults aged 20 years or older.<sup>3, 4</sup> Additionally, one in four middle-aged adults in the US and Europe will develop AF in their lifetime.<sup>5, 6</sup> These estimates suggest that AF is a condition that impacts a significant number of people with implications for their healthcare systems.

AF remains a major cause of stroke, heart failure, sudden death, and cardiovascular morbidity. In a meta-analysis of contemporary, well-controlled, randomized clinical trials in AF, the average annual stroke rate is 1.5% with an annualized death rate of 3% in anticoagulated AF patients.<sup>7</sup> A minority of these deaths are related to stroke, while sudden cardiac death and death from progressive heart failure are more frequent, emphasizing the need for interventions beyond anticoagulation.<sup>8, 9</sup> AF is also associated with high rates of hospitalization, commonly for AF management, but often hospitalization is also due to heart failure, myocardial infarction, and treatment associated complications.<sup>10-12</sup> Additionally, patients with AF have significantly poorer quality of life than healthy controls, experiencing a variety of symptoms including lethargy, palpitations, dyspnea, chest pain, sleeping difficulties, and mental distress.<sup>12-16</sup>

Treatment for AF includes thromboembolic risk management, heart rate control, and heart rhythm control, which includes cardioversion and catheter ablation. The 2016 ESC AF Guideline indicates that catheter ablation of AF is effective in restoring and maintaining sinus rhythm in patients with symptomatic paroxysmal, persistent, and probably long-standing persistent AF in general as second-line treatment after failure of or intolerance to antiarrhythmic drug therapy.<sup>17</sup> The 2014 AHA/ACC/HRS AF Guidelines, 2016 ESC AF Guidelines, and 2017 HRS/EHRA/ECAS/APHRS/SOLAECE Expert Consensus on AF Ablation all provide a Class I recommendation (Level of Evidence: A) for catheter ablation to maintain sinus rhythm for patients with symptomatic, drug refractory, paroxysmal AF.<sup>17-19</sup> Contact force sensing ablation catheter systems are a technology that is growing in adoption for AF ablation. These contact force sensing catheter systems provide catheter operators additional feedback by allowing the operator to know how much force is being applied by the catheter tip on the cardiac wall. Recently the 2017 HRS/EHRA/ECAS/APHRS/SOLAECE Expert Consensus on AF Ablation also went on to provide targeted contact force recommendations (Class IIa recommendation, Level of evidence C) during the ablation.<sup>19</sup>

The TactiCath family of catheters has been studied extensively. The early generation TactiCath catheters were investigated in the TOCCATA, EFFICAS I and II, and TOCCASTAR clinical trials. The next generation, TactiCath Quartz, implemented an updated contact force sensing mechanism, which was studied in the TOCCASTAR Supplemental Clinical Study and long-term follow up data are currently being collected in the TactiCath Quartz Post Approval Study (TQPAS). These previous clinical trials have investigated the safety and effectiveness of the previous generations of TactiCath

ablation catheters for the treatment of drug refractory, symptomatic AF.<sup>20-23</sup> 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.

While preclinical testing has demonstrated TactiCath SE ablation catheter safety, this has not been demonstrated in clinical use for the US population. This clinical trial seeks to demonstrate that this latest iteration of the TactiCath catheter has an acceptable acute safety profile.

### 3 Device(s) To be Used in the Clinical Investigation

The devices manufactured by St. Jude Medical listed in Table 1 will be used in this clinical trial.

**Table 1: Identification of Devices used in the Clinical Trial**

Device name	Model(s)
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 v1.04 or greater	H700488 (US) H700489 (OUS)
EnSite Precision™ Cardiac Mapping System	EE3000
EnSite Precision Software v2.2 or greater (OUS) and 2.0.2 (US)	H702496
Contact Force Module	H702500
TactiCath™ Ablation Catheter, Sensor Enabled™ Catheter Catalog Installation v1.1 (US only)	H702530
Cool Point™ Pump v24 or greater	IBI-89003 (US) 85784 (OUS)

*US Only:*

The investigational system to be used during the clinical trial ablation procedures includes the TactiSys Quartz Equipment (PN-004 400) and Ampere RF Generator (H700488), which, when used in combination with the TactiCath SE, are considered investigational.

EnSite Precision requires an update to the catheter catalog so that TactiCath SE can be connected and used with EnSite Precision. EnSite Precision uses the catheter catalog to store information about the catheters, including information related to the magnetic coil in the catheter (i.e. coil location and coil offset) that is required for accurate performance. The EnSite Precision catheter catalog update, implemented in the TactiCath Ablation Catheter, Sensor Enabled, Catheter Catalog Installation v1.1 (H702530), is considered investigational software and will be installed on the commercially available EnSite Precision software v2.0.2 to enable use of TactiCath SE.

Use of the Ampere generator, TactiSys Quartz Equipment, and TactiCath SE EnSite Precision Installer in conjunction with the TactiCath SE catheter in the TactiSense IDE trial at US study sites is investigational. A label indicating each device is considered part of an investigational system when used in the TactiSense IDE trial will be affixed by Abbott personnel to the Ampere RF Generator and TactiSys Quartz Equipment already in commercial use at US study sites. The Ampere generator and TactiSys Quartz Equipment will be obtained by US study sites through their usual commercial channels. The TactiCath Ablation Catheter, Sensor Enabled, Catheter Catalog Installer v1.1 will be installed onto commercially available EnSite Precision units (v2.0.2 software) as part of site activation.

The EnSite Precision Cardiac Mapping System, EnSite Precision Software v2.0.2, Contact Force Module, and Cool Point™ Pump are not part of the investigational system and will be used as commercially indicated.

*All other geographies where TactiCath SE is commercially available:*

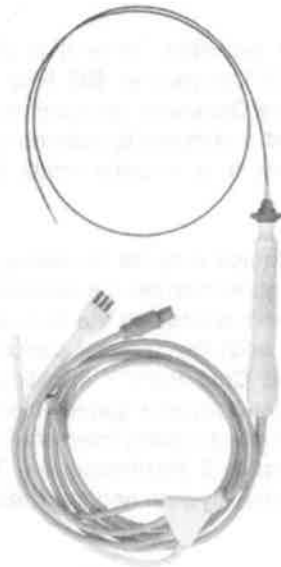
All products to be used during the clinical trial are market released, and will be utilized according to approved labeling, Instructions for Use, and medical standard of care guidelines.

### **3.1 Device Description and Intended Purpose**

#### **3.1.1 TactiCath Sensor Enabled Ablation Catheter**

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

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

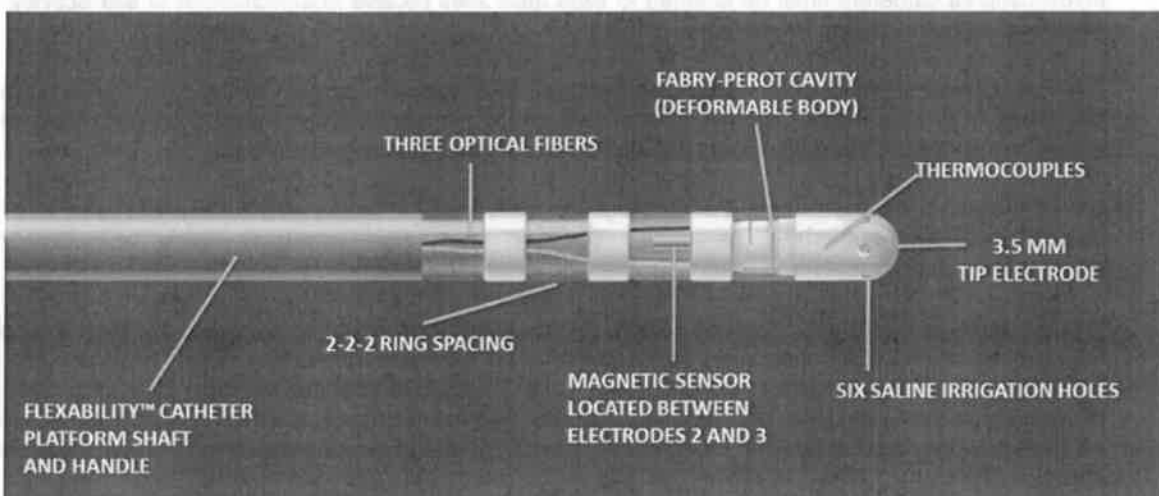
**Figure 1 Uni-Directional TactiCath SE****Figure 2 Bi-Directional TactiCath SE****United States – Proposed Indication**

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

This clinical trial is being done to demonstrate acute safety for this proposed indication.

**Outside of the United States**

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

**Figure 3 Exposed View of TactiCath SE Tip**



### 3.1.2 Ampere Generator

Investigational sites will already have the Ampere Generator available, since it is commercially released. The Ampere Generator generates radiofrequency (RF) current at 485 KHz to be used during RF catheter ablation procedures of the heart. The Ampere Generator operates in conjunction with an external Disposable Indifferent Patch (DIP) electrode and a compatible ablation catheter with an associated cable. The Ampere Generator delivers RF power in a unipolar mode between the ablation catheter's distal electrode and the DIP electrode.

The Ampere Generator features a color LCD screen and easy-to-use controls for setting the desired ablation parameters and for monitoring ablation progress. The generator can be controlled from the front panel of the main unit or by an optional remote control unit connected via fiber optic cables. Additional accessories to the generator include an optional footswitch the operator can use to turn on or off RF delivery. When connected with a compatible Abbott Cool Point™ irrigation pump, the Ampere Generator provides additional pump control options for use with an irrigated ablation catheter. The Ampere Generator is designed to be used with ablation catheters having integrated temperature sensors, and can measure temperature from a thermistor or up to 2 thermocouples. The Ampere Generator provides for connection to an electrophysiologic recording system and the EnSite Precision cardiac mapping system.

#### *Indication for Use*

The Ampere™ Generator is intended for use with compatible cardiac ablation catheters according to the indications for use of the compatible cardiac ablation catheter.

### 3.2 Device Handling and Storage

Sponsor requires all investigational products be stored according to the labeling and Instruction for Use. Commercially available devices should be stored per standard practice of the hospital. Investigational catheters (US only) must be stored in a secure area to prevent unauthorized access or use. In the US, the commercially available TactiSys Quartz Equipment and Ampere generator can be stored per standard practice of the hospital. The TactiCath Ablation Catheter, Sensor Enabled Catheter Catalog Installation v1.1 will only be handled by Abbott personnel to perform the catheter catalog update on commercially available EnSite Precision Software v2.0.2.

### 3.3 Device Accountability (US Only)

Investigational catheters shall be shipped to sites after sites receive documentation of site activation and shipping authorization is complete.

The Principal Investigator or an authorized designee must maintain records of the date of receipt, the identification of each investigational catheter (e.g. batch number, serial number or unique code), the subject identification, the date of use, the expiration date and the final disposition.

Storage locations for the catheters at investigational sites will be locked with access restricted only to investigators and authorized personnel. Sponsor must also maintain device accountability documenting all shipments and returns of investigational catheters.

The Ampere generator and TactiSys Quartz Equipment will be obtained by US study sites through their usual commercial channels. Serial numbers of Ampere Generator and TactiSys Quartz Equipment that have the label and are used in the TactiSense IDE trial will be noted on a device accountability log. The TactiCath Ablation Catheter, Sensor Enabled, Catheter Catalog Installation v1.1 will only be handled by Abbott personnel, and will not be in the possession of the investigational site.

## 4 Clinical Investigation Design

### 4.1 Clinical Investigation Design

This is a prospective, multi-center, single-arm clinical trial to demonstrate the acute safety and effectiveness of the TactiCath SE catheter for the treatment of PAF against a performance goal. One hundred fifty six (156) subjects will be enrolled at up to 35 investigational sites in the US, Europe, and Australia. Only sites that enroll at least one subject will be part of the analysis population. No center may contribute more than 20% of the total number of enrollments without sponsor pre-approval to exceed this proportion and at least 50% of subjects must be from the United States.

[REDACTED] Subjects will be followed for 12 months after the index ablation procedure and then exit the clinical trial. [REDACTED]

[REDACTED] The pre-market approval (PMA) clinical report will be submitted when at least 140 subjects have been enrolled, had the investigational catheter inserted into their vasculature, and either experienced an event as defined in section 4.3.1, completed their 30 day follow up visit, or have been lost to follow up per section 5.7.

### 4.2 Objective

The objective of this clinical trial is to demonstrate the acute safety and effectiveness of ablation with the TactiCath SE catheter for the treatment of drug refractory recurrent symptomatic PAF and is intended to support market approval of the TactiCath SE ablation catheter in the United States.

### 4.3 Endpoints

There are two primary endpoints and ten descriptive endpoints for this trial.

#### 4.3.1 Primary Safety Endpoint

The primary safety endpoint is the rate of device or procedure-related serious adverse events occurring within 7 days of the index procedure. SAEs related solely to arrhythmia recurrence (without coexisting conditions such as thromboembolism, worsening heart failure, etc.) will not be considered primary safety endpoint events. The SAEs that will be included in this endpoint are:

- Atrial-esophageal fistula
- AV block
- Cardiac perforation/ Tamponade
- Death
- Diaphragmatic paralysis
- Gastroparesis
- Hospitalization
- Myocardial Infarction
- Pericarditis
- Pneumothorax
- Pulmonary edema
- Pulmonary vein stenosis
- Stroke
- Thromboembolism
- Transient ischemic attack
- Vascular access complication

These events must meet the criteria listed in Appendix C to be included in the primary endpoint as adjudicated by the clinical events committee (CEC). Atrial-esophageal fistula, cardiac perforation/tamponade, and pulmonary vein stenosis that occur >7 days post procedure through 30 days will also contribute to the primary endpoint.

#### 4.3.2 Primary Effectiveness Endpoint

The primary effectiveness endpoint is acute procedural success, where acute procedural success is defined as confirmation of entrance block in all pulmonary veins.

#### 4.3.3 Descriptive Endpoints

There are ten types of descriptive endpoints. Descriptive endpoints are reported using summary statistics and no hypothesis testing will be performed.

1. Ablation data collected during the procedure, including:

- Power
  - Temperature
  - Irrigation flow rate
  - Contact force
  - Procedure time
  - Total ablation time
  - Total fluoroscopy time
  - Total RF application time
  - Usage of Automark
2. Proportion of index cases achieving  $\geq 90\%$  lesions with  $\geq 10\text{g}$  contact force
  3. Serious adverse events and adverse events related to the procedure and/or ablation catheter through 30 days post index ablation
  4. Serious adverse events and adverse events related to the procedure and/or ablation catheter through 1 year post index ablation
  5. One-year success defined as freedom from symptomatic AF/AFL/AT lasting at least 30 seconds without a new Class I or III AAD or a higher dosage of pre-existing AAD as assessed from the end of the 3-month blanking period to 12 months following the ablation procedure.
  6. One-year drug-free success defined as freedom from any AF/AFL/AT lasting at least 30 seconds or any Class I or III AAD after removal from antiarrhythmic drug therapy as assessed from the end of the 3-month blanking period to 12 months following the ablation procedure.
  7. Changes in EQ-5D-5L scores from baseline to follow up at 3, 6, and 12 months
  8. Changes in AFEQT scores from baseline to follow up at 3, 6, and 12 months
  9. Cardiovascular-related health care utilization through 12 months post index ablation
  10. Force time integral (FTI) and lesion index (LSI)

NOTE: For endpoints 5 and 6, a full 10-second 12-lead ECG recording of arrhythmia may be substituted for a 30-second recording unless there is evidence that the recorded arrhythmia is short-lived and less than 30 seconds.

#### 4.4 Study Population

The intended trial population is adults with symptomatic paroxysmal atrial fibrillation that have not responded to medical therapy. No vulnerable populations will be included in this trial.

##### 4.4.1 Inclusion Criteria

A patient will be eligible for clinical trial participation if he/she meets the following criteria:

- 1) Plans to undergo a catheter ablation procedure due to symptomatic PAF that is refractory or intolerant to at least one Class I or III antiarrhythmic drug
- 2) Physician's note indicating recurrent self-terminating AF
- 3) One electrocardiographically documented AF episode within 6 months prior to the index ablation procedure
- 4) At least 18 years of age
- 5) Able and willing to comply with all trial requirements
- 6) Informed of the nature of the trial, agreed to its provisions and has provided written informed consent as approved by the Institutional Review Board/Ethics Committee (IRB/EC) of the respective clinical trial site.

#### 4.4.2 Exclusion Criteria

A patient will be excluded from enrollment in the clinical trial if he/she meets any of the following criteria:

- 1) Persistent or long-standing persistent atrial fibrillation (AF)
- 2) Four or more cardioversions in the past 12 months
- 3) Active systemic infection
- 4) Known presence of cardiac thrombus
- 5) Implanted with implantable cardiac defibrillator (ICD)
- 6) Arrhythmia due to reversible causes including thyroid disorders, acute alcohol intoxication, and other major surgical procedures in the preceding 3 months
- 7) Myocardial infarction (MI), acute coronary syndrome, percutaneous coronary intervention (PCI), or valve or coronary bypass grafting surgery within preceding 3 months
- 8) Left atrial diameter > 5.0 cm
- 9) Left ventricular ejection fraction < 35%
- 10) New York Heart Association (NYHA) class III or IV
- 11) Previous left atrial surgical or catheter ablation procedure
- 12) Left atrial surgical procedure or incision with resulting scar
- 13) Previous tricuspid or mitral valve replacement or repair
- 14) Heart disease in which corrective surgery is anticipated within 6 months
- 15) Bleeding diathesis or suspected procoagulant state
- 16) Contraindication to long term antithromboembolic therapy
- 17) Presence of any condition that precludes appropriate vascular access
- 18) Renal failure requiring dialysis
- 19) Known sensitivity to contrast media (if needed during the procedure) that cannot be controlled with pre-medication
- 20) Severe 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 severe chronic symptoms
- 21) Pregnant or nursing
- 22) Presence of other anatomic or comorbid conditions that, in the investigator's opinion, could limit the patient's ability to participate in the clinical trial or to comply with follow up requirements, or impact the scientific soundness of the clinical trial results
- 23) Patient is currently participating in another clinical trial or has participated in a clinical trial within 30 days prior to screening that may interfere with this clinical trial
- 24) Patient is unlikely to survive the protocol follow up period of 12 months
- 25) Body mass index > 40 kg/m<sup>2</sup>
- 26) Vulnerable subject

#### 4.4.3 Enrollment of Medicare Beneficiaries (US only)

This clinical investigation will enroll appropriate Medicare beneficiaries that qualify based on the inclusion and exclusion criteria set forth in the trial. The IDE clinical trial adheres to all standards of Medicare coverage requirements set forth by CMS's IDE and clinical trial coverage policies. Section 7 (Risks and Benefits) describes how all enrolled subjects, including Medicare beneficiaries, may be affected by the device under investigation.

Subjects enrolled in the clinical investigation are expected to overlap with the Medicare population based on demographic characteristics and cardiovascular risk factors; therefore, the clinical investigation results are expected to be generalizable to the Medicare population.

#### 4.4.4 Historically Underrepresented Demographic Subgroups

The Sponsor intends to implement FDA's guidance on sex-specific data in medical device clinical studies to ensure adequate representation of women and other traditionally underrepresented demographic subgroups in this clinical investigation. As noted in the 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 study 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 study follow-up requirements

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

- 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
- The Sponsor will have informed consent materials in alternative languages and will work with sites and IRBs/ECs on recruitment materials

## 5 Procedures

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

Enrolled subjects (as defined in section 5.2) will undergo a pulmonary vein isolation procedure with the TactiCath SE catheter. After discharge from hospitalization post-procedure, the subject will have follow-up visits at 7 days and 30 days and 3, 6 and 12 months. Upon completion of the 12-month follow-up visit, the subject will be considered to have completed the follow-up requirements of this clinical investigation. The Principal Investigator should arrange for appropriate care of subjects following study completion.

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

### 5.1 Informed Consent Process

The Principal Investigator or his/her authorized designee will conduct the Informed Consent Process, as required by applicable regulations and the center's IRB/EC. This process will include a verbal discussion with the subject on all aspects of the clinical study that are relevant to the subject's decision to participate, such as details of clinical study procedures, anticipated benefits, and potential risks of clinical study participation. During the discussion, the Principal Investigator or his/her authorized designee will avoid any improper influence on the subject and will respect the 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. No study procedures will occur until subject consent is obtained. The template informed consent is provided under separate cover.

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

The Principal Investigator or his/her authorized designee will document the informed consent process in the subject's hospital and/or research charts. The date of signature will be entered on an applicable electronic Case Report Form (eCRF).

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

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

## 5.2 Point of Enrollment

A subject is considered enrolled in the clinical trial from the moment the subject has provided written informed consent.

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

Notification of enrollment to the Sponsor is considered to have occurred when the Sponsor has received the applicable eCRF.

## 5.3 Scheduled Procedures

The Principal Investigator is responsible for ensuring all clinical investigation data is collected as required per CIP scheduled procedures. Physical exams, including the neurological assessment, must be performed by a physician. NIH Stroke Scale must be administered by a certified assessor.

### 5.3.1 Baseline

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

- Document the informed consent process
- Confirm enrollment criteria
- Subject demographics
- Complete medical history, cardiac arrhythmias and documentation of PAF
- Complete QOL (EQ-5D-5L<sup>26</sup> & AFEQT<sup>27</sup>)
- Complete physical exam (including neurological assessment), NIH Stroke Scale (NIHSS) assessment, ECG, & NYHA assessment. NOTE: If these were done as standard of care prior to consent, they may be used if they were done within 30 days prior to index ablation procedure. Subjects with new findings on the neurologic assessment/NIHSS are required to have a formal neurological consult and follow-up diffusion-weighted MR imaging of the brain. If contra-indicated for MR, then an alternate form of imaging may be performed. Subjects should also be re-evaluated against the inclusion/exclusion criteria to ensure they are still eligible.
- A urine pregnancy test should be performed for women of child-bearing potential.
- Document anti-arrhythmic drug (AAD) history, including maximum ineffective dosages and anticoagulant usage
- Assessment for atrial thrombus must be performed within one day of the ablation procedure. Standard of care may be used for this assessment. It is recommended that transesophageal echocardiography (TEE) be performed prior (within 1 day) to the index ablation procedure to identify any left atrial thrombus. In case of a finding of atrial thrombus, the procedure will not

be scheduled and the subject placed on anticoagulation until freedom from thrombus can be confirmed. They may be rescreened once provided it is within 90 days of initial consent.

It is recommended to follow pre-ablation anticoagulation guidelines from the 2017 HRS/EHRA/ECAS/APHRS/SOLAECE Expert Consensus Statement on Catheter and Surgical Ablation for Atrial Fibrillation<sup>19</sup>

Any subjects who do not meet inclusion/exclusion criteria prior to the insertion of the TactiCath SE into their vasculature will be exited from the trial.

### 5.3.2 Ablation Procedure

The ablation procedure will be performed no more than 14 days after consent. This section describes the activities performed and information collected at the ablation procedure visit.

- The procedure should be performed following the Instructions for Use.
- It is strongly recommended that a strategy of uninterrupted anti-coagulation be in place for peri-operative management.
- It is strongly recommended that vascular access be obtained using ultrasound to minimize complications.
- It is recommended that heparin be administered prior to or immediately following transeptal puncture during AF catheter ablation procedures and adjusted to achieve and maintain an ACT of at least 300 seconds. Administration of protamine following AF catheter ablation to reverse heparin is acceptable.
- If assessment for presence of atrial thrombus was not performed prior to the initiation of the ablation procedure, an intracardiac echocardiography (ICE) or TEE assessment must be performed at the time of the procedure to exclude atrial thrombus. In case of a finding of atrial thrombus, the procedure will be postponed and the subject placed on anticoagulation until freedom from thrombus can be confirmed. They may be rescreened once provided it is within 90 days of initial consent.
- If no atrial thrombus is found, a standard treatment scheme of mapping and ablation will be conducted during the interventional procedure. It is required that confirmation of entrance block be performed.
- In the absence of a clinical or induced arrhythmia, additional ablation lesion sets (e.g., prophylactic linear lesions, ablation of CFAE sites, etc.) should not be performed.
- Subjects will receive ablations to achieve pulmonary vein isolation (PVI). The recommended ablation parameters are as follows:
  - Power (10-30W)
  - Contact force (target 20 g, 10-30 g)
  - Temperature (37 – 50 °C)
  - Irrigation flow rate (17 - 30 ml/min)
- In addition to PVI, subjects with documented atrial flutter, AT or other SVT (spontaneous or induced) may undergo additional targeted ablation as clinically indicated.
- For subjects who receive cavotricuspid isthmus (CTI) ablation for typical atrial flutter, It is required that bi-directional block be re-confirmed 30 minutes after initial block is achieved.
- Consistent with data published in the 2017 HRS/EHRA/ECAS/APHRS/SOLAECE Expert Consensus Statement on Catheter and Surgical Ablation for Atrial Fibrillation<sup>19</sup>, the following standard of care peri-procedure precautions are strongly recommended to minimize risks to subject safety:
  - 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. An alternative is esophageal deviation.
  - Termination of energy is strongly recommended if a >1°C rise in esophageal temperature is observed.

- Intracardiac echocardiography (ICE) – use of a phased-array ICE probe during the procedure to guide septal puncture and to monitor catheter position and manipulation is strongly recommended.
- Use of robotic systems to assist in the procedure is not allowed.
- Please refer to the catheter's IFU for further details.
- PVI must be documented and verified via entrance block with a multipolar catheter at or beyond 30 minutes from the last ablation lesion for each vein.
- Use of adenosine and / or isoproterenol is acceptable to assist in finding gaps.
- Cardioversion is allowed after PVI to assist with checking for isolation.
- The data from the entire procedure recorded on the commercial EnSite system should be anonymized and backed up on a USB drive and sent to the sponsor within reasonable timelines.
- It is strongly recommended that the operator personally evaluates the subject on the evening of the procedure as well as on the following morning, and maintains active surveillance of the subject's postoperative care and condition.

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

#### **Post Ablation Anticoagulation Strategy**

The following recommendations are adapted from the 2017 HRS/EHRA/ECAS/APHRS/SOLAECE Expert Consensus Statement on Catheter and Surgical Ablation for Atrial Fibrillation<sup>19</sup>:

- 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<sup>a</sup>.
- Systemic anticoagulation with warfarin<sup>a</sup> or novel oral anticoagulation (NOAC) is recommended for at least 2 months post catheter ablation of AF and systemic anticoagulation beyond 2 months post ablation should be based on the patient's stroke risk profile and not on the perceived success or failure of the ablation procedure.
- Adherence to AF anticoagulation guidelines is recommended for patients who have undergone an AF ablation procedure, regardless of the apparent success or failure of the 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.

#### **5.3.3 Pre-Discharge Procedure**

The following post-treatment evaluations will be performed within 72 hours (or as indicated) after the treatment procedure and before discharging the subject:

- TTE within 24 hours post-procedure is recommended to document absence of pericardial effusion.
- Complete physical exam (including neurological assessment).
- Complete NIH Stroke Scale (NIHSS) assessment (must be done at hospital discharge or 24±12 hours after the procedure, whichever is later). Subjects with new findings on the neurologic assessment are required to have a formal neurological consult and follow-up

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<sup>a</sup> Time in therapeutic range (TTR) should be > 65%-70% on warfarin.



diffusion-weighted MR imaging of the brain. If contra-indicated for MR, then an alternate form of imaging may be performed.

- Document AAD and anti-coagulant usage.
- Document adverse events and protocol deviations.

#### 5.3.4 Scheduled Follow-ups

Subjects will undergo the following assessments described below at 7 and 30 days, and at 3, 6 and 12 months post ablation procedure.

##### 7-Day (7 ± 2 days) Follow-up

- Complete physical exam (including neurological assessment).
- Complete NIHSS. Subjects with new findings on the neurologic assessment are required to have a formal neurological consult and follow-up diffusion-weighted MR imaging of the brain. If contra-indicated for MR, then an alternate form of imaging may be performed.
- Document adverse events and protocol deviations.
- Document anti-arrhythmic and anti-coagulant drug usage.
- If there are symptoms present that suggest pulmonary vein stenosis (e.g. shortness of breath, cough, and hemoptysis), complete CT or MRI imaging of pulmonary veins.

##### 30-Day (30 ± 7 days) Follow-up

- 12-lead ECG
- Document adverse events and protocol deviations.
- Document anti-arrhythmic and anti-coagulant drug usage.
- If there are symptoms present that suggest pulmonary vein stenosis (e.g. shortness of breath, cough, and hemoptysis), complete CT or MRI imaging of pulmonary veins.

##### 3-Month (90 ± 14 days), 6-Month (183 ± 21 days), 12-Month (365 ± 21 days) Follow-up

- Complete QOL (EQ-5D-5L & AFEQT)
- 12-lead ECG
- 24-hour Holter monitor at the 12-Month Follow-up
- Document adverse events and protocol deviations.
- Document AAD and anti-coagulant usage.
- If there are symptoms present that suggest pulmonary vein stenosis (e.g. shortness of breath, cough, and hemoptysis), complete CT or MRI imaging of pulmonary veins.
- Provide subject a trans telephonic monitor to record monthly heart rhythm and symptomatic episodes during follow up from 3 to 12 months.

#### 5.3.5 Re-ablation Procedure and Anti-Arrhythmic Drug Usage

Subjects may be re-treated with ablation up to two times during the 90-day blanking period between days 31 and 80 after the index procedure. Re-ablation cannot be performed within 30 days of the latest ablation procedure. Re-treatment during this interval will not constitute a treatment failure and must be performed with the TactiCath SE catheter. Re-ablation per standard of care after the blanking period may be performed if recurrence is detected using any commercially available catheter. This will be counted as a treatment failure.

During the blanking period, it is recommended that any current antiarrhythmic medication be continued following the ablation procedure. Current AADs should be withdrawn 4-6 weeks after ablation, unless clinically contraindicated to assess for recurrence of symptoms and the necessity for re-ablation during the blanking period.

If documented symptomatic AF recurs during the 3-month blanking period and the patient requires antiarrhythmic drug therapy, a previously ineffective but tolerated antiarrhythmic drug may be re-initiated to allow for the assessment of its effectiveness when combined with ablation.

All Class I and Class III AADs will be discontinued at the end of the blanking period. Beta-blockers, calcium channel blockers or digitalis may be used during the 9-month chronic effectiveness assessment period if prescribed for reasons unrelated to arrhythmia management. Subjects are encouraged to continue their use through the end of the study unless it is determined to be unnecessary or detrimental by the investigator. Subjects who experience a recurrence of symptomatic PAF after the blanking period (treatment failure) should retry a previously failed AAD before a new medication is prescribed to evaluate the effectiveness of combined ablation and drug therapy.

#### **5.4 Investigation Specific Tests and Activities**

The following table summarizes the investigation specific tests and activities.

Test/Activity	Frequency	Responsible Party	Notes
ECG	Baseline and periodic	Investigator	Standard 12-lead ECG
Vital Signs	Baseline and periodic	Investigator	Heart rate, blood pressure, temperature, oxygen saturation
ECG Holter	During treatment	Investigator	24-hour monitoring
Exercise Test	Baseline and periodic	Investigator	Standard treadmill test
Lab Tests	Baseline and periodic	Investigator	Electrolytes, renal function, liver function, etc.
Drug Levels	Baseline and periodic	Investigator	Thrombolytic, antiarrhythmic, etc.
Ablation Procedure	Once	Investigator	Radiofrequency catheter ablation
ECG Mapping	Baseline and periodic	Investigator	Electroanatomical mapping
ECG Implantation	Once	Investigator	Implantation of Class I/III AAD
ECG Follow-up	Baseline and periodic	Investigator	ECG monitoring post-procedure
ECG Implantation	Once	Investigator	Implantation of Class II AAD
ECG Follow-up	Baseline and periodic	Investigator	ECG monitoring post-procedure



**Abbott**

Study Document No: SJM-CIP-10216 Ver. E  
Study Name: TactiSense IDE

Clinical Investigation Plan

**Table 2 List of all clinical investigation specific tests and activities**

Study Activity	Enrollment/ Baseline	Procedure (within 14 days of consent)	Pre- Discharge	7-Day Visit (± 2 days)	30-Day Visit (± 7 days)	3-month Visit (± 14 days)	6-month Visit (± 21 days)	12-month Visit (± 21 days)
Eligibility Check	X							
Informed Consent Process	X							
Demographics / Medical History	X							
Physical Examination (including neurological assessment)	X		X	X				
NIHSS	X		X	X				
Diffusion-weighted MRI - Brain	(X)		(X)	(X)				
CT or MRI of pulmonary veins				(X)	(X)		(X)	(X)
Urine pregnancy test	(X)							
NYHA	X							
Record Antiarrhythmic / Anti- coagulant Medication	X		X	X	X	X	X	X
Confirm absence of thrombus (per standard of care)**	X	(X)						
Ablation procedure		X						
Trans thoracic echocardiogram		X*						
Trans telephonic monitoring***						X	X	X
12-Lead ECG	X				X	X	X	X
24-hour Holter-monitoring								
QOL (EQ-5D-5L & AFEQT)	X					X	X	X
Adverse Events	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)
Deviation	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)
Withdrawal	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)
Health Care Utilization				(X)	(X)	(X)	(X)	(X)

(X) if applicable

\*Recommended post procedure to exclude pericardial effusion.

\*\*Must be done within one day of procedure (day of or day prior to).

\*\*\*Collected monthly and whenever symptoms are present from 3 to 12 months post ablation procedure.

### 5.5 Description of Activities Performed by Sponsor Representatives

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

### 5.6 Subject Study Completion

Subject participation in the clinical investigation will conclude upon completion of the 12-Month visit. Upon completion of subject participation in the clinical investigation, the subject will return to standard of care.

### 5.7 Subject Withdrawal

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

A subject will be considered 'Lost to Follow-up' after one missed visit(s) and a minimum of two unsuccessful phone calls from investigational site personnel to the subject or subject's contact to schedule the next follow-up visit. These two phone calls must be documented in the subject's hospital records. If the subject is deemed lost to follow-up, a letter should be sent to the subject's last known address or to the subject's general practitioner (GP) and a copy of the letter must be maintained in the subject's hospital records.

### 5.8 Clinical Events Committee (CEC)

A CEC will be responsible for providing an independent review and adjudication of adverse events. The CEC will make the final determination whether or not an adverse event meets the criteria for the primary endpoint. The primary function, responsibilities and membership of the CEC will be described in detail in a CEC charter.

### 5.9 Core Lab

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

- Trans telephonic monitoring (TTM)
- 24-hour Holter monitoring
- 12-lead ECG

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 and adjudicate atrial arrhythmias. Findings will be communicated to the investigator and the sponsor.

## 6 Statistical Considerations

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

### 6.1 Hypotheses

There are two primary endpoints for this study and ten types of descriptive endpoints. Both the primary endpoints must be met for trial success.

### 6.1.1 Primary Safety Endpoint Hypothesis

The performance goal is set at 16.2% based on experience with the TactiCath ablation catheter (a prior generation of the TactiCath SE catheter, see below for further detail). The hypothesis is formally expressed as:

$$H_0: P \geq 16.2\%$$

$$H_a: P < 16.2\%$$

where P is the percentage of subjects with a primary safety endpoint event. The hypothesis will be tested based on a one-sided exact test of binomial proportions at the one-sided 0.05 alpha level. Rejection of the null hypothesis will indicate study success. The performance goal of 16.2% is set to be equal to that for previous generations of the TactiCath catheter.

#### 6.1.1.1 Analysis Methodology

The primary safety endpoint event rate will be calculated based on the number of subjects experiencing a primary safety endpoint divided by the total number of subjects in the analysis population. Relatedness of the event to the catheter and to the procedure will be determined by the CEC. The null hypothesis will be rejected if the upper bound of the one-sided 95% confidence interval for the proportion of subjects with a primary safety endpoint is less than 16.2%. Subjects without an event that are lost to follow up without a visit at or beyond their 30-day follow up visit window will be excluded from this analysis.

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

### 6.1.1.3 Analysis Population

The analysis population for this endpoint will include all enrolled subjects who have also had the TactiCath SE inserted into their vasculature, and either had an event or completed a visit at or beyond their 30-day follow up visit window. Subjects without an event that are lost to follow up without a visit at or beyond their 30-day follow up visit window will be excluded from this analysis.

### 6.1.1.4 Subgroup Analysis

Subgroup analyses will be performed to examine the consistency of results for the primary safety endpoint. Analysis will be based on Fisher's exact test. No subgroup specific labeling claims are desired for this endpoint and no adjustments for multiplicity will be made. Subgroups to be examined include, but are not limited to, those defined by achieving >90% of lesions with  $\geq 10$ g contact force, age (both <65 vs  $\geq 65$  and age  $\geq$  median vs < median), sex, and race/ethnicity.

## 6.1.2 Primary Effectiveness Endpoint Hypothesis

The performance goal is set at 90% based on experience from previous IDE trials of approved devices relying on pulmonary vein isolation for effectiveness. The hypothesis is formally expressed as:

$$H_0: P < 90\%$$
$$H_A: P \geq 90\%$$

where P is the percentage of subjects with acute success. The hypothesis will be tested based on a one-sided exact test of binomial proportions at the one-sided 0.05 alpha level. Rejection of the null hypothesis will indicate study success.

### 6.1.2.1 Analysis Methodology

The primary effectiveness endpoint event rate will be calculated based on the number of subjects experiencing a primary effectiveness endpoint divided by the total number of subjects in the analysis population. The null hypothesis will be rejected if the lower bound of the one-sided 95% confidence interval for the proportion of subjects in this trial with the primary effectiveness endpoint is greater than 90%.

[REDACTED]

### 6.1.2.3 Analysis Population

The analysis population for this endpoint will include enrolled subjects who have also had the TactiCath SE inserted into their vasculature.

### 6.1.2.4 Subgroup Analysis

Subgroup analyses will be performed to examine the consistency of results for the primary effectiveness endpoint. Analysis will be based on Fisher's exact test. No subgroup specific labeling claims are desired for this endpoint and no adjustments for multiplicity will be made. Subgroups to be

[REDACTED]

examined include, but are not limited to, those defined by age (both <65 vs ≥65 and age ≥ median vs < median), sex, and race/ethnicity.

### 6.1.3 Descriptive Endpoint #1

Descriptive endpoint #1 is ablation data collected during the procedure, including:

- Power
- Temperature
- Irrigation flow rate
- Contact force
- Procedure time
- Total ablation time
- Total fluoroscopy time
- Total RF application time
- Usage of Automark

#### 6.1.3.1 Analysis Methodology

Descriptive statistics will be generated for all variables.

#### 6.1.3.2 Analysis Population

The analysis population for this endpoint will include all enrolled subjects who have also had the TactiCath SE inserted into their vasculature and radiofrequency energy was delivered.

### 6.1.4 Descriptive Endpoint #2

Descriptive endpoint #2 is the proportion of index cases achieving ≥ 90% lesions with ≥10g contact force.

#### 6.1.4.1 Analysis Methodology

Subjects with at least 90% of lesions with ≥10g achieved will be divided by the analysis population. Corresponding exact two-sided 95% binomial confidence intervals will also be calculated.

#### 6.1.4.2 Analysis Population

The analysis population for this endpoint will include all enrolled subjects who have also had the TactiCath SE inserted into their vasculature and radiofrequency energy was delivered.

### 6.1.5 Descriptive Endpoint #3

Descriptive endpoint 3 is defined as serious adverse events and adverse events related the device and/or ablation catheter through 30 days post ablation.

#### 6.1.5.1 Analysis Methodology

The number and percentage of subjects experiencing adverse events will be summarized, by seriousness and relatedness. Corresponding exact two-sided 95% binomial confidence intervals will also be calculated. Subjects who terminate the study prematurely without experiencing any adverse events through 30 days post ablation will not be considered as having any events for this analysis.

#### 6.1.5.2 Analysis Population

The analysis population for this endpoint will include all enrolled subjects who have also had the TactiCath SE inserted into their vasculature.

#### 6.1.6 Descriptive Endpoint #4

Descriptive endpoint 4 is defined as serious adverse events and adverse events related the device and/or ablation catheter through 1 year post ablation.

##### 6.1.6.1 Analysis Methodology

The number and percentage of subjects experiencing adverse events will be summarized, by seriousness and relatedness. Corresponding exact two-sided 95% binomial confidence intervals will also be calculated. Subjects who terminate the study prematurely without experiencing any adverse events through 1 year post ablation will not be considered as having any events for this analysis.

##### 6.1.6.2 Analysis Population

The analysis population for this endpoint will include all enrolled subjects who have also had the TactiCath SE inserted into their vasculature.

#### 6.1.7 Descriptive Endpoint #5

Descriptive endpoint #5 is one-year success, defined as freedom from symptomatic AF/AFL/AT lasting at least 30 seconds without a new Class I or III AAD or a higher dosage of pre-existing AAD as assessed from the end of the 3-month blanking period to 12 months following the ablation procedure.

A full 10-second 12-lead ECG recording of arrhythmia may be substituted for a 30-second recording unless there is evidence that the recorded arrhythmia is short-lived and less than 30 seconds.

##### 6.1.7.1 Analysis Methodology

Freedom from AF will be calculated as the number of subjects without a failure as defined in section 6.1.7 divided by the total number of subjects in the analysis population. Corresponding exact two-sided 95% binomial confidence intervals will also be calculated.

##### 6.1.7.2 Analysis Population

The analysis population for this endpoint will include all enrolled subjects who have also had the TactiCath SE inserted into their vasculature and who have completed their 1-year visit or crossed the 1-year visit window without the visit but with an event as defined above for the descriptive endpoint #5. In addition, the analysis will be run on the subset of subjects who also meet descriptive endpoint #2 (achieving  $\geq 10$ g contact force).

#### 6.1.8 Descriptive Endpoint #6

Descriptive endpoint #6 is one-year drug-free success, defined as freedom from any AF/AFL/AT lasting at least 30 seconds or any Class I or III AAD after removal from antiarrhythmic drug therapy as assessed from the end of the 3-month blanking period to 12 months following the ablation procedure.

A full 10-second 12-lead ECG recording of arrhythmia may be substituted for a 30-second recording unless there is evidence that the recorded arrhythmia is short-lived and less than 30 seconds.

##### 6.1.8.1 Analysis Methodology

Freedom from AF will be calculated as the number of subjects without a failure as defined in section 6.1.8 divided by the total number of subjects in the analysis population. Corresponding exact two-sided 95% binomial confidence intervals will also be calculated.

##### 6.1.8.2 Analysis Population

The analysis population for this study will be based on all subjects in whom a study device was introduced and who have completed their 1-year visit or crossed the 1-year visit window without the



visit but with an event as defined above for the descriptive endpoint #6. In addition, this analysis will be performed on the following subsets of subjects:

- Subjects who are also off of antiarrhythmic medication at the end of the blanking period.
- Subjects who also meet descriptive endpoint #2 (achieving  $\geq 10g$  contact force).

#### 6.1.9 Descriptive Endpoint #7

Descriptive endpoint #7 is change in EQ-5D-5L scores from baseline to follow up at 3, 6, and 12 months.

##### 6.1.9.1 Analysis Methodology

Changes in EQ-5D-5L score between baseline and follow up visits will be summarized with descriptive statistics. Scores will be used to calculate utility values and QALYs.

##### 6.1.9.2 Analysis Population

The analysis population for this endpoint will include all enrolled subjects who have also had the TactiCath SE inserted into their vasculature, have a baseline EQ-5D-5L, and who have completed their applicable follow up visit.

#### 6.1.10 Descriptive Endpoint #8

Descriptive endpoint #8 is change in AFEQT scores from baseline to follow up at 3, 6, and 12 months.

##### 6.1.10.1 Analysis Methodology

Changes in AFEQT between baseline and follow up visits will be summarized with descriptive statistics to assess change in functional improvement.

##### 6.1.10.2 Analysis Population

The analysis population for this endpoint will include all enrolled subjects who have also had the TactiCath SE inserted into their vasculature, have a baseline AFEQT, and who have completed their applicable follow up visit.

#### 6.1.11 Descriptive Endpoint #9

Descriptive endpoint #9 is cardiovascular-related health care utilization through 12 months post index ablation.

##### 6.1.11.1 Analysis Methodology

Descriptive statistics will be generated for all variables.

##### 6.1.11.2 Analysis Population

The analysis population for this endpoint will include all enrolled subjects who have also had the TactiCath SE inserted into their vasculature and who have health care utilization data available.

#### 6.1.12 Descriptive Endpoint #10

Descriptive endpoint #10 is force time integral (FTI) and lesion index (LSI).

##### 6.1.12.1 Analysis Methodology

FTI and LSI will be derived from the available Ensite Precision data. Descriptive statistics will be generated for both variables.

### 6.1.12.2 Analysis Population

The analysis population for this endpoint will include all enrolled subjects who have also had the TactiCath SE inserted into their vasculature.

[REDACTED]

[REDACTED]

### 6.3 Multiplicity

Both primary endpoints must pass hypothesis testing for the trial to be a success. Descriptive endpoints and subgroup analyses are not intended to support labeling claims. Therefore, multiplicity adjustment is not applicable.

[REDACTED]

[REDACTED]

### 6.5 Timing of Analysis

The primary endpoint analysis will be performed and the pre-market approval (PMA) clinical report will be submitted when 140 subjects have data available to assess the primary safety and effectiveness endpoints.

### 6.6 Success Criteria

The trial will be considered successful if the null hypotheses for both the primary safety and effectiveness endpoints are rejected.

### 6.7 Interim Analysis

No interim analysis is planned for this clinical investigation.

### 6.8 Statistical Criteria for Termination

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

### 6.9 Deviations from Statistical Plan

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

[REDACTED]

## 7 Risks and Benefits

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.

### 7.1 Risks Associated with the Device Under Investigation

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

#### 7.1.1 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

#### 7.1.2 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.

#### 7.1.3 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
- Assessment of continuing safety of subjects in the clinical investigation by internal Abbott safety personnel

#### 7.2 Possible interactions with concomitant treatments

There are no known interactions with concomitant treatments.

#### 7.3 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.

#### 7.4 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.

#### 7.5 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.

## 8 Requirements for Investigator Records and Reports

### 8.1 Deviations from CIP

A deviation is defined as an instance(s) of failure to follow, intentionally or unintentionally, the requirements of the CIP. The investigator should not deviate from the CIP.

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

The PI must maintain accurate, complete, and current records, including documents showing the date of and reason for each deviation from the CIP. Relevant information for each deviation will be documented as soon as possible on the applicable eCRF. The site will submit the eCRF to the Sponsor.

The PI is required to adhere to local regulatory requirements for reporting deviations to IRB/EC.

An investigator shall notify the Sponsor and the reviewing IRB/EC of any deviation from the investigational plan to protect the life or physical well-being of a subject in an emergency. Such notice shall be given as soon as possible, but in no event later than 5 working days after the emergency occurred. Except in such an emergency, prior approval by the Sponsor is required for changes in or deviations from a plan, and if these changes or deviations may affect the scientific soundness of the plan or the rights, safety, or welfare of human subjects, FDA and IRB/EC approval is also required.

### 8.2 Safety Reporting

Safety surveillance within this study and safety reporting performed both by the investigator and Sponsor starts as soon as the subject is enrolled. Safety surveillance and reporting will continue until the last investigational visit has been performed, the subject is deceased, the subject concludes their participation in the clinical investigation or the subject withdraws from the clinical investigation. All adverse event data including deaths will be collected throughout the time period defined above and will be reported to the Sponsor on an eCRF. Additional information on an adverse event should be updated within the appropriate case report form. Unchanged, chronic, non-worsening or pre-existing conditions are not AEs and should not be reported.

For the purposes of this clinical investigation, the following events will be reported (see Appendix B for definitions):

- Serious adverse events
- Adverse events that are considered related to either the ablation catheter or the ablation procedure by the investigator

Recurrence of AF, AFL, or AT are not considered reportable adverse events unless they occur in a severity, frequency, or other manner that is significantly worse than the subject's baseline condition. These are considered lack of effectiveness and will be reported as a recurrence on the appropriate case report form.

Non-cardiac related abnormal laboratory values will not be considered AEs unless:

- The investigator determined that the value is clinically significant,
- The abnormal lab value required intervention, or
- The abnormal lab value required subject termination from the study.

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

Clinical Site	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.

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

#### 8.2.1 Unanticipated Adverse Device Effect (US Only)

If an unanticipated adverse device effect occurs, the investigator must notify the Sponsor and the IRB/EC immediately, but no later than 3 calendar days of the investigator's knowledge of the event. The Sponsor will take any steps necessary to investigate the event, and, as appropriate, will be responsible for notifying FDA and all other participating IRBs/ECs and investigators.

#### 8.3 Source records

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

#### 8.4 Records Retention

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

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

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

### 9 Clinical Data Handling

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

#### 9.1 Protection of Personally Identifiable Information

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

#### 9.2 Data Management Plan

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

Subject data will be captured in a validated electronic data capture (EDC) system hosted by the Sponsor.

Only authorized site personnel will be permitted to enter the eCRF 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.

### **9.3 Document and Data Control**

#### **9.3.1 Traceability of Documents and Data**

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

#### **9.3.2 Recording Data**

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

## **10 Monitoring**

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

Monitoring will be conducted according to a study-specific monitoring plan. Prior to beginning the clinical investigation, the Sponsor will contact the investigator or designee to discuss the clinical investigation and data requirements. A designated monitor will periodically review the subject records and associated source documents. The investigator shall make subject and clinical investigation records available to the clinical monitor for monitoring.

## **11 Compliance Statement**

### **11.1 Statement of Compliance**

In addition to applicable regional or local laws and regulations, this clinical investigation will be conducted in compliance with the most current version of the World Medical Association (WMA) and Declaration of Helsinki and 21 CFR Parts 50, 54, 56 and 812. In the event of any conflicts, local laws and regulations will have precedence and in such cases, good faith efforts will be made to adhere to the intent of the other documents.

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

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

### 11.2 Quality Assurance Audits and Regulatory Inspections

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

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

### 11.3 Repeated and Serious Non-Compliance

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

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

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

## 12 Suspension or Premature Termination of the Clinical Investigation

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

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

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

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

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



### **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**

Publications or presentations of clinical investigation methods or results will adhere to the Sponsor's publication policy, which is based on Good Publication Practices and International Committee of Medical Journal Editors (ICMJE) guidelines. A copy of the policy will be provided upon request of the investigator.

### **15 Reporting Results on ClinicalTrials.gov Website**


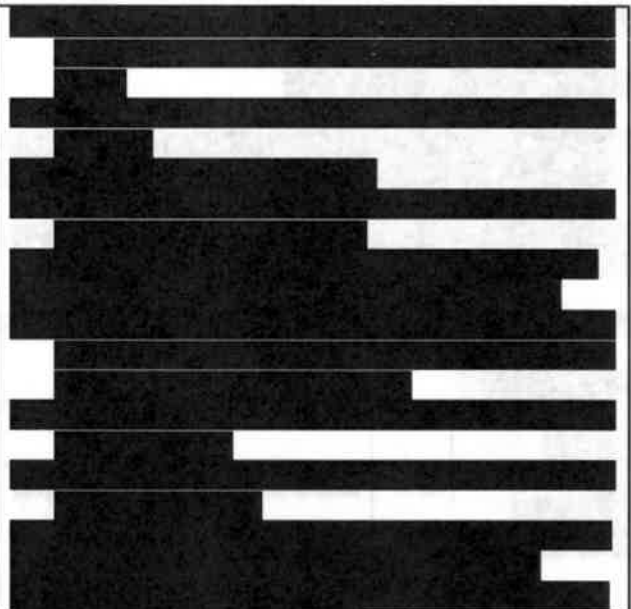



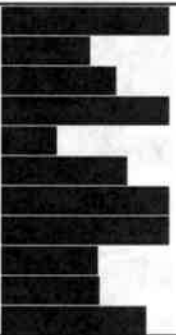

This clinical investigation will be registered on ClinicalTrials.gov as required by US federal regulations. Sponsor shall be responsible for any such registration and results posting as required by ClinicalTrials.gov. Institution and/or Principal Investigator(s) shall not take any action to register the Trial. A full report of the pre-specified outcomes, including any negative outcomes, will be made public through the ClinicalTrials.gov website according to the requirements of Section 801 of the FDA Amendments Act.



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## Appendix B Definitions

### Non-study Specific Definitions

#### Adverse Event (AE)

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

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

This definition includes events related to the procedures involved.

#### Serious Adverse Event (SAE)

An adverse event that led to any of the following:

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

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

#### Unanticipated Adverse Device Effect (UADE)

As defined in 21 CFR §812.3, unanticipated adverse device effects (UADE) are defined as any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the CIP or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

#### Vulnerable Subject

Vulnerable subject is defined as individual whose willingness to volunteer in a clinical investigation could be unduly influenced by the expectation, whether justified or not, of benefits associated with participation or of retaliatory response from senior members of a hierarchy in case of refusal to participate.

EXAMPLE Individuals with lack of or loss of autonomy due to immaturity or through mental disability, persons in nursing homes, children, impoverished persons, subjects in emergency situations, ethnic minority groups, homeless persons, nomads, refugees, and those incapable of giving informed consent. Other vulnerable subjects include, for example, members of a group with a hierarchical structure such as university students, subordinate hospital and laboratory personnel, employees of the Sponsor, members of the armed forces, and persons kept in detention.

### Study Specific Definitions

#### ACT

Active clotting time

#### Blanking Period

The blanking period is the 90 days immediately following the index ablation procedure. During this time, recurrences of arrhythmias are not counted towards the trial effectiveness end point.

#### Device-Related

Exposure to the TactiCath SE device has occurred and the device is more likely than other alternative causes to be responsible for the adverse event or it cannot be ruled out that the device is not responsible for the adverse event.

*Documentation of AF-related Symptoms*

Documentation by a physician evaluating the patient that the patient experiences symptoms that could be attributable to AF. This does not require a time-stamped ECG, Holter, or event monitor at the precise time of symptoms.

*Index Ablation Procedure*

This refers to the initial procedure where ablations were performed to treat atrial fibrillation within this trial.

*Long-standing Persistent Atrial Fibrillation*

Long-standing persistent AF is defined as continuous AF of greater than 12 months duration.

*NIHSS*

This is the National Institutes of Health Stroke Scale. It is a standard assessment for stroke which can be accessed at the following website: [https://www.ninds.nih.gov/sites/default/files/NIH\\_Stroke\\_Scale.pdf](https://www.ninds.nih.gov/sites/default/files/NIH_Stroke_Scale.pdf)

*Paroxysmal Atrial Fibrillation*

Paroxysmal AF is defined as AF that terminates spontaneously or with intervention within 7 days of onset.

*Persistent Atrial Fibrillation*

Persistent AF is defined as continuous AF that is sustained beyond 7 days.

*Physical Exam*

This is a standard of care physical exam, conducted by an investigator that includes a neurological assessment.

*Procedure-Related*

Determination of TactiCath SE procedure relationship includes assessment of AEs for relationship to any of the following: discontinuation of anticoagulation medication for the TactiCath SE procedure, administration of local or general anesthesia, or the TactiCath SE procedure. Relationship of TactiCath SE procedure will be assessed regardless of the temporal relationship to the TactiCath SE procedure.

*Symptomatic AF/AFL/AT*

AF/AFL/AT that results in symptoms that are experienced by the patient. These symptoms can include but are not limited to palpitations, presyncope, syncope, fatigue, and shortness of breath.

## Appendix C Primary Safety Endpoint Criteria

The following criteria will be used by the CEC to determine whether or not the events listed below constitute a device or procedure related serious adverse event included in the primary endpoint.

**Table 4: Primary Safety Endpoint Criteria**

Primary Serious Adverse Event	Criteria
Atrial esophageal fistula	Development of a connection between the atrium and the lumen of the esophagus
AV block	New, persistent 2 <sup>nd</sup> or 3 <sup>rd</sup> degree AV block not attributable to a vasovagal reaction or medication effect and requiring permanent pacing
Cardiac Perforation / Tamponade	Pericardial effusion that results in hemodynamic compromise, requires elective or urgent pericardiocentesis, or results in a 1-cm or more pericardial effusion as documented by echocardiography.
Death	Adverse event resulting in subject death
Diaphragmatic paralysis	Change in baseline diaphragmatic function as evidenced by elevation of a hemi-diaphragm above its normal position or loss of normal respiratory excursion but not due to a pulmonary process such as atelectasis and persisting longer than the end of the procedure
Gastroparesis	Vagal nerve injury that results in gastric dysmotility requiring intervention or hospitalization
Hospitalization (initial or prolonged)	Adverse event leading to new hospital admission or prolongation of initial hospital stay beyond expected timeframe due to ablation procedure-related cause. Excludes hospitalization solely for arrhythmia recurrence.
Myocardial Infarction	Irreversible necrosis of heart muscle secondary to prolonged ischemia with at least one of the following three criteria: <ul style="list-style-type: none"> <li>• Detection of ECG changes indicative of new detection of ECG changes indicative of new ischemia (new ST-T wave changes or new LBBB) that persist for more than 1 hour</li> <li>• Development of new pathological Q waves on an ECG</li> <li>• Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality</li> </ul>
Pericarditis	Inflammation of the pericardium resulting in chest discomfort/pain associated with either pericardial rub and/or ECG changes that requires or prolongs hospitalization
Pneumothorax	Abnormal collection of air in the pleural space between the lung and the chest wall that prolongs 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: <ul style="list-style-type: none"> <li>• Symptoms (e.g. dyspnea)</li> <li>• Physical findings (e.g. rales, hypoxemia)</li> <li>• Radiologic findings</li> <li>• Respond to diuretic therapy</li> <li>• Require hospitalization</li> </ul>
Pulmonary Vein stenosis	Reduction in the diameter of a pulmonary vein (PV) or PV branch >70% confirmed via imaging (CT or MRI)
Stroke	Brain disorder involving loss of brain functions (that persists for > 24 hours) that occur when the blood supply to any part of the brain is interrupted as determined by the consulting neurologist
Thromboembolism	An arterial or venous thrombus that results in deep vein thrombosis, pulmonary embolism, or peripheral arterial embolism
Transient ischemic attack	Acute episode of temporary (< 24 hrs.) and focal loss of cerebral function of vascular (occlusive) origin as determined by the consulting neurologist
Vascular access complications	Adverse event related to vascular access requiring surgical repair, blood transfusion (e.g., groin hematoma, AV fistula) or significant intervention such as thrombin injection (e.g., pseudoaneurysm)

**Appendix D Labels**

Sample Instructions for Use available upon request under separate cover.

**Appendix E Sample Informed Consent Form**

Provided upon request under separate cover.



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