| Abbott | Clinical Investigation Plan Cover Page |
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| NCT Number: NCT03882021 |
| WAVE-MAP AF |
| High-Density Wave Mapping in Subjects with Atrial Fibrillation as a Predictor of Recurrence After a Single Ablation Procedure Using a PVI-Only Strategy |
| Study Document No: ABT-CIP-10275 |
| Version A |
| Date: 20-FEB-2019 |

Sponsor

Abbott
5050 Nathan Lane North
Plymouth, MN 55442
USA

[redacted]

# Clinical Investigation Plan

## CRD_968

## WAVE-MAP AF

**High-Density Wave Mapping in Subjects with Atrial Fibrillation as a Predictor of Recurrence After a Single Ablation Procedure Using a PVI-Only Strategy**

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| Version | A |
| Date | 20FEB2019 |
| Planned Number of Sites and Region(s) | Up to 20 Sites Worldwide |
| Clinical Investigation Type | Prospective, single arm, multi-center clinical investigation. |
| Abbott Medical Expert | [redacted] |
| Sponsor | Abbott<br>5050 Nathan Lane North<br>Plymouth, MN 55442<br>USA |
| Electronic Data Capture Software | Oracle Clinical |
| CIP Author of Current Version | [redacted] |

[redacted]

# Clinical Investigation Plan

SITE PRINCIPAL INVESTIGATOR SIGNATURE PAGE

The Principal Investigator at each participating site may be required to sign that he/she agrees to adhere to the CIP and all applicable regulatory requirements. If this is required per regulations, include the below signature page.

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

Site Principal Investigator

| |
|---|
| Printed name: |
| Signature: |
| Date: |

# Clinical Investigation Plan

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# Clinical Investigation Plan

**COMPLIANCE STATEMENT:**

This clinical investigation will be conducted in accordance with this Clinical Investigation Plan, the Declaration of Helsinki, ISO 14155:2011 standards 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 Ethics Committee (EC) of the respective clinical site and as specified by local regulations.

# Clinical Investigation Plan

## 1.0 INTRODUCTION

This document is a clinical investigation plan (CIP) for the WAVE-MAP AF clinical investigation. This clinical investigation is intended to characterize the left atrial substrate using the Advisor™ HD Grid Mapping Catheter, Sensor Enabled™ in an HD Wave configuration and correlate different factors with 12-month success after a single ablation procedure using a pulmonary vein isolation (PVI) approach without further substrate modification. This clinical investigation will be conducted as a post-market study and is intended to support marketing claims for the Advisor™ HD Grid Mapping Catheter, Sensor Enabled™ (GRID). [redacted] This clinical investigation is sponsored by Abbott.

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

### 1.1 Background and Rationale

#### 1.1.1 Background

It has been estimated that 20.9 million men and 12.6 million women have Atrial Fibrillation (AF) worldwide.[12] AF has a prevalence of approximately 3% in adults aged 20 years or older.[3,4] Additionally, one in four middle-aged adults in the US and Europe will develop AF in their lifetime.[5,6] In Australia, 5% of people aged 55 years or older have AF, and this number is projected to rise to 6% by 2034[7]. 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.[8] 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.[9,10] 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.[11,12,13] 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.[14,15,16,17]

AF is generally divided into three different types based on the frequency of the AF: paroxysmal, persistent, and long-standing persistent. Paroxysmal AF (PAF) is defined as AF that terminates spontaneously or with intervention within 7 days of onset. Persistent AF (PsAF) is defined as continuous AF that is sustained beyond 7 days. Long-standing persistent AF (LSAF) is defined as continuous AF of greater than 12 months duration.

Per Calkins, et al in the 2017 HRS/EHRA/ECAS/APHRS/SOLAECE Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation (2017 Consensus)[18], catheter ablation is a treatment option for all three types. Pulmonary vein isolation (PVI) is a recommended approach by the consensus paper for all de novo AF ablation procedures. PVI alone does not cure all AF, and other techniques have been studied to supplement PVI ablation and improve outcomes. Substrate modification beyond

isolation of the pulmonary veins is one type of supplementary ablation. Outcomes of substrate modification, when added to PVI, have shown mixed results. Further characterization of the atrial substrate is needed to identify ablation targets to improve outcomes. Several studies have shown some benefit identifying low-voltage zones (LVZs) and ablating those targets in addition to PVI for persistent atrial fibrillation. Not all subjects have LVZs though, and mapping is critical to identify which subjects will respond to PVI only, and which require further substrate modification. It is hypothesized that it is more advantageous to characterize subjects by the amount of LVZ substrate in the left atria, rather than into PAF, PsAF, or LSAF, for the purposes of identifying the optimal treatment approach.

There are two traditional means of identifying LVZs: delayed enhancement magnetic resonance imaging (DEMRI) and traditional mapping catheters. DEMRI must be performed outside of the EP lab. The usefulness of DEMRI for detecting fibrosis requires extensive MRI experience and is dependent on image contrast and continuity parameters. When collecting points using traditional mapping catheters, only a single bi-pole is considered for any give acquisition. This makes voltage measurements susceptible to inaccuracies resulting from misalignment of the bi-pole with the propagating wave-front.

GRID was introduced to the European market in 2017. The GRID, with equispaced multipolar grid electrodes, provides known bi-pole spacing in orthogonal directions. GRID can discriminate voltage differences in two directions which provides enhanced directionality and amplitude detection. This is done by using an HD Wave electrode configuration with AutoMap (with best duplicate enabled) during electro anatomical map creation (see Appendix IX). It is hypothesized that electro anatomical mapping using the GRID with HD Wave will provide high-density and high-resolution mapping for improved insight to the extent of structural disease.

In this study, the aim is to use the GRID to characterize the atrial substrate and develop a model for predicting recurrence rates after a single procedure using a PVI only approach and a contact catheter.

### 1.1.2 Rationale for Conducting this Clinical Investigation

This study will provide insight into how substrate characteristics, as measured by GRID, can identify subjects who will not benefit from additional substrate modification beyond PVI. This may result in future recommendations for treatment based on HD Wave mapping of baseline substrate so that additional, unnecessary ablations along with their potential risks can be avoided. There have been no studies to date correlating substrate characteristics, as measured using HD Wave mapping, to outcomes. [redacted]

## 2.0 CLINICAL INVESTIGATION OVERVIEW

### 2.1 Clinical Investigation Objectives

The primary objective of this study is to characterize low-voltage substrate, as identified via HD Wave mapping in sinus rhythm, and identify associations with 12-month recurrence rates after a single pulmonary vein isolation (PVI) with a contact force RF ablation catheter.
Other objectives of this study include:

- Analyze additional maps and data collected with GRID and associations with 12-month recurrence rates, such as:

[redacted]

- Voltage maps using different configurations recreated post procedure[1]
- Voltage maps using different thresholds for low-voltage
- Fractionation maps

[redacted]

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

### 2.2.1 Name of the Device(s) Under Investigation

All devices used in this clinical study must have proper regulatory approval and will be used according to their indications for use and Instructions for Use (IFU).

The devices that will be used in this clinical study are summarized in Table 1.

**Table 1. Clinical Study Devices**

| Device name | Model/Type | Manufacturer |
|---|---|---|
| Advisor™ HD Grid Mapping Catheter, Sensor Enabled™ | D-AVHD-DF16 | SJM |
| EnSite Precision™ Cardiac Mapping System v 2.2 or later | H702496 | SJM |
| Advisor™ HD Grid Mapping Catheter, Sensor Enabled™ Software Kit *(License entitlement to use GRID with EnSite Precision 2.2)* | H702519 | SJM |
| Sensor Enabled™ Diagnostic Catheter Cable | D-AVSE-CBL22 | SJM |
| EnSite Precision™ Surface Electrode Kit | EN0020-P | SJM |
| EnSite™ AutoMap Module | H702498 | SJM |
| EnSite™ AutoMark Module | H702499 | SJM |
| EnSite™ Contact Force Module | H702500 | SJM |
| TactiCath™ Contact Force Ablation Catheter, Sensor Enabled™ | A-TCSE-D<br>A-TCSE-F<br>A-TCSE-J | SJM |

[1] For example, after receiving the EnSite case archive from the site, the Sponsor would recreate what the voltage map would have looked like using a Standard configuration as opposed to the HD Wave configuration to compare differences.

[redacted]

| | | |
|---|---|---|
| | A-TCSE-DD<br>A-TCSE-FF<br>A-TCSE-JJ<br>A-TCSE-DF<br>A-TCSE-FJ | |
| TactiSys™ Quartz Equipment | PN-004 400 | SJM |
| Cool Point™ Pump v24 or greater | 85784 (OUS) | SJM |
| Ampere™ RF Generator v1.04 or greater | H700489 (OUS) | SJM |

Additional commercially available tools may be used in this clinical study per physician's discretion and per device IFUs unless specifically prohibited in this CIP.

### 2.2.2 Indication for Use

The Advisor™ HD Grid Mapping Catheter, Sensor Enabled™, is indicated for multiple electrode electrophysiological mapping of cardiac structures in the heart, i.e., recording or stimulation only. This catheter is intended to obtain electrograms in the atrial and ventricular regions of the heart.

All devices will be used according to their approved labelling in this study.

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

## 3.0 CLINICAL INVESTIGATION DESIGN

This is a post-market, single-arm, multi-center, prospective interventional study of the Advisor™ HD Grid Mapping Catheter, Sensor Enabled™. This study is aimed at determining correlations between pre-ablation mapping characteristics and outcomes after catheter ablation of atrial fibrillation. [redacted]

Endpoints will be analyzed when all subjects have completed their 12-month follow up visits.

### 3.1 Clinical Investigation Procedures and Follow-up Schedule

Subjects will be followed until they complete their 12-month visit. Clinical Investigation visits will occur at Baseline (confirmation of eligibility), Index Procedure, 3 months, 6 months, and 12 months. The flow chart below summarizes the visits and study procedures.

[redacted]

# Clinical Investigation Plan

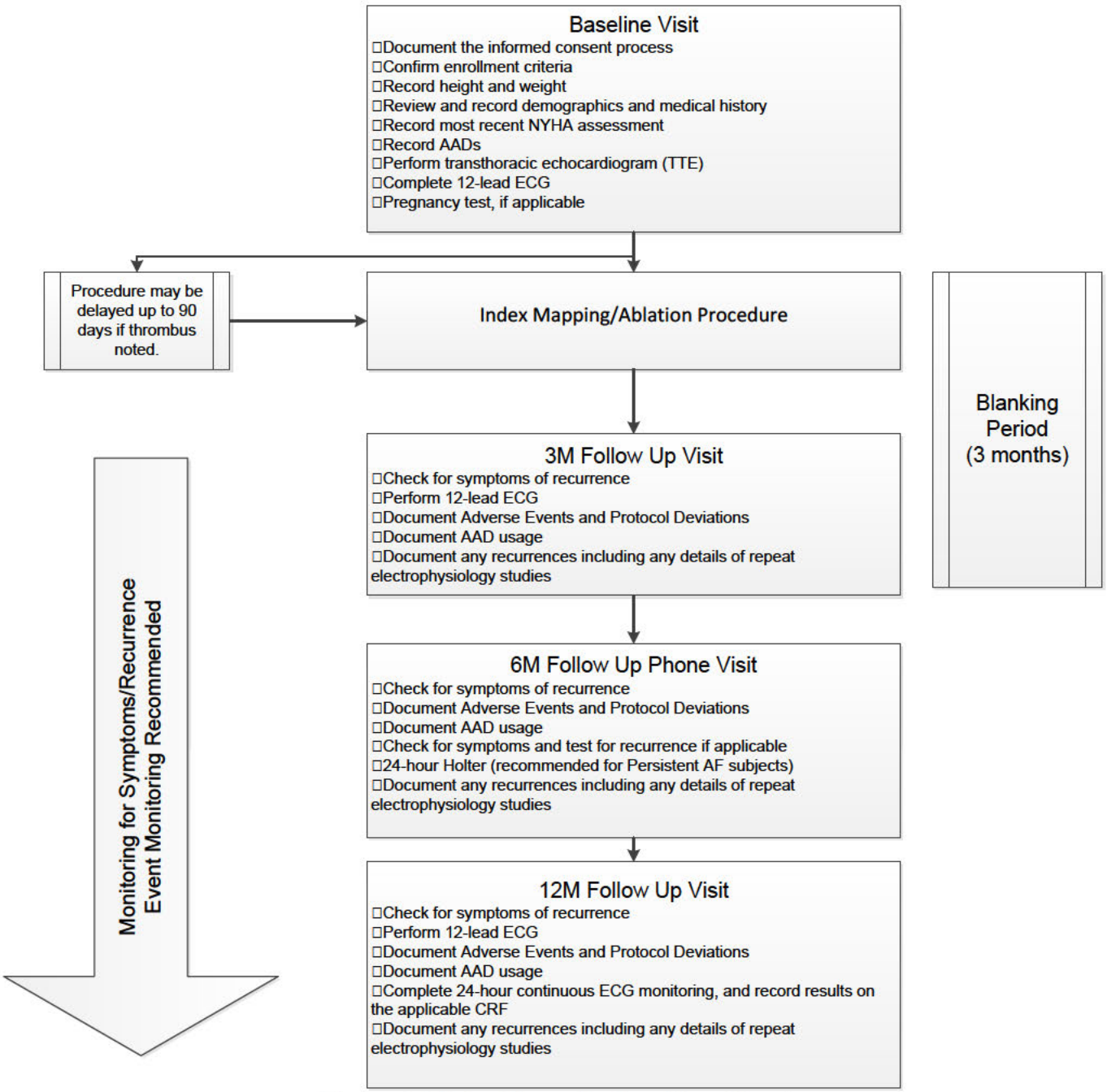



**Figure 1 Clinical Investigation Flow Chart**

## 3.2 Measures Taken to Avoid and Minimize Bias

Measures taken to avoid or minimize bias include the following:

- All analyses of mapping data will be centralized and performed using proprietary software by an independent reviewer.

[redacted]

- To minimize selection bias, investigators are required to screen consecutive patients with planned de novo AF ablation procedures and record them on a screening log.
- Strict inclusion/exclusion criteria are included in this CIP.
- A standardized mapping and ablation protocol has been defined.
- Individuals taking measurements from EnSite maps will not have access to the outcome data of the associated subject.

### 3.3 Suspension or Early Termination of the Clinical Investigation

While no formal statistical rule for early termination of the clinical investigation for insufficient effectiveness of the device under investigation is defined, the Sponsor reserves the right to discontinue the clinical investigation at any stage or reduce the follow-up period with suitable written notice to the investigator. Possible reason(s) may include, but are not limited to:

- A new unreasonable risk to the participating subjects has been identified such as an unanticipated increase in complaint rates related to the study.
- Further product development is cancelled.

Should the clinical investigation be discontinued by the Sponsor, subjects will be followed per routine hospital practice with device-related AEs reported to the Sponsor as per vigilance/commercial reporting requirements. The investigator shall return all clinical investigation materials to the Sponsor and provide a written statement to the EC (if applicable). All applicable clinical investigation documents shall be subject to the same retention policy as detailed in Section 11.0.

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

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

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

## 4.0 ENDPOINTS

### 4.1 Primary Endpoint and Rationale

The primary outcome is one-year success, defined as freedom from AF/AFL/AT after removal from antiarrhythmic drug therapy as assessed from the end of the 3-month blanking period to 12 months following a single ablation procedure.

Occurrence of isthmus-dependent atrial flutter, if confirmed during electrophysiology testing, should not be considered a failure for this outcome.

This endpoint is based on the recommendations from the 2017 HRS consensus paper.[18]

[redacted]

## 4.2 Additional Data

Additional data to be collected will include the following:

- Acute procedural success, defined as electrical isolation of all pulmonary veins.
- Success post blanking period through 12 months using different definitions, including:
    - Freedom from symptomatic AF/AFL/AT after removal from AAD therapy
    - Single procedure clinical success defined as freedom from symptomatic AF/AFL/AT without a new or increased dose of class I or III AAD
- 
- Data from EnSite maps using both HD Wave and Standard mapping modes[2] in both sinus rhythm and AF including but not limited to:
    - Left atrial area using different boundaries (e.g. with and without LAA, etc.)
    - Low voltage area and proportion of left atria with low voltage using different cutoffs for voltage
- Rates of recurrence not due to PVI gap for subjects with repeat electrophysiology studies
- LA volume and diameter
- Adverse events including any device-, procedure-, or death-related events
- Other baseline characteristics including but not limited to:
    - Time with AF
    - Type of AF
    - Sex
    - BMI
    - General medical history
    - Cardiovascular history
    - Arrhythmia history
    - NYHA classification
    - LVEF
    - Presence of pacemaker
- Procedural characteristics, including but not limited to:
    - Power, temperature, and contact force
    - Procedure time
    - Mapping time
    - Cardioversions (if applicable)

[2] Difference in each measurement between the different mapping modes will be compared.

- Anesthesia
- Fluoroscopy time

# 5.0 SUBJECT SELECTION AND WITHDRAWAL

## 5.1 Subject Population

This clinical investigation will enroll male and female subjects from the general atrial fibrillation population. Subjects must meet all eligibility criteria and provide written informed consent prior to conducting any investigation-specific procedures not considered standard of care.

## 5.2 Subject Screening and Informed Consent

### 5.2.1 Subject Screening

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

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

To minimize bias throughout the enrollment period for this study, consecutive de novo AF patients with planned ablation must be screened[3], offered the study if they meet criteria, and added to a screening log.

Potential patients presenting at the clinical sites will be fully informed about the clinical investigation, following the established Informed Consent process (described in Section 5.2.2). Patients meeting all inclusion criteria and no exclusion criteria will be asked to sign an Informed Consent form if they wish to participate in the clinical investigation.

Once a duly dated and signed Informed Consent form is obtained, the clinical investigation-specific procedures may begin.

### 5.2.2 Informed Consent

The Patient Informed Consent form must receive approval from the Sponsor and EC/IRB prior to beginning clinical investigation enrollment.

The Investigator or his/her authorized designee (if applicable) will conduct the Informed Consent process, as required by applicable regulations and the center's 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

[3] This does not necessarily mean that the patient must be approached if their medical records indicate that they would not qualify.

[redacted]

benefits to which the subject is otherwise entitled. Withdrawal from the clinical investigation will not jeopardize their future medical care or relationship with the investigator.

During the discussion, the Principal Investigator or his/her authorized designee will avoid any improper influence on the subject and will respect subject's legal rights. Financial incentives will not be given to the subject. Subjects may be compensated for time and travel directly related to the participation in the clinical investigation. 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 EC. The subject shall have adequate time to review, ask questions, and consider participation. The Principal Investigator or his/her authorized designee will make efforts to ensure that the subject understands the information provided. If the subject agrees to participate, the Informed Consent form must be signed and dated by the subject and thereafter by the person obtaining the consent prior to any clinical investigation-specific procedures. The signed original will be filed in the subject's hospital or research charts, and a copy will be provided to the subject.

Failure to obtain informed consent from a subject prior to clinical investigation enrollment should be reported to Sponsor within 5 working days and to the reviewing center's EC according to the 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 (if applicable) 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

Incapacitated individuals, defined as 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.

## 5.3 Eligibility Criteria

### 5.3.1 General Eligibility Criteria

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

### 5.3.2 Inclusion Criteria

#### 5.3.2.1 General Inclusion Criteria

1. Documented atrial fibrillation with planned endocardial ablation procedure
2. Age 18 years or older

3. Able and willing to provide written informed consent prior to any clinical investigation related procedure
4. Able and willing to complete all required study procedures through 12 months

### 5.3.3 Exclusion Criteria

5.3.3.1 General Exclusion Criteria

1. Long-standing persistent atrial fibrillation defined as continuous AF greater than 12 months in duration
2. Previous ablation or surgery in the left atria
3. Implanted left atrial appendage occluder
4. Implanted mitral or tricuspid valve replacement
5. Implanted cardiac defibrillator (ICD)
6. Participation in another clinical investigation that may confound the results of this study
7. Pregnant or nursing
8. Presence of other anatomic or comorbid conditions, or other medical, social, or psychological conditions that, in the investigator's opinion, could limit the subject's ability to participate in the clinical investigation or to comply with follow-up requirements, or impact the scientific soundness of the clinical investigation results.
9. Life expectancy less than 12 months

## 5.4 Subject Enrollment

A patient is considered enrolled in the clinical investigation from the moment the patient provides written informed consent, has been confirmed to meet all inclusion criteria and none of the exclusion criteria and has had the mapping catheter inserted into the subject's vasculature.

## 5.5 Subject Withdrawal

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

- Subject death
- Subject voluntary withdrawal
- Subject lost-to follow-up as described below
- Subject has a thrombus **and** is withdrawn per Section 6.2
- Index ablation procedure is aborted prior to collection of at least one of the required maps.
- Operator is not able to achieve pulmonary vein isolation.
- Subject becomes a screen failure after consent

[redacted]

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

No additional follow–up will be required or data recorded from subjects once withdrawn from the clinical investigation.

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

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

If subjects are enrolled into the clinical investigation and are later found to have met exclusion criteria or not all inclusion criteria after the ablation procedure, these subjects will continue follow-up in the clinical investigation and may be included in the analysis population. A protocol deviation must be completed on the applicable CRF. Such subjects identified prior to the index procedure should be identified as screen failures and a protocol deviation is not necessary.

Lost-to-Follow-up

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

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

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

## 5.6 Number of Subjects

[redacted]. Individual study centers will be allowed to enroll 20% (~60 subjects) of the maximum total trial enrollment without additional approval. Centers may have their maximum enrollment number increased with prior Sponsor

[redacted]

approval. Enrollment will be limited to a maximum 110 paroxysmal AF cases, 110 early persistent AF (7 days to 3 months duration), and 110 non-early persistent AF (>3 months to 12 months duration) without Sponsor pre-approval.

### 5.7 Total Expected Duration of the Clinical Investigation

[redacted]

## 6.0 TREATMENT AND EVALUATION OF ENDPOINTS

The following sections describe the recommended and required procedures for this investigation. Unless otherwise noted, it is recommended that the site follow standard of care for any activities not specifically stated in this CIP.

### 6.1 Baseline Procedures (within 14 days of index procedure)

The following procedures should be conducted at the baseline visit:

- Document the informed consent process
- Confirm enrollment criteria
- Record height and weight
- Review and record demographics and medical history (including, but not limited to cardiovascular and arrhythmia history)
- Record most recent NYHA assessment
- Record AADs
- Perform transthoracic echocardiogram (TTE)[4]
    - Measure left atrial diameter
    - Measure left atrial volume
    - Measure left ventricular ejection fraction
    - Note any other abnormalities detected
- Complete 12-lead ECG (a previous 12-lead ECG may be used if done within 14 days of index procedure)
- Pregnancy test, if applicable[5]

It is recommended that class I and III AADs be withdrawn 48 hours prior to the ablation procedure to facilitate induction of AF for the mapping protocol (see section 6.2.1).

[4] If a TTE was performed in the last 6 months and the required data can be collected, this procedure can be skipped at baseline.

[5] The pregnancy test should follow the site's standard of care prior to the ablation procedure. It does not have to be during the baseline visit. This applies only to subjects who would have a pregnancy test per the sites standard of care (e.g. women of child-bearing potential).

[redacted]

# Clinical Investigation Plan

If the subject is identified as pregnant prior to the ablation procedure, they will be identified as a screen failure and the screening log will be updated.

## 6.2 Index Procedure

The subject should be prepped for an electrophysiology study per the site's standard of care. If there is a thrombus noted the procedure can be delayed up to 90 days post consent until the thrombus has been resolved and the investigator has assessed it to be safe to proceed. In this case, data recorded from the baseline visit will be revisited to note any changes (e.g. updated medical history and medications). If the investigator determines after 90 days the thrombus has not resolved, the subject should be identified as a screen failure and the screening log will be updated.

### 6.2.1 Mapping Protocol

Prior to any ablation, perform the following steps with the GRID as the only mapping catheter using an HD Wave configuration. HD Wave configuration is defined as any configuration only collecting from electrodes with two orthogonal bi-poles. It is recommended to use the configuration from **Figure 2**. See Appendix VIII for further details.

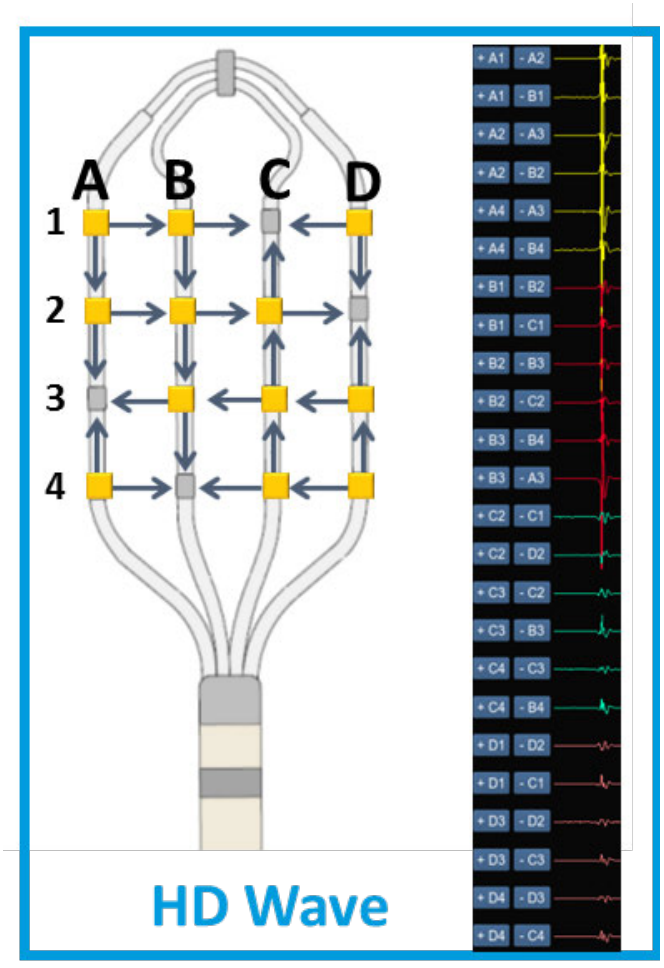


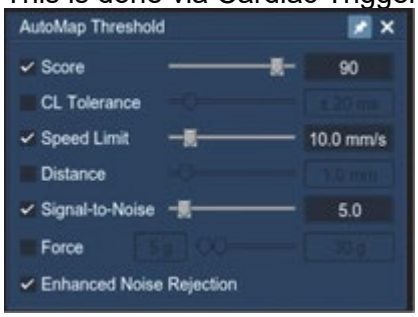

**Figure 2 Recommended HD Wave Configuration**

# Clinical Investigation Plan

- Start recording (F4) an EnSite Segment – label 'LA geometry'.
- Build LA geometry with GRID.
- End Geometry (F4) collection EnSite recording segment.

- Their first geometry may be a OneMap in sinus rhythm[6] (SR)
- Then record that segment label "SR OneMap'

- Collect Cardiac Triggered SR Map.
- This is done via Cardiac Triggered AutoMap




- Keep GRID in position for a **recommended 5 cardiac cycles (2 minimum)**

Upon completion, attempt to induce AF[7], and continue.

- Start a new map in Non- Cardiac Triggered mode (i.e. mapping in AF)
- **Set Map Settings of Interior Projection/Exterior Projection to 6/6 mm.**
- **Set Map Settings of Interpolation to 6 mm.**

  {Consider OneMap to do the geometry collection and mapping}

- Set up Map to collect with GRID.
- Use the CFE Mean map as guidance for map point collection
- CFE Mean: Suggested settings of Sensitivity 0.05 mV (above noise floor). Refractory 80 ms. Width 10 ms.
- Set up CFE Mean map: Suggested CFE Mean Color High of 250 ms and Color Low of 80 ms.
- Set up CFE Mean map with **Segment Length of 8 seconds.**

- Start recording (F4) an EnSite Segment – label 'LA AF Map'.
- **Set Auto Map Criteria as follows. Stable Distance to 5mm. Distance to 3mm.**

- Manually acquire first Auto Map point and then the Auto Map criteria will collect points based on its criteria.

  ***The catheter operator should aim, subject to their own discretion, to color the entire LA geometry using the above Auto Map settings.***

[6] If sinus rhythm cannot be achieved, this map can be captured in another regular rhythm.
[7] If subject is in AF initially, the AF map can be collected first, then collect the SR map after cardioversion.

- At each anatomical location, catheter operator aims to hold GRID in place for 8 seconds.
- End recording (F4) of Map collection segment.

After the procedure, the complete deidentified EnSite case should be submitted to Abbott per their instructions. This data will be analyzed independently of the investigator for purposes of avoiding bias and ensuring consistent measurements across all sites.

If the procedure is aborted for any reason prior to the collection of at least one voltage map, the subject should be withdrawn from the study. If the operator is not able to achieve pulmonary vein isolation, the subject should be withdrawn from the study once any ongoing serious adverse events have resolved or 30 days, whichever comes first.

### 6.2.2 Treatment Strategy for Ablation

Selected sites use a PVI-only strategy as standard of care for all de novo ablation of AF. After completing the mapping protocol, ablate the pulmonary vein antrum to isolate the veins using a wide area circumferential ablation (WACA) technique[8] with the TactiCath™ Contact Force Ablation Catheter, Sensor Enabled™ (TactiCath SE). If isthmus dependent flutter is identified and confirmed by electrophysiological testing (e.g. entrainment maneuvers), ablation of the cavo tricuspid isthmus is recommended in the right atrium. No deviations from standard of care[9] should be performed unless medically necessary. The AutoMark™ feature should be turned on for automated lesion-level data capture based on user-defined settings. Event Markers should be used to note physician comments about changes in rhythm[10].

PVI should be confirmed bidirectionally using the GRID and confirmed after a recommended 20-minute wait time to ensure isolation is achieved. In addition, use of isoproterenol or adenosine are allowed per the investigator's discretion to confirm block.

If arrhythmias remain after pulmonary vein isolation, it is recommended to treat with cardioversion and/or medication unless there is a medical necessity to perform additional ablation.

## 6.3 Post–Procedure and Early Follow Up

Sites should follow standard of care for use of AAD during the blanking period to address symptoms during healing. It is recommended to exclude Amiodarone due to its long half-life, since the effects of amiodarone could continue past the blanking period impacting recurrence rates.

All other aspects of care should follow the site's standard practice from discharge through the end of the 3-month blanking period.

## 6.4 Follow-up Assessments

The following sections describe the follow-up visits and procedures. All windows are stated with respect to the index procedure unless otherwise noted. It is recommended to follow the HRS Consensus guidelines for follow-up screening depending on type of AF (e.g. paroxysmal vs. persistent). A 12-lead

[8] This may include ablation to address the carina within the WACA circle per the investigator's discretion.
[9] Site's standard of care is PVI-only, so no other substrate modification should be performed.
[10] For example, "AF resolved to sinus rhythm during ablation of lesion #23".

ECG is recommended any time the subject returns to the clinic from 3- to 12-months post index procedure.

### 6.4.1 3-Month Follow Up (77 to 105 Days Post Index Procedure)

The blanking period ends on the day of the 3-month follow up visit. It is recommended the subject not be taking any class I or III AAD after the 3-month visit unless there is recurrence of AF. At the 3-month visit, the following procedures will be completed:

- Check for symptoms of recurrence
- Perform 12-lead ECG
- Document Adverse Events and Protocol Deviations
- Document AAD usage
- Document any recurrences including any details of repeat electrophysiology studies
- Instruct the subject to contact the site if they experience any symptoms of recurrence. If there are any symptoms noted after the 3-month visits through the 12-month visit, check for recurrence using 12-lead ECG or other form of monitoring per site's standard practice.

It is also recommended to provide the subject with an event monitor for recording at regular intervals (e.g. monthly) or for symptomatic events through the 12-month visit.

After the 3-month visit through the end of the study, any signs or symptoms of recurrence should be recorded, and the subject should have either a 12-lead ECG or other form of ECG monitoring per the site's standard practice to determine if recurrence has occurred.

### 6.4.2 6-Month (169 to 197 Days) Follow Up Phone Visit

Within two weeks of the 6-month time point post index procedure, the subject will be contacted via telephone (or seen in-clinic if standard of care) for the following assessments

- Check for symptoms of recurrence
- Document Adverse Events and Protocol Deviations
- Document AAD usage
- If there are symptoms of recurrence present, the subject should have either a 12-lead ECG or other form of ECG monitoring to determine if recurrence has occurred.
- Document any recurrences including details of any repeat electrophysiology studies

For persistent AF subjects, it is also recommended that a 24-hour holter be performed at the 6-month time point.

### 6.4.3 12-Month Follow Up Visit (335 to 395 Days Post Index Procedure)

The 12-Month visit will include the following procedures:

- Check for symptoms of recurrence
- Perform 12-lead ECG

# Clinical Investigation Plan

- Record Adverse Events and Protocol Deviations. Make sure to record the status of each ongoing event at the time of study exit.
- Document AAD usage
- Complete 24-hour continuous ECG monitoring[11], and record results on the applicable CRF
- Document any recurrences including any details of repeat electrophysiology studies

[11] This does not have to be done on the day of the visit. It can be done any time during the 12-month visit window.

### 6.4.4 Schedule of Events

The following tables summarizes the schedule of events.

*Table 2 Summary of Clinical Investigation Procedures*

| CIP Activity | Enrollment/ Baseline (within 14 days of index procedure) | Index Procedure | 3-Month (77 to 105 Days) | 6-Month phone call (169 to 197 Days) | 12-Month (335 to 395 Days) |
|---|---|---|---|---|---|
| Informed Consent Process | X | | | | |
| Record Height and Weight | X | | | | |
| Demographics | X | | | | |
| Medical History | X | | | | |
| NYHA assessment | X | | | | |
| Record AAD | X | | X | X | X |
| Thrombus assessment per SOC | X | (X) | | | |
| Mapping Protocol | | X | | | |
| PVI | | X | | | |
| Submit EnSite Data | | X | | | |
| Transthoracic Echo (TTE) | X | | | | |
| 12-lead ECG | X | | X | Y | X |
| Pregnancy Test | (X) | | | | |
| Symptom check | | | X | X | X |
| Check/Document Recurrence | | | (X) | (X) | (X) |
| 24-hour continuous ECG | | | | Y[12] | X |
| Event recording[13] | | | Y | Y | Y |
| Adverse Event | (X) | | (X) | (X) | (X) |
| Deviation | (X) | | (X) | (X) | (X) |
| Withdrawal | (X) | | (X) | (X) | (X) |
| Death | (X) | | (X) | (X) | (X) |

(X) if applicable
X = required
Y = recommended

## 7.0 ADVERSE EVENTS

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

[12] A 24-hour holter is recommended for persistent AF subjects at 6 months post ablation procedure.
[13] Event recording is recommended at regular intervals from 3 to 12 months post ablation procedure and for symptomatic events.

## 7.1 Definition

### 7.1.1 Adverse Event

An adverse event (AE) is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the medical device under investigation.

This definition includes events related to the medical device(s) under investigation and the mapping/ablation procedures involved. For users or other persons, this definition is restricted to events related to the medical devices under investigation.

### 7.1.2 Serious Adverse Event

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

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

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

## 7.2 Device Relationship

Determination of whether there is a reasonable possibility that a 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).

## 7.3 Adverse Event

### 7.3.1 Adverse Event Reporting

Safety surveillance and reporting starts as soon as the patient is enrolled in the clinical investigation. Safety surveillance and reporting will continue until the last follow-up visit has been performed, the subject is deceased, the subject concludes participation in the clinical investigation or the subject withdraws from the clinical investigation. Adverse event data, including deaths, will be collected

throughout the time period defined above and will be reported to the Sponsor on a CRF. Additional information with regard to an adverse event should be updated within the appropriate CRF.

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

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.

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

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

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

- Adverse events that are considered to be related to any of the study devices or the mapping/ablation procedure by the investigator
- Serious adverse events resulting in death

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.

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

SAE Reporting

The investigator should report applicable 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 than those outlined above. |

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 EC according to the institution's EC reporting requirements.

### 7.3.2 Device Complaint Reporting

The investigator is responsible for reporting all complaints to the manufacturer of a device that meets the definition of a complaint. A complaint is defined as any written, electronic or oral communication that

alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness or performance of a device after it is released for distribution.

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

## 8.0 STATISTICAL CONSIDERATIONS

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

### 8.1 Analysis Populations

[redacted]

### 8.2 Statistical Analyses

[redacted]

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

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

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

[redacted]

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The following lists describe the analysis methods for the additional evaluations that will be analyzed in the ENR population:

- LA volume and diameter (CONT)
- Adverse events including any device-, procedure-, or death-related events (CAT)
- Other baseline characteristics including but not limited to:
  - Time with AF (CONT)
  - Type of AF (CAT)
  - Sex (CAT)
  - BMI (CONT)
  - General medical history (CAT)
  - Cardiovascular history (CAT)
  - Arrhythmia history (CAT)
  - NYHA classification (CAT)
  - LVEF (CONT)
  - Presence of pacemaker (CAT)

The following lists describe the analysis methods for the primary endpoint and additional evaluations that will be analyzed in the PTE population:

- [redacted]

[14] Difference in each measurement between the different mapping modes will be compared.

[redacted]

### 8.3 Sample Size Calculation and Assumptions

[redacted]

### 8.4 Timing of Analysis

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

### 8.5 Subgroup Analysis

No subgroup analyses are planned for this clinical investigation.

### 8.6 Multiplicity

[redacted]

### 8.7 Procedures for Accounting for Missing Data

Every effort will be made to collect all required data. [redacted]

### 8.8 Planned Interim Analysis

[redacted]

### 8.9 Statistical Criteria for Termination

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

### 8.10 Success Criteria

[redacted]

[redacted]

### 8.11 Deviations from Statistical Plan

Any changes to the planned statistical analyses will be documented in the final report.

## 9.0 DIRECT ACCESS TO SOURCE DATA/DOCUMENTS

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

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

## 10.0 QUALITY CONTROL AND QUALITY ASSURANCE

### 10.1 Selection of Clinical Sites and Investigators

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

### 10.2 CIP Amendments

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

Acknowledgement/approval by the 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.

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## 10.3 Training

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

## 10.4 Monitoring

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

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

## 10.5 Deviations from CIP

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

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

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

## 11.0 DATA HANDLING AND RECORD KEEPING

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

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

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

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

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

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## 11.1 Protection of Personally Identifiable Information

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

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

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

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

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

## 11.2 Data Management Plan

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

## 11.3 Source Documentation

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

- Medical history/physical condition of the subject before involvement in the clinical investigation sufficient to verify CIP entry criteria
- Dated and signed notes on the day of entry into the clinical investigation referencing the Sponsor, CIP number, subject ID number and a statement that informed consent was obtained

- Dated and signed notes from each subject visit (for specific results of procedures and exams)
- Adverse events reported and their resolution, including supporting documents, such as discharge summaries, catheterization laboratory reports, ECGs, and lab results including documentation of site awareness of SAEs and of investigator assessment of device relationship for SAEs.
- CIP-required laboratory reports and 12-lead ECGs, reviewed and annotated for clinical significance of out of range results (if applicable).
- 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
- Any other data required to substantiate data entered into the CRF
- Patient reported outcome measures may be completed using CRF worksheets. These serve as the source documentation.

### 11.4 Case Report Form Completion

Primary data collection based on source-documented hospital and/or clinic chart reviews will be performed clearly and accurately by site personnel trained on the CIP and CRF completion. The investigator will ensure accuracy, completeness, legibility and timeliness of the data reported to the Sponsor on the CRFs and in all required reports.

Data on CRFs will be collected for all subjects that are enrolled into the clinical investigation.

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

### 11.5 Record Retention

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

## 12.0 ETHICAL CONSIDERATIONS

### 12.1 Ethics Committee Review and Approval

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

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

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

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

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

## 13.0 CLINICAL INVESTIGATION CONCLUSION

The clinical investigation report will be completed within one year of the last visit of the last subject. [redacted]

The clinical investigation will be concluded when:

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

## 14.0 PUBLICATION POLICY

The data and results from the clinical investigation are the sole property of the Sponsor. The Sponsor shall have the right to access and use all data and results generated during the clinical investigation. The Investigators will not use this clinical investigation-related data without the written consent of the Sponsor for any purpose other than for clinical investigation completion or for generation of publication materials, as referenced in the Clinical Trial Agreement. Single-center results are not allowed to be published or presented before the multi-center results. Any proposals for publications or presentations by the investigators must be reviewed and approved by the Sponsor in a timely manner to enable Sponsor review in compliance with the Sponsor's publication policy set forth in the Clinical Trial Agreement.

The Sponsor will be responsible for determining whether to register the clinical investigation on www.clinicaltrials.gov or any other clinical trials, in accordance with the International Committee of Medical Journal Editors guidelines, or any other applicable guidelines. In the event Sponsor determines that the clinical investigation should be registered, Sponsor shall be responsible for any such registration and results posting as required by the ClinicalTrials.gov website. Institution and/or Principal Investigator(s) shall not take any action to register the clinical investigation.

## 15.0 RISK ANALYSIS

### 15.1 Anticipated Clinical Benefits

Subjects participating in this clinical study are not expected to experience any additional benefit compared to patients who are not participating in this clinical study that also undergo cardiac ablation, as the clinical study will follow local standard practice. Medical science may benefit from your participation which may lead to benefits for future patients with AF. The information gathered in this clinical study will add to the understanding of treatment options for other patients with AF.

[redacted]

# Clinical Investigation Plan

## 15.2 Foreseeable Adverse Events and Anticipated Adverse Device Effects

The most commonly known risks for any ablation procedure are listed below:

- Bleeding or infection at the site where your catheter was inserted
- Damage to your blood vessels where the catheter may have scraped as it traveled to your heart
- Puncture of your heart
- Damage or swelling to the sack which surrounds your heart, making it difficult for the heart to beat strongly
- Damage to your heart valves
- Damage to your heart's electrical system, which could worsen your arrhythmia and could require a pacemaker to correct
- Blood clots in the legs or lungs (venous thromboembolism);
- Stroke or heart attack
- Narrowing of the veins that carry blood between your lungs and heart (pulmonary vein stenosis)
- Damage to your kidneys from dye used during the procedure
- Low blood pressure

## 15.3 Risks Associated with Participation in this Clinical Investigation

The required elements of this CIP are considered standard of care, except for additional diagnostic mapping. This mapping procedure is anticipated to last 0 to 30 minutes longer than the site's standard of care. No additional exposure to radiation, additional ablation, or changes to treatment approach are required by the mapping protocol. Considering electrophysiology studies typically last several hours, this risk is considered to be minor.

## 15.4 Steps Taken to Control or Mitigate Risks

In-depth recommendations, special precautions and instructions regarding the use of each device can be found in the applicable instructions for use.

## 15.5 Risk to Benefit Rationale

Use of GRID to facilitate electro anatomical mapping in the heart is believed to not introduce any unanticipated risks compared to current practice. Catheter ablation is a recognized safe and effective treatment of cardiac arrhythmias.

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## APPENDIX I: ABBREVIATIONS AND ACRONYMS

| Abbreviation/Acronym | Definition |
|---|---|
| AAD | Antiarrhythmic Drug |
| ACT | Active Clotting Time |
| AE | Adverse Event |
| AF or AFib | Atrial Fibrillation |
| AFL | Atrial Flutter |
| AT | Atrial Tachycardia |
| AV | Atrio-Ventricular |
| CEC | Clinical Events Committee |
| CF | Contact Force |
| CFAE | Complex Fractionated Atrial Electrograms |
| CIP | Clinical Investigation Plan or Protocol |
| CT | Computed Tomography |
| CTI | Cavo Tricuspid Isthmus |
| DMP | Data Management Plan |
| DVT | Deep Vein Thrombosis |
| EC | Ethics Committee |
| ECG | Electrocardiogram |
| eCRF | electronic Case Report Form |
| EDC | Electronic Data Capture |
| FTI | Force Time Integral |
| ICD | Implantable Cardiac Defibrillator |
| ICF | Informed Consent Form |
| IFU | Instructions for Use |
| IRB | Institutional Review Board |
| LSI | Lesion Index |
| MI | Myocardial Infarction |
| MRI | Magnetic Resonance Imaging |
| NYHA | New York Heart Association |
| PAF | Paroxysmal Atrial Fibrillation |
| PCI | Percutaneous Coronary Intervention |
| POD | Post-Operative Day |
| PsAF | Persistent Atrial Fibrillation |
| PV | Pulmonary Vein |
| PVI | Pulmonary Vein Isolation |
| RF | Radiofrequency |
| SAE | Serious Adverse Event |

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## APPENDIX II: DEFINITIONS

| Term | Definition |
|---|---|
| Documentation of Paroxysmal AF for Inclusion | AF lasting up to 7 days that is documented by (1) physician's note within 12 months of consent indicating recurrent self-terminating AF AND (2) one electrocardiographically documented AF episode |
| Documentation of Persistent AF for Inclusion | AF sustained beyond 7 days and less than 1-year that is documented by (1) a physician's note within 12 months of consent 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 |
| Early Persistent AF | Early persistent AF is defined as AF that is sustained beyond 7 days but is less than 3 months in duration. |
| Non-Early Persistent AF | Persistent AF sustained beyond 3 months but is less than 12 months in duration. |

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## APPENDIX III: SITE CONTACT INFORMATION

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

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## APPENDIX IV: LITERATURE REVIEW

The following literature was reviewed for the development of this CIP and summarizes the topic of low-voltage zones in the left atria, and their association with one-year success.

| Clinical Investigation | Objective | Study Arms | Patient population | Endpoints | Results |
|---|---|---|---|---|---|
| Lin, et al[19]<br>High-resolution mapping of pulmonary vein potentials improved the successful pulmonary vein isolation using small electrodes and inter-electrode spacing catheter | Determine if smaller electrodes with a closer inter-electrode spacing may improve the mapping resolution and outcome | Substrate mapping of the left atrium and residual pulmonary vein (PV) potentials during sinus rhythm was sequentially performed using a Navistar Thermocool (3.5-mm) and PentaRay (1-mm) in 33 patients (Group 1) that underwent repeat atrial fibrillation (AF) procedures. PV gap identification and electrophysiological characteristics were compared. Arrhythmia freedomwas compared with a propensity matched (1:2) control group (66 patients, Group | Paroxysmal and Persistent AF | Arrhythmia freedom at one year | In the Group 1 patients, the total area of residual PV potentials measured using the 1-mm catheter was larger than that measured by the 3.5-mm catheter. Overall 1.97 ± 0.59 (1–3) and 1.49 ± 0.62 (1–3) PVs were identified by the 1-mm electrode and 3.5 mm catheters, respectively (P = 0.02). The gaps not identified by the 3.5 mm catheter had a smaller width and lower voltage. Radiofrequency catheter ablation in the areas with residual PV potentials identified by the 1-mm catheter resulted in complete electrical isolation of the PVs. Arrhythmia freedom at one year of follow-up was achieved |

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| Clinical Investigation | Objective | Study Arms | Patient population | Endpoints | Results |
|---|---|---|---|---|---|
| | | 2) undergoing repeat AF procedures guided by wide inter-electrode spacing catheter. | | | in 26 of 33 (78.8%) patients in Group 1, which was significantly higher than the matched control group (33/66 [50%], P < 0.05). |
| Yagishita, et al[20] Identification and electrophysiological characterization of early left atrial structural remodeling as a predictor for atrial fibrillation recurrence after pulmonary vein isolation | Determine optimal bipolar voltage cutoff for identifying mildly affected low-voltage area | PVI only ablation Control without AF and structural heart disease | Patients with PAF, PsAF, or LSAF undergoing a PVI-only ablation | Recurrence of AF | During the median 2.4 years, patients with mild low-voltage area (<1.1mV) had higher recurrence rates (p<0.001) and presence of mild low-voltage area was an independent predictor for recurrence in multivariate analysis (hazard ratio 3.944) |
| Yagishita, et al[21] Long-Term Outcome of Left Atrial Voltage-Guided Substrate Ablation During Atrial Fibrillation: A Novel Adjunctive Ablation Strategy | Determine long-term outcomes after low-voltage area (LVA) ablation with PVI for AF | Presence of LVA No LVA (non-LVA group) Both groups had PVI. Only LVA group had additional substrate modification. | Patients with PAF, PsAF, or LSAF | Recurrence of AF | After the index procedure, 72% of total population was free of AF after 12M. There was no difference in the recurrence (log-rank P-0.746), and complications (0% vs 7%, P=0.125) between the groups. Neither LVA nor Non-LVA was an independent predictor for the recurrence in a multivariate analysis. |

# Clinical Investigation Plan

| Clinical Investigation | Objective | Study Arms | Patient population | Endpoints | Results |
|---|---|---|---|---|---|
| Yagishita, et al[22]<br>Correlation of Left Atrial Voltage Distribution Between Sinus Rhythm and Atrial Fibrillation: Identifying Structural Remodeling by 3-D Electroanatomic Mapping Irrespective of the Rhythm | Compare point by point electro anatomical voltage mapping (EAVM) obtained during AF and SR in the same patient presenting for AF ablation | Single arm consecutive patients compared to 6 controls<br><br>The CARTO3-RMT and Stereotaxis systems were used for EAVM during AF and SR. The geometry fill threshold was set at 15 for a uniform, high-resolution EAVM. | 27 consecutive patients presenting for RF ablation for symptomatic AAD refractory PAF, PsAF, or LSAF.<br><br>Excluded re-ablation | LA and PV Antra voltage compared in both SR and AF | There was a significant linear bipolar voltage correlation between SR and AF(r = 0.707, P < 0.001, Y = 1.515X + 0.786).<br>LA bipolar voltage in PAF patients was higher than non-PAF in SR (2.24 ± 1.51 vs. 1.56 ± 1.53 mV) and in AF (0.81 ± 0.60 vs. 0.58 ± 0.62 mV, both for P < 0.001).<br>The pulmonary vein antra voltage was significantly lower than other LA regions in PAF (1.28 ± 0.79 vs. 2.54 ± 1.50 mV, P < 0.001) and Non-PAF patients (1.13 ± 1.04 vs. 1.86 ± 1.72 mV, P < 0.001), while no voltage differences was found in the control group (P = 0.998). |
| Kircher, et al[23]<br>Individually tailored vs. standardized substrate modification during radiofrequency catheter | Compare efficacy and safety of PVI plus voltage-guided ablation vs. PVI with or | Control: PVI with linear ablation (persistent) or without linear ablation (paroxysmal) | 124 persistent or paroxysmal AF<br>No previous ablation allowed | Freedom from arrhythmia (>30sec) via 7-day holter at 12M | After a mean follow-up of 12 ± 3 months, significantly more patients in the LVA ablation group were free from atrial |

# Clinical Investigation Plan

| Clinical Investigation | Objective | Study Arms | Patient population | Endpoints | Results |
|---|---|---|---|---|---|
| ablation for atrial fibrillation: a randomized study | without linear ablation depending on the type of AF. | Treatment: PVI plus ablation of low-voltage areas | | | arrhythmia recurrence >30 s off antiarrhythmic drugs (AADs) after a single procedure (primary endpoint) compared with control group patients [40/59 (68%) vs. 25/59 (42%), log-rank P = 0.003]. Arrhythmia-free survival on or off AADs was found in 33/59 control group patients (56%) and in 41/59 LVA ablation group patients (70%) (adjusted log-rank P = 0.10). During the 7 day Holter monitoring period at 12 months, significantly more patients in the LVA ablation group were free from arrhythmia recurrence on or off AADs [45/50 (90%) vs. 33/46 (72%), P = 0.04]. |
| Jadidi, et al[24]<br>Ablation of Persistent Atrial Fibrillation Targeting Low-Voltage Areas With Selective | Determine if PVI plus ablation of selective atrial low-voltage sites may be | Group 1: PVI plus ablation of low-voltage areas<br>Group 2: Matched control of 66 | 85 consecutive persistent AF patients | Single procedure arrhythmia freedom | Single-procedural freedom at 13 months median follow-up was 59/85 (69%) in group 1 compared to 31/66 |

# Clinical Investigation Plan

| Clinical Investigation | Objective | Study Arms | Patient population | Endpoints | Results |
|---|---|---|---|---|---|
| Activation Characteristics. | more successful than PVI only | patients with PVI only | | | (47%) in group 2 (p<0.001) |
| Schreiber, et al[25]<br>Catheter ablation of atrial fibrillation with box isolation of fibrotic areas: Lessons on fibrosis distribution and extent, clinical characteristics, and their impact on long-term outcome | Report outcomes using box isolation of fibrotic areas (BIFA) in patients with fibrotic atrial cardiomyopathy (FACM) | Retrospective analysis compared PVI + BIFA (n=92) to non-fibrosis reference group with PVI only (n=49) | 92 de novo persistent and paroxysmal patients with PVI + BIFA based on detection of significant fibrotic areas defined as <0.5mV | Arrhythmia free | For BIFA ablation, single and multiple procedure arrhythmia-free survival was 68.8% and 82.8% with 1.2 procedures/patient and a follow-up time of 16.3 ± 8.2 months after the index procedure. FACMI+II pts showed a significantly better outcome compared to FACM III+IV pts (single procedure: 81.0 vs. 40.9%, P < 0.001, multiple procedure 92.8 vs. 61.4%, P < 0.001). Non-fibrosis reference group had single/multiple procedure success rates of 84.4% and 93.7% respectively with 1.1 procedures. |
| Yamaguci, et al.[26]<br>Long-term results of pulmonary vein antrum isolation in patients with atrial fibrillation: an | To examine the impact of left atrial (LA) low-voltage zones (LVZs) on atrial fibrillation (AF) | Single arm with PVAI only | 76 paroxysmal and persistent AF<br>Low voltage zones were identified in 32% of cases | AF recurrence through 24M | During 24+7 months of follow-up, 15 patients (63%) with LVZs and 10 (19%) without had AF recurrences off antiarrhythmic drugs |

# Clinical Investigation Plan

| Clinical Investigation | Objective | Study Arms | Patient population | Endpoints | Results |
|---|---|---|---|---|---|
| analysis in regards to substrates and pulmonary vein reconnections. | recurrence after pulmonary vein antrum isolation (PVAI) without LA substrate modification. | | | | (log-rank P , 0.001). A multivariate logistic regression analysis revealed that LVZ areas [odds ratio (OR): 1.12 per 1 cm2, 95% confidence interval (CI): 1.04–1.23, P < 0.001] and ATP-induced reconnection (OR: 2.08, 95% CI: 1.01–4.91, P < 0.046) were significant predictors of recurrence.<br>In those with LVZs, the LVZ area was strongly correlated with the LA body volume (r = 0.81, P < 0.001) and a unique predictor of recurrence (OR: 1.17 per 1 $cm^2$, 95% CI: 1.01–1.55, P = 0.031), while in those without an LVZ,ATP induced PV reconnection was a unique predictor (OR: 3.24, 95% CI: 1.15–15.39, P = 0.025). |

# Clinical Investigation Plan

*Table 3 Summary of Relevant Review Articles*

| Article | Subject | Summary |
|---|---|---|
| Calkins, et al. [18]<br>2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation: Executive summary. Calkins et al. *Heart Rhythm*. 2017; 14: e275-e444. | The main objective of the document is to improve patients care by providing a foundation of knowledge for those involved with catheter ablation of atrial fibrillation. A second major objective is to provide recommendations for designing clinical trials of AF ablation. | The purpose of the 2017 Consensus Statement is to provide a state-of-the-art review of the field of catheter and surgical ablation of AF and to report the findings of a writing group convened by five international societies. Reflecting both the worldwide importance of AF, as well as the worldwide performance of AF ablation, this document is the result of a partnership between the Heart Rhythm Society (HRS), European Heart Rhythm Association (EHRA), European Cardiac Arrhythmia Society (ECAS), the Asia Pacific Heart Rhythm Society (APHRS), and the Latin American Society of Cardiac Stimulation and Electrophysiology (SOLAECE). The consensus statement provides guidance on clinical definitions of AF, a discussion of electrophysiological features of AF, and the role of catheter ablation to treat PsAF along with safety and effectiveness reporting guidelines. |
| Rolf et al.[27]<br>Electro Anatomical Mapping of Atrial Fibrillation: Review of the Current Techniques and Advances. *J A Fib.* 2014; 7. | The objective of this review was to outline contemporary and upcoming electro anatomical key technologies focusing on new mapping tools and strategies in the context of AF catheter ablation. | This review discussed how electro anatomical mapping technologies have facilitated mapping processes and enabled complex AF ablation strategies Electro anatomical mapping technologies and the benefits of use in AF ablation are discussed. There is focused review of specific mapping strategies including activation mapping, entrainment mapping, mapping of complex fractionated electrograms, multipolar mapping, mapping of high dominant frequencies, focal and rotor mapping and modulation, voltage mapping and substrate imaging, and ripple mapping. |
| Saini et al.[28]<br>Scar homogenization in Atrial Fibrillation Ablation: Evolution and Practice. *J A Fib.* 2017; 10. | The objective of this review was to discuss the evidence behind the use of scar homogenization in AF | This review discussed the association between fibrosis and atrial fibrillation along with methods for defining atrial scar. A thorough review of clinical trials that have targeted atrial substrate for AF ablation is included that identifies evidence in support of, and against, a substrate guided approach to AF ablation. The review concludes with highlighting |

# Clinical Investigation Plan

| Article | Subject | Summary |
|---|---|---|
| | ablation, its evolution and scope in delivering optimal outcomes. | the pitfalls of a substrate guided approach to AF ablation including variation in scar maps, discussion of an appropriate endpoint for substrate modification, and if scar is truly static substrate that encompasses all abnormal atrial substrate. |
| Nery, et al[29]<br>Characterization of Low-Voltage Areas in Patients With Atrial Fibrillation: Insights From High-Density Intracardiac Mapping | Characterization of low-voltage left atrial substrate in AF | This review determined the optimal catheter ablation strategy for persistent atrial fibrillation remains unknown. Current data highlight the need for a better understanding of the substrate and mechanisms of arrhythmia maintenance in the persistent AF population. Catheter ablation based on low-voltage (scar) substrate has recently emerged as a promising strategy for ablation of atrial fibrillation. Further research is needed to assess the role of voltage-based ablation for persistent AF. |

# Clinical Investigation Plan

## APPENDIX V: INFORMED CONSENT FORM

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

# Clinical Investigation Plan

## APPENDIX VI: MONITORING PLAN

A copy of the Monitoring Plan can be obtained upon request from the Sponsor for the clinical investigation.

# Clinical Investigation Plan

## APPENDIX VII: CASE REPORT FORMS

A copy of sample Case Report Forms can be obtained upon request from the Sponsor for the clinical investigation.

# Clinical Investigation Plan

## APPENDIX VIII: GRID ELECTRODE CONFIGURATIONS

**HD Wave Electrode Configuration**
For the purposes of this clinical study, HD Wave electrode configuration will be considered any configuration that only utilizes mapping data collected at electrodes with orthogonal bi-poles. Orthogonal bi-poles are defined as a pair of perpendicular bi-poles originating from a single electrode with one bi-pole configured across two separate splines and one bi-pole configured along the spline. Automap settings will be set to select the 'best duplicate' at each electrode with orthogonal bi-poles.

An example of GRID with HD Wave configuration is depicted in **Figure 3**. This HD Wave configuration utilizes bi-poles both along each spline of the catheter (A, B, C, and D) and across GRID catheter splines (A-B, B-C, and C-D) as depicted by the dark arrows. Bipolar electrogram voltages along the splines are configured as in the along-the-spline configuration described below; using electrode pairs 1-2, 2-3, and 3-4 on each spline. Bipolar electrogram voltages across the splines are recorded using electrode pairs of the same number/position on adjacent splines (A1-B1, B1-C1, C1-D1, A2-B2, B2-C2, C3-D3, A3-B3, B3-C3, C3-D3). Automap settings will be set to select the 'best duplicate' at each electrode shown in yellow.

An alternate example of GRID with HD Wave configuration is depicted in **Figure 4**. Bipolar electrograms are configured as depicted by the dark arrows. Bipolar electrogram voltages along the splines are configured using the following electrode pairs and directionality: A1-A2, A2-A3, A4-A3, B1-B2, B2-B3, B3-B4, C2-C1, C3-C2, C4-C3, D1-D2, D3-D2, D4-D3. Bipolar electrogram voltages across the splines are configured using the following electrode pairs and directionality: A1-B1, B1-C1, D1-C1, A2-B2, B2-C2, C2-D2, B3-A3, C3-B3, D3-C3, A4-B4, C4-B4, D4-C4. Automap settings will be set to select the 'best duplicate' at each electrode shown in yellow.

# Clinical Investigation Plan

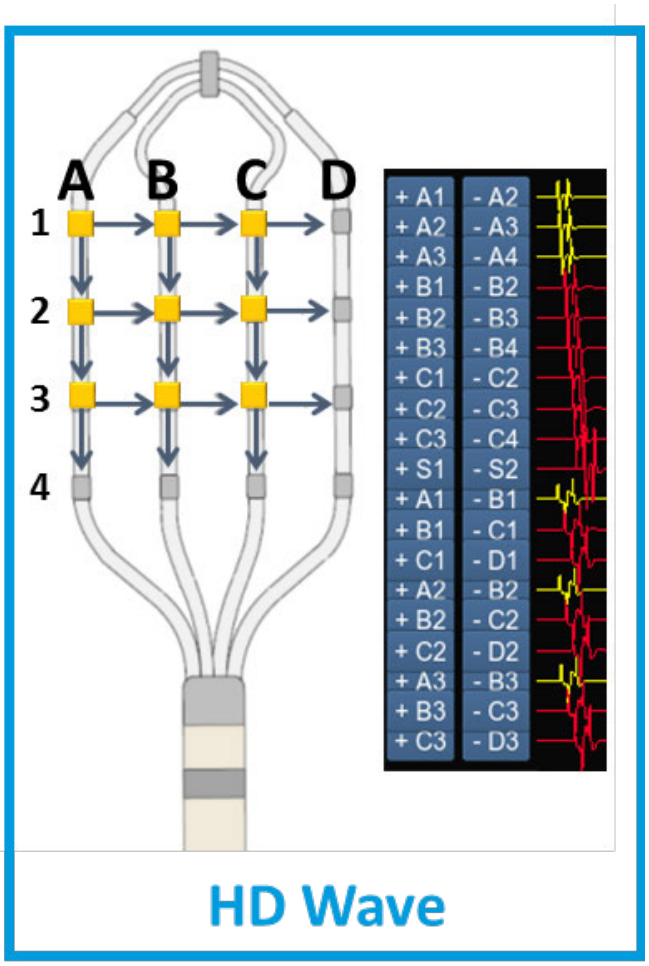


**Figure 3. Example of GRID HD Wave Electrode Configuration**

# Clinical Investigation Plan

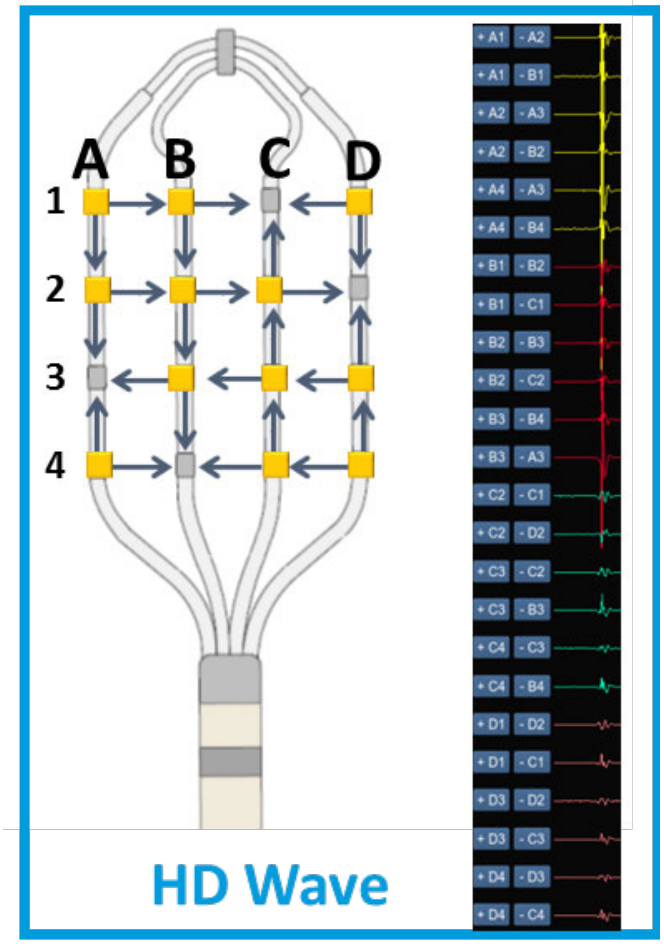


**Figure 4. Example of alternative GRID HD Wave electrode configuration**

**Along-the-Spline Configuration**
This configuration utilizes bi-poles, or electrogram pairs, along each of the GRID catheter splines (labeled A, B, C, and D). On each spline, electrodes are numbered 1 through 4, with 1 being the most distal electrode. Bipolar electrogram voltages are recorded using electrode pairs 1-2, 2-3, and 3-4. An additional bi-pole is recorded using the shaft electrodes (S1-S2).

# Clinical Investigation Plan

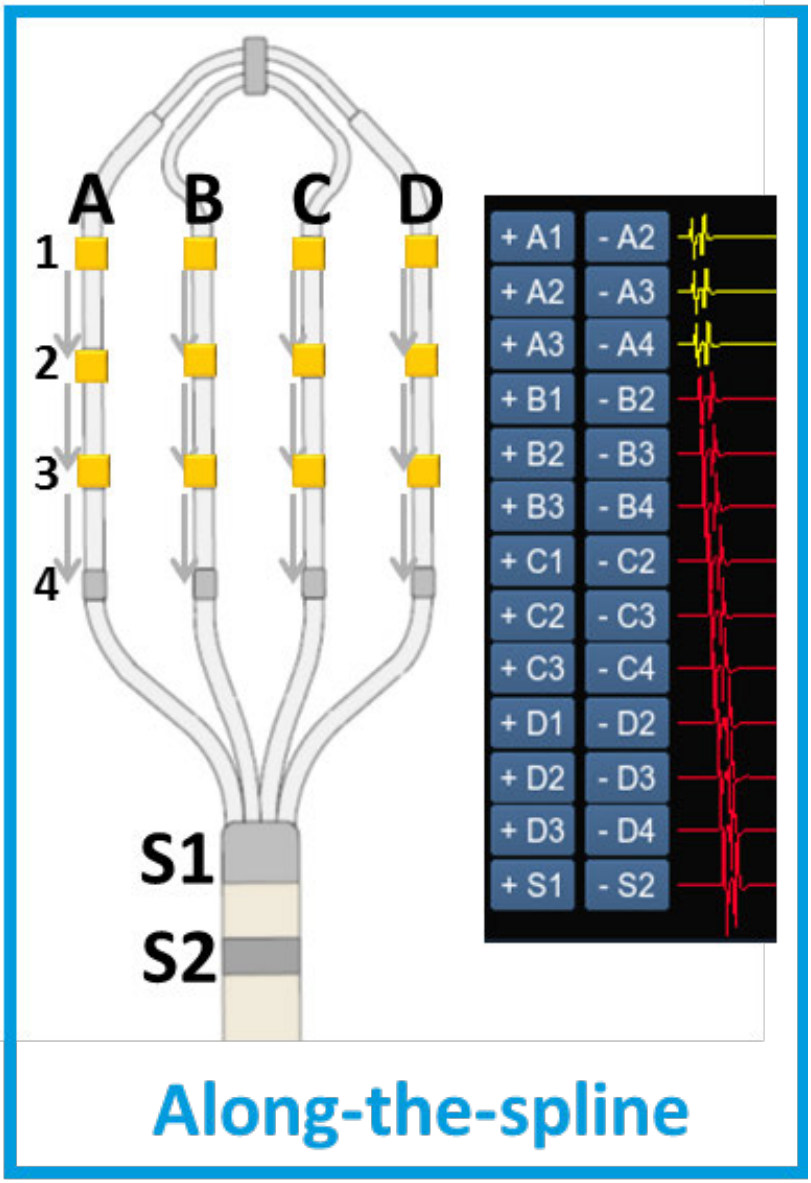


**Figure 5. Along-the-spline GRID Electrode Configuration**

**Other Configurations**

For the purposes of this clinical study, any electrode configuration that does not meet the definition of HD Wave or along-the-spline configuration (i.e. use of all bipoles employing a combination of electrodes with orthogonal bipoles and electrodes with only along the spline configurations) will be classified as 'other'.

## APPENDIX IX: REVISION HISTORY

This CIP may be amended as appropriate by the Sponsor. Rationale will be included with each amended version in the revision history table below. The version and date of amendments will be documented.

EC and relevant Regulatory Authorities, if applicable, will be notified of amendments to the CIP.

# Clinical Investigation Plan

## APPENDIX X: CIP SUMMARY

| | |
|---|---|
| **Clinical Investigation Name and Number** | WAVE-MAP AF |
| **Title** | High-Density Wave Mapping in Subjects with Atrial Fibrillation as a Predictor of Recurrence After a Single Ablation Procedure Using a PVI-Only Strategy |
| **Purpose/ Objective(s)** | The primary objective of this study is to characterize low-voltage substrate, as identified via HD Wave mapping in sinus rhythm and identify associations with 12-month recurrence rates after a single pulmonary vein isolation with a contact force RF ablation catheter.<br>Other objectives of this study include:<br>• Analyze additional maps and data collected with GRID and associations with 12-month recurrence rates, such as:<br>  ○ Voltage maps using different configurations recreated post procedure<br>  ○ Voltage maps using different thresholds for low-voltage<br>  ○ Fractionation maps<br>• Collect mapping data in AF to support future research and development.<br>• Support future study designs to identify optimal treatment approaches for individual patients. |
| **Number of Subjects Required for Inclusion in Clinical Investigation** | [redacted] |
| **Clinical Investigation Design** | This is a single-arm, multicenter, post-market study. There will be no randomization. The purpose of the study is to determine correlations between low-voltage substrate, as identified via HD Wave mapping, and recurrence of atrial fibrillation after a single pulmonary vein isolation with a contact force RF ablation catheter. |
| **Primary Endpoint** | The primary outcome is one-year success, defined as freedom from AF/AFL/AT after removal from antiarrhythmic drug therapy as assessed from the end of the 3-month blanking period to 12 months following a single ablation procedure. |
| **Subject Follow-up** | Subjects will have follow-up visits at 3, 6, and 12 months post ablation procedure. The 6-month visit can be conducted via telephone. |
| **Inclusion Criteria** | 1. Documented atrial fibrillation with planned endocardial ablation procedure<br>2. Age 18 years or older |

[redacted]

# Clinical Investigation Plan

| | |
|---|---|
| | 3. Able and willing to provide written informed consent prior to any clinical investigation related procedure<br>4. Able and willing to complete all required study procedures through 12 months |
| **Exclusion Criteria** | 1. Long-standing persistent atrial fibrillation defined as continuous AF greater than 12 months in duration<br>2. Previous ablation or surgery in the left atria<br>3. Implanted left atrial appendage occluder<br>4. Implanted mitral or tricuspid valve replacement<br>5. Implanted cardiac defibrillator (ICD)<br>6. Participation in another clinical investigation that may confound the results of this study<br>7. Pregnant or nursing<br>8. Presence of other anatomic or comorbid conditions, or other medical, social, or psychological conditions that, in the investigator's opinion, could limit the subject's ability to participate in the clinical investigation or to comply with follow-up requirements, or impact the scientific soundness of the clinical investigation results.<br>9. Life expectancy less than 12 months |

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