SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Cardiac ablation percutaneous catheter, intended for treatment of symptomatic, drug refractory, recurrent, paroxysmal atrial fibrillation
Device Trade Name:	INTELLANAV STABLEPOINT™ Ablation Catheter & Force Sensing System on the RHYTHMIA HDX™ Mapping System
Device Procode:	OAD, OAE
Applicant's Name and Address:	Boston Scientific Corporation 4100 Hamline Ave North St. Paul, Minnesota 55112-5798
Date(s) of Panel Recommendation:	N/A
Premarket Approval Application (PMA) Number:	P150005/S074
Date of FDA Notice of Approval:	February 26, 2024

The original PMA P150005 for the Blazer Open-Irrigated Ablation Catheter was approved on February 24, 2016, and is indicated for cardiac electrophysiological mapping, delivering diagnostic pacing stimuli, and radiofrequency ablation of sustained or recurrent Type I Atrial Flutter in patients age 18 or older. The panel-track supplement P150005/S014 was approved on December 21, 2017, to expand the indications to include drug refractory, recurrent, symptomatic, paroxysmal atrial fibrillation (PAF) in patients age 18 years or older, when used with a compatible mapping system. The SSEDs to support the prior indications are available on the CDRH website and are incorporated by reference here. The current supplement was submitted to introduce a new model of the device called the INTELLANAV STABLEPOINT™ Ablation Catheter & Force Sensing System on the RHYTHMIA HDx™ Mapping System.

II. INDICATIONS FOR USE

The INTELLANAV STABLEPOINT Catheter, when used with a compatible Radiofrequency Controller and Irrigation Pump, is indicated for:

- Cardiac electrophysiological mapping
- Delivering pacing stimuli
- RF ablation of sustained or recurrent typical atrial flutter in patients age 18 or older
- Treatment of drug refractory, recurrent, symptomatic, Paroxysmal Atrial Fibrillation (PAF) in patients age 18 years or older, when used with a compatible mapping system

III. CONTRAINDICATIONS

The INTELLANAV STABLEPOINT Catheter is contraindicated for use:

- In patients with active systemic infection;
- In patients with a mechanical prosthetic heart valve through which the catheter must pass;
- In patients with conditions where insertion into or manipulation in the cardiac chambers is unsafe as these conditions (e.g., presence of intracardiac thrombus or myxoma, history of recent cardiac surgery with atriotomy, etc.) may increase the risk of systemic embolism or cardiac perforation;
- In patients who are unable to receive heparin or an acceptable alternative to achieve adequate anticoagulation;
- In patients who have vena cava embolic protection filter devices and/or known femoral thrombus who require catheter insertion from the femoral approach;
- In patients who are hemodynamically unstable;
- In patients with a contraindication to an invasive electrophysiology procedure where insertion or manipulation of a catheter in the cardiac chambers is deemed unsafe, such as but not limited to, a recent previous cardiac surgery (e.g., ventriculotomy or atriotomy, Coronary Artery Bypass Graft [CABG], PTCA/PCI/coronary stent procedure/unstable angina) and/or in patients with congenital heart disease where the underlying abnormality increases the risk of the ablation (e.g. severe rotational anomalies of the heart or great vessels);
- Via transseptal approach in patients with an intra-atrial baffle or a foramen ovale patch.
- Via retrograde transaortic approach in patients with a prosthetic aortic valve.

Do not use this device:

- With a long sheath less than 8.5F or a short introducer less than 8.5F
- In the coronary vasculature

The IntellaNav StablePoint Catheter Cable (RC03 and RC04) and IntellaNav StablePoint Connection Box do not have any specific contraindications themselves. Users should read and understand the specific indications, contraindications, warnings, and precautions included with IntellaNav StablePoint Ablation Catheter, RHYTHMIA HDx System and IntellaNav StablePoint Connection Box used in conjunction with the IntellaNav StablePoint Cable.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the INTELLANAV STABLEPOINT™ Ablation Catheter & Force Sensing System on the RHYTHMIA HDX™ Mapping System labeling.

V. DEVICE DESCRIPTION

The INTELLANAV STABLEPOINT™ Ablation Catheter ("IntellaNav StablePoint catheter" or "the catheter") & Force Sensing System on the RHYTHMIA HDX™ Mapping System ("Force Sensing System") is a single-use, disposable, bi-directional steerable, multi-electrode, open-irrigated radiofrequency (RF) ablation catheter. When used with a compatible RF controller and irrigation pump, it can be used to deliver RF energy to target locations on the endocardium. When used with a compatible mapping and navigation system, the catheter can be tracked in 3D space, display intracardiac electrograms and/or create electro-anatomical maps. An external recording system can also be used to display intracardiac electrograms or configure channels for delivering pacing stimuli. A compatible mapping and navigation system is also required for the feedback on contact force and local impedance via DIRECTSENSE technology. DIRECTSENSE is a software feature on the RHYTHMIA HDx Mapping System that provides a display of local impedance, which reflects tissue properties closest to the catheter distal electrode when enabled by a compatible BSC Ablation Catheter. The Force Computation Software Module is loaded on the RHYTHMIA HDx Mapping System, which performs the force visualization. In order to deliver radiofrequency energy, the IntellaNav StablePoint Catheter and Cable must be connected to a compatible RF generator and Irrigation Pump System via the Connection Box.

The catheter is only compatible with the Boston Scientific Corporation (BSC) Open-Irrigated (OI) Ablation System and the RHYTHMIA HDx Mapping System. The catheter connectivity is similar to that of existing BSC navigation-enabled catheters and includes the choice of two cables, along with a modified connection box, to connect the catheter to both the Maestro™ 4000 RF generator and the RHYTHMIA HDx Mapping System. The IntellaNav StablePoint Connection Box ("connection box") connects the catheter to both the Maestro™ 4000 RF Generator and the RHYTHMIA HDx Mapping System (Figure 1). The Maestro 4000 RF Generator and MetriQ™ Irrigation Pump do not require modification for compatibility with the catheter and therefore are out of scope of this Panel-Track Supplement.

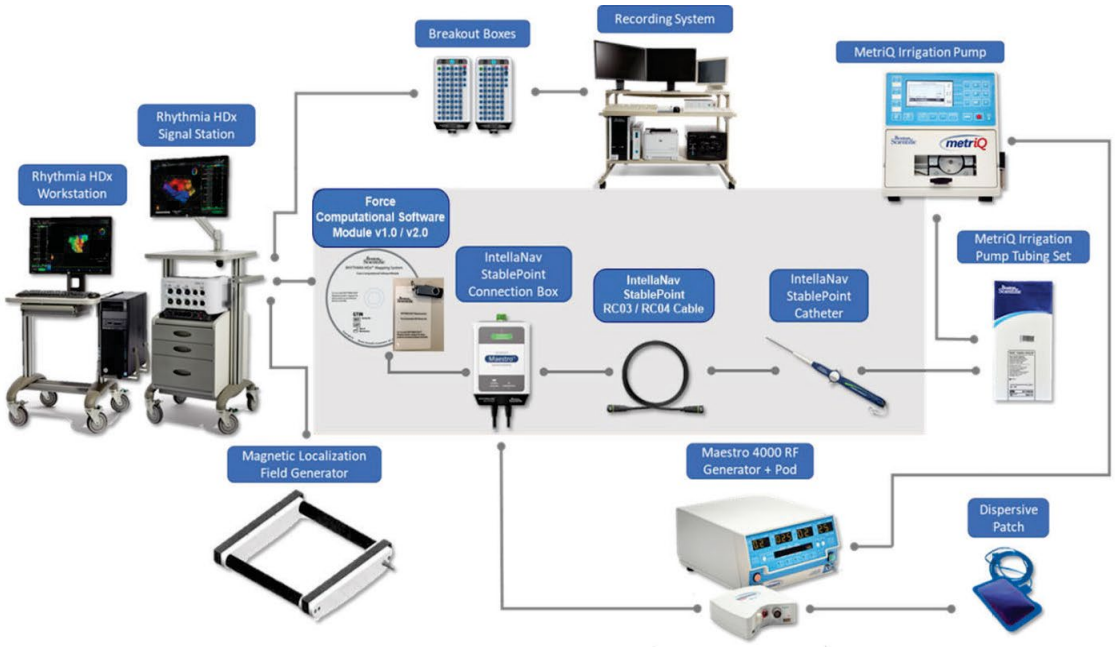


Figure 1: IntellaNav StablePoint System Connectivity Representation Diagram Using Maestro 4000

A. IntellaNav StablePoint Catheter

The catheter is a steerable, quadripolar, open-irrigated ablation catheter designed to deliver RF energy to its 4 mm tip electrode for cardiac ablation. The catheter shaft is 7.5F with 8F ring electrodes. The catheter is compatible with introducers or sheaths with a minimum inner diameter of 8.5F.

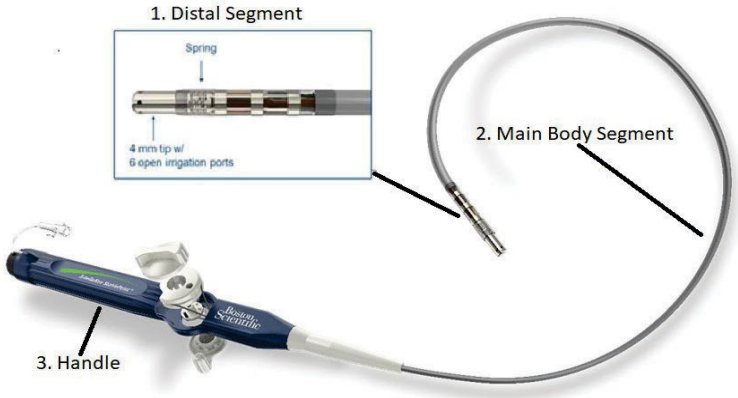


Figure 2: IntellaNav StablePoint Catheter

The catheter incorporates a position sensor for magnetic tracking and navigation when used with a compatible RHYTHMIA™ Mapping System. The catheter also includes force sensing technology embedded in the distal tip to transmit real-time feedback on the mechanical interaction between the tip electrode and myocardial tissue. Additionally, the catheter is enabled to measure changes in local dielectric properties in the proximity of the tip electrode to the myocardial tissue via DIRECTSENSE technology.

For ablation, the catheter is designed to be used with a commercially available RF controller, an irrigation pump and irrigation tubing set that meet the catheter flow rate requirements, a commercially available Connection Box, and a dispersive pad (indifferent electrode). For mapping, navigation, and visualization of force and DIRECTSENSE information, the catheter is designed to be used with a compatible RHYTHMIA HDx Mapping System and associated accessories.

The catheter incorporates an open-irrigated cooling mechanism through a tip that is partitioned into two chambers. The proximal chamber circulates normal saline (0.9%) within the tip to cool the proximal end of the tip electrode and mitigate overheating while the distal chamber allows the fluid to exit through six irrigation holes, thereby cooling the tip/tissue interface. A luer connection at the proximal end of the handle connects the catheter to the irrigation tubing set, allowing the irrigation pump to generate the flow of saline to the catheter. A thermocouple temperature sensor embedded in the tip provides feedback on the tip cooling.

The electrode segment comprises a tip electrode and three ring electrodes. All the electrodes can be used for recording intracardiac electrograms (EGMs) or delivering pacing stimuli from external systems. The tip electrode transmits RF energy for cardiac ablation. The catheter interfaces with standard RF controllers and recording

equipment through the Connection Box. The handle includes the electrical connector for the cable connection to the Connection Box.

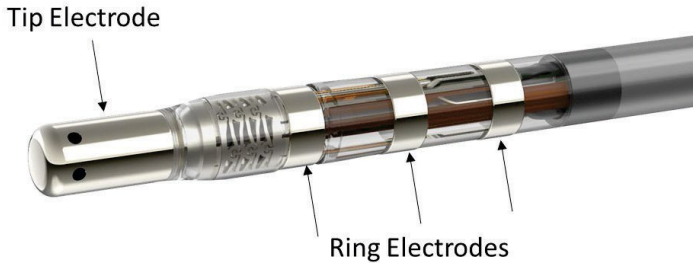


Figure 3: IntellaNav StablePoint Catheter Components

The catheter, when used with a compatible RHYTHMIA HDx Mapping System, provides a display of local bipolar impedance that measures the dielectric properties closest to the catheter tip electrode. This diagnostic measure can be used in conjunction with other diagnostic elements (e.g., electrogram amplitude, fluoroscopy, intracardiac echocardiography, and tactile feedback) to inform the user on stability and proximity of the catheter electrodes to the endocardial surface.

During the application of RF energy, the local impedance measure provides additional feedback on tissue response near the RF electrode as a result of RF energy delivery. During RF application, the impedance signal changes due to tissue heating; local impedance may not represent catheter proximity or stability, or relative position of the catheter tip-to-tissue.

During the application of RF energy, a compatible RHYTHMIA HDx Mapping System provides a measure of local impedance as a numerical value widget, a power bar graphic, a tip graphic in orange, and a real-time graph. The value widget is updated to display the change in local impedance from the onset of ablation. The change in local impedance is displayed in orange to match the other ablation color indicators and can be displayed as an absolute, relative, or percent value. Once RF energy is terminated, the real-time graph will continue to display an orange overlay to temporally indicate that ablation has occurred at previous data epochs.

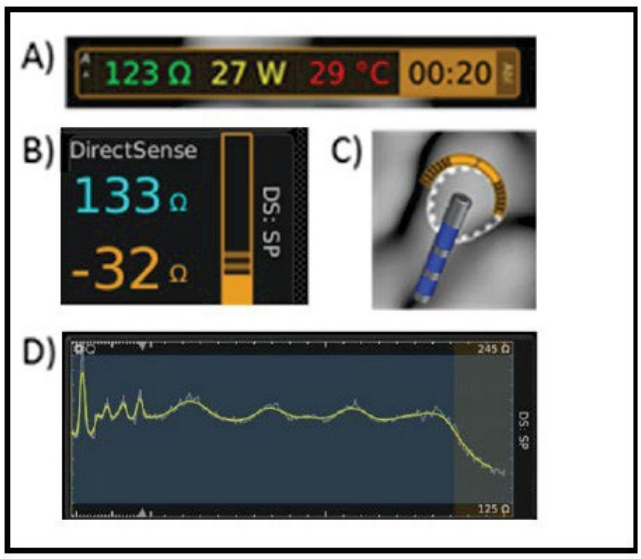


Figure 4: Local Impedance Elements during RF Ablation ((A) generator parameters widget; (B) numerical value (average impedance) widget during RF; (C) catheter tip graphic during RF; (D) local impedance vs. time trace during RF)

Changes in the local impedance during RF delivery require stable catheter position. Fluoroscopy or other visualization techniques such as echocardiography are used to verify catheter location during RF delivery. Incorrect catheter localization may lead to misinterpretation of the impedance measure and an incorrect clinical conclusion or patient injury.

A compatible RHYTHMIA HDx Mapping System provides the visualization of the force information in a similar set of widgets, including a catheter tip visualization, a force value widget, a force angle indicator, and a real-time force graph. The real-time force graph will also have an orange overlay during RF delivery that will persist over the segment that represents the ablation while those data are in the field of view. The average contact force and the variability of contact force can be used within the context of other additional parameters (e.g., catheter position, fluoroscopy, intracardiac electrograms, and tactile feedback) to aid in the position of the catheter prior to and during RF delivery.

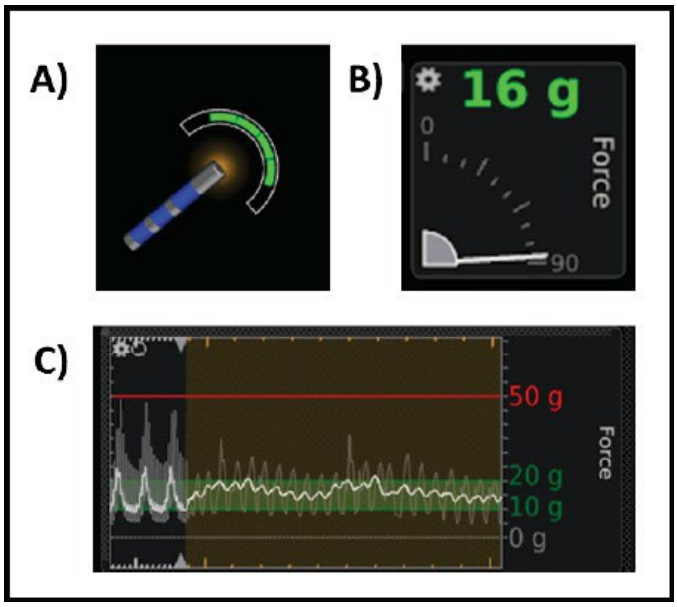


Figure 5: Visualization of Force on Compatible RHYTHMIA HDx Mapping System ((A) catheter tip visualization; (B) force value widget and force angle indicator; (C) force real-time graph with user defined range of interest and user defined high force threshold)

B. IntellaNav StablePoint Catheter Cable (RC03 and RC04)

The IntellaNav StablePoint Catheter Cable (RC03 and RC04) connects the IntellaNav StablePoint Catheter to the RHYTHMIA HDx Mapping System via the Connection Box. The cable transmits RF energy to the IntellaNav StablePoint Catheter and facilitates transmission of signals from the electrodes, force sensor, temperature sensors, location sensor, and catheter identifier. Both the RC03 and RC04 cables are 6.6-ft- (200 cm) long flexible electrical cable with identical 41-pin locking connectors on each end.

Figure 6: IntellaNav StablePoint Catheter Cable

C. IntellaNav StablePoint Connection Box

The IntellaNav StablePoint Connection Box (Connection Box) is a source finished medical device, designed for use solely with the IntellaNav StablePoint Catheter and the Maestro 4000 RF Generator, that provides a connection between the IntellaNav StablePoint Catheter, via the Cable, the generator, and the RHYTHMIA HDx Signal Station. The Connection Box routes intracardiac signals, location, and force information sensed by the ablation catheter to the mapping system and prevents RF energy from affecting catheter localization and other mapping system features. The Connection Box passes catheter tip temperature and catheter tip impedance information, as well as RF energy between the RF generator and ablation catheter and contains the hardware required for measuring the force from the sensors in the catheter.

Figure 7: IntellaNav StablePoint Connection Box

D. Force Computational Software Model

The Force Computation Software Module (FCM) is a software application, which runs on a computer inside the RHYTHMIA HDx Signal Station (SiS). The FCM reads the force data packets and performs a data integrity check to ensure the Connection Box data have not been compromised during transfer. When the FCM is installed, and a compatible IntellaNav StablePoint Catheter is connected to the RHYTHMIA HDx Mapping System, the force visualization features become available to the user. While force computation is performed by the FCM, force visualization is performed by the RHYTHMIA HDx software version 4.0 or greater.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the correction of symptomatic, drug refractory, recurrent, paroxysmal atrial fibrillation.

- Treatment with medicines that help control the rate and/or rhythm of the heart and other medicines that reduce the likelihood of clots forming (known as medical or pharmacologic therapy).
- Cardioversion to restore the heart's normal rhythm (with electrical shock or medicine).
- Implantable devices that control the rate of the heart.
- Implantable devices that reduce the likelihood of clots forming.
- Catheter ablation with other devices approved in the United States.

Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The INTELLANAV STABLEPOINT™ Ablation Catheter & Force Sensing System on the RHYTHMIA HDX™ Mapping System has been marketed in the European Union, Japan, Australia, and other countries. The INTELLANAV STABLEPOINT™ Ablation Catheter & Force Sensing System on the RHYTHMIA HDX™ Mapping System has not been withdrawn from the market in any country for any reason related to safety and effectiveness.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) associated with the use of the device.

- Pain or discomfort, for example:
  - Angina
  - Chest pain
  - Non-cardiovascular pain
- Cardiac arrest
- Death
- Hypertension
- Hypotension
- Infection/inflammation/exposure to biohazardous material
- Edema/heart failure/pleural effusion
- Procedural related side effects, for example:
  - Allergic reaction (including anaphylaxis)
  - Genitourinary complication
  - Side effects related to medication or anesthesia
  - Radiation injury/tissue burn
  - Renal failure/insufficiency
  - Vasovagal response
- Respiratory distress/insufficiency/dyspnea
- Arrhythmia (new or exacerbated)
- Conduction pathway injury (heart block, nodal injury, etc.)
- Nerve injury, for example:
  - Phrenic nerve injury
  - Vagal nerve injury
- Gastrointestinal disorders
- Vessel trauma, including:
  - Perforation
  - Dissection
  - Coronary artery injury
  - Vasospasm
  - Occlusion
  - Hemothorax
- Cardiac trauma, for example:
  - Cardiac perforation/cardiac tamponade/pericardial effusion
  - Valvular damage
  - Stiff left atrial syndrome
- Injury related to tissue damage and/or adjacent structures, for example:
  - Esophageal injury

    - Pulmonary injury
    - Catheter entrapment
- Fistula, for example:
    - Atrio-esophageal fistula
    - Bronchopericardial fistula
- Pulmonary vein (PV) stenosis and its symptoms, for example:
    - Cough
    - Shortness of breath
    - Fatigue
    - Hemoptysis
- Surgical and access complications, for example:
    - Hematoma/seroma
    - Arteriovenous (AV) fistula
    - Bleeding
    - Pseudoaneurysm
    - Pneumothorax
    - Residual atrial septal defect
- Injury due to embolism/thromboembolism/air embolism/foreign body embolism
    - Cerebrovascular Accident (CVA)/stroke
    - Transient Ischemic Attach (TIA)
    - Myocardial infarction
    - Neurological impairment and its symptoms, for example:
        - Cognitive changes, visual disturbances, headache, motor impairment, sensory impairment, and speech impairment
    - Pulmonary embolism
    - Asymptomatic cerebral embolism.

For the specific adverse events that occurred in the clinical study, please see Section X below.

IX. SUMMARY OF NON-CLINICAL STUDIES

For non-clinical testing, verification and validation were performed at the device, system, and software levels. Testing was performed to evaluate biocompatibility, sterility, packaging performance, and shelf-life. Tests were developed in accordance with FDA-recognized voluntary consensus standards, non-FDA-recognized consensus standards, and product specifications. The non-clinical tests performed were similar to those performed for the Blazer Open-Irrigated (OI) Catheter under https://www.accessdata.fda.gov/cdrh_docs/pdf15/P150005b.pdf and https://www.accessdata.fda.gov/cdrh_docs/pdf15/P150005S014B.pdf.

A. Laboratory Studies

Design Verification

Catheter and Cable

Table 1 – Design Verification Testing

Test Name	Description	Result
Visual Inspection, Deflection, and Contraction	To identify manufacturing defects or anomalies caused by preconditioning.	Pass
Electrical	To evaluate DC lead resistance of each ring electrode circuit and isolation of the ring electrodes.	Pass
Irrigation Flow Rate	To evaluate the flow characteristics of the catheter.	Pass
Loop Buckle Force	To quantify the force required to buckle the loop lumen.	Pass
Tip Stiffness	To evaluate the force required to pull the catheter when it is deflected.	Pass
Side Force	To quantify the side force generated by a deflected rotated catheter tip.	Pass
Catheter Soak	To simulate clinical usage.	Pass
Steering through Vascular Model	To evaluate catheter integrity during sheath insertions.	Pass
In-Bath Rotation and Deflection	To evaluate catheter integrity during manipulation.	Pass
Handle to Shaft Flexion Fatigue	To evaluate flexural reliability.	Pass
Catheter Initialization Check	To verify recognition on the CARTO 3 System.	Pass
Ablation Cycling	To evaluate catheter integrity following simulated ablation cycles.	Pass
Irrigation Flow Rate	To evaluate flow characteristics.	Pass
DC Resistance	To evaluate DC lead resistance of each ring electrode circuit and isolation of the ring electrodes.	Pass
Visual Inspection, Deflection, and Contraction	To identify manufacturing defects or anomalies caused by postconditioning.	Pass
Torque Test of Entire Catheter	To evaluate catheter integrity during rotation.	Pass
Tensile Test of Loop to Housing	To quantify the tensile strength required to break the full length of a catheter.	Pass
Tensile Test of Transition Joint of Soft Tip to Shaft	To quantify the tensile strength required to break the full length of a catheter.	Pass
Tensile Test of Transition Joint of Shaft to Handle	To quantify the tensile strength required to break the full length of a catheter.	Pass
Sidearm/Luer Hub Torque Test	To evaluate the torque resistance of the irrigation side arm.	Pass
Sidearm/ Luer Hub Pull Test	To evaluate the tensile strength of the irrigation side arm.	Pass

Voluntary Consensus Standards

The IntellaNav StablePoint Catheter and Force-Sensing System demonstrated conformity with the following FDA-recognized and non-recognized voluntary consensus standards.

- ISO 10993-1:2018
- ISO 10993-4:2017
- ISO 10993-5:2009
- ISO 10993-10:2021
- ISO 10993-11:2017
- ISO 10993-12:2021
- ISO 10993-18:2020
- ISO 10993-23:2021
- EN ISO 14155:2020
- IEC 60601-1:2005 + A1:2012
- IEC 60601-1-2:2014
- IEC 60601-2-2:2017
- EN 55011:2009
- CISPR 11:2009 + A1:2010
- EN ISO 14644-1:2015
- EN ISO 14644-2:2015
- EN 17141:2020
- EN 1041:2008 + A1:2013
- EN ISO 15223-1:2021
- ISO 20417 COR:2021
- ANSI/AAMI/ISO 11607-1:2019
- ANSI/AAMI/ISO 11607-2:2019
- EN ISO 13485:2016/AC:2016/AC:2018
- EN ISO 14971:2019
- EN ISO 10555-1:2013 + AMD1:2017
- EN ISO 80369-1:2018
- EN ISO 80369-7:2021
- ISO 11135:2014 + AMD:2018
- ISO 11138-1:2017
- ISO 11138-2:2017
- EN 556-1:2001 + COR:2006
- EN ISO 10993-7:2008 + A1:2022
- EN ISO 11737-1:2018 + A1:2021
- EN ISO 11737-2:2020
- ISO 17664-2:2021
- ISO 14161:2015

- ISO 17665-1:2006(R)2013
- ANSI/AAMI ST72:2019
- ASTM D4169:2016
- ASTM F1886:2016
- ASTM F 88/F88M:2015
- ASTM F1980:2016
- ASTM F2096:2019
- IEC 60601-1-6:2013
- ISO 62366

B. Animal Studies

Pre-clinical animal studies were performed to evaluate characteristics of the IntellaNav StablePoint Catheter and Force-Sensing System that could not be evaluated through bench or clinical studies.

Design Validation & Usability

In vivo Intracardiac study in swine model

Demonstrated performance of the Force Sensing System (i.e., IntellaNav StablePoint Catheter, IntellaNav StablePoint Catheter Cable, IntellaNav StablePoint Connection Box and Force Computation Software Module) through evaluation in a simulated use environment and when used with RHYTHMIA HDx Mapping System, Boston Scientific Corporation Open-Irrigated (BSC OI) Ablation System and commercial pacing and recording systems in support of predefined Design Validation requirements. Tested performance included catheter manipulation in the intracardiac space (with and without a steerable sheath), pacing, acquiring intracardiac electrograms, measuring force and local impedance, and ablating at various RF powers and durations.

- Validated system connectivity
- Validated the impact of new features on existing functionality (e.g. handling, intracardiac pacing, sensing/electrogram fidelity during RF)
- Validated compatibility with associated systems and accessories (e.g. recording system, mapping system)
- N=8 independent Clinical Evaluators

Usability: *In vivo* Intracardiac study in swine model
Demonstrated that the Force Sensing System, as designed, can be used safely and effectively by people who are representative of the intended users under expected use conditions for essential and critical (high-risk) tasks.

- Assessment of the user interpretation of the force and local impedance feedback and the effect of the added parameters on workflow during simulated clinical use
- N=8 independent Clinical Evaluators + N=8 independent BSC RHYTHMIA Mapping Specialists

Safety & Performance

***In vivo* GLP Chronic Study**
Assessed the safe use of the Force Sensing System when used to create RF ablation lesions in the right atrium (RA) and left atrium (LA) at clinically relevant and upper limit RF ablation parameters through the occurrence of adverse events, complications, and collateral damage.

- 30-day study; 8 canines; 2 Clinical Evaluators with no char/coagulum observed, no pulmonary vein stenosis, deaths, or major adverse events attributable to the test articles.
- Demonstrated ability to maintain stability during RF and use local impedance and contact force information during standard workflow.

***Ex vivo* steam pop evaluation with Cardiac Tissue**
Demonstrated clinical equivalence in the rate of steam pops between the IntellaNav StablePoint and IntellaNav OI Catheters when performing RF ablation using the BSC OI Cardiac Ablation System. The study characterized therapeutic performance across a range of applied force, power and duration using freshly explanted porcine hearts as the substrate.

Lesion Formation in a Swine Thigh Muscle Preparation
Demonstrated clinical equivalence of lesion formation between the IntellaNav StablePoint Catheter and the IntellaNav OI Catheter when performing RF ablation using the BSC OI Cardiac Ablation System on thigh muscle preparation of 5 swine.

- All data collection and reporting requirements for incidence of steam pop, incidence of char/coagulum, model-specific and RF ablation parameters, catheter tip and lesion images animal health and physiological data were met for this study.

C. Additional Studies

N/A

X. SUMMARY OF PRIMARY CLINICAL STUDY(IES)

The applicant performed a clinical study titled Clinical Evaluation of the StablePoint Catheter and Force-Sensing System for Paroxysmal Atrial Fibrillation (NEwTON-AF, ClinicalTrials.gov Registration: NCT04580914) to establish a reasonable assurance of safety and effectiveness of percutaneous catheter ablation with the INTELLANAV STABLEPOINT™ Ablation Catheter & Force Sensing System on the RHYTHMIA HDX™ Mapping System for symptomatic, drug refractory, recurrent paroxysmal atrial fibrillation in the US, Canada, Europe, and Asia Pacific under IDE G200215. Data from this clinical study were the basis for the PMA approval decision. Data from studies conducted to support P150005 (Table 2) were used to support the design of the pivotal study. A summary of the clinical study is presented below.

Table 2: Previous studies conducted to support P150005 and P150005/S014

Clinical Study	Study Design	Objective	Number of Sites	Number of Subjects	Indication
BLOCk-CTI (NCT01253200)	Prospective, multi-center, single blinded, 1:1 randomized	Demonstrate that the safety and effectiveness of the Blazer OI catheter is non-inferior to the safety and effectiveness of the control catheters for treatment of Type 1 atrial flutter	26	302	Type 1 Atrial Flutter
ZERO-AF (NCT01687166)	Prospective, multi-center, single blinded, 1:1 randomized	Demonstrate that the safety and effectiveness of the Blazer OI Catheter is non-inferior to the safety and effectiveness of the control catheters for treatment of PAF	38	398	Paroxysmal Atrial Fibrillation

A. Study Design

Patients were treated between April 12, 2021, and June 3, 2023. The database for this Panel-Track Supplement reflected data collected through June 30, 2023. 321 patients were enrolled, and 299 patients were treated. There were 47 investigational sites, 45 of which enrolled at least 1 subject.

The study was a multi-center, global, prospective, single-arm clinical study to establish the safety and effectiveness of the INTELLANAV STABLEPOINT™ Ablation Catheter & Force Sensing System on the RHYTHMIA HDX™ Mapping System in the treatment of symptomatic, drug refractory, recurrent, paroxysmal AF.

A pre-specified 6-month endpoint analysis was conducted on October 24, 2022, after all 299 Treatment subjects completed 30 days of follow-up and at least 183 Treatment subjects completed 6 months of follow-up. A 12-month analysis was performed after

all Treatment subjects completed 12 months of follow-up or exited the study. The Panel Track Supplement was approved on the basis of the 12-month analysis. Core Laboratories (Core Labs) were used to evaluate event monitor recordings, 24-hour Holter Monitor recordings, and 12-lead ECG tracings.

1. Clinical Inclusion and Exclusion Criteria

   Enrollment in the NEwTON-AF study was limited to patients who met the following inclusion criteria:

   1. History of recurrent symptomatic Paroxysmal Atrial Fibrillation (PAF), defined as atrial fibrillation (AF) that terminates spontaneously or with intervention (either procedure or drug therapy) within seven days of onset. Minimum documentation includes the following:
      - a physician's note indicating recurrent self-terminating atrial fibrillation (AF) which includes at least two symptomatic AF episodes in the patient's history within the last 6 months prior to enrollment, and
      - any electrocardiographically documented AF episode within 12 months prior to enrollment.
   2. Subjects who are eligible for an ablation procedure for PAF according to 2017 HRS expert consensus statement on catheter ablation of atrial fibrillation;
   3. Subjects refractory or intolerant to at least one class I or class III antiarrhythmic medication or contraindicated to any class I or III medications;
   4. Subjects who are willing and capable of providing informed consent;
   5. Subjects who are willing and capable of participating in all testing associated with this clinical investigation at an approved clinical investigational center;
   6. Subjects whose age is 18 years or above, or who are of legal age to give informed consent specific to state and national law.

   Patients were not permitted to enroll in the NEwTON-AF study if they met any of the following exclusion criteria:

   1. Subjects with New York Heart Association (NYHA) Class III or IV heart failure < 180 days prior to enrollment.
   2. Left atrial diameter > 5.0 cm or left atrial volume >50 ml/m² indexed based on the most recent echocardiography.
   3. Left ventricular ejection fraction < 35% based on the most recent echocardiogram.
   4. Continuous AF lasting longer than seven (7) days.
   5. Subjects who have undergone any previous left atrial cardiac ablation (RF, Cryo, surgical).

6. Atrial fibrillation secondary to electrolyte imbalance, thyroid disease, or reversible or non-cardiac cause.
7. Subjects who have undergone any cardiac ablation or any surgery within 30 days prior to enrollment.
8. Currently implanted with a pacemaker, ICD, CRT device, or an implanted arrhythmia loop recorder.
9. Active systemic infection.
10. Unstable angina or ongoing myocardial ischemia.
11. Myocardial Infarction (MI) within 90 days prior to enrollment.
12. Evidence of myxoma, left atrial thrombus or intracardiac mural thrombus.
13. Previous cardiac surgery (i.e., ventriculotomy, atriotomy, CABG, PTCA, PCI, coronary stenting procedures) ≤90 days prior to enrollment.
14. Severe valvular disease, including mechanical prosthetic mitral or tricuspid heart valves (patients with successful mitral valve repair allowed – annular ring constitutes repair).
15. Any prior history of documented cerebral infarct, TIA or systemic embolism [excluding a post-operative deep vein thrombosis (DVT)] <180 days prior to enrollment.
16. Moderate or severe mitral stenosis (severity assessed on the most recent TTE ≤180days prior to enrollment. Defined as pulmonary artery systolic pressure >30 mmHg).
17. Presence of left atrial appendage closure device.
18. Interatrial baffle, closure device, patch, or patent foramen ovale (PFO) occluder.
19. Subjects who, in the judgment of the investigator, have a life expectancy of less than two (2) years.
20. Women of childbearing potential who are, or plan to become, pregnant during the time of the study (method of assessment upon investigator's discretion).
21. Amiodarone use within 60 days prior to enrollment.
22. Any carotid stenting or endarterectomy.
23. Stage 3B renal disease or higher (estimated glomerular filtration rate, eGFR <45 mL/min).
24. Known coagulopathy disorder (e.g., von Willebrand's disease, hemophilia).
25. Any known contraindication to an AF ablation.
26. Any known contraindication for anticoagulation (e.g., patients unable to receive heparin or an acceptable alternative to achieve adequate anticoagulation).
27. Vena cava embolic protection filter devices and/or known femoral thrombus that prevents catheter insertion from the femoral approach.
28. Known sensitivity to contrast media (if needed during the procedure) that cannot be controlled with pre-medication.
29. Rheumatic Heart Disease
30. Presence of intramural thrombus, tumor or other abnormality that precludes vascular access, or manipulation of the catheter.

31. Subjects unable or unwilling to complete follow-up visits and examinations for the duration of the clinical study.
32. Subjects who are currently enrolled in another investigational study or registry that would directly interfere with the current study, except when the subject is participating in a mandatory governmental registry, or a purely observational registry with no associated treatments; each instance must be brought to the attention of the sponsor to determine eligibility.

2. Follow-up Schedule

All patients were scheduled to return for follow-up examinations at pre-discharge, 1-month, 3-months, 6-months, and 12-months postoperatively.

Preoperatively, a baseline assessment was performed within 30 days of enrollment and before the index procedure. Data collected during the baseline assessment included date, eligibility criteria, demographic data (as allowed), physical assessment, cardiovascular/pulmonary exam (including lung and heart auscultation), medical history, cardiac assessments, laboratory blood tests, pregnancy test, 12-lead electrocardiogram (ECG), quality of life questionnaires (AFEQT and EQ-5D-5L), National Institutes of Health Stroke Scale (NIHSS), antiarrhythmic drug (AAD) history, current AAD and anticoagulation regimen, reportable adverse events, and protocol deviations.

Postoperatively, the objective parameters measured during the study included, as appropriate, physical assessment, quality of life questionnaires, NIHSS, cardiac computed tomography (CT) or magnetic resonance imaging (MRI) to assess pulmonary vein (PV) stenosis), neurology consultation, echocardiography, 12-lead ECG, phrenic nerve palsy assessment, 24-hour Holter monitor, arrhythmia/event monitor, documentation of intervention for AF/atrial tachycardia (AT)/atrial flutter (AFL), device deficiencies, medications, adverse events, and protocol deviations. Adverse events and complications were recorded at all visits.

Table 3: Previous studies conducted to support P150005 and P150005/S014

				Blanking Period			Effectiveness Evaluation Period			Other	
Procedure/Assessment	**ENROLLMENT**	**BASELINE**	**INDEX PROCEDURE** (Day 0)	**PRE-DISCHARGE** (0-7 days)	**1-MONTH FOLLOW-UP** (30± 10 days)	**REPEAT PROCEDURE** (:S 90 days)	**03-MONTH FOLLOW-UP** (91± 14 days)	**06 MONTH FOLLOW-UP** (180 ± 30 days)	**12 MONTH FOLLOW-UP** (365 ± 30 days)	**UNSCHEDULED FOLLOW-UP**	**REPEAT PROCEDURE** (> 90 days)
Informed Consent	X										
Eligibility Criteria	X	X	X								
Pregnancy Test, if necessary		X									
Demographics		X									
Medical history		X									
Physical Assessment		X		X	X		X	X	X	X	
Blood Tests		X[1]									
Cardiovascular/Pulmonary Exam		X		X	X						
Quality of Life Questionnaires (EQ-5D-5L and AFEQT)		X					X[7]	X[7]	X[7]		
NIH Stroke Scale (NIHSS)		X		X[6]		X[6]					X[6]
Cardiac CT or MRI to assess PV diameter/stenosis		X		X[5]	X[5]		X[5]	X[5]	X[5]	X[5]	
Neurology Consultation				X[4]		X[4]					X[4]
Echocardiography to assess cardiac size and function		X[2]									
Screening for LA thrombus (TEE/ICE)		X[3]	X[3]			X[3]					X[3]
Procedural Data			X			X					X
RHYTHMIA HDx Export (Electronic Case Data)			X			X					X
12-Lead ECG		X	X	X	X	X	X	X	X	X	X
Phrenic Nerve Palsy Assessment				X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]	X[8]
Holter Monitor (24H)								X	X		
Arrhythmia/Event Monitor				X	X		X	X	X	X	
Documentation of intervention AF/AT/AFL (if any)					X	X	X	X	X	X	X
Device Deficiency Assessment			X			X					X
Medications (AAD/Anticoagulants)	X	X	X	X	X	X	X	X	X	X	X
Adverse Events Assessment	X	X	X	X	X	X	X	X	X	X	X
Protocol Deviations	X	X	X	X	X	X	X	X	X	X	X

Abbreviations: D = day(s), H = hour(s), NIH = National Institutes of Health, ECG = electrocardiogram, M = Month, TTE = trans-thoracic echocardiogram, TEE = trans-esophageal echocardiogram, CT = Computed Tomography, MRI = Magnetic Resonance Imaging

[1]Blood tests up to 90 days prior to enrollment
[2]TTE/TEE only required if data not available within 180 days prior to enrollment
[3] TEE within 48 hours prior to the index procedure or ICE during the procedure.
[4] Neurology consult was only required if NIHSS scale worsened from the previous assessment. If it is suspected the patient experienced a new cerebral ischemic event, a cerebral vascular imaging/DW-MRI scan was required
[5]Cardiac CT/MRI scan was considered post-procedure if PV stenosis was suspected.
[6]NIHSS at Pre-Discharge must be performed between Day 1 and Day 7 after the procedure and completed by a NIHSS certified administer.
[7]Quality of Life Instruments (AFEQT and EQ-5D-5L) were highly recommended prior to the remaining clinical assessments
[8]Phrenic Nerve Palsy Assessment at discharge and at follow-up visits was only applicable for subjects who had phrenic nerve palsy detected during the index or repeat procedure. Subjects were assessed per standard of care.

3. Clinical Endpoints

Primary Safety Endpoints

With regards to safety, the study included Primary Safety Endpoints at 30 days and 12 months.

The Primary Safety Endpoint at 30 days consisted of the following acute primary safety endpoint events, counted through 7 days post-index procedure or hospital discharge, whichever was later, unless denoted as an event counting through 30 days post-index procedure.

- Death
- Myocardial infarction (MI)
- Vagal Nerve Injury/Gastroparesis
- Transient ischemic attack (TIA)
- Stroke/Cerebrovascular accident (CVA)
- Thromboembolism
- Pericarditis
- Cardiac tamponade/perforation*
- Pneumothorax
- Major vascular access complications
- Pulmonary edema/heart failure
- AV block**
- Atrial esophageal fistula*
- Severe pulmonary vein stenosis (70% reduction in the diameter of the PV or PV branch from baseline)*

**Atrial esophageal fistula, cardiac tamponade/perforation and severe pulmonary vein stenosis occurring up to 30 days post-index-procedure will count as primary safety endpoint events*
***AV block not attributable to medication effect or vasovagal reaction.*

The endpoint was evaluated by the primary safety event-free rate at 30-days post-procedure, which was assessed at the time of the 6-month analysis.

The Primary Safety Endpoint at 12 months consisted of the following acute primary safety endpoint events, counted through 7 days post-index procedure or hospital discharge, whichever was later, unless denoted as an event counting through 30 days or 12 months post-index procedure.

- Death
- Myocardial infarction (MI)
- Vagal Nerve Injury/Gastroparesis
- Transient ischemic attack (TIA)
- Stroke/Cerebrovascular accident (CVA)
- Thromboembolism
- Pericarditis
- Pneumothorax
- Major vascular access complications
- Pulmonary edema/heart failure
- AV block
- Cardiac tamponade/perforation*
- Atrial esophageal fistula**
- Severe pulmonary vein stenosis (≥70% reduction in the diameter of the PV or PV branch from baseline)**
- Persistent phrenic nerve palsy**

**Counted through 30 days post-index procedure*
***Counted through 12 months post-index procedure*

Hypothesis

- Ho: The primary safety endpoint event-free rate at 30-days post procedure ≤90%
- Ha: The primary safety endpoint event-free rate at 30-days post procedure >90%

Analysis Methods

The 30-day primary safety event-free rate was calculated using Kaplan-Meier methodology. Subjects who withdrew from the study prior to 30 days without experiencing an event were censored on the date of their last study visit. The 95% one-sided lower confidence limit of the observed safety event-free rate at 30 days was compared to the performance goal of 90%. The lower confidence limit was calculated as the pointwise confidence limit using the log-log methodology.

Primary Effectiveness Endpoints

With regards to effectiveness, the study included Primary Effectiveness Endpoints at 6 months and 12 months.

Acute Procedural Success

Acute Procedural Success was defined as a subject that successfully had confirmed pulmonary vein isolation, by demonstration of entrance block at a minimum and no evidence of exit conduction with the study catheter only. This endpoint was assessed at 6 months.

Hypothesis

- Ho: The acute procedural success rate ≤92%
- Ha: The acute procedural success rate >92%

Analysis

The 97.5% one-sided Clopper-Pearson lower confidence limit of the observed acute procedural success rate was calculated. If the lower confidence limit was greater than the performance goal of 92%, the null hypothesis was rejected.

Primary Effectiveness at 6 Months and 12 Months

The primary effectiveness endpoint at 6 and 12 months consisted of endpoint events monitored according to the schedule discussed above.

Hypothesis

- Ho: The primary effectiveness event-free rate ≤60%
- Ha: The acute procedural success rate >60%

Primary effectiveness endpoint events included the following:

- Acute procedural failure:
    - Failure to achieve acute procedural success in the index procedure or in a repeat procedure during the blanking period.
    - Acute procedural success is defined as the achievement of electrical isolation of all PVs using the IntellaNav StablePoint Catheter only. Electrical isolation of a PV is demonstrated by entrance block after a 20-minute waiting period. If exit block testing is performed, the PV will only be considered as isolated if both entrance and exit block testing are successful.
- Use of amiodarone post-index procedure
- Use of non-study ablation catheter in the index procedure or in a repeat procedure during the blanking period
- More than one repeat procedure during the blanking period (90 days post-index procedure)
- Surgical ablation of Atrial Fibrillation (AF)/Atrial Tachycardia (AT)/Atrial Flutter (AFL) post-index procedure

- Documented AF, or new onset of AFL or AT between 91 days and 183* days postindex procedure captured by one of the following methods:
    - ≥30 seconds in duration recording from the study-specific event monitor or Holter monitor
    - ≥10 seconds 12-lead electrocardiography (ECG)
- Any of the following interventions for AF, or new onset of AFL or AT between 91 days and 183 days post-index procedure:
    - Repeat procedure
    - Electrical and/or pharmacological cardioversion
    - Prescribed any AAD (AADs for endpoint will consist of all Class I/III, including Amiodarone, and any Class II/IV medications taken for control of AF/AT/AFL recurrence.

Analysis

The Kaplan-Meier (KM) 6 month (183-day) primary effectiveness event-free rate was calculated using all available data at the time of the 6-month analysis. This analysis was pre-specified to occur when 299 Treatment subjects had been enrolled and completed their 30-Day follow-up and at least 183 Treatment subjects had completed their 6-month follow-up. Event-free subjects who withdrew from the study or died prior 6 months due to a device- or procedure-related adverse event were considered to have an endpoint event at the time of study exit. Subjects who withdrew from the study or died prior to 6 months without experiencing an event, as well as event-free subjects who were still active in the study at the time of the 6-month analysis snapshot, were censored on the date of their last study visit or arrhythmia/event monitor use, whichever was later. The 97.5% one-sided lower confidence limit of the observed 6-month primary effectiveness event-free rate was compared to the performance goal of 60%. The lower confidence limit was calculated as the pointwise confidence limit using the log-log methodology. The same methodology was used to calculate the primary effectiveness event-free rate at 12 months. The 12-month primary effectiveness event-free rate was used to support approval of the Panel Track Supplement.

Primary effectiveness events at 6 and 12 months were defined as:

- Acute procedural failure
    - Failure to achieve acute procedural success in the index procedure or in a repeat procedure during the blanking period.
    - Acute procedural success was defined as the achievement of electrical isolation of all PVs using the catheter only. Electrical isolation of a PV is demonstrated by entrance block after a 20-minute waiting period. If exit block testing was performed, the PV was only considered as isolated if both entrance and exit block testing was successful.
- Use of amiodarone post-index procedure
- Use of non-study ablation catheter in the index procedure or in a repeat procedure during the blanking period.

- More than one repeat procedure during the blanking period (90 days post-index procedure)
- Surgical ablation of AF/AT/AFL post-index procedure
- Documented atrial fibrillation, or new onset of atrial flutter or atrial tachycardia between 91 days and 183 days post-index procedure captured by one of the following methods:
    - ≥30 seconds in duration from the study specific event monitor or Holter monitor
    - ≥10 second 12-lead ECG
- Any of the following interventions for atrial fibrillation, or new onset atrial flutter or atrial tachycardia between 91 days and 183 days post-index procedure:
    - Repeat procedure
    - Electrical and/or pharmacological cardioversion
    - Prescribed any AAD*

**AADs for endpoint will consist of all Class I/III, including amiodarone, and any Class II/IV medications taken for control of AF/AT/AFL recurrence.*

B. Accountability of PMA Cohort

At the time of database lock, of 321 patients enrolled in the PMA study, 299 patients completed the index procedure, and 288 patients were available for analysis at the completion of the study, the 12-month post-operative visit.

Table 4 – Study Cohort Accountability

		Visit Completed*			
Visit	**Overall Compliance**	**In Window**	**Early**	**Late**	**Missed**
Pre-Discharge	299/299 (100%)	299 (100%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
1 Month Follow-Up	295/297 (99.3%)	273 (91.6%)	3 (1.0%)	19 (6.4%)	2 (0.7%)
3 Month Follow-Up	289/296 (97.6%)	260 (87.5%)	3 (1.0%)	26 (8.8%)	7 (2.4%)
6 Month Follow-Up	292/296 (98.6%)	273 (92.2%)	2 (0.7%)	17 (5.7%)	4 (1.4%)
12 Month Follow-Up	288/291 (99.0%)	262 (90.0%)	2 (0.7%)	24 (8.2%)	3 (1.0%)
Total	**1463/1479 (98.9%)**	**1367 (92.3%)**	**10 (0.7%)**	**86 (5.8%)**	**16 (1.1%)**

**Results in these columns provide the percentage of visits out of all subjects active in the study beyond the visit window.*

Table 5 – Overall 12-lead ECG and 24-hour Holter Compliance

Visit	12-Lead ECG Compliance	24-Hour Holter Monitor Completion
3 Month Follow-Up	97.2% (281/289)	Not required
6 Month Follow-Up	97.9% (286/292)	94.2% (275/292)
12 Month Follow-Up	98.6% (284/288)	92.4% (266/288)
Unscheduled Follow-Up	50.0% (4/8)	Not required
Total	**97.5% (855/877)**	**93.3% (541/580)**

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for a pivotal, single-arm, catheter ablation study performed in the US.

Table 6 – Study Population Demographics

Characteristic	Measurement	Result
Age at Enrollment (years)	N	299
	Mean ± SD	62 ± 12
	Range	19-85
Sex [N (%)]	Male	181 (60.5)
	Female	118 (39.5)
Ethnicity Hispanic or Latino [N (%)]	Hispanic or Latino	5 (1.7)
Race* [N (%)]	Native American	0 (0.0)
	Asian	48 (16.3)
	Black	3 (1.0)
	Pacific Islander	0 (0.0)
	White	244 (83.0)
	Other	1 (0.3)
	Race Undisclosed	5 (1.7)

**Subjects may contribute to more than one category*

Table 7 – Study Population Baseline Parameters

Characteristic	Measurement	Result [N (%)]
Cardiac Disease History	None	127 (42.5)
	Ischemic Cardiomyopathy	1 (0.3)
	Non-ischemic Cardiomyopathy	8 (2.7)
	Myocardial Infarction	3 (1.0)
	Angina Pectoris	12 (4.0)
	Congenital Heart Disease	1 (0.3)
	Congestive Heart Failure	16 (5.4)
	Cerebrovascular Disease	4 (1.3)
	Peripheral Vascular Disease	8 (2.7)
	Hypertension	131 (43.8)
	Pulmonary Hypertension	8 (2.7)
	Dyslipidemia	93 (31.1)
	Pulmonary Embolism	4 (1.3)
	DVT	6 (2.0)
	Other Cardiovascular Disease	17 (5.7)
Neurological Medical History	None	287 (96.0)
	Carotid Artery Disease	2 (0.7)
	TIA	7 (2.3)
	CVA	3 (1.0)
Cardiac Procedure History	None	269 (90.0)
	PTCA	9 (3.0)
	Stent	15 (5.0)
	CABG	5 (1.7)
	Pacemaker/ICD/CRT	0 (0.0)
	Cardiac Valve	0 (0.0)
	LAAC	1 (0.3)
	PFO Intervention	0 (0.0)
	ASD Intervention	0 (0.0)
	Heart Transplant	0 (0.0)
	Other Cardiovascular Procedure*	10 (3.3)

**Other cardiovascular procedures included: cardiac catheterization (5), cardioversion (3), stress test (1), and aortic repair (1)*

Table 8 – Study Population Baseline Parameters

Characteristic	Measurement	Result [N (%)]
Ventricular Arrhythmia History	None	264 (88.3)
	Ventricular Tachycardia	15 (5.0)
	Ventricular Fibrillation	0 (0.0)
	Other Ventricular Arrhythmia	25 (8.4)
Atrial Arrhythmia History	Atrial Fibrillation	299 (100.0)
	Atrial Tachycardia	23 (7.8)
	Atrial Flutter	95 (31.8)
	Type 1	95 (31.8)
	Other Atrial Arrhythmia	18 (6.0)
Brady Arrhythmia History	None	183 (61.2)
	Sinus Bradycardia	107 (35.8)
	Sinus Node Dysfunction	6 (2.0)
	Sick Sinus Syndrome / Chronotropic Incompetence	4 (1.3)
	Sinus Arrest	3 (1.0)
	AV Block 1	19 (6.4)
	AV Block 2	2 (0.7)
	AV Block 3	0 (0.0)
	Other Brady Arrhythmia	1 (0.3)
Cardiac Ablation History	None	281 (94.0)
	Any Left Atrial Ablation	0 (0.0)
	Any Cardiac Ablation	18 (6.0)
Previous Ablation Arrhythmia*	Typical AFL (CW or CCW)	10 (56)
	Atrio-Ventricular Nodal Reentrant Tachycardia (AVNRT)	4 (22)
	Other (Not Left-Sided)**	3 (17)
	Atypical AFL	2 (11)
	Non-AFL Reentrant Atrial Tachycardia	1 (6)

**Subjects may contribute to more than one category.*
*** Other previous ablation included: Wolf-Parkinson White, SVT, and one site reported "CAG showed patent coronary arteries" and was queried for correction*

D. Safety and Effectiveness Results

1. Safety Results

The analyses of safety at 30 days and 12 months were based on all treatment and attempt subjects. Adverse events are reported in Table 10.

Primary Safety Endpoint at 30 Days

299 subjects were available for the primary safety endpoint at 30 days evaluation. The key safety outcomes for this study are presented below in Table 9.

Table 9 – Primary Safety Events at 30 Days

Event Type	N (%)
Pericarditis	6 (2.0)
Major Vascular Access Complication	2 (0.7)
Pulmonary edema or heart failure	2 (0.7)
Pulmonary Thromboembolism	1 (0.3)
CVA	1 (0.3)
Cardiac Tamponade or Perforation	1 (0.3)

NOTE: Subjects may experience multiple primary safety endpoint events within 30 days.

Primary Safety Endpoint at 12 Months

299 subjects were available for the 12-month evaluation. The key safety outcomes for this study are presented below in Figure 8 and Table 10.

Figure 8: Freedom from Primary Safety Events at 12 Months

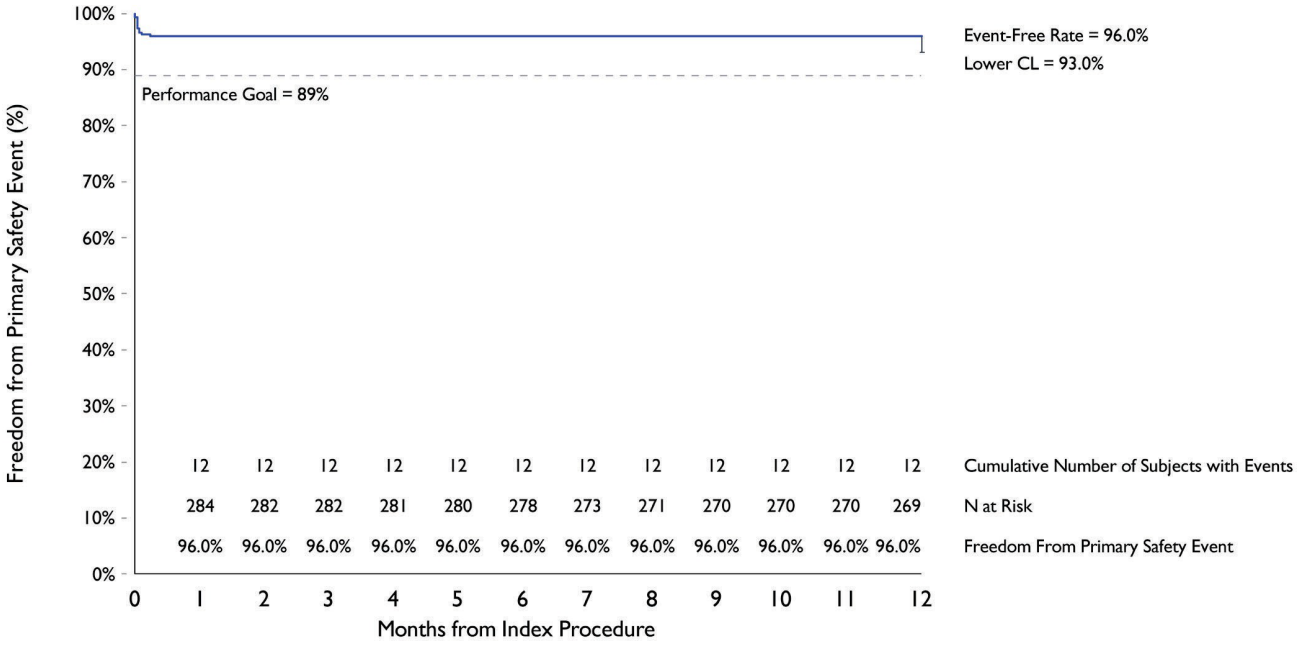


Table 10 – Primary Safety Events at 12 Months

Event Type	N Subjects (%)
Pericarditis	6 (2.0)
Major Vascular Access Complication	2 (0.7)
Pulmonary edema or heart failure	2 (0.7)
Pulmonary Thromboembolism	1 (0.3)
CVA	1 (0.3)
Cardiac Tamponade or Perforation	1 (0.3)

NOTE: Subjects may experience multiple primary safety endpoint events within 30 days.

Adverse events that occurred in the PMA clinical study

Table 11 – Primary Safety Events Listing

		CEC Adjudication	
Primary Safety Event Type	**Days Post-Index Procedure**	**Procedure Relationship**	**Device Relationship**
CVA	0	Related	Unknown
Cardiac Tamponade or Perforation	0	Related	Unknown
Major Vascular Access Complication	1	Related	Unrelated
Major Vascular Access Complication	1	Related	Unrelated
Pericarditis	1	Related	Unknown
Pulmonary edema or heart failure	1	Related	Unknown
Pericarditis	1	Related	Unknown
Pericarditis	1	Related	Unknown
Pericarditis	2	Related	Unknown
Pulmonary edema or heart failure	2	Related	Unknown
Pericarditis	3	Related	Unknown
Pulmonary Thromboembolism	3	Related	Unrelated
Pericarditis	7	Related	Unknown

FDA reviewed the listing of adverse events, including serious and non-serious adverse events, and including those adjudicated as related to the device, related to the procedure, or not related to either. The adverse events did not raise safety concerns based on a comparison to published literature and results for other devices with similar indications.

2. Effectiveness Results

The analysis of effectiveness was based on three analyses: acute procedural success, 6 months, and 12 months.

Primary Effectiveness Endpoint – Acute Procedural Success

The primary effectiveness endpoint for acute procedural success was based on 299 evaluable patients at the time of the procedure after a 20-minute waiting period. Of evaluable subjects, 294 (98.3%) reported acute procedural success and 5 (1.7%) were classified as acute procedural failures. The lower confidence bound of 96.1% was above the pre-specified performance goal of 92%. Key effectiveness outcomes are presented in Table 12.

Table 12 – Acute Procedural Success by Pulmonary Vein

Location	N	N Success (%) (95% CI)
Right superior (RSPV)	68	68 (100.0%) (94.7%-100.0%)
Right inferior (RIPV)	62	62 (100.0%) (94.2%-100.0%)
Right common (RCPV)	2	2 (100.0%) (15.8%-100.0%)
Right middle (RMPV)	1	1 (100.0%) (2.5%-100.0%)
Right PV pair	241	237 (98.3%) (95.8%-99.5%)
Left superior (LSPV)	50	49 (98.0%) (89.4%-99.9%)
Left inferior (LIPV)	43	42 (97.7%) (87.7%-99.9%)
Left common (LCPV)	20	20 (100.0%) (83.2%-100.0%)
Left PV pair	238	235 (98.7%) (96.4%-99.7%)

Primary Effectiveness Endpoint at 6 Months

The primary effectiveness endpoint at 6 months was based on 299 evaluable patients at the 6-month time point. The freedom from primary effectiveness failure at 6 months was 68.1% with the one-sided 97.5% lower confidence limit at 62.5%, which was greater than the pre-specified performance goal of 60%. Key effectiveness outcomes are presented in Table 13, Table 14, and Figure 9.

Table 13 – Primary Effectiveness Failure at 6 months by Type

Primary Effectiveness Event Type	N (% of Treatments)
Acute procedural failure	5 (1.7)
Use of amiodarone post index procedure	7 (2.3)
Use of a non-study ablation catheters in the Index Procedure or in a Repeat Procedure during the Blanking Period	1 (0.3)
More than one repeat procedure during the Blanking Period	0 (0.0%)
Surgical ablation of AF/AT/AFL post-Index Procedure	0 (0.0%)
Documented AF or new onset AT/AFL post-Blanking Period	34 (11.4)
>= 30 seconds in duration from the study specific event monitor or Holter Monitor	33 (11.0)
>= 10 second 12-lead ECG	1 (0.3)
Interventions for AF or new onset AFL/AT post-Blanking Period	48 (16.1)
Repeat procedure	0 (0.0%)
Electrical and/or pharmacological cardioversion	0 (0.0%)
Prescribed any anti-arrhythmic drug	48 (16.1)

Figure 9 – Freedom from Primary Effectiveness Failure at 6 Months

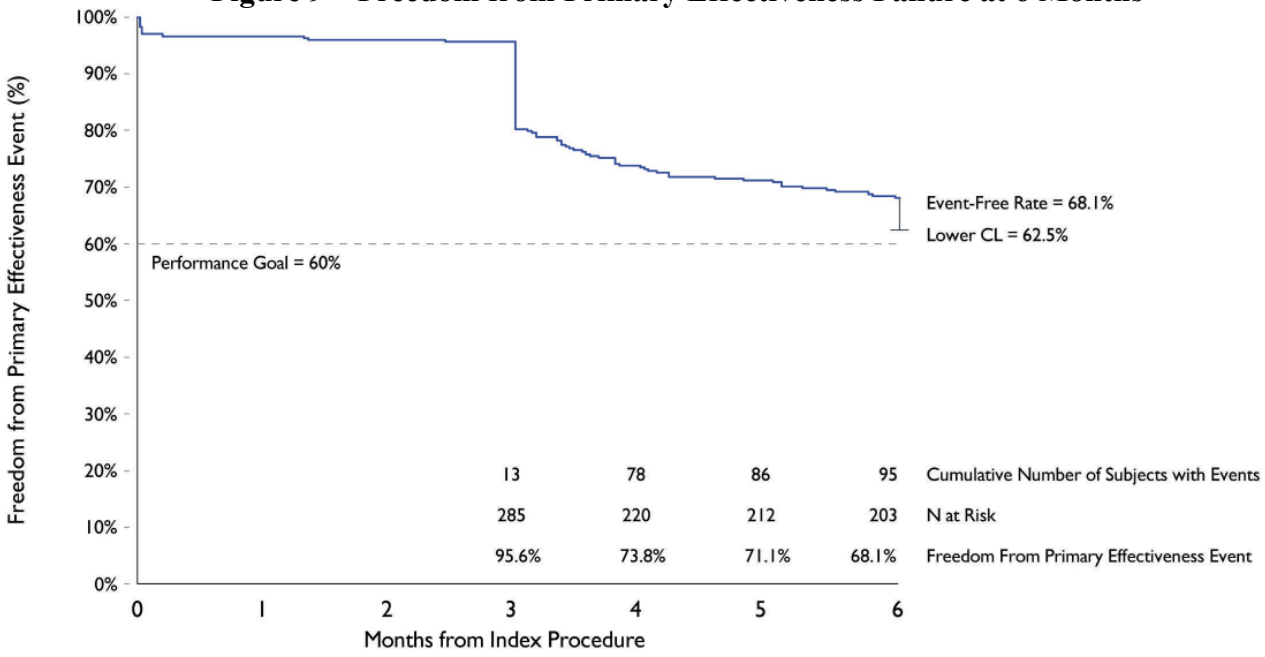


Table 14 – Data Accountability for Primary Effectiveness Endpoint at 6 Months

Data Accountability	N (%)
Complete 6-month primary effectiveness endpoint data	298 (99.7)
Completed 6-month visit or later without experiencing 6-month primary effectiveness event	203 (67.9)
Experienced 6-month primary effectiveness event	95 (31.8)
Missing 6-month primary effectiveness endpoint data	1 (0.3)

Imputation Analysis

An imputation analysis was performed to characterize the impact of missing data on the main 12-month primary safety endpoint outcome. Subjects with missing data had their 12-month endpoint outcome imputed using multiple imputation methods. Imputed outcome data was analyzed along with the data from complete data subjects to determine a 12-month Kaplan-Meier primary safety endpoint event-free rate and lower 95% confidence interval, as shown in Table 15. This represents a likely outcome if full data had been collected on all treatment subjects. The independent variables included in the imputation model are as follows:

- Age
- Sex
- Body Mass Index (BMI)
- $CHADS_2$ score
- History of ischemic cardiomyopathy
- History non-ischemic cardiomyopathy
- History of congestive heart failure
- History of hypertension
- Chronic Obstructive Pulmonary Disease (COPD)
- Diabetes
- Sleep disordered breathing
- History of Transient Ischemic Attack (TIA)
- History of Cerebrovascular Accident (CVA)
- History of Coronary Artery Bypass Graft (CABG) surgery
- History of prosthetic cardiac valve intervention
- History of heart transplant
- Cardioversion performed during index procedure

Table 15 – Imputation Analysis for Primary Safety Endpoint at 12 Months

Minimum Imputed Event-Free Rate	Maximum Imputed Event-Free Rate	Combined Event- Free Rate	Lower Confidence Limit	MI Analysis Outcome
90.0%	96.0%	94.8%	90.9%	Pass

Primary Effectiveness Endpoint at 12 Months

The primary effectiveness endpoint at 12 months was based on the 299 evaluable patients at the 12-month time point. The freedom from primary effectiveness failure at 12 months was 60.3% with the one-sided 97.5% lower confidence limit at 54.5%, which was greater than the pre-specified performance goal of 50%. Key effectiveness outcomes are presented in Table 16, Table 17, and Figure 10.

Table 16 – Primary Effectiveness Failure at 12 Months by Type

Primary Effectiveness Event Type	N (% of Treatments)
Acute procedural failure	5 (1.7)
Use of amiodarone post index procedure	7 (2.3)
Use of a non-study ablation catheters in the Index Procedure or in a Repeat Procedure during the Blanking Period	1 (0.3)
More than one repeat procedure during the Blanking Period	0 (0.0%)
Surgical ablation of AF/AT/AFL post-Index Procedure	0 (0.0%)
Documented AF or new onset AT/AFL post-Blanking Period	54 (18.1)
>= 30 seconds in duration from the study specific event monitor or Holter Monitor	53 (17.7)
>= 10 second 12-lead ECG	1 (0.3)
Interventions for AF or new onset AFL/AT post- Blanking Period	51 (17.1)
Repeat procedure	0 (0.0%)
Electrical and/or pharmacological cardioversion	0 (0.0%)
Prescribed any anti-arrhythmic drug	51 (17.1)

Figure 10 – Freedom from Primary Effectiveness Failure 12 Months

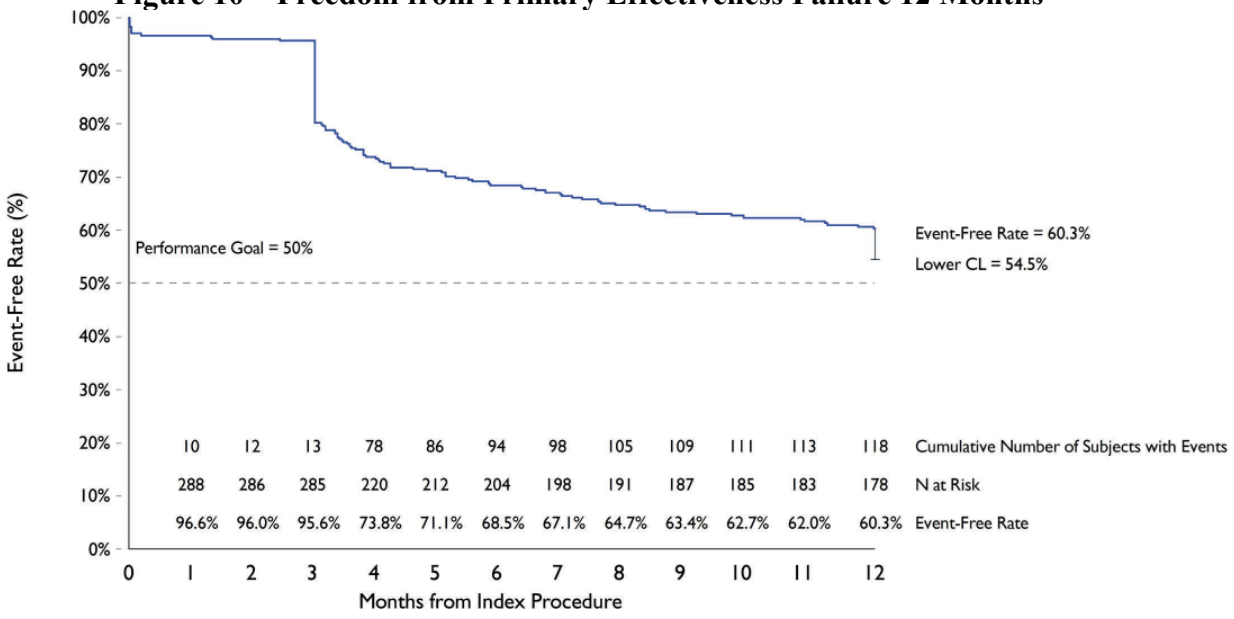


Table 17 – Data Accountability for Primary Effectiveness Endpoint at 12 Months

Data Accountability	N (%)
Complete 12-month primary effectiveness endpoint data	296 (99.0)
Completed 12-month visit or later without experiencing primary effectiveness event	178 (59.5)
Experienced primary effectiveness event	118 (39.5)
Missing 12-month primary effectiveness endpoint data	3 (1.0)

Secondary Endpoint Analysis – Safety

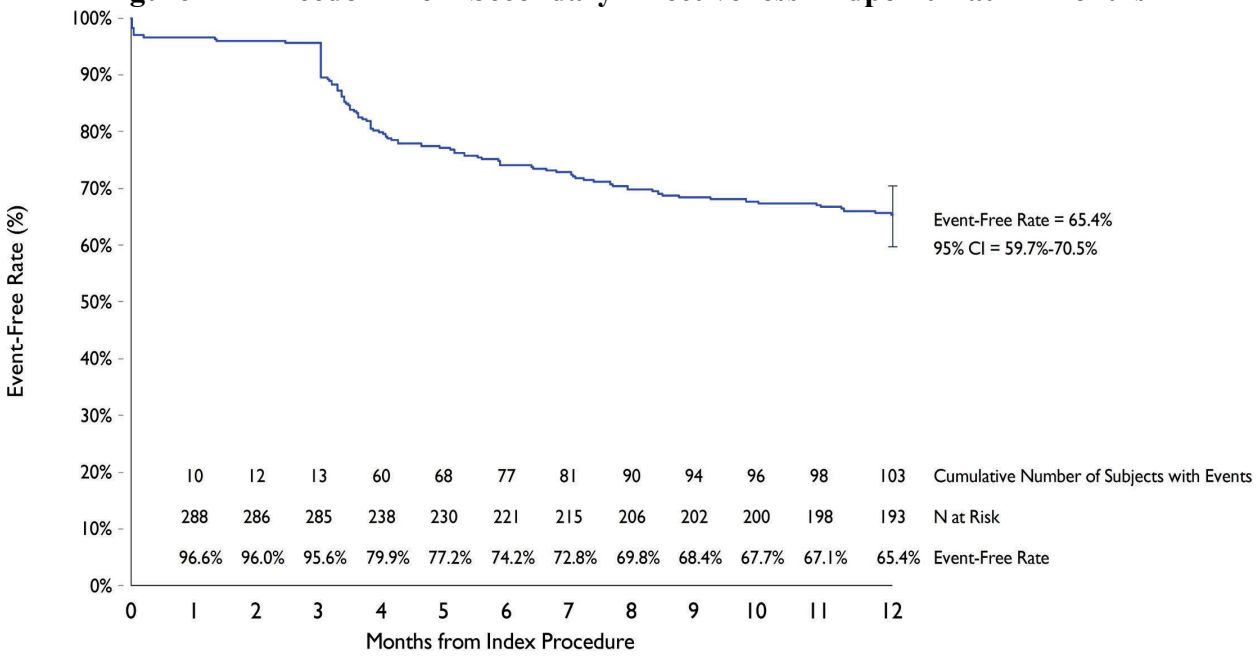
- Secondary Safety Endpoint – SAE and AE Rates

Table 18 – Summary of Adverse Events by Relatedness

Adverse Event Classification	Number of Events (Number of subjects, % of Treatments)
Total Adverse Events	156 (97, 32.4%)
Primary Safety Events [1]	13 (12, 4.0%)
Serious [2][4]	
Yes	72 (47, 15.7%)
No	84 (64, 21.4%)
Device and/or Procedure Relatedness [2][3][4]	
Causal	33 (30, 10.0%)
Probable	25 (23, 7.7%)
Possible	27 (24, 8.0%)
Not related	71 (52, 17.4%)

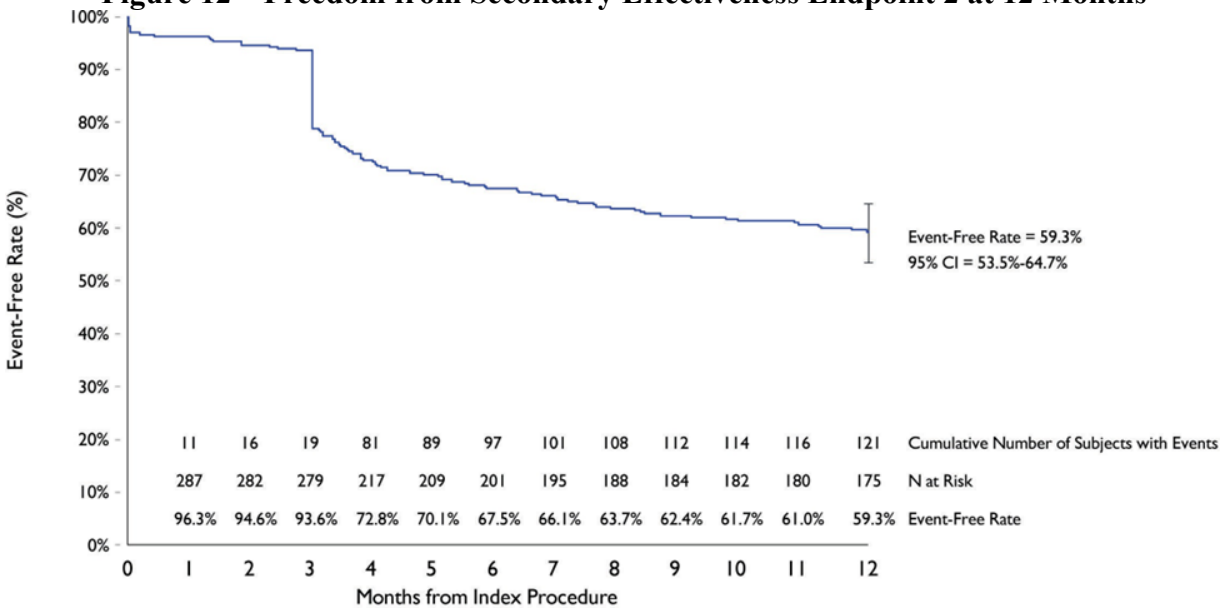
- Secondary Effectiveness Endpoint 1 – New or Increased AADs

Figure 11 – Freedom from Secondary Effectiveness Endpoint 1 at 12 Months



- Secondary Effectiveness Endpoint 2 – Single Procedure Success

Figure 12 – Freedom from Secondary Effectiveness Endpoint 2 at 12 Months



- Secondary Effectiveness Endpoint 3 – Symptomatic Recurrence
  8.5% (9/106) of subjects experiencing AF/AFL/AT episodes >=30s at any time reported at least 1 symptomatic episode.

Table 19 – List of Standard Symptoms

STANDARD SYMPTOMS
ANXIETY
CAN'T SLEEP
CHEST PAIN
DIZZINESS
FATIGUE
HEADACHE
NAUSEA
PALPITATIONS
SHORTNESS OF BREATH
SLEPT POORLY
STRESSED
SWEATING

- Quality of Life Questionnaires (AFEQT and EQ-5D-5L)

Table 20 – Quality of Life Questionnaire Completion

Questionnaire	Baseline % (n/N)	3-Month % (n/N)	6-Month % (n/N)	12-Month % (n/N)
AFEQT	99.7% (298/299)	100.0% (289/289)	100.0% (292/292)	99.3% (286/288)
5Q-5D-5	99.7% (298/299)	100.0% (289/289)	100.0% (292/292)	99.3% (286/288)

Table 21 – Quality of Life Questionnaire score through follow-up visits

		Baseline		Month 3 Follow- Up		Month 6 Follow- Up		Month 12 Follow-Up	
Questionnaire	Component	N	Mean +/- SD	N	Mean +/- SD	N	Mean +/- SD	N	Mean +/- SD
AFEQT	Overall Score	298	60.5 +/- 21.2	289	86.6 +/- 15.3	292	85.8 +/- 16.7	286	87.5 +/- 14.8
	Daily Activity Component Score	298	59.1 +/- 28	289	84.5 +/- 20.6	292	83.7 +/- 21.8	286	85.8 +/- 18.9
	Symptom Component Score	298	64.5 +/- 24.6	289	90.7 +/- 14.7	292	88.5 +/- 16.2	286	89.9 +/- 15
	Treatment Concerns Component Score	298	59.8 +/- 21.9	289	86.5 +/- 14.7	292	86.6 +/- 15.8	286	88.2 +/- 15
EQ-5D-5L	Overall Score	298	75.3 +/- 15.8	289	81.9 +/- 13.8	292	83 +/- 12.9	286	83.3 +/- 12.8

Table 22 – Qualify of Life Change from Baseline to 12-Month Follow-Up

Questionnaire	Component	Change from Baseline to 12M (95% CI)	P-Value
AFEQT	Overall Score	26.5 (23.9, 29)	<.0001
	Symptom Component Score	25 (21.9, 28.1)	<.0001
	Daily Activity Component Score	26.1 (22.8, 29.3)	<.0001
	Treatment Concerns Component Score	28 (25.2, 30.7)	<.0001
EQ-5D-5L	Overall Score	7.4 (5.6, 9.3)	<.0001

- Freedom from Recurrence of AF and New Onset of AT/AFL Between 91 and 365 days from Index Procedure

Figure 13 – Freedom from AF Recurrence

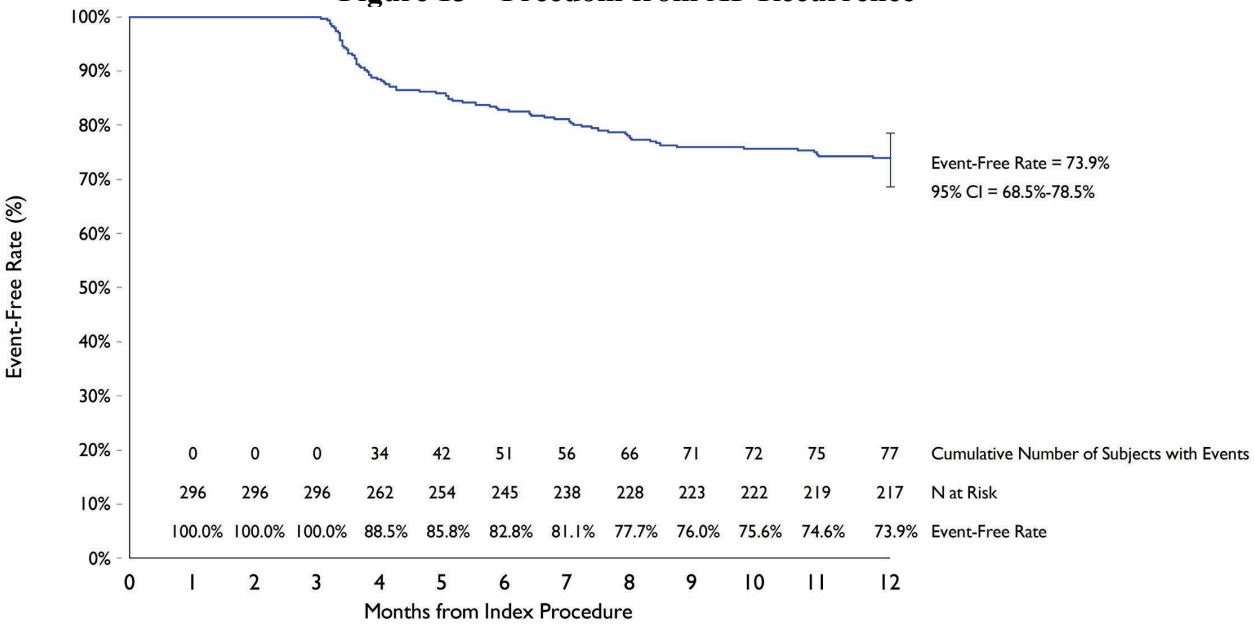


Figure 14 – Freedom from New Onset of AT

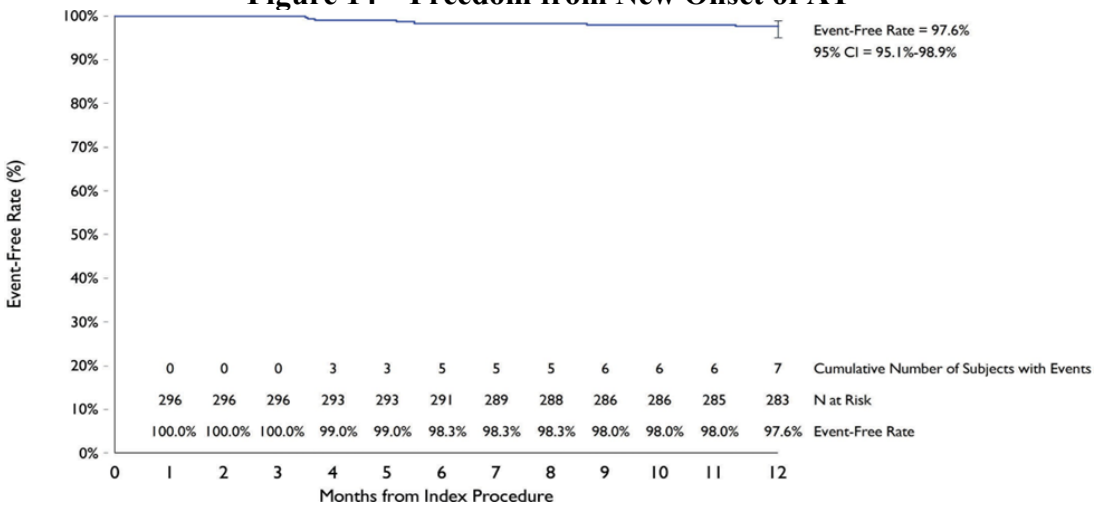
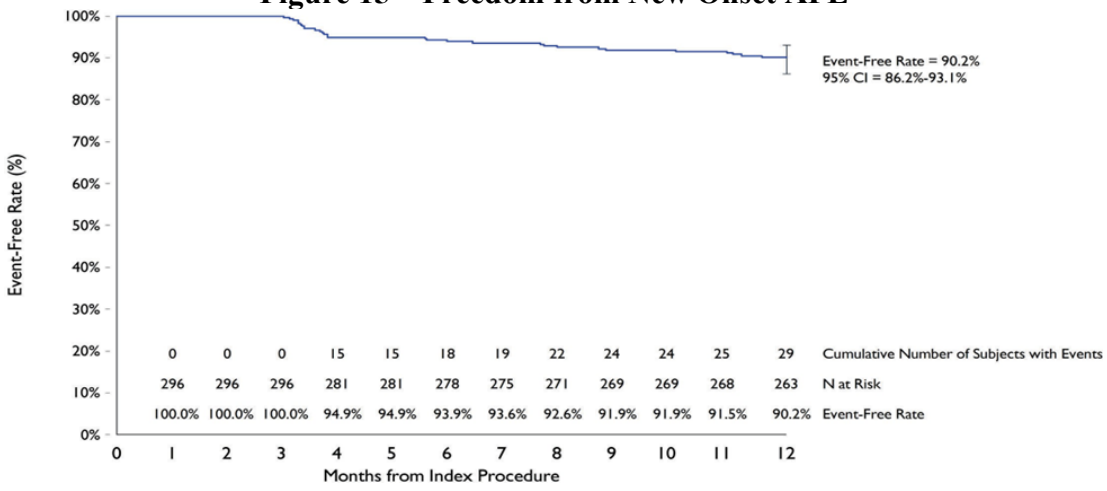
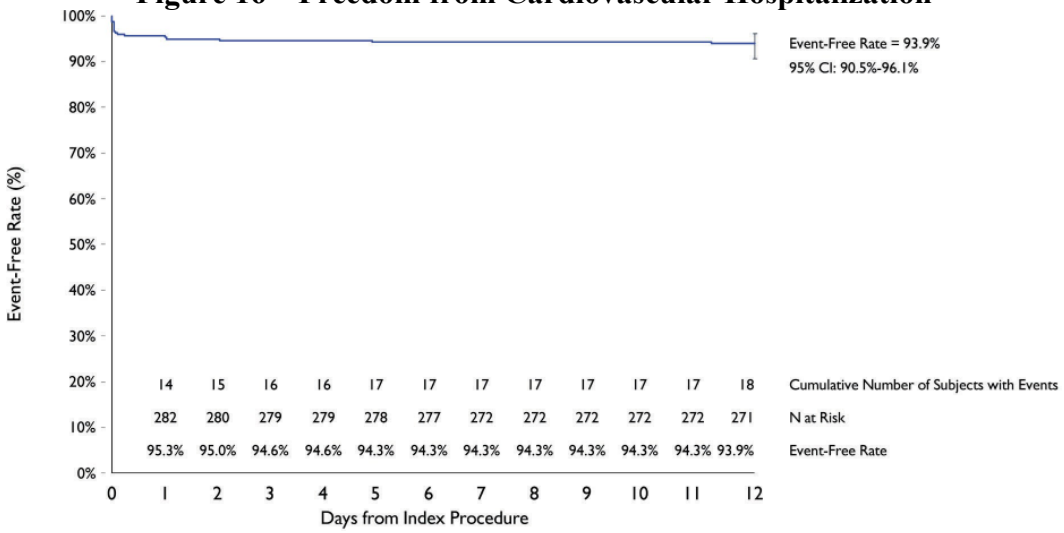


Figure 15 – Freedom from New Onset AFL



- Freedom from Cardiovascular Hospitalization at 12 Months

Figure 16 – Freedom from Cardiovascular Hospitalization



- RHYTHMIA HDx Ablation Parameter Data

Table 23 – RHYTHMIA HDx Ablation Parameter Data

Characteristic	Measurement	Treatments with PVI Only (N=166)	Treatments with PVI and Point-by-Point Applications Only (N=163)
Mean power (W)	N	4,811	4,711
	Mean ± SD	43.69 ± 7.70	43.61 ± 7.71
	Range	18.40 - 50.30	18.40 - 50.30
Max temp (C)	N	4,811	4,711
	Mean ± SD	29.60 ± 2.67	29.57 ± 2.69
	Range	22.90 - 41.70	22.90 - 41.70
RF Duration (sec)	N	16,702	16,254
	Mean ± SD	11.6 ± 6.3	11.5 ± 6.3
	Range	3.0 - 67.1	3.0 - 67.1
Local impedance baseline (Ohm)	N	16,533	16,086
	Mean ± SD	155.11 ± 20.54	155.14 ± 20.64
	Range	74.80 - 297.10	74.80 - 297.10
DIRECTSENSE drop (Ohms)	N	16,533	16,086
	Mean ± SD	21.16 ± 11.07	21.34 ± 11.07
	Range	0.00 - 211.30	0.00 - 211.30
% DIRECTSENSE drop from baseline	N	16,533	16,086
	Mean ± SD	13.3% ± 5.9%	13.4% ± 5.9%
	Range	0.0% - 94.0%	0.0% - 94.0%
Max raw force (g)	N	16,069	15,623
	Mean ± SD	28.17 ± 14.97	28.51 ± 14.85
	Range	0.80 - 101.30	0.80 - 101.30
Min raw force (g)	N	16,069	15,623
	Mean ± SD	5.89 ± 4.90	5.93 ± 4.92
	Range	0.00 - 44.10	0.00 - 44.10
Mean filtered force (g)	N	16,071	15,625
	Mean ± SD	14.04 ± 7.14	14.19 ± 7.09
	Range	0.40 - 61.20	0.40 - 61.20
NOTE: One unintentional ablation with a mean power of 9.6W is excluded from this summary. Based on a review of the data, the user had not yet set the generator to 50W for the first application. This application was halted early, the generator was set to 50W and the ablation was repeated in this location.			

- Ablation Duration by Power

Table 24 – Ablation Duration by Power

Power	Measurement	Duration (sec)
<20W	N	50
	Mean ± SD	10.9 ± 3.2
	Range	4.5 - 20.3
20 to 30W	N	535
	Mean ± SD	12.6 ± 5.2
	Range	3.1 - 29.9
>30 to 40W	N	1297
	Mean ± SD	14.6 ± 7.8
	Range	3.2 - 39.9
>40 to <45W	N	11
	Mean ± SD	13.5 ± 7.5
	Range	3.3 - 28.5
>=45	N	2818
	Mean ± SD	9.9 ± 3.7
	Range	3.1 - 39.2
NOTE: One unintentional ablation with a mean power of 9.6W is excluded from this summary. Based on a review of the data, the user had not yet set the generator to 50W for the first application. This application was halted early, the generator was set to 50W and the ablation was repeated in this location.		

3. Subgroup Analyses

The following preoperative characteristics were evaluated for potential association with outcomes:

Table 25 – Subgroup Analyses

Covariate	Subgroup	N	Event-Free Rate (95% CI)	P-value*
Primary Safety at 12 Months				
Sex	Female	118	94.0% (87.9% - 97.1%)	0.1640
	Male	181	97.2% (93.5% - 98.8%)	
Age at time of Consent	Subjects >60 years	184	95.1% (90.8% - 97.4%)	0.3318
	Subjects <=60 years	115	97.4% (92.1% - 99.1%)	
Geography	International	131	97.7% (93.1% - 99.3%)	0.1785
	United States	168	94.6% (89.9% - 97.2%)	
Primary Effectiveness at 12 Months				
Sex	Female	118	52.0% (42.6% - 60.6%)	0.0290
	Male	181	65.7% (58.3% - 72.1%)	
Age at time of Consent	Subjects >60 years	184	55.8% (48.3% - 62.7%)	0.0528
	Subjects <=60 years	115	67.5% (58.1% - 75.3%)	
Geography	International	131	55.7% (46.8% - 63.7%)	0.0964
	United States	168	63.9% (56.1% - 70.7%)	

*For acute procedural success, p-values are from a logistic regression model of the primary endpoint outcome on the covariate. For primary safety and effectiveness at 12 months, p-values are from a log-rank test comparing time to outcome across subgroups.

4. Pediatric Extrapolation

In this premarket application, existing clinical data was not leveraged to support approval of a pediatric patient population. The NEwTON-AF study enrolled patients ages 18 or older; however, patients aged 18 through 22 (transitional adolescents) were not treated differently than adult patients.

XI. FINANCIAL DISCLOSURE

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 3 investigators of which 0 were full-time or part-time

employees of the sponsor and 3 had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: 0
- Significant payment of other sorts: 3
- Proprietary interest in the product tested held by the investigator: 0
- Significant equity interest held by investigator in sponsor of covered study: 0

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. Statistical analyses were conducted by FDA to determine whether the financial interests/arrangements had any impact on the clinical study outcome. The information provided does not raise any questions about the reliability of the data.

XII. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

N/A

XIII. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory System Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIV. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The INTELLANAV STABLEPOINT™ Ablation Catheter & Force Sensing System on the RHYTHMIA HDX™ Mapping System met all three pre-specified primary effectiveness endpoints in the NEwTON AF clinical study. The determination of a reasonable assurance of effectiveness was principally based on meeting the 12-month primary effectiveness endpoint, which indicated that 60.3% (lower 97.5% CL at 54.5%) of subjects remained free from a primary effectiveness endpoint event at 12 months. This result met the pre-specified performance goal of 50%. Of the subjects who experienced a primary effectiveness event, 18.1% experienced documented AF or new onset AT/AFL post-blanking period and 1.7% experienced acute procedural failure. Complete 12-month primary effectiveness endpoint data were available for 99.0% of subjects. A tipping point analysis was performed to characterize the impact of missing data, which indicated that the performance goal would be met even if all subjects with missing data were considered primary effectiveness failures. The data indicated that the INTELLANAV STABLEPOINT™ Ablation Catheter & Force

Sensing System on the RHYTHMIA HDX™ Mapping System is supported by a reasonable assurance of effectiveness.

B. Safety Conclusions

The risks of the device are based on nonclinical laboratory and animal studies as well as data collected in a clinical study conducted to support PMA approval as described above. Nonclinical laboratory and animal studies evaluated the safety of the INTELLANAV STABLEPOINT™ Ablation Catheter & Force Sensing System on the RHYTHMIA HDX™ Mapping System with respect to biocompatibility, sterility, electrical safety, electromagnetic compatibility, usability, and performance. With respect to clinical data, the INTELLANAV STABLEPOINT™ Ablation Catheter & Force Sensing System on the RHYTHMIA HDX™ Mapping System met the two pre-specified primary safety endpoints in the NEwTON AF clinical study. In 299 subjects, 13 primary safety events occurred through 30 days in 12 subjects. This resulted in a primary safety rate at 30 days of 96.0% (lower 95% CL of 93.6%) which met the pre-specified performance goal of 90%. No patients experienced atrial esophageal fistula, cardiac tamponade/perforation, or severe pulmonary vein stenosis. The data indicated that the INTELLANAV STABLEPOINT™ Ablation Catheter & Force Sensing System on the RHYTHMIA HDX™ Mapping System is supported by a reasonable assurance of safety.

C. Benefit-Risk Determination

The probable benefits of the device are also based on data collected in a clinical study conducted to support PMA approval as described above. The benefits include freedom from atrial fibrillation and other atrial tachyarrhythmias at a likelihood determined to be acceptable by the clinical community. Additional benefits include likely improvement in quality of life. The rate of adverse events was lower than the pre-defined performance goal.

The probable risks of the device are also based on data collected in a clinical study conducted to support PMA approval as described above. The risks include those associated with any electrophysiology catheterization procedure (e.g., access site complications) and those specific to the ablation catheter (e.g., pericarditis).

Additional factors to be considered in determining probable risks and benefits for the INTELLANAV STABLEPOINT™ Ablation Catheter & Force Sensing System on the RHYTHMIA HDX™ Mapping System device included: (1) the lack of a concurrent control arm in the NEwTON AF study and (2) the lack of continuous electrocardiographic monitoring leading to sub-optimal compliance with rhythm monitoring strategies.

1. Patient Perspective
   This submission either did not include specific information on patient perspectives or the information did not serve as part of the basis of the decision to approve or deny the PMA for this device.

In conclusion, given the available information above, the data support that for the treatment of drug-refractory, recurrent, symptomatic paroxysmal atrial fibrillation the probable benefits outweigh the probable risks.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use.

XV. CDRH DECISION

CDRH issued an approval order on February 26, 2024.

The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XVI. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.

XVII. REFERENCES

N/A