STATISTICAL ANALYSIS PLAN (SAP)

reMARQable:

nMARQ™ Pulmonary Vein Isolation System for the Treatment of Paroxysmal Atrial Fibrillation

Protocol Version 5.2
Closeout Plan (Apr 18, 2017)

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SAP Version: 1.0

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nMARQ™ Pulmonary Vein Isolation System for the Treatment of Paroxysmal Atrial Fibrillation

Protocol Version 5.2 & Closeout Plan (Apr 18, 2017)

The following individuals have reviewed this version of the Statistical Analysis Plan and are in agreement with the content:

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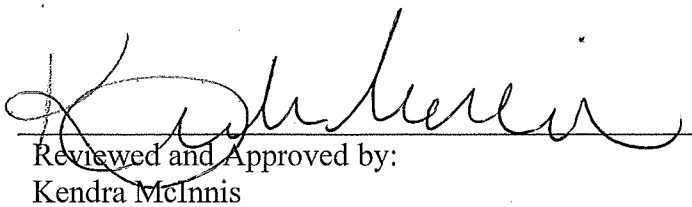	7 DEC 2017
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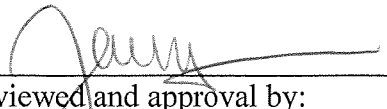	7 Dec 2017
Reviewed and approval by: Jennifer Walcott Director of Clinical Trials Management, JNJ Medical Devices	Date

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1.0 REVISION HISTORY

Version	Date	Author(s)	Description of Change
1.0	Dec 04, 2017	Tiffany Tan and Bonnie Zhang	First Version per Protocol v 5.2 and Closeout Plan (Apr 18, 2017)

2.0 Introduction

This statistical analysis plan contains a detailed description of the data presentations and statistical analyses that will be included in the reMARQable clinical study report. Due to the discontinuation of the worldwide commercialization of the nMARQ catheter and generator technologies, the study sponsor (Biosense Webster) decided to terminate the study (IDE # G120289) prior to study completion. The Closeout Plan was approved without conditions by FDA on July 18, 2017. Therefore, the statistical methods and analyses described here are based on those presented in Section 7 of the Closeout Plan (April 18, 2017) and supersede the methods outlined in the reMARQable IDE study protocol. Any deviation from the analysis plan will be documented as such in the study report.

3.0 Study Design

3.1 Study Objectives

3.1.1 *Primary Objectives*

- To demonstrate the safety of the nMARQ™ catheter system (nMARQ; Test device) compared to the THERMOCOOL® Navigational Family of catheters (TC; Control device) for treating subjects with drug-refractory symptomatic paroxysmal atrial fibrillation (PAF) based on the occurrence of early-onset (within 7 days of ablation procedure) primary adverse events.
- To demonstrate the effectiveness of the nMARQ (Test device) compared to the TC (Control device) for subjects with symptomatic PAF based on the difference in proportion of freedom from documented, symptomatic AF/AT/AFL through 12 months post ablation follow-up.

3.1.2 *Secondary Objectives: Subpopulation Neurological Assessment (SNA)*

To evaluate the comparative incidence of pre- and post-ablation symptomatic and asymptomatic cerebral emboli using MRI evaluation in a subset of the Main Study Phase PAF population. The presence of emboli-associated neurological deficits will also be evaluated, using the National Institute of Health Stroke Scale (NIHSS). MoCA, mRS and general neurological assessments.

3.2 Design

In accordance with the protocol, following the Calibration Roll-In phase of up to 5 nMARQ subjects per investigational site, the design of the Main Study will be carried out as a prospective, multi-center, randomized (1:1 concurrent nMARQ™ Catheter System [nMARQ] vs ThermoCool® Navigational Family of catheters [TC]), controlled, two-arm, single-blind, clinical study.

A cap of 777 subjects will be enrolled at up to 50 sites in the United States (U.S.) and other regions may be included in the study.

A Bayesian adaptive trial design is employed. Several Bayesian aspects will be employed and crucial parameters of the trial will be determined by the accruing data using a completely prospective design. The following is an overview of the design:

1) The sample size of the trial will be determined by Bayesian adaptive techniques. At the time we reach 250, 300, 350, 400, and 450 subjects in the ITT population, the trial may stop for expected success or for futility. If the trial stopped for expected success then all subjects will be followed through to the final efficacy endpoint (12-months post procedure). A cap of 500 subjects in the ITT population will be employed.

2) An interim analysis will be conducted 16-weeks after enrollment ends for early success. If the predictive probability of final success is greater than 99%, then trial success will be declared. All subjects will have complete safety data and all subjects will be followed through their trial completion.

Per the Closeout Plan, the enrollment, follow-up schedule, adaptive design for sample size determination, and the interim analysis will be changed. No enrollment or interim analysis will be conducted after the approval date of the Closeout Plan (July 18, 2017). Additionally, due to the termination of the study, the interim analysis at 300 ITT subjects was cancelled. The follow-up schedule for subjects who have not completed their 3-year follow-up visits nor exited the study will follow the procedures described within of the Closeout Plan. Details will also be provided in the following section of “Interval Windows”.

4.0 Treatment Assignment

Eligible subjects who sign the study informed consent form and satisfy all inclusion and exclusion criteria will be randomized into one of two treatment groups:

- **Test Group [nMARQ Group]:** subjects who undergo catheter ablation with the nMARQ™ system.
- **Control Group [TC Group]:** subjects who undergo catheter ablation with a device from the approved THERMOCOOL® Navigational Family of catheters.

5.0 Randomization and Blinding Procedures

5.1 Randomization

Per Protocol, dynamic randomization will be defined and executed to balance the two treatment groups by site and gender via the Medidata Balance interactive web-based randomization system (IWRS). The designated personnel at each site will be required to access the electronic randomization system to obtain the randomization assignment after entering stratification factors. The randomization treatment assignment and related information (e.g., randomization date and stratification factors) will be passed on to the electronic data capture system and integrated with the subject's clinical study data.

The Work Instruction (WI) of Procedures for Handling Data and Results in the reMARQable clinical study (BDM-0005) was developed to define the procedures for sharing data and results in the reMARQable Clinical Study. Some of the data to be collected in this study have the potential to unblind the study team. To preserve the blind and the integrity of the data, teams of blinded and unblinded personnel have been formed for this study. Their roles and responsibilities are defined in this document. Procedures for the handling and transfer of unblinded data are also described.

5.2 Interim Monitoring Committee (IMC)

The Interim Monitoring Committee (IMC) is an independent expert advisory group commissioned by Biosense Webster (BWI; sponsor) to perform and evaluate the Bayesian adaptive analysis for the sponsor's study entitled, "nMARQ™ Pulmonary Vein Isolation System for the Treatment of Paroxysmal Atrial Fibrillation."

The IMC is responsible for conducting the interim Bayesian analyses, verifying that the algorithms are performing correctly, ensuring that the trial adaptations are being conducted as planned, and make recommendations to BW. The IMC is not responsible for oversight of other effectiveness and safety analyses.

An IMC charter (version 2.1, Sep 12, 2016) has been developed to describe the roles and responsibilities of the IMC, identifies the members, describes the purpose and timing of its meetings, and describes the decision-making process, including voting procedures. The Charter provides the procedures for ensuring confidentiality and proper communication, and an outline of the content of the Closed Session Reports that will be provided to the sponsor. This Charter also outlines the meeting schedules and format and explains the administrative procedures that will be followed. The appendices contain the contact information for persons relevant to the IMC and the study.

5.3 Unblinding

After the FDA approval of the Closeout Plan, the blinded study team, including the blinded biostatistician and programmers, will be unblinded for the final CSR. In addition, per the memo regarding the interim analysis for the 2nd interim look (dated Jun 01, 2017), a 2nd interim look will not be conducted and thus there would be no further IMC meetings. Therefore, the Senior Management Steering Committee (SMSC) would also be unblinded.

6.0 Interval Windows

Per protocol, subjects are required to complete follow up visits through 3 years post initial ablation procedure. The follow-up visits at 1 month, 3 months, 6 months, 9 months, and 12 months will consist of an office visit.

Follow-up visits should be scheduled according to the following timeframes: 1 month -23/+12 days (M-1, day 7-42), 3 month ± 20 days (M-3, day 70-110), 6 months ± 30 days, (M-6, day 150-210), 9 month ± 40 days (M-9, Day 235-315) and 12 month ± 45 days (M-12, Day 316-405). The 2 and 3-year post-ablation telephone calls should occur within ± 45 days of their index ablation procedure anniversary.

Follow-up visit schedule will not reset if subject undergoes a repeat AF ablation procedure.

At each visit, the following assessments should be performed:

Assessments	**BL**	**D/C**	**D7**	**M1** D7-42	**M3** D70-110	**M6** D150-210 **M9** D235-315	**M12** D316-405	**UNS**	**Y2** ±45D **Y3** ±45D
Clinic visit	●			●	●	●	●	●	
Patient Information (Demographics) and Consent	●								
Medical history	●								
Pregnancy Test[1]	●								
TTE[2]	●	●							
Imaging for detection of LA thrombus (e.g., TEE, ICE, CT, MRI)[3]	●								
ECG[4]	●	●		●	●	●	●	●	
TTM[5]					●	●	●	●	
CT/MRA **nMARQ GROUP ONLY**	●[6]				●				
Cardiac medication	●			●	●	●	●	●	
Adverse events	●	●	●[7]	●	●	●	●	●	●[7]
AFL/AT/AF recurrence and repeat ablation				●	●	●	●	●	●[7]
CCS-SAF Scale	●				●	●	●		
Cerebral MRI[8]	●[9]	●[10]		●[11]	●[11]	●[11]	●[11]	●[12]	
Neurological Exam[8]	●[9]	●[10]		●[11]	●[11]	●[11]	●[11]	●[12]	
NIH Stroke Scale[8]	●[9]	●[10]		●[11]	●[11]	●[11]	●[11]	●[12]	
mRS	●[9]				●				
MoCA	●[9]			●	●[11]	●[11]	●[11]	●[12]	

1. In all women of child-bearing age and potential. To be completed within 24 hours prior to ablation procedure.
2. Completed within 30 days prior to ablation period.
3. To be completed the day before or the day of the ablation procedure.
4. To be collected if completed as standard of care.
5. Dispensation of TTM device at Month 3.
6. Within 30 days prior to ablation procedure.
7. To be assessed via phone follow-up.
8. Only for SNA subjects.

9. To be performed within 72 hours prior to ablation procedure.
10. To be completed within 72 hours post-ablation procedure.
11. To be undertaken if neurologic symptoms and/or cerebral ischemic lesions identified in a prior evaluation.
12. To be completed only if: (i) a previously mandated test was missed; or, (ii) subject reports neurologic difficulties between scheduled follow-up visits and unscheduled assessment per investigator approval.

Per the Closeout plan, the follow up schedule has been modified to accommodate the early termination of the study. Enrolled subjects were be required to complete follow up visits through 3 months post index ablation. Subjects who had yet to complete their 3-month follow-up visit by the release date of the study Closeout plan remained in follow-up through their 3-month visit. For these subjects, the 3-month visit was considered the subjects exit visit from the study.

Subjects who completed their 3-month follow-up visit prior to the implementation of the Closeout plan at each individual site (i.e. after IRB approval of the Closeout plan) received a telephone call to assess the occurrence of adverse events and recurrence of AF/AFL/AT since the last visit. This telephone call was considered the subjects exit visit for the study. If a subject visit coincides with the exit telephone call, the adverse events and AF/AFL/AT recurrence assessment may be conducted at that visit. Sites will be closed after subject follow-up and necessary data cleaning is completed.

7.0 Primary and Secondary Endpoint(s) and Associated Hypotheses

7.1 Primary Endpoints

The primary safety endpoint for this study is the incidence of early-onset (within 7 days of the ablation procedure) primary AEs. Pulmonary vein (PV) stenosis or atrio-esophageal fistula that occurs greater than one week (7 days) post-procedure shall be deemed a Primary AE.

The primary effectiveness endpoint is defined as freedom from documented symptomatic AF/AT/AFL based on electrocardiographic data during the effectiveness evaluation period (Day 91-365). Additionally, if a subject meets the failure mode criteria (see protocol section 8.2), the subject will be considered as chronic effectiveness failure.

7.2 Secondary Endpoints

Acute Effectiveness:

- Acute effectiveness is defined as complete PVI confirmation as documented by confirmed entrance block (i.e., complete PVI with or without the use of the toolkit's focal catheter).

One-Year Effectiveness:

- Freedom from AF/AFL/AT off antiarrhythmic drug therapy as assessed from the end of the 3-month blanking period to 12 months following the ablation procedure.

Long-Term Effectiveness:

- Freedom from AF/AFL/AT off antiarrhythmic drug therapy as assessed from the end of the 3-month blanking period to 2 year following the ablation procedure.
- Freedom from AF/AFL/AT off antiarrhythmic drug therapy as assessed from the end of the 3-month blanking period to 3 year following the ablation procedure.

Long Term Safety:

- Incidence of AEs and serious adverse events (SAEs) during the 12 month follow-up period post ablation procedure.
- Assessment of PV stenosis at 3 months post-ablation.
- Incidence of AEs and serious adverse events (SAEs) during the 2nd and 3rd year follow-up period post ablation procedure.

7.3 Additional Endpoints

- % PV isolation by study devices, by subject and by PV
- Repeat ablation rate (for AF/AFL/AT)
- Cardiac specific hospitalization rate
- Total fluoroscopy time
- Overall procedure time
- Ablation procedure related parameters
- Device use per targeted PV

7.4 Subpopulation Neurological Assessment (SNA) Endpoints

- Incidence of symptomatic and asymptomatic cerebral emboli pre- and post-ablation.
- Frequency, anatomic location, and size (diameter and volume) of cerebral emboli by MRI testing at baseline, post-ablation and during follow-up (if lesions observed).
- Incidence of new or worsening neurologic deficits, post-ablation and during follow-up.
- NIHSS score, Montreal Cognitive Assessment and Modified Rankin Scale pre- and post-ablation and during follow-up.

8.0 Level of Significance

Per Closeout Plan, no formal statistical hypothesis and inferential statistics will be formulated and performed for study endpoints. Two-sided 95% confidence intervals will be constructed for the safety endpoints.

9.0 Analysis Sets

The following analyses populations will be used to complete the analyses of the data:

9.1 Intent-to-Treat Population (ITT)

The ITT subject population will include all randomized patients who have the ablation catheter inserted. They will be analyzed as randomized. Lost-to-follow-up and withdrawn / early termination subjects post randomization are included in the ITT population. Calibration Roll-in cases will not be included.

9.2 As-Treated Population (AT)

The AT subject population will include all randomized patients who have the ablation catheter inserted. They will be categorized by the treatment received if this deviates from the treatment randomized. Calibration Roll-in cases will not be included.

9.3 Per Protocol Population (PP)

The PP subject population will include randomized subjects who satisfy the following criteria. Calibration Roll-in subjects will not be included.

- have undergone RF ablation,
- are treated with the study catheters as randomized (nMARQ or TC),
- are in compliance (no major protocol deviations) with the study protocol, and
- have been treated for the study-related arrhythmia.

9.4 Safety Population (SP)

The SP will include all subjects who have undergone insertion of an ablation catheter. The subjects will be analyzed according to the actual treatment received by subjects regardless of the Group they are randomized to. The calibration roll-in and discontinued roll-in cases will be included in the SP.

9.5 SNA Population (SNAP)

The SNAP will include all subjects who are enrolled and randomized within the Main Study and who further satisfy specific inclusion and exclusion criteria and provide additional consent to participate in the SNA. Eligible SNA subjects will have undergone RF delivery with the study ablation catheters and will have successfully completed pre- and post-ablation brain MRI examinations, NIHSS Questionnaires, and general neurological assessments.

9.6 SNA Evaluable Population (SNAEP)

SNA Evaluable Population includes subjects who have provided consent to participate in the SNA, satisfy specific eligibility criteria, receive RF ablation, had both the pre- and post- MRI performed and completed one or more post-ablation neurological assessments.

10.0 Sample Size Justification

Per protocol, trial simulation was carried out to evaluate the performance characteristics of the trial. For each scenario, 10,000 simulated trials were summarized to create the performance characteristics of that trial. Under the assumptions of equivalent effectiveness success rate at 55% and equivalent safety event rate at 8.6% in both groups, at an experiment-wise error rate of 0.05, an adaptive sample size of 250-500 (mean sample size of 417) will provide 80% power for trial success, meeting both effectiveness and safety endpoints, and 82.8% power and 87.4% power for meeting effectiveness and safety endpoints individually. The probability of early trial success is 36.8%. In the simulation, the non-inferiority margin is 15% for effectiveness and 8% for safety. The primary AE rate in the first 7-days is simulated as a Bernoulli random variable with a specified probability; the occurrence of effectiveness failure and timing of the failure are based upon a three-piece exponential time-to-failure model.

These trial simulations assume a primary AE rate of 8.6% for both Test and Control groups under the alternative hypothesis. Based on P030031/S011 data, the overall primary AE rate was 10.8%. However, this primary AE rate included 3 study subjects deemed primary safety failures solely due to hospitalization for AF recurrence. The incidence of primary AEs excluding those 3 subjects was 8.6%. Thus, an 8.6% primary AE rate is used for the purpose of trial simulations.

These trial simulations assume an equivalent success rate of 55% for both Test and Control groups under the alternative hypothesis using the chronic definition of effectiveness failures as defined in the protocol. These assumptions are based upon review of data from recent pivotal P030031/S011 AF THERMOCOOL® Trial where the chronic success rate in the NAVISTAR® THERMOCOOL® Group at 1 year follow-up was 62.7% (64/102) for all sites and 43.3% (29/67) for US data only. Therefore, it is estimated that the chronic success rate for both the nMARQ™ System and THERMOCOOL® at 12-month follow-up will be around 55%.

The sample size in the Main Study may vary from 250 to 500 due to the adaptations to the trial.

As for the SNA sub-study, At least 60 subjects (≥30 Test subjects and ≥30 Control subjects) from the already enrolled and randomized subjects of the Main Study will be selected in sequence for the SNA. The sample size is not intended for statistical comparisons by treatment group; however, 30 subjects in each arm will provide at least 91% probability of observing at least one event if the true event rate is at 8-14%.

Therefore, the total sample size for this IDE study to be up to 777 subjects (500/0.95+250), based upon the 250-500 subjects required for the effectiveness evaluation, up to 250 Calibration Roll-in subjects and 5% potential subject attrition rate before randomization. Up to 250 roll-in subjects using the nMARQ™ System are expected in this study because up to 50 sites will enroll up to 5 roll-in subjects each to reduce the influence of learning curve on effectiveness results. It is also estimated that no more than 5% of enrolled patients will either not meet the inclusion/exclusion criteria or be lost to contact or withdrawn prior to the randomization. The enrollment will be concluded when study outcomes meet the early stopping criteria or when 500 subjects have been randomized in the Main Study.

Per Closeout Plan, study enrollment will be stopped after receiving the FDA approval of the Closeout plan (dated Jul 18, 2017). The total sample size of the final CSR will be based on the actual enrollment status up to Jul 18, 2017. As for the SNA study, the enrollment has been halted after achieving total of 76 enrolled SNA subjects. The SNA final report was submitted and reviewed by FDA on Jan 21, 2016.

11.0 Data Monitoring Committee (DMC)

No Data Monitoring Committee will be constituted for the study.

12.0 Analyses to be Conducted

Per the Closeout Plan, a final Clinical Study Report (CSR) will be submitted to the FDA. The CSR will be formatted similar to an annual progress report. Descriptive statistics and data listing will be presented for demographic and baseline characteristics, subject disposition, ablation procedure data, device accountability and safety data. No inferential statistics will be performed. Efficacy data will not be reported. All the analysis methods described in the following sections are based on the Closeout Plan and will be performed for the CSR.

The SNA final analysis report, dated November 10, 2015, was submitted to the FDA on December 21, 2015 (G120289 / S012). The FDA approved the supplement on January 21, 2016 and determined that the enrollment cap could be removed based on the current results of the subpopulation neurological assessment. Therefore, the study results of the SNA sub-study won't be included in the final CSR.

12.1 General Conventions

- Summary Statistics

For continuous variables (e.g., age), summary statistics will include the sample size (n), mean, standard deviation, and median, minimum, maximum, and quartiles.

For categorical and ordinal variables, summary statistics will include the sample size (n) and percentage (%) for each unique category. Confidence limits for binary variables, will be computed using the exact binomial distribution unless otherwise specified.

- Study Days

The analysis of data will require that the number of days since the initial ablation is calculated. The Study Day will be calculated as: (date of the occurrence of event – initial ablation date).

> Note: The day of initial ablation is considered Study Day 0. The "event" in the above definition includes: completion of/exit from the study, onset of AEs, etc.

- Data Display

Data displays will include three types - summary tables, data listings and figures. Unless stated otherwise, data listings will be produced for all critical data points.

- Reporting of Numerical Values

Means, standard deviations, medians, and confidence intervals will be reported to one decimal place more than the data reported on the CRF or by the laboratory/vendor. Minimum and maximum will be reported to the same number of decimal places displayed on the CRF or by the laboratory/vendor.

- Statistical Software

SAS 9.3 and SAS studio will be used to execute the statistical analyses per this plan.

12.2 Subject Disposition

- **Excluded Subjects:** subjects who have signed the ICF, but are found to not meet the study eligibilities, PRIOR to insertion of the study catheter. Excluded subjects will not be included in either the effectiveness or safety analyses of the study catheters.

- **Evaluable Subjects**: all enrolled subjects who have the study catheter inserted. (Calibration Roll-in, discontinued Roll-in and randomized subjects.)
  - **Discontinued Subjects:** evaluable subjects who have the study catheter inserted but do not undergo ablation (i.e., no RF energy is delivered with the study catheter). Subjects will be categorized as "discontinued" if ablation is not possible due to equipment failure or if their arrhythmia is determined at the time of electrophysiology study to be a non-study arrhythmia; e.g., AFL instead of PAF (required for subject enrollment per study inclusion criteria). Discontinued subjects will remain in follow-up for 30 days as part of the safety

cohort. If an SAE is reported for a discontinued subject, they will be followed until event resolution.

- **Calibration Roll-in Subjects**: enrolled subjects who have the study catheter inserted and RF delivered during the Calibration Roll-in Phase. These subjects will be included as part of the analyses for secondary safety endpoints but not analyses for the primary endpoints. Calibration roll-in cases are not randomized and will be limited to not more than 5 subjects enrolled and treated at each site.
- **Lost to Follow-up Subjects:** subjects who are enrolled and evaluable, but contact is lost after most recent follow-up visit (despite 3 documented attempts to contact the subject).
- **Withdrawn / Early Termination Subjects:** subjects who withdraw consent for study participation or are withdrawn by the investigator (as described in Section 6.10) or are terminated from the study prior to completion of all follow-up visits.
- **Completed Subjects:** enrolled subjects who have not been excluded, discontinued, expired, withdrawn, early terminated or lost-to-follow-up from the study prior to the final study visit.

Figure 1 summarizes the study enrollment and accountability and explains the subject flow.

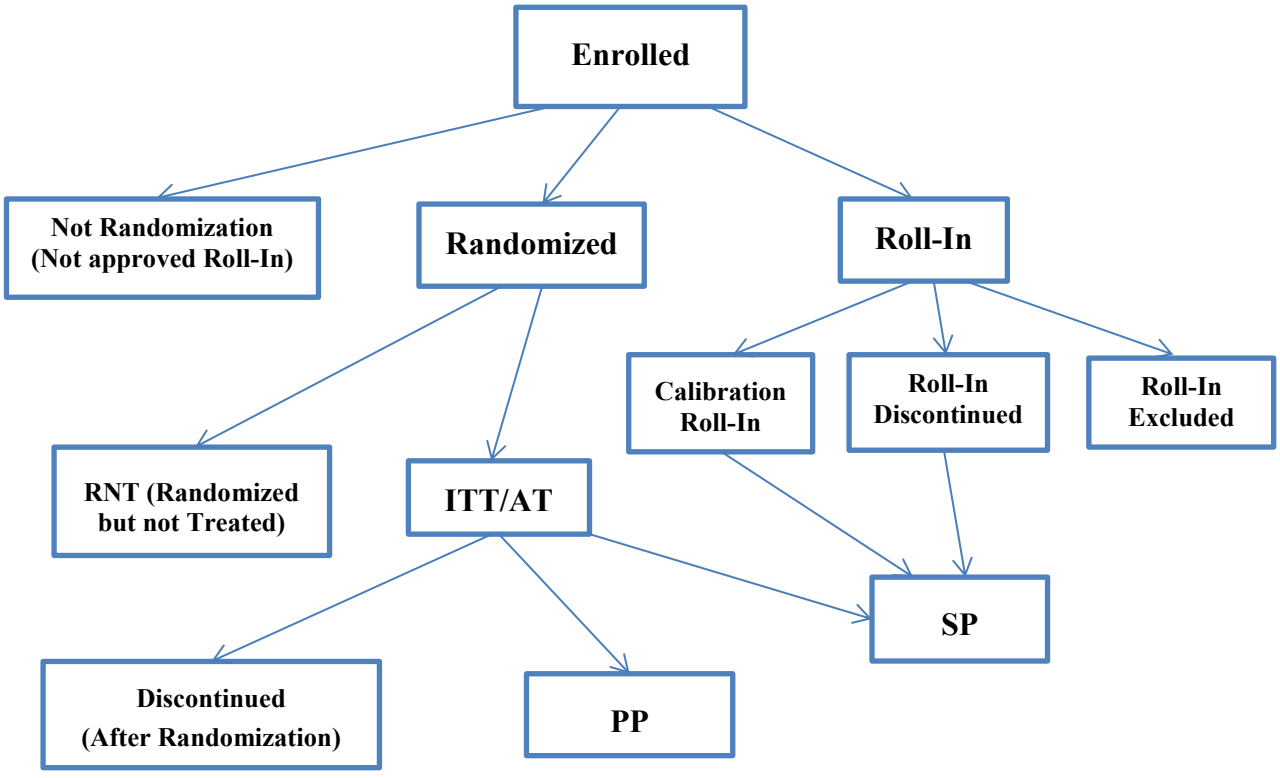

Figure 1: Subject Flowchart

Disposition of all enrolled subjects will be summarized. Listing per subjects' reasons of exclusion, discontinuation, withdrawal/early termination due to study close out, and lost to follow-up will be provided.

12.3 Demographics and Baseline Characteristics

Demographics data, including age, gender, race and ethnicity, will be summarized overall and by treatment group for the enrolled subjects, randomized subjects and roll-in subjects.

Baseline characteristics, including Medical History, Atrial Fibrillation History, CHADS2 score, Canadian Cardiovascular Society Severity in Atrial Fibrillation (CCS-SAF) scale, Failed AAD Medication History at screening, TTE Exam, Visualization of LA Thrombus assessment, and ECG, will be summarized overall and treatment group for all enrolled subjects, randomized subjects and roll-in subjects. Descriptive statistics for continuous and categorical variables will be presented.

12.4 Endpoint Analyses

Descriptive statistics and two-sided 95% confidence intervals will be presented for the safety data. Analyses of safety data will be performed in the proposed analysis populations excluding the subjects with missing outcomes.

12.4.1 *Primary Safety Endpoints*

The incidence of early-onset Primary Adverse Events is the percentage of patients with at least one primary adverse event with onset on Day 0 through Day 7 except for pulmonary vein (PV) stenosis and atrio-esophageal fistula that could occur greater than one week (7 days) post-procedure. The number of primary adverse events (PAE) and the number of subjects experiencing primary adverse events will be reported.

The primary safety outcomes will be presented in the SP, AT populations and for Calibration Roll-in subjects. Listing of PAEs will be provided for subjects in SP.

12.4.2 *Secondary Safety Endpoints*

- ***Incidence of AEs and Serious (Non-Primary) AEs during 12 Month Follow-up***

Incidence of Serious Non-Primary AEs and All AEs during the 12 months follow-up will be reported by coded AE categories in three timeframes (ablation to ≤7 days, >7 to 30 days post ablation and >30 days). AEs will be evaluated by causality and treatment groups using descriptive statistics.

The primary safety outcomes will be presented in the SP, AT populations and for Calibration Roll-in subjects. Listing of will be provided for subjects in the SP.

- ***PV Stenosis at 3 Months Post Ablation***

Incidence of PV narrowing 3 months post ablation (<50%, 50-70%, ≥70% diameter reduction in diameter of pulmonary vein from baseline CT/MRA scan) will be reported overall and by

ablation targets. The percent of subjects with PV narrowing for subjects undergoing an RF ablation procedure using nMARQ system will be presented descriptively.

The outcomes of 3-month PV narrowing will be presented in the ITT subjects in the nMARQ group and for Calibration Roll-in subjects.

- ***Incidence of AEs and Serious (Non-Primary) AEs during 2nd and 3rd Year Follow-up***

All AEs, including Serious Non-Primary AEs and Non-serious AEs, during the 2nd (366-730 days post the index procedure) and 3rd year (>730 days post the index procedure) follow-up period will be summarized by coded AE categories, causality, timeframes and treatment groups using descriptive statistics.

The outcomes of 2nd- and 3rd-year (S)AEs will be presented in the SP, AT populations and for Calibration Roll-in subjects. Listing will be provided for subjects in the SP.

12.4.3 *Other Endpoints / Assessments*

- ***Ablation Procedural***

Descriptive statistics of the number of index and repeat ablation procedures performed throughout the study will be reported. The number of index and repeat procedures will be summarized overall and by treatment group. The number of subjects undergoing repeat ablation will also be summarized by timeframe of <90, 91-365 and > 365 days post the index procedure.

The type of investigational catheter used in the index procedure will also be summarized for subjects in the SP overall and by treatment group and roll-in subjects.

The ablation procedure data will be presented in the SP.

- ***Device Malfunction***

The investigational device malfunction will be reported by type of study device, associated catalog number, lot number, and description of events. All enrolled subjects with each device malfunction category will be listed out. All malfunction will be reported for SP, including those occurred prior to the catheter insertion.

- ***Protocol Deviations***

The number of subjects reported protocol deviations and number of deviations occurred will be summarized by type of protocol deviation and sponsor adjudicated major/minor category. All enrolled subjects under each protocol deviation category will be listed out accordingly.

The following lists the pre-defined major/minor protocol deviation categories.

Major:

- Inclusion criteria #1, #2, #3, (version 4.1 of the protocol), #5
- All Exclusion are considered major (#1-27)
- The verification procedure of a 30 minute waiting period from the last RF application at a PV target is “NOT Done”

Minor:

- All other inclusion criteria are considered minor
- All non-major protocol deviations are considered minor

In additional to the protocol deviations captured by CRF, overall TTM compliance rate will be calculated as part of the assessment of the study protocol deviation. TTM compliances will be presented in the ITT population and for calibration roll-in subjects.

- ***Follow-up Duration***

Follow-up duration is defined as the number of days between the date of the index procedure and the date of subject completes/exits the study. The follow-up duration will be summarized and displayed by histogram. Listing of subjects' follow-up duration will be provided for all evaluable subjects.

12.5 Plans for Interim Analyses

The 1st interim analysis had been conducted when number of subjects in the ITT population reached 250. The 2nd interim analysis was not conducted due to the decision of early termination of the study. The memo of "Interim Analysis for 2nd Interim Look" (dated June 01, 2017) documented the request and the rational of ceasing the 2nd interim analysis.

Due to the early termination of the study, no further interim analyses will be performed to validate whether the enrollment should be terminated or not.

12.6 Handling of Missing data

Missing data will be queried for reasons and will not be imputed for the analysis for the final CSR.

12.7 Sensitivity Analyses

No sensitivity analysis will be performed for the final CSR.

12.8 Subgroup Analysis

No subgroup analysis by factors other than treatment group will be performed for the final CSR.

12.9 Assessment of Site Homogeneity

Site homogeneity will not be tested for the final CSR.

13.0 List of Tables, Figures and Listings

Please refer to the Appendix A for the table, figure and listing shells of the CSR.