Abbott	Clinical Investigation Plan Cover Page

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ABLATOR
Ablation Observational Registry
Study Document No: SJM-CIP-10032
Version B
Date: 20-Oct-2015

Sponsor

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CRD N° : CRD_723
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ABLATOR Ablation Observational Registry

Protocol

CRD_723

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Revision History				
Amendment N°	Project Version	Date	Rationale	Details
NAP	Ver. A	17SEP2014	Initial release	NAP
NAP	Ver. B	19OCT2015	Increase to 2000 patients and 100 centers. Added US as a potential geography. Updated section 6 statistical considerations. Added 2 objectives.	NAP

1 Background

Atrial Fibrillation (AF) prevalence in the western world is high and increasing, from 0.9%[1]up to 24.2% in men over 85 years[2]. These estimates are consistent with earlier US based data, which indicate that the number of individuals with AF is expected to double between now and 2050.

AF ablation is now recognized as a second line therapy[3], sometimes used as primary therapy prior to failure of an antiarrhythmic drug (AAD)[4]. The most common approach to AF ablation is based on Pulmonary Vein Isolation (PVI), but multiple alternate approaches are being used and studied (i.e. lines, complex fractionated electrograms (CFE), rotors, epicardial approach).

Radiofrequency (RF) energy is still predominantly used, with 3D mapping for both anatomical navigation and electrical mapping.

St. Jude Medical (SJM) provides a wide range of devices that can be used during atrial fibrillation (AF) ablation procedures and has recently introduced new devices such as the FlexAbility Ablation catheter with enhanced maneuverability and innovative irrigation and TactiCath Ablation Catheter with contact force sensing[5].

Multiple papers address the treatment of AF from a clinical perspective[6-9]. This registry aims at collecting a large sample of real world cases focusing on the synergy between various tools and investigating their impact on procedural and clinical effectiveness. The outcomes will support recommendations for optimal techniques, evaluate overall procedural costs, provide feedback to designers for improved tools, create supporting data for randomized controlled trials designs and provide information on operator's choices from a vast variety of sites.

2 Registry Design

2.1 Purpose

The purpose of this registry is to assess the performance and clinical effectiveness of a combination of SJM mapping and ablation products in the treatment of subjects with atrial fibrillation (AF.

2.2 Objectives

- To confirm patient safety as part of the post market surveillance study.
- To assess performance of a combination of SJM products during procedures
- To assess the learning curve with a combination of SJM products.
- To collect operator feedback on a combination of SJM products
- To compare the acute and long-term effectiveness according to technique used.
- To analyze procedure efficiency according to technique used.

2.3 Investigation Type

Post-market, international, multi-center, prospective, single arm observational registry.

This observational registry will be conducted in approximately 100 centers worldwide.

2.4 Subject Population

All patients from participating sites who are indicated for an atrial fibrillation ablation procedure and willing to provide written Informed Consent may be enrolled in this registry.

Point of Enrollment

Patients are considered enrolled in this registry following provision of written Patient Informed Consent.

Expected duration of each subject's participation

The expected duration of each subject's participation is 1 year.

Expected duration of the registry

The expected duration of this registry is approximately 3 years: 2 years of enrollment and 1 additional year of follow up.

Number of Patients required to be included in the registry

Up to 2,000 patients will be enrolled in this registry.

2.5 Devices Used

In order to ensure a minimum level of uniformity across site practices and to enable comparison of acute and long-term effectiveness as well as procedure efficiency according to technique used, a combination of 2 types of devices from the pre-specified list must be used to be eligible in this registry.

List of devices to be used in this registry:

Combination of a minimum of 2 devices amongst:

Europe, Middle East Canada, Australia and New Zealand

- Ablation catheter: TactiCath or FlexAbility
- Access with steerable sheath: Agilis NxT
- Versatile diagnostic catheters: Inquiry Afocus II DL, Optima or Reflexion Spiral

In case of advanced mapping, EnSite Velocity must be used.

US

- Ablation catheter: TactiCath
- Access with steerable sheath: Agilis NxT
- Versatile diagnostic catheters: Inquiry Afocus II DL, Optima or Reflexion Spiral

In case of advanced mapping, EnSite Velocity must be used.

Asia

- Ablation catheter: Family of Therapy CoolFlex catheters
- Access with steerable sheath: Agilis NxT
- Versatile diagnostic catheters: Inquiry Afocus II DL, Optima or Reflexion Spiral

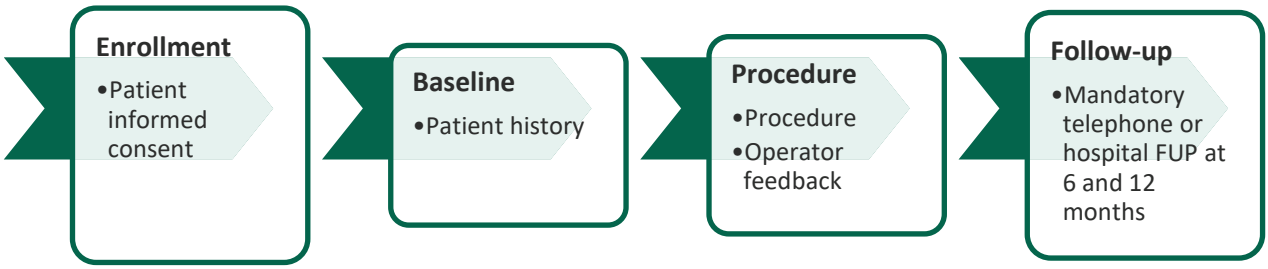
In case of advanced mapping, EnSite Velocity must be used.

Only SJM commercially available shelf-stock will be used for the Registry. The manuals shipped with the SJM devices should be consulted. Successor models of the current approved devices can be used as well once they become available and market approved.

3 Data collection

3.1 Registry Flow Chart

Figure 2: Flow Chart



All procedures will follow site standard of care at the site.

3.2 Case Report Forms Content

Table 1: Data Collection

Visit / CRFs	Enrollment & Baseline	Ablation Procedure	6 and 12 Months
Enrollment: Informed Consent Process	X		
Baseline: Demographics, Cardiovascular History, AF History, Medical History	X		
Ablation procedure		X	
Device user experience		X	
Follow Up Log*			X
Repeat procedure			(X)
Cardiovascular Serious Adverse Event	(X)	(X)	(X)
Withdrawal	(X)	(X)	(X)
Death	(X)	(X)	(X)

(X) if applicable
* Telephone or office visit

Enrollment & Informed Consent Process

The investigator is responsible for screening subjects for this registry and for obtaining patient informed consent, as applicable per local regulations. Provision of the Informed Consent is mandatory. Informed Consent is required from all patients (or their legal representatives) prior to participation in the investigation. The process of obtaining Informed consent shall comply with the most recent version of the declaration of Helsinki, ISO 14155 and all applicable regulations. The principal investigator or his/her authorized designee will conduct the Informed Consent Process. This process will include a verbal discussion with the patient on all aspects of the clinical investigation that are relevant to the patient's decision to participate in the clinical investigation. It is crucial that this discussion is documented in the source documents (read hospital records of the patient).

The patient will be provided with the informed consent form that is written in a language that is understandable to the patient and has been approved by Ethics Committee. The patient is given ample time to consider participation and ask questions if necessary.

In order to avoid any possible coercion or undue improper influence on, or inducement of the patient to participate, the Sponsor requests the investigator to only sign the informed consent form once the patient has signed and dated the document and therefore decided to participate in the investigation.

Informed Consent of a patient shall always be indicated by personally dated signature of the patient and by the investigator responsible for conducting the informed consent process. It is crucial that the signature of the informed consent is documented in the source documents (read hospital records of the patient).

One original signed consent document must be retained on file by the investigator and a second original signed consent document is provided to the subject (investigator's responsibility).
The patient's legal rights will not be waived nor the appearance that these will be waived. Native non-technical language, understandable for the patient, will be used. Important new information that becomes available throughout the Registry will have to be provided in writing to new and existing patients. If relevant, all affected patients shall be asked to confirm their continuing informed consent in writing.

Baseline Visit

The following baseline information will be collected;
- Patient demographics
- Atrial fibrillation History (such as type, frequency, duration of atrial fibrillation and other arrhythmias other than AF),
- Cardiovascular history (NYHA class, LA diameter, LV EF% and degree of valvular heart disease),
- Cardiac medical history (pre-existing cardiac conditions and cardiac procedures).

Ablation procedure

- Devices used
- Ablation parameters
- Ablation success definition and result
- Operator feedback (Device combination chosen, device maneuverability, ease of use in combination with other device)
- Number, experience and type of attending personnel
- Definition of standard of care (follow-up procedures and occurrence)

6 and 12 Month Follow-up (+/- 30 days)

- Recurrence of atrial arrhythmias: list of atrial arrhythmias since last visit, classify episodes, duration of the episodes, (only events with source data evidence are to be recorded).
- Changes in therapy (new antiarrhythmic drug, redo procedures).
- In case of Repeat Ablation Procedures, reconnections and new ablations will be recorded.

Cardiovascular Serious Adverse Event

An adverse event is reportable in this registry when the event is deemed of cardiovascular origin and has the potential of leading to:

- Death
- A serious deterioration in the health of the subject, that can either result in:
    - A life-threatening illness or injury OR
    - A permanent impairment to a body structure or a body function OR
    - An in-patient or prolonged hospitalization OR
    - A medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function OR
    - A malignant tumor
- Fetal distress, fetal death or a congenital abnormality or birth defect

A planned hospitalization for a pre-existing condition is not considered a serious adverse event.

Potential Cardiovascular Serious Adverse Events (SAEs) include but are not limited to the following:

Abnormal ECG, Angina (chest pain), Arrhythmia, AV fistula, Complete heart block, Coronary artery injury, Cardiac perforation, Cardiac Thromboembolism, CHF exacerbation – fluid overload, Component damage to ICD or implantable pacemaker, Death, Dislodgement of implantable cardiovertor defibrillator of permanent pacing lead, Endocarditis, Exacerbation of pre-existing atrial fibrillation, Heart Failure, Hypotension, Inadvertent AV block (complete heart block), Left atrial/esophageal fistula, Myocardial infarction, Obstruction/perforation/damage of the vascular system, Palpitation, Pericardial effusion/cardiac tamponade, Pericardial effusion without tamponade, Pericarditis, Pulmonary vein dissection, Pulmonary vein stenosis, Pulmonary vein thrombus, Temporary or complete heart block, Unintended (in)complete AV, sinus node, heart block/damage, Vessel wall/valvular damage or insufficiency and Ventricular arrhythmia requiring defibrillation.

Procedure for assessing, recording and reporting SAEs:

Cardiovascular SAEs must be reported following local regulation, no later than 7 days from site being made aware of the event. All cardiovascular SAEs between patient enrollment and end of registry must be reported to the sponsor and to the local ethics committees, as per local regulations.

Should an SAE occur, complete and submit an Adverse Event form to St. Jude Medical.

Additional information can be requested, if necessary, by the Sponsor for reporting of SAEs to regulatory authorities. The investigator must notify the Ethics Committee, if appropriate, in accordance with national and local laws and regulations.

Death

All patient deaths that occur during this registry must be reported to SJM within 72 hours of the center becoming aware of the death. An Adverse Event form should be completed for all deaths at all sites.

Protocol Deviations

Investigators are required to adhere to the study protocol, signed Investigator's Agreement, applicable federal (national) or state/local, laws and regulations, and any conditions required by the Ethics Committee or applicable regulatory authorities. A protocol deviation is used to describe situations in which the study protocol was not followed. All deviations from the study protocol must be reported to SJM.

Withdrawals

All reasonable efforts should be made to retain the patient in the Registry. If a patient concludes their participation in the registry, the patient's future management will not be changed by this decision, whether it is voluntary or otherwise. Should a patient withdraw and conclude participation in the registry, document the information in the withdrawal form (CRF) as soon as possible.

4 Registry Conduct

4.1 Sponsor obligations

Sponsor personnel will:

- Propose the registry to participating sites
- Train and provide the site personnel with access and training to an Electronic Data Capture platform
- Monitor subject data collected in the registry

4.2 Investigator obligations

The principal investigator and delegates are required to adhere to the Protocol in order to prevent subjects being exposed to unreasonable risks. On top of that, the principal investigator and delegates are required to be compliant with the signed Study Agreement, applicable national or local laws and regulations, and any conditions required by the appropriate Ethics Committee

4.3 Monitoring

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

4.4 Investigation Termination

The Sponsor reserves the right to stop the registry at any stage, with appropriate written notice to the investigator.
Possible reasons for early termination of the registry by the sponsor, either at local, national or international level, may include, but are not limited to:

- Sponsor's decision
- Request from Regulatory bodies
- Request of Ethics Committee(s)
- Occurrence of unanticipated SAE related to a device which cannot be prevented in future cases

If applicable the registry will be terminated according to applicable regulations.

4.5 Statement of Compliance

The registry will be performed in accordance with the most current versions of the World Medical Association (WMA) Declaration of Helsinki, ISO 14155 and any regional and/or national regulations and will be compliant to this International Standard and any regional and national regulations, as appropriate.

The investigator shall not start enrolling patients or requesting informed consent from any patient prior to obtaining Ethics Committee approval and Competent Authority approval, if applicable, and authorization from the sponsor in writing.

In case additional requirements will be imposed by the Ethics Committee or Competent Authority they shall be followed, if appropriate.

5 Risks and Benefits of the clinical investigation

This registry will follow site standard practice procedures, therefore there are no risks or benefits associated with participating in this registry for the patient. A long term benefit for therapy delivery is expected based on the scientific outcome of the registry data analysis.

6 Statistical considerations

This is a post-market, international, multi-center, single arm observational registry. The objectives of this Registry are as follows:

- To confirm patient safety as part of the post market surveillance study.
- To assess performance of a combination of SJM products during procedures
- To assess the learning curve with a combination of SJM products.
- To collect operator feedback on a combination of SJM products
- To compare the acute and long-term effectiveness according to technique used.
- To analyze procedure efficiency according to technique used.

Up to 2,000 patients will be enrolled in this registry, which is expected to be adequate to address the objectives of this registry. Descriptive statistics will be used to summarize baseline and demographic data, procedural information, adverse events and recurrence of atrial arrhythmias. Continuous variables may be summarized using either mean, standard deviation and range, or median and interquartile range as applicable. Categorical variables will be summarized as frequencies and proportions. Kaplan-Meier time to event analysis may be used to summarize recurrent atrial arrhythmias. To assess learning curve, appropriate statistical analysis will be used to assess the influence of physician experience on procedural outcomes or adverse events.

7 Data Management

Data from this registry will be analyzed by SJM and may be transferred SJM's locations outside of Europe and/or any other worldwide regulatory authority in support of a market-approval application.

The physician is required to enter the data through an electronic data capture (EDC) system within 10 days of the visit.

8 Document Retention

The principal investigator (PI) shall maintain a copy of all registry records (e.g., informed consent documents, Registry records, etc.) which support CRFs of this registry, must be retained in the files of the responsible Investigator for a minimum of 15 years following notification by SJM that all Investigations (not merely the Investigators portion) are completed, terminated, or discontinued.

If the participating physician retires, relocates, or for other reasons withdraws from the

responsibility of keeping the registry records, custody must be transferred to a person who will accept responsibility. SJM must be notified in writing of the name and address of the new custodian.

9 Amendments

This protocol, Case Report Forms (CRFs), Informed Consent form, other patient information, or other Registry documents shall be amended as needed throughout the registry. A justification statement shall be included with each amended section of a document. The amendments to the protocol and the subject's Informed Consent shall be notified to, or approved by, the Ethic Committees and regulatory authorities, if required. The version number and date of amendments shall be documented.

10 Publication Policy

The Investigator shall strictly comply with the Publication agreement related to "Ablator registry".

SJM is the legal owner of the entire Clinical Study database. Decisions on the timing and content of Publication(s) from the Registry will be coordinated by SJM.

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Appendix A: Data Collection Method

Sponsor/Investigators are required to prepare and maintain adequate and accurate case histories to record all observations and other data pertinent to the investigation on each subject. Source documents include all original records from which CRFs derive their data. Worksheets can be provided. The purpose of these worksheets is to aid investigators in the capture of clinical investigational data and ensure all protocol required data, which is not captured in medical records, is recorded to support data for the investigation. These worksheets will not be a copy of the CRFs, but will contain entry blanks for study required data not routinely collected by the investigators. All documentation pertaining to clinical assessments and medical evaluations should be signed and dated by the appropriate clinical personnel. Electronic Data Capture (EDC) will be used for this investigation.