Abbott	Clinical Investigation Plan Cover Page

NCT Number: NCT03260244
EnSite Precision Observational Study
A Clinical Evaluation using EnSite Precision Cardiac Mapping System (software version 2.0.1 or higher) in a Real-World Environment
Study Document No: SJM-CIP-10159
Version A
Date: 26-Jun-2017

Sponsor

Abbott
5050 Nathan Lane North
Plymouth, MN 55442
US

[redacted]

EnSite Precision Observational Study
A Clinical Evaluation using EnSite Precision Cardiac Mapping System (software version 2.0.1 or higher) in a Real-World Environment
CRD_871
Study Document No: SJM-CIP-10159
Version A
Date: 26-Jun-17
Clinical Investigation Plan (CIP)

Sponsor

St. Jude Medical / Abbott
5050 Nathan Lane North
Plymouth, MN 55442
US

[redacted]

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 study.

Principal Investigator

Printed name:
Signature:
Date:

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[redacted]

1 Synopsis

1.1 Objective(s)

The objectives of this study are as follows:

- To quantify and characterize the usage of the EnSite Precision™ Cardiac Mapping System (software version 2.0.1 or higher) modules
- To characterize the mapping duration and point usage when using multipolar catheters with the EnSite™ AutoMap module
- To characterize the relationship of the system usage to patient outcomes in a variety of electrophysiological (EP) procedures and clinical settings.

1.2 Devices Used

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

The following devices will be used in this clinical study:

Table 1: Identification of Clinical Study Devices

Device name	Model/Type	Manufacturer	Region/ Country	Investigational or Market Released
EnSite Precision™ Software	V2.0.1 or higher	SJM	Worldwide	Market Released
EnSite Precision™ Module, Sensor Enabled	H702473	SJM	Worldwide	Market Released
EnSite Precision™ Surface Electrode Kit	EN0020-P	SJM	Worldwide	Market Released
EnSite™ AutoMap Module	H702498	SJM	Worldwide	Market Released
AutoMark Module	V1.0	SJM	Worldwide	Market Released

Additional commercially available tools may be used in this clinical study, per physician's discretion and per their IFUs.

1.3 Indications for Use

The EnSite Precision™ Cardiac Mapping System is a catheter navigation and mapping system capable of displaying the three-dimensional (3D) position of conventional and sensor enabled electrophysiology catheters, as well as displaying cardiac electrical activity as waveform traces and as dynamic 3-D isopotential maps of the cardiac chamber. The contoured surfaces of these three-dimensional maps are based on the anatomy of the patient's own cardiac chamber.

The EnSite Precision™ Cardiac Mapping System (including AutoMap) is a suggested diagnostic tool in patients for whom electrophysiology studies have been indicated.

The EnSite Precision™ system interfaces to either MediGuide™ Guided Medical Positioning System or the EnSite Precision™ Module to combine and display magnetic processed patient positioning and orientation mapping information.

When used with compatible hardware, the AutoMark module is intended to automatically catalog and display various parameters associated with radiofrequency (RF) information on the 3D model in real-time.

1.4 Design

This is a prospective, multicenter, post-market, observational study designed to quantify and characterize the usage of the EnSite Precision™ Cardiac Mapping System in a real-world environment.

[redacted]

1.5 Endpoints

The endpoints for evaluating the objectives are as following:

- Summary of subjects that used EnSite™ AutoMap and AutoMark module
- Summary of EnSite™ Automap and AutoMark module software settings used per arrhythmia
- Assessment of EnSite™ AutoMap Module including:
  - Mapping time associated with (re-)mapping one or multiple arrhythmias per catheter type used in a single subject
  - Used Points per Minute per catheter type stratified by arrhythmia type and mapping type
- Rate of acute success based on pre-defined procedural endpoints
- Freedom from arrhythmia recurrence through 12 months
- Number of repeat ablations up to 12 months
- Summary of NavX patch placement locations used
- Number of gaps in lesions identified requiring touch-up ablation
- Changes in EQ-5D quality of life score at 6 and 12 months
- Number of unscheduled visits and hospitalizations due to arrhythmias
- Overall procedure time
- Overall system stability

1.6 Study Population

The intended population for this study is patients over the age of 18 years who are eligible for a cardiac EP mapping and RF ablation procedure using the EnSite Precision™ Cardiac Mapping.

1.7 Inclusion/Exclusion Criteria

1.7.1 Inclusion Criteria

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

- Indicated for a cardiac EP mapping and RF ablation procedure using a 3D mapping system per IFU
- Over 18 years of age
- Able to provide informed consent for study participation and willing and able to comply with the protocol described evaluations and follow up schedule

1.7.2 Exclusion Criteria

Subjects who meet any of the following exclusion criteria must be excluded from the study:

- Patients who are only presenting with:
  - Atrioventricular Nodal Reentrant Tachycardia (AVNRT)

[redacted]

  - Atrioventricular Reentrant Tachycardia (AVRT)
- Planned cryoablation procedure
- Implanted with a neurostimulator
- Contraindication to anticoagulation
- Known presence of cardiac thrombus
- Recent (<3 months) myocardial infarction or unstable angina or coronary artery by-pass
- Currently enrolled in a clinical study/investigation evaluating another device or drug that would confound the results of this study
- Pregnant or nursing
- Individuals whose willingness to volunteer in a study, in the judgement of investigator or public authorities, could be unduly influenced by lack of or loss of the autonomy due to immaturity, or mental disability, or adverse personal circumstances, or hierarchical influence

1.8 Enrollment

A subject is considered enrolled in the clinical study from the moment the subject has provided a written Informed Consent.

1.9 Study Assessments

Refer to Section 6, Procedures for the Clinical Study Procedures Table

2 Introduction

This document is a clinical investigation plan (CIP) for the EnSite Precision Observational Study. This clinical study is intended to quantify and characterize the usage of the EnSite Precision™ Cardiac Mapping System (Software version 2.0.1 or higher) in a real-world environment. This study will be conducted in patients who are indicated for a cardiac EP mapping and RF ablation procedure using a 3D system.

This document describes the rationale and procedures used for a prospective, multicenter, observational study. The clinical study is sponsored by St. Jude Medical / Abbott.

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

3 Background and Justification for Clinical Study

Atrial fibrillation (AF) is a common cardiac rhythm disturbance and increases in prevalence with advancing age. Approximately 1% of patients with AF are <60 years of age, whereas up to 12% of patients are 75 to 84 years of age. More than one third of patients with AF are >80 years of age. In the United States, the percentage of Medicare Fee-for-Service beneficiaries with AF in 2010 was reported as 2% for those <65 years of age and 9% for those ≥ 65 years of age.

The mechanisms causing and sustaining AF are multifactorial, and can be complex and difficult for clinicians to manage (January, et al., 2014). Ablation is increasingly used for AF and is superior to pharmacological therapy for patients with early (paroxysmal) to advanced (persistent) AF (Wright & Narayan, 2015).

Sustained ventricular tachycardia (VT) and ventricular fibrillation (VF) are typically a manifestation of significant structural heart disease and often associated with a high risk of sudden cardiac death. Implantable cardioverter defibrillators (ICDs) remain the mainstay of therapy for prevention of sudden cardiac death associated with these arrhythmias. However, ICDs treat the arrhythmia after it occurs and does not prevent the arrhythmia. Recurrent ventricular arrhythmias can lead to multiple ICD shocks that are painful, decrease quality of life and cause post-traumatic stress disorder. Spontaneous VT and ICD shocks are also associated with an increased risk of death and progressive heart failure. Antiarrhythmic drugs, notably amiodarone, reduce arrhythmias for some patients, but have limited efficacy for long-term management, particularly for scar-related re-entrant arrhythmias. In addition, antiarrhythmic drugs have the potential for significant adverse effects that includes negative inotropy, pro-arrhythmia and non-cardiac organ toxicities that limit their long-term use. Catheter ablation offers an alternative therapy for preventing arrhythmias, and can be life-saving when frequent episodes (VT storm) threaten survival. (Nof, Stevenson, & John, 2013) (Pedersen, et al., 2014)

The incidence and treatment complexity of these arrhythmias represent an opportunity for the EnSite™ Velocity Cardiac Mapping System due to the increased case complexity and duration, as mapping system precision is a key requirement to maximize the success of these challenging procedures. As a result, the EnSite Precision™ System was developed to introduce features such as Delayed Enhancement Magnetic Resonance Imaging (DE-MRI) image integration, lesion marking automaticity, automatic mapping, and workflow flexibility to aid in the success of complex ablation procedures. This clinical study is intended to understand how the EnSite Precision™ System is utilized in the treatment of complex ablation procedures.

4 Devices Used

4.1 Identification and Description of the Clinical Study Devices

4.1.1 Identification

All of the devices used in this study, must have received proper regulatory clearance and must be market released.

The following devices will be used in this clinical study according to their IFU.

Table 2: Identification of Clinical Study Devices

Device name	Model/Type	Manufacturer	Region/ Country	Investigational or Market Released
EnSite Precision™ Software	V2.0.1 or higher	SJM	Worldwide	Market Released
EnSite Precision™ Module, Sensor Enabled	H702473	SJM	Worldwide	Market Released
EnSite Precision™ Surface Electrode Kit	EN0020-P	SJM	Worldwide	Market Released
EnSite™ AutoMap Module	H702498	SJM	Worldwide	Market Released
AutoMark Module	V1.0	SJM	Worldwide	Market Released

Additional commercially available tools may be used in this clinical study, per physician's discretion and per their IFUs.

4.1.2 Device Description and Intended Purpose

The EnSite Precision™ Cardiac Mapping System is a catheter navigation and mapping system capable of displaying the three-dimensional (3D) position of conventional and sensor enabled electrophysiology catheters, as well as displaying cardiac electrical activity as waveform traces and as dynamic 3-D isopotential maps of the cardiac chamber. The contoured surfaces of these three-dimensional maps are based on the anatomy of the patient's own cardiac chamber.

The EnSite Precision™ Cardiac Mapping System (including AutoMap) is a suggested diagnostic tool in patients for who electrophysiology studies have been indicated.

The EnSite Precision™ system interfaces with either MediGuide™ Guided Medical Positioning System or the EnSite Precision™ Module to combine and display magnetic processed patient positioning and orientation mapping information.

When used with compatible hardware, the AutoMark module is intended to automatically catalog and display various parameters associated with RF information on the 3D model in real-time.

4.1.3 Device Handling and Storage

Only commercially available shelf-stock will be used. All devices will be handled and stored per standard practice of the hospital.

5 Clinical Study Design

5.1 Clinical Study Design

This is a prospective, multicenter, post-market, observational study designed to quantify and characterize the usage of the EnSite Precision™ Cardiac Mapping System in a real-world environment.

[redacted]

5.2 Objectives

The objectives of this study are as follows:

- To quantify and characterize the usage of the EnSite Precision™ Cardiac Mapping System (software version 2.0.1 or higher) modules
- To characterize the mapping duration and point usage when using multipolar catheters with the EnSite™ AutoMap module
- To characterize the relationship of the system usage to patient outcomes in a variety of electrophysiological (EP) procedures and clinical settings.

5.3 Endpoints

The endpoints for evaluating the objectives are as following:

- Summary of subjects that used EnSite™ AutoMap and AutoMark module
- Summary of EnSite™ Automap and AutoMark module software settings used per arrhythmia
- Assessment of EnSite™ AutoMap Module including:
    - Mapping time associated with (re-)mapping one or multiple arrhythmias per catheter type used in a single subject
    - Used Points per Minute per catheter type stratified by arrhythmia type and mapping type
- Rate of acute success based on pre-defined procedural endpoints
- Freedom from arrhythmia recurrence through 12 months
- Number of repeat ablations up to 12 months
- Summary of NavX patch placement locations used
- Number of gaps in lesions identified requiring touch-up ablation
- Changes in EQ-5D quality of life score at 6 and 12 months
- Number of unscheduled visits and hospitalizations due to arrhythmias
- Overall procedure time
- Overall system stability

5.4 Study Population

The intended population for this clinical study is patients over the age of 18 years who are eligible for a cardiac EP mapping and RF ablation procedure using the EnSite Precision™ Cardiac Mapping System.

[redacted]

5.4.1 Inclusion Criteria

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

- Indicated for a cardiac EP mapping and RF ablation procedure using a 3D mapping system per IFU
- Over 18 years of age
- Able to provide informed consent for study participation and willing and able to comply with the protocol described evaluations and follow up schedule

5.4.2 Exclusion Criteria

Subjects who meet any of the following exclusion criteria must be excluded from the clinical study:

- Patients who are only presenting with:
  - Atrioventricular Nodal Reentrant Tachycardia (AVNRT)
  - Atrioventricular Reentrant Tachycardia (AVRT)
- Planned cryoablation procedure
- Implanted with a neurostimulator
- Contraindication to anticoagulation
- Known presence of cardiac thrombus
- Recent (<3 months) myocardial infarction or unstable angina or coronary artery by-pass
- Currently enrolled in a clinical study/investigation evaluating another device or drug that would confound the results of this study
- Pregnant or nursing
- Individuals whose willingness to volunteer in a study, in the judgement of investigator or public authorities, could be unduly influenced by lack of or loss of the autonomy due to immaturity, or mental disability, or adverse personal circumstances, or hierarchical influence

6 Procedures

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

Subjects will undergo a cardiac mapping and RF ablation procedure using the EnSite Precision™ Cardiac Mapping System per the IFUs of all devices used during the procedure. After the post-procedure hospital discharge, the subject will have 3 in-clinic visits: at 1 month, 6 months and 12 months post-procedure. Upon completion of the 12-month follow-up visit, the subject will be considered to have completed the follow-up requirements of this clinical study. 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.

6.1 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 subject's legal rights. The subject shall be provided with the informed consent form (refer to Appendix F) 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.

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 Case Report Form (CRF).

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 study, 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.

6.2 Point of Enrollment

A subject is considered enrolled in the clinical study from the moment the subject has provided a written Informed Consent.

6.3 Scheduled Procedures

The Principal Investigator is responsible for ensuring all clinical study data is collected as required per CIP scheduled procedures.

6.3.1 Baseline Visit (within 10 days from Informed Consent)

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

- Demographics - include subject's age and gender
- Physical information - include subject's height, weight (measurements taken during visit)
- Cardiac History (most recent value prior to baseline visit)
- Arrhythmia History
- 12 Lead ECG information (most recent information prior to baseline visit)
- Antiarrhythmic medication - indicate both the medication that failed and the medication (if any) the patient is currently taking
- Current anticoagulant medication
- Completion of the EQ-5D questionnaire (refer to Appendix H for additional information)

Record the required information on the Baseline form.

6.3.2 Procedure Visit (within 14 days from Baseline)

The procedure should be performed according to the IFU of the EnSite Precision™ Cardiac Mapping System, the IFUs of the AutoMark and EnSite™ AutoMap modules and any other medical devices used during the procedure.

Subjects will be prepared according to the standard ablation procedures and standard practice of the center.

The following information will be collected during the Procedure Visit:

- Mapping and ablation tools used during the procedure
- Procedural characteristics (set up and timing)
- AutoMap settings used (if applicable)
- AutoMark setting used (if applicable)
- Field Scaling used

Sponsor representatives can be involved in providing support during the procedure.

The entire case (procedure) should be recorded and stored on a study-specific USB (password-protected), provided by the Sponsor, and returned within reasonable timelines to the Sponsor.

A User Experience form should be completed once by every physician performing a procedure for this study, preferably after the first study related procedure performed by that physician.

Protocol deviations (refer to section 9.1 for details) that were observed during the procedure will also be recorded at this time.

NOTE: A separate guideline for additional information on supplementary data collection will be available. This guideline is not mandatory, however, it may assist in increasing knowledge and understanding of the treatment options for patient with arrhythmias.

6.3.3 Scheduled Follow-ups

In-clinic follow-up visits are scheduled at 1 month, 6 months and 12 months after procedure. The scheduled visit windows are calculated from the index procedure.

6.3.3.1 1-Month Visit (within 30 days from procedure)

The 1-month visit needs to be performed within 30 days post procedure, depending on the hospital's standard practice for 1st follow-up post procedure.

The following information is collected:

- Arrhythmia recurrence
  - For the purpose of this clinical study, recurrence of arrhythmia is deemed to have occurred only when the arrhythmia is documented on ECG or during a period of monitoring e.g. holter-monitoring or implantable cardiac monitor. Atrial arrhythmias 30 seconds or longer will be collected. Ventricular arrhythmias treated by an ICD, or lasting 20 seconds or longer will be collected.
- Antiarrhythmic / Anticoagulant medication
- Healthcare Utilization information when applicable
- Protocol deviation, when applicable

6.3.3.2 6- and 12-Month Visit (± 30 days)

At each visit, the following information is collected:

- Arrhythmia recurrence
  - For the purpose of this clinical study, recurrence of arrhythmia is deemed to have occurred only when the arrhythmia is documented on ECG or during a period of monitoring e.g. Holter-monitoring or implantable cardiac monitor. Atrial arrhythmias 30 seconds or longer will be collected. Ventricular arrhythmias treated by an ICD, or lasting 20 seconds or longer will be collected.
- Antiarrhythmic / Anticoagulant medication
- Completion of the EQ-5D questionnaire

- Holter monitoring* at 12-Month visit (for patients treated for AF)
- Healthcare Utilization information when applicable
- Protocol deviation, when applicable

***Holter Monitoring (AF only)**
Subjects with AF will be issued a holter monitor at the 12-month visit and instructed to obtain a 48-hour recording. A core laboratory will review each recording and report findings to the Sponsor.

NOTE: The Sponsor may request access to other patient data during the required protocol follow up visits or throughout the follow up period, which may include, but is not limited to, data from implanted device(s).

Record the required information on the appropriate CRF(s). Documentation of arrhythmia (e.g. ECG printouts, holter printouts, session records), where applicable, should be retrieved and submitted electronically through EDC to the Sponsor.

Sponsor representatives can be involved in providing support during the follow-up procedures.

6.4 Unscheduled Visits

An unscheduled visit is defined as any healthcare visit (e.g. office visit, outpatient visit, urgent care, observational visit, ER visit, hospitalization) between scheduled follow-ups, due to a cardiovascular event.

Such visits need to be documented by completing the Health Care Utilization form.

6.5 Study Flow Chart

The Study Flow Chart (fig. 1) and Table 3 below summarize subject flow and requirements of this clinical study.

Figure 1: Study Flow Chart

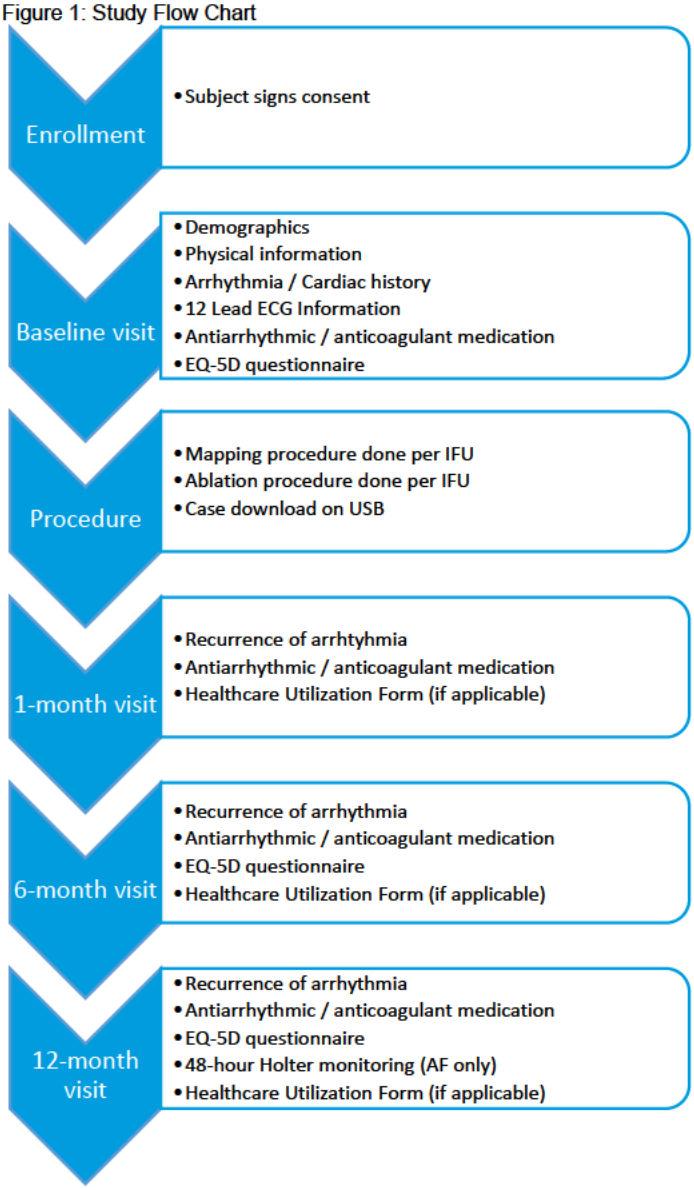


Table 3: List of all clinical study specific tests/activities and procedures

Visit / Study Activity	Enrollment	Baseline Visit (Max 10 days from Informed Consent)	Procedure Visit (Max 14 days after baseline)	1-month Visit (Within 30 days post procedure)	6-month Visit (± 30 days)	12-month Visit (± 30 days)
Eligibility check	X					
Informed Consent Process	X					
Demographics		X				
Physical information		X				
Cardiac History		X				
Arrhythmia History		X				
12 Lead ECG		X				
Antiarrhythmic / Anti-coagulant Medication		X		X	X	X
EQ-5D questionnaire		X			X	X
Mapping of cardiac structures			(X)			
RF Ablation			(X)			
User Experience			(X)[1]			
Obtain Procedure USB			X			
Arrhythmia Recurrence				(X)	(X)	(X)
48-hour Holter-monitoring (AF only)						(X)[2]
Healthcare Utilization information				(X)	(X)	(X)
Deviation	(X)	(X)	(X)	(X)	(X)	(X)
Withdrawal	(X)	(X)	(X)	(X)	(X)	(X)

(X) If applicable

[1] Only required for first procedure performed by physician

[2] Only required for patients treated for AF

6.6 Description of Activities Performed by Sponsor Representatives

Trained Sponsor personnel may perform certain activities to ensure compliance to the CIP and may provide technical expertise.

While Sponsor representatives may perform these activities, the Principal Investigator remains responsible for ensuring all clinical study data is collected as required per CIP.
Sponsor personnel will not:

- Administer the informed consent process
- Practice medicine
- Provide medical diagnosis or treatment to subjects
- Discuss a subject's condition or treatment with a subject without the approval and presence of a health care practitioner
- Independently collect study data

6.7 Subject Study Completion

Subject participation in the clinical study will conclude upon completion of the 12-Month visit and 48-hour holter monitoring (if applicable). Upon completion of subject participation in the clinical study, the subject will return to standard of care.

6.8 Subject Withdrawal

Subjects must be informed about their right to withdraw from the clinical study 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 study 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 study until completion of the clinical study.

A subject will be considered 'Lost to Follow-up' after one missed visit and a minimum of two unsuccessful phone calls from study 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.

6.9 Study Committees

6.9.1 Publication Committee (PC)

A Publication Committee shall be established to oversee study publications. Publication Committee membership may include Principal Investigators, a representative of the Sponsor and a statistician. The Publication Committee will be responsible for identifying, selecting and approving publication proposals and determining authorship according to a Publication Plan. A Publication Committee charter will define membership of the committee and outline the roles and responsibilities of the committee, as well as rules to define authorship.

7 Statistical Considerations

The following section describes the statistical methods for the observational study and justification of the design.

7.1 Endpoints

The endpoints for evaluating the objectives are as following:

- Summary of subjects that used EnSite™ AutoMap and AutoMark module
- Summary of EnSite™ Automap and AutoMark module software settings used per arrhythmia
- Assessment of EnSite™ AutoMap Module including:
    - Mapping time associated with (re-)mapping one or multiple arrhythmias per catheter type used in a single subject
    - Used Points per Minute per catheter type stratified by arrhythmia type and mapping type
- Rate of acute success based on pre-defined procedural endpoints
- Freedom from arrhythmia recurrence through 12 months
- Number of repeat ablations up to 12 months
- Summary of NavX patch placement locations used
- Number of gaps in lesions identified requiring touch-up ablation
- Changes in EQ-5D quality of life score at 6 and 12 months
- Number of unscheduled visits and hospitalizations due to arrhythmia
- Overall procedure time

- Overall system stability

7.1.1 Analysis Methodology

The endpoints will be summarized descriptively based on available data or measurements in the analysis population. No hypothesis testing will be performed.

Summary of subjects that used EnSite™ AutoMap and AutoMark module:

- Overall usage of EnSite™ AutoMap Module:
  This will be summarized by the number and proportion of subjects with a procedure that use EnSite™ AutoMap.
- Overall usage of AutoMark module:
  This will be summarized by the number and proportion of subjects with a procedure that use AutoMark.

Summary of EnSite™ Automap and AutoMark Module software settings used per arrhythmia:

- Usage of EnSite™ AutoMap Module features:
  Among the subjects with EnSite™ AutoMap module features used during the procedure, the initial settings of EnSite™ AutoMap features listed below will be summarized descriptively by each arrhythmia, as number and proportion or mean and standard deviation as appropriate.

  AutoMap Settings:
  - Score Threshold (%)
  - Cycle length tolerance (ms)
  - Speed limit (mm/s)
  - Distance threshold (mm)
  - Signal-to-Noise ratio (number)
  - Force lower limit (grams)
  - Force upper limit (grams)
  - Enhanced Noise rejection enabled? (Y/N)
  - Independent Scoring Interval enabled? (Y/N)

- Usage of AutoMark Module features:
  Among the subjects with AutoMark features used during the procedure, the AutoMark features listed below will be summarized descriptively as number and proportion or mean and standard deviation as appropriate.

  AutoMark Parameters (values and diameters of Lesion Color and Lesion Size Metrics):
  - Energy (Joules)
  - Time (Seconds)
  - Impedance Drop (Ohms)
  - Impedance Drop (%)
  - Average Power (Watts)
  - Maximum Power (Watts)
  - Average Temperature (Degrees Celsius)
  - Max. Temperature (Degrees Celsius)
  - Average Force (Grams)
  - Max. Force (Grams)
  - *LSI (number) → OUS only*
  - *FTI (gr/s) → OUS only*

AutoMark placement settings:
- AutoMark Spacing (mm)
- Min AutoMark Time (s)
- Away Time (s)

Mapping time associated with (re-)mapping one or multiple arrhythmias per catheter type used in a single subject:
- Mapping time will be summarized (e.g. as mean, median, standard deviation, minimum and maximum) across arrhythmia types and for each type of arrhythmia per catheter, as appropriate for the following map types:
  - Manual
  - AutoMap
  - Combination Manual Map / AutoMap
  - TurboMap™

Used Points per Minute per catheter type stratified by arrhythmia type and mapping type:
- Mapping points per minute used will be summarized (e.g. as mean, median, standard deviation, minimum and/or maximum) across arrhythmia types and for each type of arrhythmia per catheter as appropriate, with following map types:
  - Manual mapping
  - AutoMap
  - Combination Manual Map / AutoMap
  - TurboMap™

Rate of acute success based on pre-defined procedural endpoints (refer to Appendix C):
- The number and proportion of subjects with acute success will be summarized.

Freedom from arrhythmia recurrence: Arrhythmia recurrence is defined as documented atrial arrhythmia for 30 seconds or longer or documented ventricular arrhythmia either treated by ICD or lasting 20 seconds or longer throughout the follow-up period.
- This analysis will be performed using the Kaplan-Meier (KM) analyses. The start date is the date of the index procedure. For subjects who do not experience an event, their follow up duration will be defined from the start date to the date of death, withdrawal, or last follow-up, whichever occurred later.
- Time to arrhythmia recurrence is defined as time from index procedure to the date of the first recurrence. For subjects with AF, events occurring within the blanking period (defined as the first 90 days after the index procedure) will be excluded from the analysis.

Number of repeat ablations up to 12 months. This will be summarized as:
- Total count of repeat ablations up to 12 months among all subjects in the analysis population defined in section 7.1.3
- Total number of subjects who experience at least one repeat ablation up to 12 months among all subjects in analysis population defined in section 7.1.3

Summary of NavX Patch placement locations used
- The number and proportion of subjects with NavX patches (Surface Electrode Patches) placed by location

Number of gaps in lesions identified during the procedure that require touch-up ablation:
- The number and proportion of subjects with gaps in lesions identified will be summarized and reported.
- The summary of number of gaps identified will be reported.
- The number and proportion of subjects where the AutoMark Module assisted in identifying these gaps will be summarized and reported.

Changes in EQ-5D quality of life score at 6 and 12 months:

- Changes in EQ-5D at 6 months from baseline, and changes in EQ-5D score at 12 months from baseline will be summarized.

Number of unscheduled visits and hospitalizations due to arrhythmia:

- The number of unscheduled visits due to arrhythmia, or hospitalizations due to arrhythmia will be summarized per subject and presented as the number of subjects

Overall procedure time:

- Overall procedure time for the index procedure will be summarized e.g. as mean, standard deviation, minimum and/or maximum. Procedure time will be derived as (Procedure stop time (Last catheter out) - Procedure start time (first catheter in)).

Overall system stability:

- Proportion of subjects with the system stable throughout the procedure. System stability will be based on the opinion of the investigator.

7.1.2 Sample Size Determination

[redacted]

7.1.3 Analysis Populations

[redacted]

7.1.4 Subgroup Analysis

There are no pre-specified subgroup analysis for this clinical study.

7.1.5 Missing Data

All data available for the endpoints specified among the analysis population will be used. Missing data will not be imputed.

7.2 Justification of Clinical Study Design

The EnSite Precision™ Cardiac Mapping System is a newly developed system that introduces features such as DE-MRI image integration, lesion marking automaticity, automatic mapping, and workflow flexibility to aid in the success of complex ablation procedures. Utilization of this system in the treatment of complex ablation procedures and its impact on patient outcomes is not well characterized. This clinical study is designed to collect a broad range of usage scenarios, therefore this clinical study has limited patient selection criteria and data collection is focused on EnSite Precision™ Cardiac Mapping System usage and patient outcomes.

The data collected from the procedure (performed per IFU and per standard practice of the physician) as well as the 12 month follow up period enables the Sponsor to review the system's standard practice

[redacted]

usage. This information will be added to the current knowledge and understanding of treatment options for patients with arrhythmias, which can assist the Sponsor to provide future recommendations for best practices to improve patient outcomes.

7.3 Overall Sample Size

[redacted]

7.4 Timing of Analysis

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

7.5 Success Criteria

[redacted]

7.6 Interim Analysis

[redacted]

7.7 Statistical Criteria for Termination

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

7.8 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.

8 Risks and Benefits

The risks associated with the EnSite Precision™ Cardiac Mapping System can be found in the Instructions for Use. The clinical study does not require any additional procedures or assessments over the standard of care. There are no additional risks introduced to subjects due to participation in this study.

8.1 Risks Associated with the Clinical Study Device

8.1.1 Anticipated Adverse Device Effects

Refer to applicable IFU for list of Anticipated Adverse Device Effects.

8.1.2 Risks Associated with Clinical Study Assessments

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

[redacted]

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

8.2 Risk Control Measures

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

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

8.3 Possible interactions with concomitant treatments

There are no interactions with concomitant medical treatments and/or concurrent medical interventions compared to standard practice.

8.4 Anticipated Benefits

The aim of this clinical study is to collect information on the use and the performance of the EnSite Precision™ Cardiac Mapping System.

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

8.5 Risk-to-Benefit Rationale

Catheter ablation is a recognized safe and effective treatment of cardiac arrhythmias. The EnSite Precision™ Cardiac Mapping System is believed to not introduce any unanticipated risks compared to current practice

8.6 History of Device Modifications or Recall

There have been no modifications or recalls in relation to safety and clinical performance of the EnSite Precision™ Cardiac Mapping System.

9 Requirements for Investigator Records and Reports

9.1 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, e.g. failure to adhere to the inclusion/exclusion criteria. 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 CRF. The site will submit the CRF to the Sponsor.

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

9.2 Safety Reporting

The devices used in this clinical study are market released and should be used according to IFU. As there are no safety driven endpoints, adverse events will not be collected during this clinical study. Complaints will be managed via the sponsor's standard Postmarket Surveillance process.

9.2.1 Subject Death

Subject deaths shall be reported to the IRB/EC as per local regulations and shall be reported on a Withdrawal form.

9.2.2 Complaints

The investigator will be responsible for reporting all complaints they became aware of during the study. 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.

The investigator must notify the Post Market Surveillance Department by submitting the information on the device via email to [redacted] as soon as possible after becoming aware of the complaint. This information will not be collected on a CRF for the study.

9.3 Source Records

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

To facilitate data collection during the EP procedure, worksheets may be provided to the site where source data can be collected.

9.4 Records Retention

The Sponsor and the Principal Investigators will maintain the clinical study 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 if required by local regulations) after the conclusion of the clinical study 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.

10 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.

10.1 Protection of Personally Identifiable Information

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

10.2 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 study 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 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.

10.3 Document and Data Control

10.3.1 Traceability of Documents and Data

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

10.3.2 Recording Data

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

11 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.

12 Compliance Statement

12.1 Statement of Compliance

This clinical study will be conducted in compliance with the most current regional and local laws and regulations. Principles of Good Clinical Practice will be followed as based on the most current version of the World Medical Association (WMA) Declaration of Helsinki.

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 study. 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 study, 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 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 study specific insurance will be provided by the Sponsor.

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

12.3 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 study, the Sponsor will either secure compliance or, at its sole discretion, terminate the investigator's participation in the clinical study. 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.

13 Suspension or Premature Termination of the Clinical Study

The Sponsor reserves the right to terminate the clinical study 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 study 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 study or when so instructed by the IRB/EC or regulatory authority, the Sponsor may suspend the clinical study while the risk is assessed. The Sponsor will terminate the clinical study 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 study 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 study 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 study, and the Principal Investigator or authorized designee will promptly inform the enrolled subjects at his/her investigational site, if appropriate.

14 Clinical Study Conclusion

The clinical study 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 study closure.

15 Publication Policy

Publications or presentations of clinical study methods or results will adhere to 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. Publication planning and authorship determinations will be overseen by Publications Committee (see section 6.9.1), and investigators will be notified via email about the dissemination of study data and opportunities for involvement as authors on publications/presentations.

16 Reporting Results on ClincalTrials.gov Website

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

Appendix A: CIP Revisions

Procedure for CIP Amendments

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 number and date of amendments will be documented.

The acknowledgement of the amended CIP by the Principal Investigators will be collected on the signature pages.

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

Revision History

Appendix B: Bibliography

January, C. T., Wann, L. S., Alpert, J. S., Calkins, H., Cleveland, J. C., Cigarro, J. E., . . . M, N. (2014). 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. *Circulation*, e-199 - e267.

Nof, E., Stevenson, W. G., & John, R. M. (2013). Catheter Ablation for Ventricular Arrhythmias. *Arrhythmia & Electrophysiology Review*, 45 - 52.

Pedersen, C. T., Kay, G. N., Kalman, J., Borggrefe, M., Della-Bella, P., Dickfeld, T., . . . Kirchhof, P. (2014). EHRA/HRS/APHRS Expert Consensus on Ventricular Arrhythmias. *Heart Rhythm*, e166 - e196.

Wright, M., & Narayan, S. M. (2015). Ablation of Atrial Fibrillation. *Trends Cardiovasc Med.*, 409-419.

Appendix C: Definitions

Non-study Specific Definitions

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.

Complaint
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.

Study Specific Definitions

Arrhythmia recurrence
For the purpose of this clinical study, recurrence of arrhythmia is deemed to have occurred only when the arrhythmia is documented on ECG or during a period of monitoring e.g. Holter-monitoring, implantable cardiac monitor, ICD, CRT… Atrial arrhythmias must be 30 seconds or longer. Ventricular arrhythmias are any treated by ICD or 20 seconds or longer.

Blanking period (AF only)
The 3-month (90 days) period of time following a procedure in which AF episodes can occur as part of the body's healing response. Any arrhythmia activity during that blanking period is not counted in the study's results and is not used in determining success or failure of the procedure.

Acute success
For the purpose of this study, acute success is attained when one (or multiple) predefined procedural endpoints, have been realized. These predefined procedural endpoints include, but are not limited to:

- Abolition of all clinical ventricular ectopies and unstable ventricular arrhythmias
- Bidirectional block across CTI
- Block across mitral isthmus
- Confirmation of vagal reflexes
- CS isolation
- Documentation of block at a critical isthmus of conduction
- Elimination and noninducibility of tachycardia following ablation
    - With burst pacing
    - With Isoproterenol
    - With programmed atrial and ventricular stimulation
- Elimination of dormant conduction
- Elimination of LAVA
- Elimination of local Purkinje potentials
- Lines connecting scar to anatomic conduction barrier
- Lines parallel to scar border zone

[redacted]

- Pulmonary Vein capture with exit block
- Pulmonary Vein electrical isolation
- Scar homogenization
- Superior Vena Cava isolation
- Termination of tachycardia during RF energy application

[redacted]

Appendix D: Abbreviations

3D	Three-Dimensional
AF	Atrial Fibrillation
AVNRT	Atrioventricular Nodal Reentry Tachycardia
AVRT	Atrioventricular Reentrant Tachycardia
CIP	Clinical Investigation Plan
CRF	Case Report Forms
CRT	Cardiac Resynchronization Therapy
DE-MRI	Delayed Enhancement Magnetic Resonance Imaging
DMP	Data Management Plan
EC	Ethics Committee
ECG	Electrocardiogram
EDC	Electronic Data Capture
EP	Electrophysiological Procedure
ER	Emergency Room
ICD	Implantable Cardioverter Defibrillator
ICMJE	International Committee of Medical Journal Editors
IFU	Instructions For Use
IRB	Institutional Review Board
OUS	Outside the United States
PVC	Premature Ventricular Contractions
RF	Radiofrequency
SVT	Supraventricular Tachycardia
US	United States
USB	Universal Serial Bus
VF	Ventricular Fibrillation
VT	Ventricular Tachycardia
WMA	Word Medical Association

Appendix E: Case Report Form

The Final CRFs will be kept under a separate cover and are available upon request.

Appendix F: Informed Consent Form

[redacted]

[redacted]

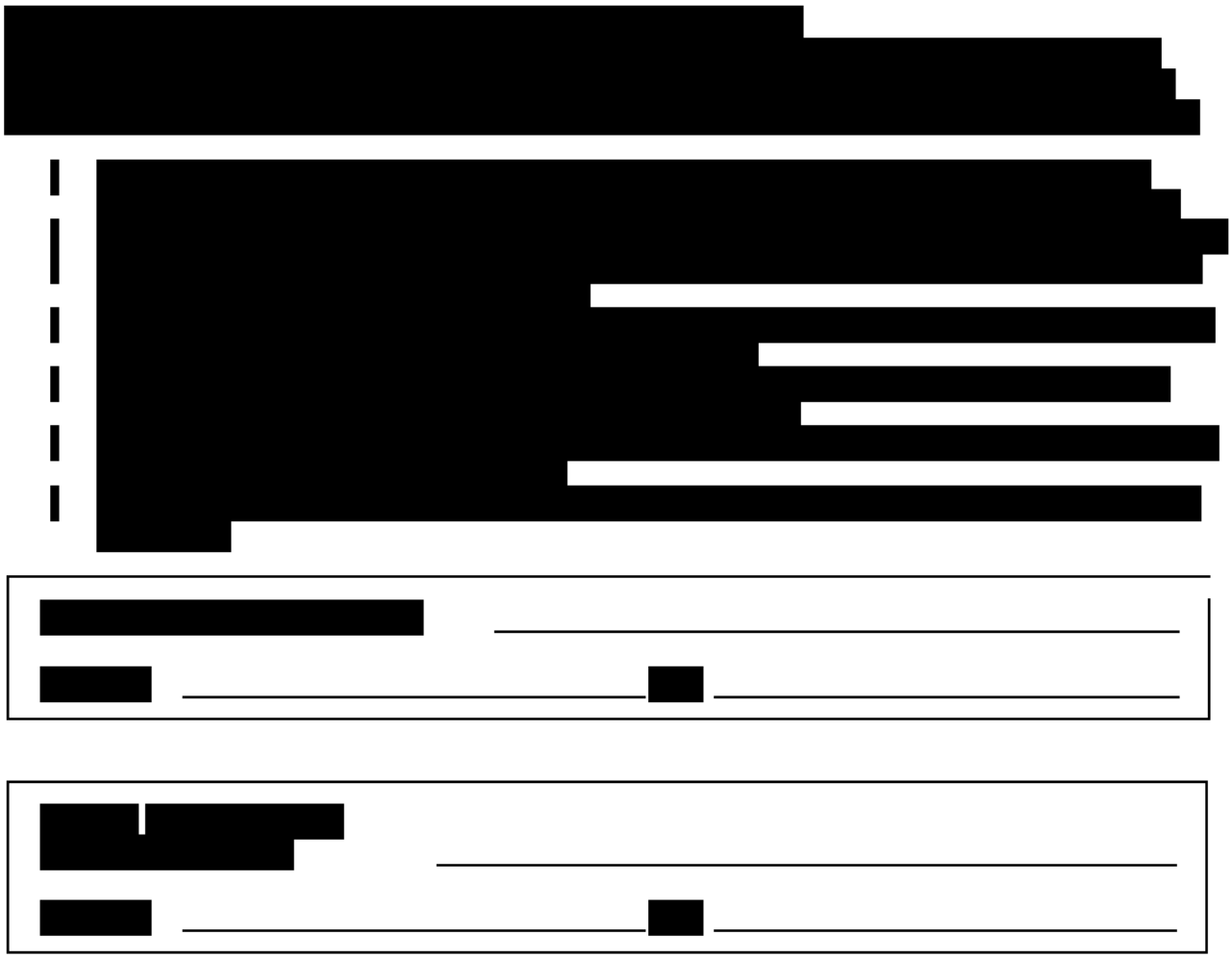
[redacted]

[redacted]

[redacted]

[redacted]

[redacted]



Appendix G: Percentage by Arrhythmia type

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

Appendix H: EQ-5D Questionnaire

The subject should be asked to indicate his/her health state by ticking or placing a cross in the box against the most appropriate statement in each of the 5 dimensions.
This decision results in a 1-digit number expressing the level selected for that dimension. The digits for 5 dimensions can be combined in a 5-digit number describing the subject's health state.

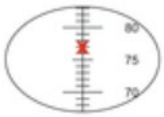
The EQ-5D-5L descriptive system should be scored, for example, as follows:

This example identifies the health state '12345'.

NB: *There should be only ONE response for each dimension*
NB: Missing values *can be coded as '9'.*
NB: Ambiguous values *(e.g. 2 boxes are ticked for a single dimension) should be treated as missing values.*

Scoring the EQ VAS

The EQ VAS should be scored, for example, as follows:



For example this response should be coded as 77

NB: Missing values *should be coded as '999'.*
NB: *If there is a discrepancy between where the respondent has placed the X and the number he/she has written in the box, administrators should use the number in the box.*

The EQ VAS records the subject's self-rated health on a 20 cm vertical, visual analogue scale with endpoints labelled 'the best health you can imagine' and 'the worst health you can imagine'. This information can be used as a quantitative measure of health as judged by the individual respondents.