Boston Scientific

INTELLANAV STABLEPOINT™

Ablation Catheter

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BSC (MB eIFU Template 8.2677 x 11.6929 A4, 92524324F), eIFU, MB, INTELLANAV STABLEPOINT US, en, 51590762-01B

℞ **ONLY**

Caution: Federal Law (USA) restricts this device to sale by or on the order of a physician.

REUSE WARNING

Contents supplied STERILE using an ethylene oxide (EO) process. Do not use if sterile barrier is damaged. If damage is found, call your Boston Scientific (BSC) representative.

For single use only. Do not reuse, reprocess or resterilize. Reuse, reprocessing or resterilization may compromise the structural integrity of the device and/or lead to device failure which, in turn, may result in patient injury, illness or death. Reuse, reprocessing or resterilization may also create a risk of contamination of the device and/or cause patient infection or cross-infection, including, but not limited to, the transmission of infectious disease(s) from one patient to another. Contamination of the device may lead to injury, illness or death of the patient.

Carefully read all ancillary device instructions prior to use. Observe all contraindications, warnings and precautions noted in these directions. Failure to do so may result in patient complications.

DEVICE DESCRIPTION

The INTELLANAV STABLEPOINT Ablation Catheter (henceforth referred to as the INTELLANAV STABLEPOINT Catheter) is a non-pyrogenic, steerable quadripolar open-irrigated ablation catheter designed to deliver Radiofrequency RF) energy to the 4 mm catheter tip electrode for cardiac ablation. The catheter shaft is 7.5F with 8F ring electrodes. The INTELLANAV STABLEPOINT Catheter is compatible with introducers or sheaths with a minimum inner diameter of 8.5F.

The INTELLANAV STABLEPOINT Catheter incorporates a position sensor for magnetic tracking and navigation, when used with a compatible RHYTHMIA Mapping System. Additionally, the catheter has an embedded force sensor in the distal tip to transmit real-time feedback on the mechanical interaction between the RF tip electrode and myocardial tissue and the catheter is enabled to measure changes in local dielectric properties in the proximity of the tip electrode.

Note: See corresponding Instructions for Use (IFU) for the compatible RHYTHMIA Mapping System for additional information on the contact force visualization and the local impedance measurement, hereby referred to as DIRECTSENSE on the INTELLANAV STABLEPOINT Catheter.

The INTELLANAV STABLEPOINT Catheter is capable of accessing power up to 50 Watts when connected to a compatible RF Controller. The INTELLANAV STABLEPOINT Catheter is designed to be used with a commercially available RF Controller (also called RF Generator) not exceeding 50 Watts or 133 Vpk, an Irrigation Pump and Irrigation Tubing Set that meets the catheter flow rate requirements[1], a commercially available Connection Box, and a dispersive pad (indifferent electrode). For mapping, navigation, and visualization of force and DIRECTSENSE information, the INTELLANAV STABLEPOINT Catheter is designed to be used with a compatible RHYTHMIA Mapping System.

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One (1) sterile INTELLANAV STABLEPOINT Catheter

Operating Principle

The INTELLANAV STABLEPOINT Catheter incorporates an open-irrigated cooling mechanism through a tip that is partitioned into two chambers. The proximal chamber circulates heparinized 0.9% normal saline within the tip to cool the proximal end of the tip electrode and mitigate overheating while the distal chamber allows the fluid to flow through six irrigation holes into the patient's vasculature, 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.

[1] Must be capable of delivering flow rates of 2mL/min (Standby), 17 mL/min (Low Power Ablation Flow Rate at 30 W), and 30 mL/min (High Power Ablation Flow Rate at 31 W - 50 W).

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The electrode segment is comprised of a tip electrode and three ring electrodes. All the electrodes can be used for recording intracardiac electrograms (EGM) or delivering pacing stimuli from external systems. The tip electrode transmits RF energy for cardiac ablation. The INTELLANAV STABLEPOINT 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 mapping system. The INTELLANAV STABLEPOINT Catheter is shown in Figure 1.

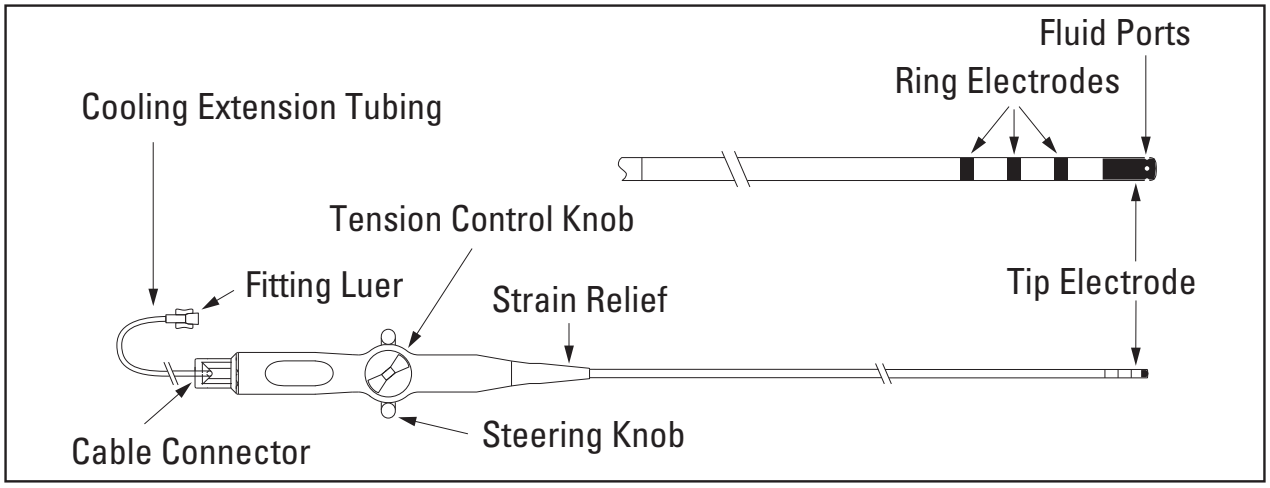


Figure 1. INTELLANAV STABLEPOINT Catheter

Local Impedance During Ablation – DIRECTSENSE

Please refer to the Instructions for Use of the compatible RHYTHMIA Mapping System for instructions on how to use the DIRECTSENSE software feature in conjunction with the INTELLANAV STABLEPOINT Catheter.

The INTELLANAV STABLEPOINT Catheter, when used with a compatible RHYTHMIA Mapping System, provides a display of local bipolar impedance that measures the dielectric properties closest to the catheter tip electrode. This diagnostic metric 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.

Note: Local impedance is not an indicator of contact force.

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. During RF application, the impedance signal changes due to tissue heating; local impedance may not represent catheter proximity or stability nor relative position of the catheter tip-to-tissue.

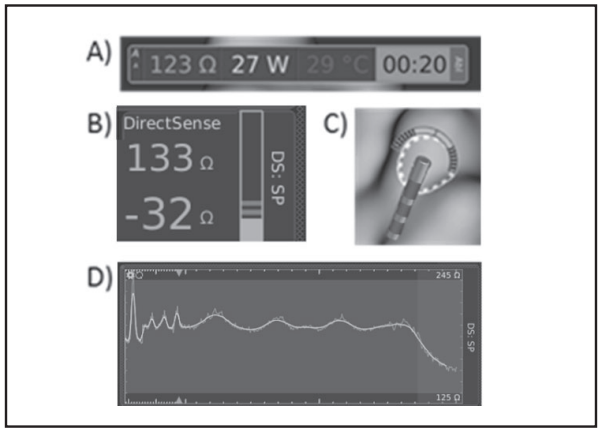
Note: Local impedance during ablation is only supported by a compatible RHYTHMIA Mapping System.

Note: RF ablation effectiveness is influenced by a number of factors including: tissue thickness, contact, force, stability, catheter orientation, power, duration, and irrigation flow. Users should consider these factors when performing ablation and confirm effectiveness through functional endpoints such as arrhythmia termination or establishing conduction block.

To ensure correct use of DIRECTSENSE, the distal portion of the catheter should have the tip and ring electrodes outside of the sheath.

During the application of RF energy, a compatible RHYTHMIA Mapping System provides a measure of local impedance as a real-time graph, a power bar graphic, a numerical value widget, and a tip graphic (Figure 2). 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 accordance with the other ablation color indicators and can be displayed as an absolute or percent value.

Once RF energy is terminated, the real-time graph will continue to display an overlay to temporally indicate that ablation has occurred at previous data epochs.



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.

Figure 2. Local impedance elements during RF ablation

Note: Please refer to the instructions for use of the compatible RHYTHMIA Mapping System for images of the local impedance elements in the associated software version.

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

The clinical utility of DIRECTSENSE RF has not been established; users should select ablation settings and limits (e.g., temperature limit, irrigation flow rate, power level, RF duration) in accordance with the Operational Instructions below.

Force Visualization on RHYTHMIA

A compatible RHYTHMIA Mapping System provides the visualization of the force information in a similar set of widgets comprised of a catheter tip visualization, a force value widget, a force angle indicator, and a real time force graph (Figure 3). 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 that data is 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 positioning of the catheter prior to and during RF delivery.

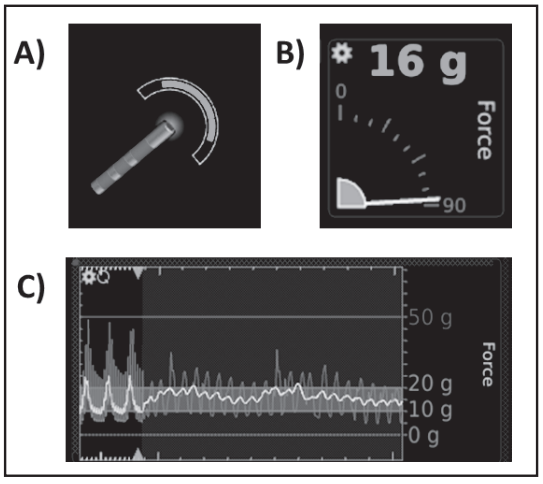


Figure 3. Visualization of Force on Compatible RHYTHMIA Mapping System

Please refer to the instructions for use of the compatible RHYTHMIA Mapping System for images of the force visualization elements in the associated software version.

Materials

This device is made with a metal alloy which contains cobalt. Current scientific evidence supports that metal alloys containing cobalt used in medical devices do not cause an increased risk of cancer or adverse reproductive effects.

Non-pyrogenic

This device meets pyrogen limit specifications for all patient-contacting parts.

User Information

The INTELLANAV STABLEPOINT Catheter is to be used by physicians thoroughly trained in invasive cardiology and in the open-irrigated techniques of RF powered catheter mapping and ablation, in the specific approach to be used, and in a fully-equipped electrophysiology lab. Assistance to prepare and run the system may only be provided by appropriately trained personnel.

INDICATIONS FOR USE

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

- Cardiac electrophysiological mapping
- Delivering diagnostic pacing stimuli
- RF ablation of sustained or recurrent typical atrial flutter in patients age 18 years 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

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 or a short introducer < 8.5 F.
- in the coronary vasculature.

WARNINGS

- If the visibility of the EP catheters is compromised for any reason, the user should stop and not resume ablation therapy until catheter visibility is established in order to prevent patient injuries such as perforation, heart block and injury to adjacent structures.
- Cardiac mapping and ablation procedures should be performed only by physicians thoroughly trained in invasive cardiology and in the techniques of open-irrigated RF powered catheter mapping and ablation, and in the specific approach to be used, in a fully-equipped electrophysiology lab.
- Administer appropriate levels of peri-procedural anticoagulation therapy for patients undergoing left-sided and transseptal cardiac procedures. There is an increased risk of thromboemboli if appropriate anticoagulation levels are not maintained while the transseptal sheath and/or catheter is in the left side of the heart. Administer anticoagulation therapy during and post-procedure according to the institution's standards to minimize bleeding and thrombotic complications.
- Carefully read all equipment and ancillary device instructions required for the procedure prior to use. Observe all contraindications, warnings, and precautions noted in these directions. Failure to do so may result in patient complications.
- Before using, inspect the INTELLANAV STABLEPOINT Catheter for any defects or physical damage, including electrical insulation on the cables and the catheter shaft that, if used, may cause patient and/or user injury. Do not use defective or damaged devices. Replace damaged equipment if necessary. No modification of this equipment is allowed.
- Using the INTELLANAV STABLEPOINT Catheter at lower than the prescribed flow rates specified in the Operational Instructions may increase the potential for thrombus, coagulum, and char that may result in embolism.
- Electromagnetic Interference (EMI) from any source during normal operation may adversely affect the visualization and tracking of the catheter during the procedure, which can cause patient injuries such as perforation, heart block and injury to adjacent structures.
- Carefully follow the power and the correlating flow rate procedures as specified in the Operational Instructions. Performing ablation with high power, insufficient flow rate, excessive contact force and/or excessive RF duration without moving the tip of the ablation catheter may lead to perforation, arrhythmias, damage to adjacent structures, and/or embolism.
- Avoid increasing power or duration of RF application beyond your standard of care to target a specific change in local impedance. Doing so may result in damage to adjacent structures, perforation caused by steam pop, arrhythmias, and/or embolism.

Note: The change in local impedance during RF delivery should not be used independent of established clinical indicators of RF tissue response (e.g., electrograms, generator impedance, pace capture). Select ablation settings and limits (e.g., temperature limit, irrigation flow rate, power level, RF duration) in accordance with the Operational Instructions below. Increases in contact force, ablation duration or power in pursuit of a specific change in local impedance are not recommended.

- The INTELLANAV STABLEPOINT Catheter is not intended to be used with an RF Controller output setting exceeding 50 Watts or 133 Vpk. The safety and performance of the INTELLANAV STABLEPOINT Catheter at powers exceeding 50 Watts has not been evaluated in a clinical trial. Exceeding recommended power settings or using flow rates lower than recommended settings may increase the risk of patient injury.
- Patients who have had a prior atrial flutter ablation procedure may be at greater risk for perforation and/or pericardial effusion with the use of this catheter system.
- Patients undergoing septal accessory pathway, Atrioventricular (AV) node reentry tachycardia, and/or atrial flutter ablation are at risk for complete AV block which requires the implantation of a temporary and/or permanent pacemaker.
- During energy delivery, the patient should not be allowed to come in contact with grounded metal surfaces to minimize the potential for electrical shock.

- Ensure that the cable/catheter connection remains dry throughout the procedure in order to prevent electric shock or other patient injuries as well as to prevent loss of device function.
- Electrodes and stimulating devices can provide paths of high frequency current. The risk of burns can be reduced but not eliminated by placing the electrodes as far away as possible from the ablation site and the Dispersive Pad. Protective impedances may reduce the risk of burns and permit continuous monitoring of the Electrocardiogram (ECG) during energy delivery.
- Before use, ensure irrigation ports are patent and jetting by infusing heparinized normal saline through the catheter tubing. Patency of irrigation ports is important to maintain cooling function and minimize risks of coagulum, fibrin, thrombus and char that may result in embolism as well as perforation caused by steam pop.
- Fibrin may accumulate in or on the sheath/catheter assembly during the procedure. Aspirate when removing the dilator or catheter.
- Do not continue using the catheter if the irrigation ports are occluded or the catheter is not functioning properly.
- Due to the design of the INTELLANAV STABLEPOINT Catheter tip, the velocity of fluid exiting the irrigation ports may change based on rate and pressure of flushing. As long as there is fluid jetting out of each port, regardless of the velocity, the catheter is functioning as designed and may be used. However, if any irrigation port has no flow (or extremely low flow compared to adjacent ports) despite attempts to flush the irrigation port, do not insert the catheter in the patient as there may be potential risk of embolism.
- Electrical recording or stimulation equipment must be isolated. Current leakage from any electrical equipment that is connected to the patient must not exceed 10 microamps for intracardiac electrodes.
- Care must be taken to ensure that any equipment used in connection with the BSC catheters be type CF, be defibrillation proof, meet IEC 60601-1 electrical safety requirements, and comply with all local regulatory requirements for specified intended use to reduce the potential risk of inadvertent electrical shock.
- Do not insert or withdraw the INTELLANAV STABLEPOINT Catheter without straightening the catheter tip (returning the steering lever to neutral position) in order to prevent entanglement/ entrapment within the valve and/or other device that may result in myocardial trauma and/or may require additional medical/surgical intervention.
- Stimulation of cardiac tissues caused by pacing stimulus and/or RF energy may lead to inadvertent induction of arrhythmias. These arrhythmias may require defibrillation that could also result in skin burns.
- Maximum Catheter Rated Voltage: 133 Vpk.
- Warnings for patients with implantable pacemakers and Implantable Cardioverter/Defibrillators (ICDs):
    - Pacemakers, implantable cardioverter/defibrillators, and leads can be adversely affected by radiofrequency energy. It is important to refer to the device manufacturer's instruction for use prior to performing ablation procedures.
    - Do not apply RF energy directly to a lead or to tissue immediately in contact with a lead because it could potentially damage the lead or lead function.
    - Temporarily reprogram pacemaker per the manufacturer guidelines during RF ablation to a non-tracking pacing mode if pacing is likely to be required during the ablation.
    - The pacemaker could be damaged by the ablation procedure. Interrogate the device fully after the ablation per the manufacturer guidelines and reprogram to preoperative sensing and pacing parameters.
    - Deactivate ICDs as they could discharge and injure the patient or be damaged by the ablation procedure.
    - Have temporary external sources of pacing and defibrillation available.
    - Perform a complete analysis of the implanted device function after ablation.
    - Fluoroscopic or appropriate imaging guidance and care must be taken during catheter advancement, manipulation, and withdrawal to avoid lead dislodgement.
    - Monitor pre- and post-measurements for sensing and pacing thresholds and impedances to determine the integrity of the lead-patient function.
    - Remember to reactivate the pulse generator after turning off the RF ablation equipment.
- Do not ablate from within the coronary artery as the resulting myocardial injury can be fatal. Adequate visualization techniques, such as fluorosocopy or intracardiac echocardiography are necessary during the transaortic approach to avoid placement of the ablation catheter in the coronary vasculature.

- During RF ablation, care must be taken not to deliver RF energy on or near the coronary artery even on the right side of the heart, as the resulting myocardial injury can be fatal.
- Ablation in contact with any other electrodes alters the function of the catheter and can lead to thrombus, coagulum, or char formation that may result in embolism.
- At no time should a INTELLANAV STABLEPOINT Catheter be advanced or withdrawn when resistance is felt, without determining the cause. Valve damage, vascular and/or cardiac perforation is a risk with any intracardiac catheter.
- Catheter entrapment within the heart or blood vessels is a possible complication of cardiac ablation procedures. The potential for catheter entrapment may be increased when the catheter is overtorqued and/or positioned in the chordae tendineae. The occurrence of this complication may necessitate surgical intervention and/or repair of injured tissue and/or valve damage.
- Do not use the INTELLANAV STABLEPOINT ablation system in the proximity of Magnetic Resonance Imaging (MRI) equipment because the MRI equipment may adversely impact the function of an RF Controller and the ablation system may adversely impact the image quality. This can also lead to loss of visibility during ablation which can cause patient injuries such as perforation, heart block and injury to adjacent structures.
- Do not use the INTELLANAV STABLEPOINT ablation system and its accessories in an oxygen rich environment or near flammable anesthetics.
- Catheter ablation procedures present the potential for significant radiation exposure, which can result in acute radiation injury as well as an increased risk for somatic and genetic effects, to both patients and laboratory staff due to the radiation beam intensity and duration of the fluoroscopic imaging. Catheter ablation should only be performed after adequate attention has been given to the potential radiation exposure associated with the procedure, and steps have been taken to minimize this exposure. Due to radiation exposure during catheter ablation, the safety and effectiveness of this device has not yet been established in pregnant and/or nursing women and pediatric patients.
- There are no data to support the safety and effectiveness of this device in the pediatric population.
- In the event of a suspected failure of the integrity of fluid flow through the catheter or the tubing set or if there is a rapid temperature rise of > 15 ˚C noted on the RF Controller, the procedure should be stopped, and the catheter withdrawn to reduce the risk of steam pop that could result in adverse events including perforation, embolism or injury to adjacent structures. Both the catheter and the Irrigation Tubing Set should be replaced. The replacement catheter and tubing set must be primed outside the body prior to insertion to reduce risk of air embolism.
- Prior to the procedure, always identify the patient's risk of volume overload. Monitor the patient's fluid balance throughout the procedure and after the procedure to avoid fluid volume overload. Some patients may have factors that reduce their ability to handle the volume overload, making them susceptible to developing pulmonary edema or heart failure during or after the procedure. Patients with congestive heart failure or renal insufficiency, and the elderly are particularly susceptible.
- Always maintain a constant heparinized normal saline infusion to prevent coagulation within the lumen of the catheter that may result in embolism.
- Excessive curves or kinking of the catheter may damage internal wires and components, including the cooling lumen. This damage may affect steering performance or force accuracy and may cause patient injury.
- Excessive manipulation of the distal tip and spring region may cause permanent damage to the contact force elements resulting in inaccurate force readings.
- Manual bending and/or twisting of the distal curve can damage the steering mechanism and cooling lumens and may cause catheter failure and patient injury.
- Do not scrub the tip electrode as this may result in irrigation port(s) occlusion and may lead to catheter failure and patient injury.
- Use both fluoroscopy, or other visualization technique such as echocardiography, and electrograms to monitor the advancement of the catheter to the area of the endocardium under investigation to avoid conduction pathway injury, cardiac perforation or tamponade.

- Do not use excessive force to advance or withdraw the catheter. The firmness of the tip dictates that care shall be taken to prevent perforation of the heart during catheter manipulation. If the force-sensing feature is active, evaluate applied force to avoid applying excessive loads.
- Local impedance is affected by many factors including tissue conductivity, contact force, catheter orientation (focal/drag) power, duration, irrigation flow, tissue changes, and electrode char/thrombus/steam pop.
- During RF, due to tissue heating, local impedance may not represent catheter proximity or stability nor relative position of the catheter tip-to-tissue, as it is when RF is OFF.
- Do not deliver RF energy with the catheter outside the target site. RF Controllers can deliver significant electrical energy and may cause patient injury.
- In the event of RF Controller cut-off (impedance or temperature), the catheter must be withdrawn and the tip electrode cleaned of coagulum before RF energy is reapplied. Ensure that all of the irrigation holes are patent prior to reuse to reduce the risk of embolism and/or perforation.
- Verify effective contact between the patient and the Dispersive Pad whenever the patient is repositioned as patient movement may disrupt Dispersive Pad contact resulting in patient injury and/or extended procedure times.
- Always verify that the tubing set, catheter and all connections have been properly cleared of air prior to inserting the catheter into the vasculature. Air entrapped in the tubing and catheter can cause potential injury or cardiac arrest. The operator is responsible for removing all air from the system.
- Patients undergoing left sided ablation procedures should be closely monitored during and post procedure for clinical manifestations of infarction, pulmonary vein injury, nerve damage, embolism and/or atrial esophageal fistula.
- Patients undergoing a long irrigated ablation procedure have the potential for greater anticoagulation and therefore Activated Coagulation Time (ACT) should be monitored closely due to the increased risk for bleeding/ hemorrhage and/or embolism.
- Patients with hemodynamic instability or cardiogenic shock are at increased risk for life-threatening adverse events and ablation must be done with extreme caution.
- The INTELLANAV STABLEPOINT Catheter is not intended to be used for internal cardioversion. Doing so may result in perforation, arrhythmias, embolism, thrombus and/or patient death.
- The long-term risks of lesions created by RF ablation have not been established. In particular, any long-term effects of lesions in proximity to the specialized conduction system or coronary vasculature are unknown.
- Inspect irrigation saline for air bubbles and remove any air bubbles prior to its use in the procedure. Air bubbles in the irrigation saline may cause embolism.
- If there is uncertainty regarding the patient's anticoagulation status or rhythm prior to the procedure, there should be a low threshold to perform a Transesophageal Echocardiogram (TEE) prior to the procedure to confirm absence of mural thrombus and/ or thrombus in the left atrial appendage.
- Do not deliver RF energy when the tip electrode is withdrawn or partially withdrawn into a sheath, to minimize the risk of char or coagulum formation.
- Guiding catheters and/or long introducer sheaths present the potential for thromboembolic events. Pre-flush and maintain lumen patency with heparinized intravenous infusion.
- Do not wipe this catheter with organic solvents such as alcohol or immerse the handle cable connector in fluids. This may result in electrical or mechanical catheter failures. It may also result in an allergic reaction from the patient.
- Irrigation flow during RF ablation may distort distal tip electrogram recordings due to the signal conductivity of the external cooling solution. Careful monitoring of additional intracardiac electrograms during RF application is recommended to reduce the possibility of inadvertent injury to adjacent structures if appropriate. Higher power coupled with higher flow rates may exacerbate the distortion of the EGM signal recordings.
- Pre-procedural anticoagulation therapy is at the discretion of the physician. However, patients with a history of thromboembolic events may require therapeutic anticoagulation therapy, pre-, during and post-ablation to reduce the incidence of major complications. Peri-procedural anticoagulation therapy is recommended for patients undergoing left-sided and transseptal cardiac procedures and should be considered for selected patients undergoing right-sided procedures.

- The safety and/or efficacy of epicardial use of the INTELLANAV STABLEPOINT Catheter has not been evaluated in a clinical trial.
- The Transseptal Puncture (TSP) presents a potential risk for perforation/ tamponade; echocardiography and/or fluoroscopic images should be used to guide the transseptal puncture and a real-time arterial blood pressure monitor should be applied. TSP may induce an air embolus; use proper aspiration and flushing techniques to minimize air embolus.
- Care should be used during multiple sheath/catheter exchanges through the transseptal puncture to avoid causing a residual atrial septal defect that would require repair.
- To avoid patient injury, manipulate the sheath carefully when performing the transseptal puncture especially if the patient has any of the following conditions:
  - Enlarged aortic root
  - Marked right atrial enlargement
  - Small left atrium
  - Marked skeletal deformity or distortion of the thoracic configuration (e.g., scoliosis)
- Any serious incident that occurs in relation to this device should be reported to Boston Scientific and the relevant local regulatory authority.

PRECAUTIONS

- The INTELLANAV STABLEPOINT Catheter is designed for use with a compatible RF Controller, Irrigation Pump and Irrigation Tubing Set that meets the catheter flow rate requirements, a compatible Mapping System, and compatible Connection Box.
- The contact force reading is for information only and is not intended to replace standard handling precautions.
- The local impedance reading is for information only and is not intended to replace standard handling precautions.
- The catheter must be warmed up prior to use. If the catheter has not reached a steady state condition prior to use, there is a potential for measurement drift to occur, which could result in an inaccurate force reading.

Note: Refer to the Instructions for Use on compatible RHYTHMIA Mapping System for instructions on how to perform warm- up.

- Ensure catheter tip is not in contact with myocardial wall or other device when zeroing the contact force reading. Failure to do so could result in inaccurate force reading.

Note: Refer to the Instructions for Use on compatible RHYTHMIA Mapping System for instructions on how to zero the catheter.

- Always zero the contact force reading following insertion into the patient or moving the catheter from one heart chamber to another.
- To ensure proper function of the contact force reading, ensure the tip electrode and distal ring electrode are outside of a sheath.

Note: Refer to the Instructions for Use on compatible RHYTHMIA Mapping System for list of sheaths that are compatible with the sheath detect software feature.

- To ensure proper function of the local impedance reading, ensure the tip electrode and all three ring electrodes are outside of a sheath.

Note: Refer to the error messages and notifications section of the compatible RHYTHMIA Mapping System instructions for use for system-related messages and indications related to DIRECTSENSE.

- When applying high force during mapping and RF application, the user should monitor the contact force visualization on the RHYTHMIA Mapping System screen to ensure the force does not exceed the operating range.

Note: Refer to the error messages and notifications section of the compatible RHYTHMIA Mapping System instructions for use for system-related messages and indications related to force range and inaccurate force reading.

- Do not place the distal end of the catheter near magnets. Magnetization of the catheter may result in degradation of magnetic tracking precision. Such degradation may be manifested by an unstable or complete loss of rendering of the position and/or orientation of the catheter by a magnetic tracking system. If this occurs, the catheter should be replaced.
- Electromagnetic Interference (EMI) produced by the INTELLANAV STABLEPOINT Catheter when used in conjunction with the RF Controller during normal operation may adversely affect the performance of other equipment.
- Do not use the temperature sensor to monitor tissue temperature. The temperature sensor located within the electrode will not reflect either electrode-tissue interface or tissue temperature due to the cooling effects of the saline irrigation of the electrode.
- Use only sterile saline and gauze pad to clean the tip.
- Verify the RF Controller is in the control mode which will deliver the amount of power specified by the power setting unless the measured temperature exceeds the temperature setting. Temperature controlled RF delivery may be affected by the cooling effects of the saline irrigation of the electrode. For example, the MAESTRO 4000 RF Cardiac Ablation Controller has these settings in the power control mode.
- Equipment/accessories carrying high frequency alternating current may cause direct coupled interference and therefore, may disrupt the operation of the RF Controller. It may be necessary to take risk control measures, such as re-orienting, relocating, or shielding the interfering equipment/accessories.
- Use only Dispersive Pads that meet or exceed IEC 60601-2-2 requirements and follow the Dispersive Pad manufacturer's instructions for use. The use of Dispersive Pads which meet ANSI/AAMI requirements (HF18) is recommended.
- Apparent low power output, high impedance reading or failure of the equipment to function correctly at normal settings may indicate faulty application of the Dispersive Pad or failure of an electrical lead.
- The INTELLANAV STABLEPOINT Catheter is highly torqueable. Avoid overtorquing. Over-rotating the handle and catheter shaft may cause damage to the distal tip or catheter assembly. Do not rotate the handle and catheter shaft more than 1½ full rotations (540°). If the desired catheter tip position is not achieved, adjust the catheter's curve to disengage the catheter tip from the heart wall before resuming rotation of the handle and catheter shaft.
- Electrophysiology catheters and systems are intended for use only in radiation shielded rooms due to electromagnetic compatibility requirements and other hospital safety guidelines.
- The risk of igniting flammable gases or other materials is inherent in electrosurgery. Precautions must be taken to restrict flammable materials from the electrosurgical suite.
- Do not use the INTELLANAV STABLEPOINT ablation system and its accessories closer than 30 cm (12 inches) to any Wireless Power Transfer (WPT) and 5G cellular devices, otherwise electromagnetic interference from those devices could result in degradation of the performance of this equipment.
- Adequate filtering must be used to allow continuous monitoring of the surface Electrocardiogram (ECG) during RF power applications.

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ADVERSE EVENTS

Potential adverse events associated with use of the INTELLANAV STABLEPOINT Catheter include, but are not limited to:

- 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
  - Physical trauma
- Fistula, for example:
  - Atrio-esophageal fistula
  - Bronchopericardial fistula

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- PV stenosis and its symptoms, for example:
  - Cough
  - Shortness of breath
  - Fatigue
  - Hemoptysis
- Surgical and access complications, for example:
  - Hematoma/seroma
  - AV fistula
  - Bleeding
  - Pseudoaneurysm
  - Pneumothorax
  - Residual atrial septal defect
- Injury due to embolism/thromboembolism/air embolism/foreign body embolism
  - Cerebrovascular Accident (CVA)/stroke
  - Transient Ischemia Attack (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

The potential adverse events may be related to the diagnostic mapping catheter(s) and/or the interventional ablation device(s) and/or the procedure. The severity and/or the frequency of these potential adverse events may vary and may result in prolonged procedure time and/or additional medical and/or surgical intervention, implantation of a permanent device such as a pacemaker, and in rare cases, may result in death. Refer to the RF Controller, Irrigation Pump, and other ancillary device instructions for additional potential adverse events related to their use with the INTELLANAV STABLEPOINT Catheter.

CLINICAL STUDIES

The safety and effectiveness of the INTELLANAV STABLEPOINT Catheter was established through the NEwTON AF clinical study, performed with the INTELLANAV STABLEPOINT Catheter, and through the BLOCk-CTI and ZERO-AF clinical studies using the BLAZER Open-Irrigated Catheter (henceforth, referred to as the BLAZER OI Catheter).

The clinical use of the INTELLANAV STABLEPOINT Catheter is supported by the BLOCk-CTI and ZERO-AF studies as the inclusion of the magnetic sensor, local impedance, force, and associated functionality does not affect the ablation therapy delivery or catheter operation because the use of imaging guidance is still required to confirm device positioning prior to and during delivery of therapy.

BLOCk-CTI

Boston Scientific conducted a clinical study (BLOCk-CTI) to establish a reasonable assurance of safety and effectiveness of radiofrequency cardiac ablation using the BLAZER OI Catheter in the treatment of type I Atrial Flutter (AFL). The clinical study was conducted using a surrogate system consisting of the Stockert 70 Radiofrequency Generator and the CoolFlow Irrigation Pump and Tubing Set. However, on the basis of the engineering testing and animal studies, the results of the BLOCk-CTI study may be extrapolated to the use of BLAZER OI Catheter with the MAESTRO RF Generator and METRIQ Pump. These data from the clinical study are summarized below.

Objective

A multi-center clinical study was conducted using the BLAZER OI Catheter. The purpose of the clinical study was to demonstrate that the BLAZER OI Investigational Catheter is non-inferior to that of the Control Catheters when used to ablate the Cavo-tricuspid Isthmus (CTI) for the treatment of sustained or recurrent type I atrial flutter.

Study Design

BLOCk-CTI (BLAZER Open-Irrigated Radiofrequency Catheter for the Treatment of Type I Atrial Flutter) was a prospective, randomized, controlled, single-blinded, multi-center U.S. investigation. A Roll-in cohort was introduced into the study for investigators to use the BLAZER OI Catheter and a Control Catheter but these subjects were not part of the endpoint analyses. In this study, the Control devices were open-irrigated radiofrequency ablation catheters that received FDA market approval for the treatment of type I atrial flutter and the Investigational device was the BLAZER OI Catheter.

Patients were treated between January 17, 2011 and January 15, 2014. The database for this Premarket Approval PMA) reflected data collected through January 15, 2014 and included 302 patients. There were 24 investigational sites. All adverse events and deaths reported in this study were reviewed and adjudicated by a Clinical Events Committee (CEC). The CEC was comprised of independent physicians, and its decisions were based upon independent physician review of data.

Study Endpoints

Primary Safety Endpoint

The Primary Safety Endpoint was the Procedure-related Complication-free rate at 7 days post-procedure. Procedure-related complications were defined as adverse events that are related to the ablation procedure or catheter and result in death, life threatening complication, or a persistent or significant disability/incapacity or required intervention to prevent impairment of a body function or damage to a body structure. The difference in Procedure-related Complication-free rates between the Randomized groups was calculated and compared against a 10 % non-inferiority margin.

Primary Effectiveness Endpoint

The Primary Effectiveness Endpoint was Acute Success. Acute Success was defined as demonstration of bi-directional cavo-tricuspid isthmus block 30 minutes following the last RF application in the CTI with the sole use of the randomized Investigational or selected Control Catheter only. Acute Success was evaluated for each Randomized group and the difference between the two groups was compared against a 10 % non-inferiority margin.

Secondary Effectiveness Endpoints

The Secondary Effectiveness Endpoint for the study was Chronic Success, evaluated separately for All Treated subjects (all subjects that had an ablation procedure) and Acute Success subjects (defined by the Primary Effectiveness Endpoints). Chronic Success was defined as freedom from recurrence of type I atrial flutter at 3 months post-procedure. Subjects who were prescribed Antiarrhythmic Drugs (AADs) for the treatment of type I AFL during the follow-up period were considered chronic failures. Chronic Success was evaluated in two Secondary Endpoints: Chronic Success in Acute Successes and Chronic Success in All Treated Subjects. The difference in chronic success rates between the Randomized groups was compared against a 10 % non-inferiority margin.

Tertiary Objectives

The following was evaluated for differences between the Investigational and Control groups as tertiary objectives:

- Total procedure time (first catheter inserted to last catheter removed)
    - Procedure time for patients without concomitant arrhythmias ablated
    - Procedure time for patients with concomitant arrhythmias ablated
- Fluoroscopy time
    - Fluoroscopy time for patients without concomitant arrhythmias ablated
    - Fluoroscopy time for patients with concomitant arrhythmias ablated
- Total number of RF applications per patient
- Cumulative RF time per patient
- Frequency and severity of arrhythmia-related symptoms at 3 months post-procedure as compared to baseline

Patient Accountability

All subjects who signed the Informed Consent form were considered enrolled in the study and counted towards the enrollment ceiling. Subjects were classified as either part of the Roll-in cohort or the Randomized cohort.

Roll-in — To facilitate the investigator's familiarity with the BLAZER OI Catheter and the EGMs, the study included a cohort of subjects considered to be "Roll-in" Subjects. Investigational sites without previous experience with the BLAZER OI Catheter or the Control Catheter were required to utilize one Roll-in subject for each treatment arm. Roll-in requirements could be waived for investigational sites that had previous experience.

Randomized — Once the Roll-in requirements were met at an investigational site, the subsequent enrolled subjects were part of the Randomized cohort, and were randomized 1:1 to receive treatment with either the Control Catheter or the Investigational Catheter.

Enrolled subjects were further classified into the subject statuses described below.

Intent — A subject who had been enrolled but then withdrawn from the study and did not undergo the protocol-required ablation procedure.

Attempt — A subject who had been enrolled and had anesthesia or sedation administered in preparation for the ablation procedure but did not receive ablation therapy with the treatment or Control Catheter Per-Protocol.

Treatment subject — A subject who had an ablation procedure and received ablation therapy with the Investigational or Control Catheter.

Each Primary Endpoint was analyzed based on Modified Intention-to-Treat (mITT), Per-Protocol (PP), and As Treated (AT) Populations. The Modified Intention-to-Treat analysis included all Randomized Treatment subjects in their Randomized group, regardless of compliance to the assigned treatment. The Per-Protocol analysis included subjects who were treated with the Randomized catheter, had complete endpoint data, and had no major protocol violations.

The As Treated analysis was done for each Primary Endpoint to account for one subject where the subject was randomized to the Investigational Catheter but mistakenly treated with the Control Catheter. The As Treated analysis included subjects in the group for which they received treatment, regardless of randomization.

Table 1 shows the disposition of subjects in the BLOCk-CTI study. There were five subjects enrolled and classified as part of the Randomized cohort, but who withdrew prior to being randomized. Subjects that were randomized and underwent an ablation procedure were referred to as Randomized Treatment subjects, and these were the subjects eligible for endpoint analyses. Among the Randomized cohort, there were 30 Randomized subjects classified as Intents (20 subjects) or Attempts (10 subjects). Since these subjects did not have an ablation procedure, they were not eligible for any endpoint analyses.

Subjects classified as Roll-ins, Not Randomized, Randomized Intents and Randomized Attempts were not included in endpoint analyses. Table 1 also summarizes the accountability of the Randomized Treatment subjects for inclusion in each endpoint analysis for each analysis type.

Table 1. Subject Disposition and Accountability for Endpoint Analysis

	Control	Investigational	Total
Enrolled Subjects			302
Roll-in Cohort	17	30	47
Not Randomized	N/A	N/A	5
Randomized Cohort	125	125	250
Intents	10	10	20
Subject did not meet eligibility criteria	4	4	8
Subject refused testing/follow-up	1	1	2
Subject withdrawn by physician	2	3	5
Insurance issues	2	1	3
Lab equipment issues	1	1	2
Attempts	4	6	10
Subject did not meet eligibility criteria	3	3	6
Lab equipment issues	1	2	3

	Control	Investigational	Total
Subject anatomical issues	0	1	1
Treatment Subjects (Eligible for Endpoint Analysis)	111	109	220
3-month follow-up visit completed	106	104	210
3-month follow-up visit not completed	5	5	10
Death	0	1	1
Withdrawals	1	3	4
Additional missed 3-month follow-ups	4	1	5
Endpoint Accountability for Randomized Treatment Subjects (N = 220)			
Primary Safety: 7-Day Procedure-Related Complications			
Modified Intentions-to-Treat	111	109	220
Per-Protocol	111	107	218
Excluded due to randomized error*	0	1	1
Excluded due to withdrawal within 7 days	0	1	1
As Treated*	112	108	220
Primary Effectiveness: Acute Success			
Modified Intentions-to-Treat	111	109	220
Per-Protocol	111	108	219
Excluded due to randomized error*	0	1	1
As Treated*	112	108	220
Secondary Effectiveness: Chronic Success in All Treated Subjects			
Modified Intention-to-Treat	111	109	220
Secondary Effectiveness: Chronic Success in Acute Success Subjects			
Modified Intention-to-Treat (Acute Success Subjects Only)	99	95	194
*One subject randomized to Investigational group was treated with the Control Catheter only.			

There were four Randomized Treatment subjects that withdrew from the study. A summary of withdrawal reasons for these subjects is included in Table 2.

Table 2. Randomized Subjects Withdrawal Summary

Reason	Control	Investigational
Subject refused testing/follow-up	0	2
Subject "lost to follow-up"	1	1
Total	1	3

Study Population Demographics and Baseline Parameters

The average age of the subjects was 66 ± 10 years for the Control group and 65 ± 11 years for the Investigational group.

For both treatment groups, the majority of subjects were male. The Control group enrolled 96 male subjects (76.8 %) and the Investigational group enrolled 102 male subjects (81.6 %). There were 29 females enrolled in the Control group, (23.2 %) and 23 female subjects enrolled in the Investigational group, (18.4 %). The demographics of the study population are typical for an atrial flutter ablation study performed in the US.

Overall, there were no imbalances in baseline characteristics between the two treatment groups as shown in Table 3.

Table 3. Baseline Characteristics (Randomized Cohort N = 250)

Characteristic	Measurement of Category	Control (N = 125)	Investigational (N = 125)	P-Value
Age (years)	N	125	125	0.66
	Mean ± SD	66 ± 10	65 ± 11	
	Range	35-85	25-91	
Gender [N (%)]	Female	29 (23.2)	23 (18.4)	0.35
	Male	96 (76.8)	102 (81.6)	
Cardiac and cardiovascular disease history	Hypertrophic cardiomyopathy [N (%)]	1 (0.8	2 (1.6)	0.56
	Ischemic cardiomyopathy [N (%)]	12 (9.6	9 (7.2)	0.49
	Non-ischemic cardiomyopathy [N (%)]	2 (1.6)	3 (2.4)	0.65
	Congestive Heart Failure (CHF) [N (%)]	22 (17.6	17 (13.6	0.38
	Coronary artery disease [N (%)]	44 (35.2)	44 (35.2)	1.00
	Hypertension [N (%)]	88 (70.4)	81 (64.8)	0.34
	Prior myocardial infarction [N (%)]	20 (16.0	23 (18.4)	0.62
	Valvular disease [N (%)]	22 (17.6	27 (21.6)	0.43
Cardiac intervention/ surgery history	Angiography/angioplasty [N (%)]	13 (10.4)	12 (9.6	0.83
	Stent [N (%)]	20 (16.0	10 (8.0	0.05
	CABG [N (%)]	25 (20.0	24 (19.2)	0.87
	Device implant (CRT) [N (%)]	1 (0.8	0 (0)	0.32
	Device implant (ICD) [N (%)]	8 (6.4)	5 (4.0)	0.39
	Pacemaker implant [N (%)]	3 (2.4)	10 (8.0	0.05
	Heart valve repair/replacement [N (%)]	5 (4.0)	12 (9.6	0.08
Significant non-cardiovascular disease history	Type II diabetes [N (%)]	35 (28.0	30 (24.0)	0.47
	Hyperlipidemia [N (%)]	75 (60.0	77 (61.6)	0.80
Conduction disorder	1st degree AV block [N (%)]	13 (10.4)	17 (13.6	0.44
	2nd degree AV block (Mobitz I) [N (%)]	2 (1.6)	9 (7.2)	0.03
	2nd degree AV block (Mobitz II) [N (%)]	2 (1.6)	0 (0)	0.16
History of non-type I AFL atrial arrhythmias	Atrial fibrillation [N (%)]	57 (45.6	72 (57.6)	0.08
	Atypical atrial flutter [N (%)]	2 (1.6)	2 (1.6)	1.00
	Sick sinus syndrome [N (%)]	9 (7.2)	7 (5.6	0.61

Results

Procedural Data

The goal of the ablation procedure was to produce bi-directional conduction block between the tricuspid annulus and inferior vena cava at the CTI. Subjects with type I atrial flutter were randomized to be treated with either the Investigational device or the Control device in the ablation procedure.

Three subjects were ablated for a concomitant arrhythmia, two subjects for atrial tachycardia and one subject for atrial fibrillation and atypical flutter, during the index procedure for type I atrial flutter.

Control Catheters Used

Investigators used a total of 112 Control Catheters as the initial catheter in the ablation procedure for 111 randomized Control subjects and one (1) randomized to the Investigation group. The ThermoCool Open-Irrigated Catheter (Biosense Webster) was the most frequently used catheter in the Control group (66/112), followed by the ThermoCool OI Nav Catheters (32/112) and the St. Jude Medical Cool Path, Therapy Cool Path, and Safire BLU Duo Ablation Catheters (14/112).

Ablation Parameters

The ablation parameters to achieve bi-directional block are shown in Table 4 for the Control and Investigational Catheters.

Table 4. Ablation Parameters*

Procedure Parameter	Measurement	Control N = 111	Investigational N = 109
RF applications with randomized catheter	N	1262	1313
	Mean ± SD	14 ± 12	15 ± 10
	Range	1-71	1-67
Ablation duration (seconds)	N	1260	1313
	Mean ± SD	96 ± 91	91 ± 78
	Range	0-999	0-742
Starting power (W)	N	1260	1306
	Mean ± SD	20 ± 2	19 ± 2
	Range	0-35	0-30
Max power (W)	N	1259	1308
	Mean ± SD	36 ± 7	37 ± 9
	Range	0-50	0-50
Average power (W)	N	1255	1301
	Mean ± SD	31 ± 7	32 ± 8
	Range	0-48	0-49
Max temperature (°C)	N	1259	1300
	Mean ± SD	38 ± 5	33 ± 3
	Range	23-63	0-72
Average temperature (°C)	N	1255	1301
	Mean ± SD	34 ± 4	29 ± 2
	Range	23-51	21-46
Max impedance (Ω)	N	1254	1299
	Mean ± SD	141 ± 51	155 ± 46
	Range	62-999	0-940
Average impedance (Ω)	N	1255	1300
	Mean ± SD	119 ± 30	132 ± 34
	Range	35-380	33-230

*Only includes data from randomized catheters.

Fluids Received During the Procedure

Procedural fluids administered via the open-irrigated catheters and non-catheter sources were recorded as shown in Table 5. The Investigational Catheter used more fluid than the Control Catheter. Patients randomized to the Control group received an ablation using any open-irrigated RF ablation catheter with FDA market approval for the treatment of type I AFL, when used in conjunction with the catheter's corresponding market-approved generator and pump. Fluid infusion rates for the Control Catheter pump(s) were programmed per the manufacturer's instructions for use and some had lower flow rates than the Investigational Catheter. The choice of the Control Catheter used during the procedure was left up to the discretion of the Investigator.

Table 5. Fluid and Flow Rates Recorded During the Ablation Procedure

Fluid infusion	Measurement	Control	Investigational
Primary flow rate for RF applications <= 30 W (mL/min)	N	110	109
	Mean ± SD	18 ± 7	20 ± 6
	Range	8-30	15-30
Primary flow rate for RF applications > 30 W (mL/min)	N	110	107
	Mean ± SD	25 ± 7	30 ± 1
	Range	13-30	15-30
Total fluid infused through ablation catheter (mL)	N	108	108
	Mean ± SD	611 ± 433	699 ± 386
	Range	20-2346	50-1881
Total fluid infused through non-catheter sources (mL)	N	109	109
	Mean ± SD	449 ± 337	544 ± 416
	Range	0-1900	0-2000
Total fluid output from the patient (mL)	N	110	109
	Mean ± SD	113 ± 304	133 ± 393
	Range	0-1300	0-2200

Primary Safety Endpoint

The objective of the Primary Safety Endpoint was to demonstrate that the proportion of subjects free from Procedure-related complications in the Investigational group is non-inferior to that in the Control group. The safety of the BLAZER OI Catheter was evaluated by the Procedure-related Complication-free rate at 7 days post-procedure. The Primary Safety Endpoint was determined after all adverse events that occurred within seven (7) days of the procedure were adjudicated by an independent Clinical Event Committee.

The Primary Safety Endpoint analysis includes all Randomized Treatment subjects (111 Control and 109 Investigational). Based on the Modified Intention-to-Treat analysis, the 7-day Procedure-related Complication-free rate was 98.2 % in the Control group and 93.6 % in the Investigational group. The difference in the 7 day Procedure-related Complication-free rate between the Control and the Investigational groups was 4.6 %. The upper 95 % confidence bound of 9.78 % was less than the non-inferiority margin of 10 %, demonstrating non-inferiority between the two groups. The results of the Primary Safety Endpoint are shown in Table 6. The Primary Safety Endpoint results were consistent across three analysis cohorts (e.g., mITT, PP and AT) and supported the safety of the BLAZER OI Catheter for the treatment of type I atrial flutter.

Table 6. Primary Safety Endpoint Results (Randomized Treatment Subjects N = 220)

Analysis Cohort	Study Group	Subjects Event-Free	Treatment Subjects	Procedure-Related Complication-Free Rate	Difference (One-sided Upper 95% Bound)	Endpoint Result
Modified Intention-to-Treat	Control	109	111	98.2%	4.6% (9.78%)	Pass
	Investigational	102	109	93.6%		
Per-Protocol	Control	109	111	98.2%	4.7 (9.98%)	Pass
	Investigational	100	107	93.5%		
As Treated	Control	110	112	98.2%	4.7% (9.89%)	Pass
	Investigational	101	108	93.5%		

Of the 220 Randomized Treatment subjects, 9 subjects (7 Investigational and 2 Control) had Procedure-related complications that are detailed in Table 7.

Table 7. Primary Safety Endpoint Events by Group (Randomized Treatment Subjects N = 220)

Primary Safety Events	Investigational Group N = 109	Control Group N = 111
Cerebrovascular Accident (CVA) resulting in death	1 (0.9 %)	0
Congestive heart failure	0	1 (0.9 %)
Hypotension	2 (1.8 %)	0
Vasovagal reaction	1 (0.9 %)	0
Junctional rhythm requiring pacemaker implantation	1 (0.9 %)	0
Pseudoaneurysm with hematoma	0	1 (0.9 %)
Pseudoaneurysm	1 (0.9 %)	0
Urinary tract infection	1 (0.9 %)	0
Total	**7* (6.4 %)**	**2 (1.8 %)**

* None of the primary safety events in the Investigational group was adjudicated by the Clinical Events Committee as related to the BLAZER OI Catheter.

There were no device-related complications reported in the Randomized Treatment subjects.

There was one death reported during the course of the clinical study that was adjudicated by the Clinical Events Committee as Procedure-related event. The subject was a 64 year old male with a medical history of Coronary Artery Disease (CAD), hypertension, and Myocardial Infarction (MI) with coronary artery bypass graft surgery. The subject also had a history of Chronic Obstructive Pulmonary Disease (COPD), hyperlipidemia and asthma. There was no prior history of embolic phenomena and the subject was Class 1 for the New York Heart Association Functional Classification. The subject was on ASA (325 mg.QD) for 21 days pre-procedure and Accupril for persistent type I atrial flutter. No anticoagulation therapy was administered prior to, during or after the ablation procedure. No Transesophageal Echocardiogram (TEE) was performed to exclude left atrial thrombus prior to the ablation procedure. The subject underwent CTI ablation using the Investigational Catheter and acute success was achieved without immediate complications. On day three post-procedure, the subject presented to the Emergency Department with left sided weakness, facial droop, aphasia and dysarthria. Head CT was negative for acute intracranial hemorrhage. The diagnosis of ischemic stroke (right MCA distribution) was made. Shortly after thrombolysis therapy with IV tPA administrated within two hours of symptom onset, the subject deteriorated. Repeat head CT showed massive parenchymal hemorrhagic transformation of the infarct with massive effect and midline shift. The subject passed away on day four post procedure.

The cause of the death was massive cerebral hemorrhage status post tPA for embolic stroke. The ischemic stroke could be attributed to inadequate peri-procedure anticoagulation and lack of pre-procedure TEE for exclusion of left atrial thrombus. Not performing a TEE prior to the ablation procedure in this subject with persistent AFL who was not anticoagulated pre-procedure was also a study protocol violation.

Primary Effectiveness Endpoint: Acute Success

The objective of the Primary Effectiveness Endpoint was to demonstrate that the proportion of subjects with Acute Success in the Investigational group was non-inferior to that in the Control group. Acute Success was defined as demonstration of bi-directional CTI block 30 minutes following the last RF application in the CTI, with the sole use of the randomized Investigational or selected Control Catheter.

The Primary Effectiveness Endpoint analysis includes all 220 Randomized Treatment subjects (111 Control and 109 Investigational). Based on the Modified Intention-to-Treat analysis, the Acute Success rate was 89.2 % in the Control group and 87.2 % in the Investigational group, respectively, as shown in Table 8. The difference in the Acute Success rates between the Control and the Investigational groups was 2.0 %. The upper 95 % confidence bound of 9.4 % was less than the non-inferiority margin of 10 %, demonstrating non-inferiority between the two groups. The results of the Per-Protocol and As Treated analyses were consistent with the mITT analysis and supported the effectiveness of the BLAZER OI Catheter for the treatment of type I atrial flutter.

Table 8. Primary Effectiveness Endpoint Results: Acute Success (Randomized Treatment Subjects N = 220)

Analysis Cohort	Study Group	Successful Procedures	Total Procedures	% Success	Difference (One-sided Upper 95% Bound)	Endpoint Result
Modified Intention-to-Treat	Control	99	111	89.2 %	2.03 % (9.37 %)	Pass
	Investigational	95	109	87.2 %		
Per-Protocol	Control	99	111	89.2 %	2.15 % (9.53 %)	Pass
	Investigational	94	108	87.0 %		
As Treated	Control	100	112	89.3 %	2.25 % (9.61 %)	Pass
	Investigational	94	108	87.0 %		

Secondary Effectiveness-Chronic Success

The objective of each of the Secondary Effectiveness Endpoints was to demonstrate that the proportion of subjects with Chronic Success in the Investigational group was non-inferior to that in the Control group. Chronic Success was evaluated for All Treated subjects and Randomized subjects who had Acute Success separately.

Subjects that were followed through 3 months or had an Electrocardiogram (ECG) documented recurrence of type I atrial flutter with less than 3 months of follow-up were considered to have complete data. Subjects that withdrew or died with no arrhythmia recurrence or did not follow the protocol with regards to follow-up requirements were considered to have incomplete data. These subjects with incomplete data were reviewed to determine if there was sufficient data to determine Chronic Success. Subjects with insufficient data to determine Chronic Success were included in the analysis, but could not be considered as Chronic Successes, and therefore counted against the endpoint.

Among the 220 Randomized Treatment subjects, 19 (ten Control and nine Investigational) had incomplete data due to death n = 1, one Investigational), request to be withdrawn n = 4, one Control and three Investigational), or missing follow-up ECG/visit (n = 14, nine Control and five Investigational).

Six subjects in the Investigational group (five Acute Successes and one acute failure) had ECG documented type I AFL recurrence during the 3-month follow-up period and thus were classified as chronic failures; no subjects from the Control group were classified chronic failures due to ECG documented type I AFL recurrence or on AADs for type I AFL during follow-up.

Chronic Success in Acute Successes

The analysis of this Secondary Endpoint was performed in the Modified Intention-to-Treat cohort and included only Randomized Treatment subjects who had Acute Success (99 Control and 95 Investigational). The Chronic Success rate was 89.9 % in the Control group and 85.3 % in the Investigational group, respectively. The difference in the Chronic Success rates between the Control and the Investigational groups was 4.64 %. The upper 95 % confidence bound of 12.64 % was greater than the non-inferiority margin of 10 %, resulting in failure to demonstrate non-inferiority between the two groups. The results of this Secondary Endpoint analysis are shown in Table 9.

Table 9. Chronic Success in Acute Successes (Randomized Treatment Subjects with Acute Success N = 194)

Analysis Cohort	Study Group	Chronic Success	Total Acute Subjects	% Success	Difference (One-sided Upper 95% Bound)	Endpoint Result
Modified Intention-to-Treat	Control	89	99	89.9 %	4.64 % (12.64 %)	Fail
	Investigational	81	95	85.3 %		

Chronic Success in All Treated Subjects

The analysis of this Secondary Endpoint was performed in the Modified Intention-to-Treat cohort and included all 220 Randomized Treatment subjects (111 Control and 109 Investigational). In this analysis, all acute failures were classified as chronic failures.

The Chronic Success rate was 80.2 % in the Control group and 74.3 % in the Investigational group, respectively. The difference in the Chronic Success rates between the Control and the Investigational groups was 5.87 %. The upper 95 % confidence bound of 15.08 % was greater than the non-inferiority margin of 10 %, resulting in failure to demonstrate non-inferiority between the two groups. The results of this Secondary Endpoint are shown in Table 10.

Table 10. Chronic Success in All Treated Subjects (Randomized Treatment Subjects N = 220)

Analysis Cohort	Study Group	Chronic Success	Total Acute Subjects	% Success	Difference (One-sided Upper 95% Bound)	Endpoint Result
Modified Intention-to-Treat	Control	89	111	80.2 %	5.87 % (15.08 %)	Fail
	Investigational	81	109	74.3 %		

Although the clinical study failed to statistically demonstrate non-inferiority in chronic success, the difference in the Chronic Success rates between the Investigational and Control groups was small (about 5 %) and is not considered clinically meaningful. The vast majority of the Acute Successes in the Investigational group had no type I atrial flutter recurrence during follow-up, supporting the effectiveness of the BLAZER OI Catheter for the treatment of type I atrial flutter.

Data Summary on Tertiary Objectives

The tertiary objectives included procedure time, fluoroscopy time, number of RF applications, RF time, and changes in frequency and severity of arrhythmia-related symptoms. These data are summarized in Table 11.

Table 11. Tertiary Objectives Summary (Randomized Treatment Subjects N = 220)

Tertiary Objective	Measurement	Control (N = 111)	Investigational (N = 109)
Total procedure time for subjects without concomitant arrhythmias ablated (minutes)	N	108	109
	Mean ± SD	94 ± 41	98 ± 34
	Minimum–Maximum	44–250	33–190
	Median	83	93
Total procedure time for subjects with concomitant arrhythmias ablated (minutes)	N	3	0
	Mean ± SD	153 ± 86	N/A
	Minimum–Maximum	84–249	N/A
	Median	127	N/A
Fluoroscopy time for subjects without concomitant arrhythmias ablated (minutes)	N	108	109
	Mean ± SD	14 ± 15	17 ± 10
	Minimum–Maximum	0–83	2–46
	Median	10	15
Fluoroscopy time for subjects with concomitant arrhythmias ablated (minutes)	N	3	0
	Mean ± SD	53 ± 65	N/A
	Minimum–Maximum	11–127	N/A
	Median	20	N/A
Total number of RF applications per patient	N	111	108
	RF applications per patient	12.4	13.6

Tertiary Objective	Measurement	Control (N = 111)	Investigational (N = 109)
Cumulative RF time per patient (seconds)	N	110	108
	Mean ± SD	1170 ± 976	1199 ± 842
	Minimum–Maximum	180–4739	159–4452
	Median	856	992
Change in frequency of arrhythmia-related symptoms (3 months-baseline)	N	106	104
	Mean ± SD	-6.9 ± 7.4	-7.8 ± 7.4
	Minimum, Maximum	-25, 15	-35, 11
	Median	-5	-6
Change in severity of arrhythmia-related symptoms (3 months-baseline)	N	106	104
	Mean ± SD	-5.3 ± 6.8	-5.9 ± 6.2
	Minimum, Maximum	-28, 11	-26, 7
	Median	-4	-4.5

Study Conclusion

The clinical study met its predefined success criterion by meeting both primary safety and effectiveness endpoints. There were no device related complications in the Investigational group. The vast majority of the subjects in whom Acute Success was obtained using the BLAZER OI Catheter were free of type I atrial flutter recurrence during 3-month follow-up. The study results support a reasonable assurance of safety and effectiveness of this BLAZER OI Catheter when used in accordance with the Indications for Use.

ZERO AF

Boston Scientific conducted a clinical study (ZERO AF) to establish a reasonable assurance of safety and effectiveness of radiofrequency cardiac ablation using the BLAZER OI Catheter in the treatment of Paroxysmal Atrial Fibrillation (PAF). The clinical study was conducted using a surrogate system consisting of the Stockert 70 Radiofrequency Generator and the CoolFlow Irrigation Pump and Tubing Set. However, on the basis of the engineering testing and animal studies, the results of the ZERO AF study may be extrapolated to the use of BLAZER OI Catheter with the MAESTRO RF Generator and METRIQ Pump. These data from the clinical study are summarized below.

Objective

A multi-center clinical study was conducted using the BLAZER OI Catheter. The purpose of the clinical study was to demonstrate that the BLAZER OI Investigational Catheter is non-inferior to that of the Control catheters when used for the treatment of drug refractory, recurrent, symptomatic paroxysmal atrial fibrillation in patients age 18 or older.

Study Design

The ZERO AF study was a prospective, 1:1 randomized, single-blinded, multi-center, controlled global investigation conducted at 39 Investigational sites (26 sites in US, 13 sites in OUS (Outside the United States)). Subjects randomized to the Investigational arm received ablation therapy with the Investigational BLAZER OI Catheter along with the St. Jude Medical EnSite NavX, EnSite Velocity Cardiac, or Boston Scientific RHYTHMIA Mapping System. The Control devices used in the study are the Biosense Webster ThermoCool SF NAV, NaviStar ThermoCool and EZ Steer ThermoCool NAV Ablation Catheters, hereafter referred to collectively as ThermoCool Catheters, and the CARTO Imaging System (Biosense Webster, Inc.). A commercially available radiofrequency generator (Stockert 70/EP-Shuttle), CoolFlow Irrigation Pump and the CoolFlow Tubing Kit were used in the study.

Subjects were enrolled between November 1, 2012 and August 26, 2015. The last Twelve-Month follow-up took place on October 13, 2016 and the study is considered complete. The database for this PMA reflected data collected through 12 months follow-up and included 398 patients.

All adverse events and deaths reported in this study were reviewed and adjudicated by a Clinical Events Committee (CEC). The CEC was comprised of independent physicians, and its decisions were based upon independent physician review of data.

Subject in-and Exclusion Criteria

The study's inclusion and exclusion criteria are summarized below.

Subjects were included in the study if they met all the inclusion criteria listed below:

- History of recurrent symptomatic PAF* with ≥ 2 episodes reported within the 365 days prior to enrollment
- At least 1 episode of PAF documented by Holter monitor, rhythm strip, Trans-telephonic Monitor (TTM), or 12-lead ECG in the 365 days prior to enrollment
- Refractory or intolerant to at least one Beta Blocker, Calcium Channel Blocker, Class I OR Class III Anti-arrhythmic Drug (AAD)
- Age 18 or above, or of legal age to give informed consent specific to state and national law
- Competent and willing to provide written informed consent to participate in the study and agree to comply with follow-up visits and evaluation

* Definition of PAF is AF episodes that last ≥ 30 seconds in duration and terminate within seven days. Clinical symptoms associated with PAF may include, but are not limited to, palpitations, syncope, light-headedness, chest pain/tightness, shortness of breath, and extreme fatigue.

Subjects were ineligible to participate if they met one of the exclusion criteria listed below:

- Have any of the following heart conditions within 90 days prior to enrollment:
  - New York Heart Association (NYHA) Class III or IV
  - Left Ventricular Ejection Fraction (LVEF) < 35 %
  - Left Atrial (LA) diameter > 5.5 cm
  - Unstable angina or ongoing myocardial ischemia
  - Transmural myocardial infarction
- Congenital structural heart disease that increases the risk of ablation or precludes catheter placement
- Undergone any left atrial catheter or surgical ablation
- Have had a coronary intervention, cardiac surgery, or other cardiac ablation within 90 days prior to enrollment
- Had > 1 Atrial Fibrillation (AF) episode lasting greater than seven days, with no episodes having lasted greater than 30 days, within the past year
- Subjects regularly prescribed amiodarone therapy during the 120 days prior to enrollment
- Contraindication to anticoagulation therapy
- Creatinine > 2.5 mg/dL or creatinine clearance < 30 mL/min within 90 days prior to enrollment
- Prosthetic mitral or tricuspid heart valves
- Confirmed cardiac thrombus within 30 days prior to enrollment
- Implanted pacemaker, ICD, or CRT leads within 180 days prior to enrollment
- History of CVA, TIA or PE within 180 days prior to enrollment
- Left atrial appendage closure device
- Any other significant uncontrolled or unstable medical condition (e.g., sepsis, acute metabolic illness, end stage COPD)
- Enrolled in any concurrent clinical trial without documented pre-approval from BSC
- Women who are pregnant or plan to become pregnant within the course of their participation in the investigation
- Life expectancy ≤ 2 years (730 days) per physician opinion

Follow-up Schedule

All patients were scheduled to return for follow-up examinations at pre-discharge, one month, two months, three months, six months and 12 months post-procedure. Adverse events and complications were recorded at all visits. Table 12 lists the protocol-required baseline, procedural, and follow-up assessments.

Table 12. Data Collection Schedule

				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** ≤ 90 days)	**03-MONTH FOLLOW-UP** 91 ± 14 days)	**06-MONTH FOLLOW-UP** 180 ± 30 days)	**12-MONTH FOLLOW-UP** 365 ± 30 days)	**UNSCEHDULED FOLLOW-UP**	**REPEAT PROCEDURE** > 90 days)
Informed Consent	X										
Eligibility Criteria	X	X	X								
Pregnacy 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 funtion		X[2]									
Screening for LA thrombus TTE/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 = Transesophageal 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 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 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.

Study Endpoints

Primary Safety Endpoint

The safety of the BLAZER OI Catheter was evaluated by demonstrating that the Investigational group primary safety endpoint event rate is non-inferior to that of the Control group. Primary Safety Endpoint events were defined as any of the following:

- Procedure-related Serious Adverse Events (SAEs) at seven days post-index procedure or hospital discharge, whichever is later
- Significant pulmonary vein stenosis (≥ 70 % reduction in diameter from baseline) occurred within 12 months of the index procedure
- Atrio-esophageal fistulas that occurred within 12 months of the index procedure

All adverse events were adjudicated by an independent committee of physicians as to their severity and relationship to the Investigational and Control catheters and/or procedure.

Primary Effectiveness Endpoint

The effectiveness of the BLAZER OI Catheter was evaluated by demonstrating that the proportion of subjects free from failure in the Investigational group is non-inferior to those in the Control group at 12 months after the index ablation procedure. Failure was defined as a Randomized subject being an acute procedure failure, having more than one repeat procedure during the Blanking Period, having a repeat procedure outside the Blanking Period, or having any of the following between 91 days and 12 months post-procedure:

- A documented symptomatic AF, AT, or AFL (≥ 30 seconds in duration or from a 10-second 12-lead ECG
- Prescribed a higher dose of a previously failed AAD*
- Prescribed a new AAD*

* AADs for this endpoint consisted of all Class I/III medications and Class II/IV medications taken explicitly for control of arrhythmia recurrence.

Secondary Effectiveness Endpoint

The Secondary Effectiveness Endpoint of acute procedural success was evaluated by demonstrating that the Investigational group acute procedural success rate is non-inferior to that of the Control group. Acute procedural success was defined as a subject that successfully had all clinically relevant PVs electrically isolated, by demonstration of entrance block at a minimum and no evidence of exit conduction with the Investigational or Control Catheter only.

Each endpoint was analyzed and evaluated for success based on Modified Intention-to-Treat and Per-Protocol PP) subject cohorts. The mITT analysis included all Randomized Treatment subjects in their Randomized group, regardless of compliance to the assigned treatment. The Per-Protocol analysis included subjects who were treated with the Randomized catheter, had complete endpoint data, and had no major protocol violations.

Accountability of PMA Cohort

All subjects who signed the Informed Consent Form were considered enrolled in the study and counted towards the enrollment ceiling. Subjects were classified as either part of the Roll-in cohort or the Randomized cohort:

Roll-in Subject – To help facilitate Investigators' familiarity with the new Investigational system, the first two subjects enrolled by the first two Investigators assigned could be classified as "Roll-in" subjects and would not undergo randomization.

Randomized Subject — After the Roll-in subject criteria or case review was satisfied for the treating physician, their subjects were randomized 1:1 to either the Investigational or Control arm of the study. Randomization was stratified by Investigational site. Study subjects were not informed of their randomization assignment. Subjects could be informed of their randomization assignment at the end of the Twelve-Month follow-up visit upon request. Subjects were further classified as Intent, Attempt, and Treatment as described below.

Intent — Refers to a subject who was enrolled but withdrew from the study and did not undergo the protocol-required ablation procedure.

Attempt — Refers to a subject who was enrolled and had anesthesia or sedation administered in preparation for the ablation procedure but did not receive ablation therapy with the Investigational or Control Catheter Per-Protocol.

Treatment — Refers to all enrolled subjects who received ablation therapy with the Investigational or Control Catheter.

Table 13 shows the subject disposition for all Roll-in and Randomized subjects. Data from Roll-in subjects are not included in endpoint analyses.

Table 13. Subject Disposition and Accountability for Endpoint Analysis

	Control	Investigational	Total
Enrolled Subjects			398
Roll-in Cohort	3	56	59
Randomized Cohort	172	167	339
Intents	5	8	13
Adverse Event	0	1	1
Did not meet eligibility criteria	2	2	4
Investigator discretion	1	1	2
Lost to follow-up	0	1	1
No longer meets protocol criteria	1	2	3
No product available	1	0	1
Withdrew from study participation	0	1	1
Attempts	3	2	5
Treatment Subjects (Eligible for Endpoint Analysis)	164	157	321
12-month follow-up visit completed	145	139	284
12-month follow-up visit not completed	19	18	37
Death	1	1	2
Withdrawals	16	16	32
Missed 12-month follow-up	2	1	3
Endpoint Accountability for Randomized Treatment Subjects (N = 321)			
Primary Safety Endpoint and Secondary Effectiveness Endpoint			
Modified Intention-to-Treat	164	157	321
Per-Protocol	160	157	317
Excluded due to randomization error*	4	0	4
Primary Effectiveness Endpoint			
Modified Intention-to-Treat	164	157	321
Complete Data	152	146	298
Imputed Data	12	11	23
Per-Protocol	148	146	294
Excluded due to randomization error*	4	0	4

	Control	Investigational	Total
Excluded due to incomplete follow-up endpoint event (includes death, withdrawal, and missed visit with no TTM in window)	12	11	23
*Four subjects randomized to the Control group were treated with the Investigational Catheter.			

There were 42 Treatment subjects (35 Randomized and 7 Roll-in) that withdrew from the study. A summary of withdrawal reasons for these subjects is included in Table 14.

Table 14. Treatment Subjects Withdrawal Summary

Reason for Withdrawal	Control N (%)	Investigational N (%)
Adverse event	1 (5.6	1 (4.2)
Investigator discretion	1 (5.6	2 (8.3)
Lost to follow-up	5 (27.8	2 (8.3)
No longer meets protocol criteria	3 (16.7	0 (0)
Study device change / revision	2 (11.1)	5 (20.8
Withdrew from study participation	4 (22.2)	12 (50)
Other	2 (11.1)	2 (8.3)
Total	**18**	**24**

Study Population Demographics and Baseline Parameters

The tables in this section include data from all Randomized subjects (N = 339).

The average age of the subjects is 59 ± 10 years for the Control group and 60 ± 11 years for the Investigational group. For both Treatment groups, the majority of subjects were male; the Control group had 107 male subjects (62 %) and the Investigational group had 105 male subjects (63 %). The male gender predominance is consistent with previous clinical studies for RF ablation of PAF. The majority of subjects for both Treatment groups were evaluated as non-heart failure; the Control group with 92 subjects (53.5 %) and the Investigational group with 76 subjects (45.5 %).

Overall, there were no significant imbalances in baseline characteristics between the two Treatment groups. Table 15 presents the demographics and physical assessment data for all Randomized patients.

Table 15. Baseline Characteristics

Characteristic	Measurement	Control (N = 172)	Investigational (N = 167)	P-Value
Age at index procedure (years)	N	172	167	
	Mean ± SD	59 ± 10	60 ± 11	0.32
	Range	31–82	22–84	
Gender [N (%)]	Female	65 (38)	62 (37)	0.9
	Male	107 (62)	105 (63)	
Height (cm)	N	169	165	
	Mean ± SD	174 ± 9	173 ± 9	0.5
	Range	150–200	150–193	
Weight (kg)	N	169	165	
	Mean ± SD	90 ± 22	89 ± 19	0.55
	Range	53–218	46–167	
Resting heart rate (bpm)	N	169	164	
	Mean ± SD	67 ± 15	71 ± 19	0.08
	Range	39–130	43–156	

Characteristic	Measurement	Control (N = 172)	Investigational (N = 167)	P-Value
Resting systolic BP (mmHg)	N	169	164	
	Mean ± SD	130 ± 20	131 ± 16	0.7
	Range	90–191	96–171	
Resting diastolic BP (mmHg)	N	169	164	
	Mean ± SD	76 ± 11	77 ± 11	0.38
	Range	48–110	50–116	
Creatinine (mg/dL)	N	166	161	
	Mean ± SD	0.9 ± 0.2	0.9 ± 0.2	0.42
	Range	0.4–1.5	0.5–2.5	
NYHA class	I	64 (37.2)	67 (40.1)	0.3
	II	13 (7.6	17 (10.2)	
	Non HF	92 (53.5)	76 (45.5)	
	Not Assessed	3 (1.7)	7 (4.2)	
Left atrial diameter (cm)	N	165	162	
	Mean ± SD	3.97 ± 0.65	3.96 ± 0.65	0.86
	Range	2.30–5.50	2.30–5.50	
LVEF (%)	N	164	161	
	Mean ± SD	60.4 ± 7.4	60.2 ± 7.2	0.76
	Range	38.0–86.0	35.0–84.0	

Pre-existing conditions and arrhythmia/conduction disorder history of Randomized subjects are summarized in Table 16 and Table 17.

Table 16. Pre-existing Conditions Recorded at Baseline

Characteristic	Category	Control (N = 172)	Investigational (N = 167)	P-Value
Cardiac/cardiovascular disease history	Dilated cardiomyopathy [N (%)]	0 (0)	3 (1.8)	0.08
	Hypertrophic cardiomyopathy [N (%)]	4 (2.3)	2 (1.2)	0.43
	Ischemic cardiomyopathy [N (%)]	3 (1.7)	5 (3.0	0.45
	Non-ischemic cardiomyopathy [N (%)]	1 (0.6	6 (3.6	0.05
	Cerebral vascular disease [N (%)]	3 (1.7)	2 (1.2)	0.68
	Congestive Heart Failure (CHF) [N (%)]	5 (2.9)	8 (4.8)	0.37
	Coronary artery disease [N (%)]	21 (12.2)	18 (10.8	0.68
	Hypertension [N (%)]	84 (48.8	98 (58.7	0.07
	Myocardial infarction [N (%)]	1 (0.6	6 (3.6	0.05
	Peripheral vascular disease [N (%)]	2 (1.2)	4 (2.4)	0.39
	Pulmonary hypertension [N (%)]	1 (0.6	2 (1.2)	0.54
	Aortic valvular disease [N (%)]	1 (0.6	5 (3.0	0.09
	Mitral valvular disease [N (%)]	7 (4.1)	7 (4.2)	0.96
	Pulmonic valvular disease [N (%)]	1 (0.6	3 (1.8)	0.3
	Tricuspid valvular disease [N (%)]	3 (1.7)	5 (3.0	0.45
	Other cardiac disease history* [N (%)]	9 (5.2)	5 (3.0	0.3

Characteristic	Category	Control (N = 172)	Investigational (N = 167)	P-Value
Cardiac intervention/ surgery history	Aneurysmectomy [N (%)]	0 (0)	2 (1.2)	0.15
	Angiography/angioplasty [N (%)]	5 (2.9)	8 (4.8)	0.37
	Stent [N (%)]	8 (4.7)	10 (6.0	0.58
	CABG [N (%)]	3 (1.7)	5 (3.0	0.45
	Device implant (CRT) [N (%)]	0 (0)	2 (1.2)	0.15
	Device implant (ICD) [N (%)]	1 (0.6	3 (1.8)	0.3
	Pacemaker implant [N (%)]	3 (1.7)	8 (4.8)	0.11
	Heart valve repair/replacement [N (%)]	0 (0)	2 (1.2)	0.15
	Other cardiac intervention/ surgery** [N (%)]	5 (2.9)	6 (3.6	0.72
Significant non-cardiovascular disease history	COPD [N (%)]	10 (5.8	5 (3.0	0.21
	Type I diabetes [N (%)]	4 (2.3)	1 (0.6	0.19
	Type II diabetes [N (%)]	18 (10.5)	18 (10.8	0.93
	Hepatic disease [N (%)]	1 (0.6	1 (0.6	0.98
	Neurologic disease [N (%)]	4 (2.3)	5 (3.0	0.7
	Renal disease [N (%)]	6 (3.5)	4 (2.4)	0.55
	GI bleed or other coagulopathies [N (%)]	2 (1.2)	4 (2.4)	0.39
	Hyperlipidemia [N (%)]	69 (40.1)	64 (38.3)	0.74
	Sleep apnea [N (%)]	27 (15.7	23 (13.8	0.62
	Other non-cardiovascular disease*** [N (%)]	44 (25.6	47 (28.1	0.59

* Other Cardiac Disease History: Aortic Atheroma, Diastolic Dysfunction, ST Abnormality, Left Ventricular Hypertrophy, Scleroderma, Syncope, Atypical chest pain, Diastolic Dysfunction, Idiopathic Pulmonary Embolism, Aortic Stenosis, Pericarditis

** Other Cardiac Intervention/Surgery History: Cardiac Ablation, Loop recorder implantation, Cardioversion, Left brachial embolectomy

*** Other Non-Cardiovascular Disease History: Allergy, Anemia, Anxiety, Cancer, Dermatological Issues, Dyslipidemia, Gastrointestinal, Gynaecological Diseases, Hypercholesterolemia, Hyperglycemia, Hyperuricemia, Hypomagnesium, Hypotension, Hypothyroidism, Medication intolerances, Musculoskeletal Diseases, Neurological Diseases, Obesity, Ophthalmological Diseases, Pulmonary Diseases, Rheumatological Diseases, Sleeping Disorders

Table 17. Arrhythmia/Conduction Disorder History

Characteristic	Category	Control (N = 172)	Investigational (N = 167)	P-Value
Arrhythmia and conduction disorder history	1st degree AV block [N (%)]	23 (13.4)	24 (14.4)	0.79
	2nd degree AV block (Mobitz 2) [N (%)]	1 (0.6	0 (0)	0.32
	3rd degree AV block [N (%)]	0 (0)	2 (1.2)	0.15
	Intraventricular conduction delay [N (%)]	12 (7.0	16 (9.6	0.38
	Left bundle branch block [N (%)]	2 (1.2)	1 (0.6	0.58
	Right bundle branch block [N (%)]	3 (1.7)	12 (7.2)	0.01
	Other conduction disorder* [N (%)]	25 (14.5)	27 (16.2)	0.68
	Atrial flutter [N (%)]	45 (26.2)	42 (25.1	0.83

* Other Conduction Disorder History: Atrial Tachycardia, Atrioventricular Nodal Reentry Tachycardia (AVNRT), Cardiac Arrest, Junctional Tachycardia, Low Voltage QRS, Mild ST/T changes, Non-sustained Ventricular Tachycardia, Premature Atrial Contractions, Premature Ventricular Contractions, Sick Sinus Syndrome, Sinus Bradycardia, Sinus Tachycardia, Supraventricular Ectopic Beat, Supraventricular Tachycardia, Syncope, Tachy-Brady Syndrome, Variable AV Block, Ventricular Fibrillation, Ventricular Tachycardia, Wolff Parkinson White Syndrome

Procedural Data

The tables in this section include data from all Randomized Treatment subjects (N = 321).

The goal of the ablation procedure was electrical isolation of all clinically relevant pulmonary veins. Use of multiple catheter curves of a single catheter type was allowed in both arms; however, use of only one catheter type was allowed. Once the Control Catheter type was selected by the Investigator and Investigators could not switch to another Control Catheter type. If multiple catheter curves of a single catheter type were required or if a catheter was changed from a unidirectional curve to a bi-directional curve, these were considered same types of catheters and would not affect the outcome determination of acute success.

The largest proportion of the Control cases were completed with the ThermoCool SF NAV (42 %) with the rest of the cases closely split between the EZ Steer ThermoCool NAV (27.4 %) and the NaviStar ThermoCool (28 %). Four Control subjects were incorrectly treated with the BLAZER OI Catheter. For the Investigational group, all index procedures were initiated with the BLAZER OI Catheter. The summary of Control devices used for study procedures is included in Table 18.

Table 18. Catheters Used in the Procedure

Catheter	Control N (%)	Investigational N (%)
BLAZER OI Catheter	4 (2.4)*	157 (100)
EZ Steer ThermoCool NAV Catheter	46 (28)	0 (0.0
NaviStar ThermoCool Catheter	45 (27.4)	0 (0.0
ThermoCool SF NAV Catheter	69 (42.1)	0 (0.0
*Four subjects were randomized to Control but treated with a BLAZER OI Catheter.		

Table 19 includes the procedural data for Randomized Treatment subjects treated with only the Randomized catheter.

Table 19. Ablation Parameters — ONLY Randomized Treatment Catheters Used for Control and Investigational

Procedure Parameter	Measurement	Control	Investigational
RF applications in the PVs	N	153	129
	Mean ± SD	38 ± 25	38 ± 30
Total RF applications for procedure	N	153	129
	Mean ± SD	42 ± 27	41 ± 32
RF time in PVs (minutes)	N	152	129
	Mean ± SD	41 ± 22	37 ± 25
Total RF time for procedure (minutes)	N	152	129
	Mean ± SD	45 ± 25	41 ± 26
Starting power (W)	N	152	129
	Mean ± SD	19 ± 4	19 ± 3
Max power (W)	N	151	128
	Mean ± SD	37 ± 6	36 ± 6
Average power (W)	N	148	125
	Mean ± SD	30 ± 5	30 ± 5
Max temperature (°C)	N	148	125
	Mean ± SD	38 ± 5	36 ± 4
Average temperature (°C)	N	148	125
	Mean ± SD	32 ± 3	31 ± 3
Max impedance (Ω)	N	148	125
	Mean ± SD	178 ± 55	195 ± 45

Procedure Parameter	Measurement	Control	Investigational
Average impedance (Ω)	N	148	125
	Mean ± SD	125 ± 21	152 ± 30

Fluids Received During the Procedure

Procedural fluid volumes administered via the open-irrigated catheters were recorded as shown in Table 20. The choice of the Control catheter used during the procedure was left up to the discretion of the Investigator. Fluid infusion rates were programmed per the manufacturer's instructions for use. As the ThermoCool SF has lower prescribed flow rates than the Investigational catheter, use of the ThermoCool SF in the study could account for the Investigational catheter having a higher mean (1.34 ± 0.71 L versus 1.18 ± 0.64 L) total fluid infusion.

Table 20. Fluid Volumes Infused During Ablation Procedure

Fluid Infusion	Measurement	Control	Investigational
Fluid infused from catheter sources (L)	N	162	155
	Mean ± SD	1.18 ± 0.64	1.34 ± 0.71
	Range	0.20–4.00	0.10–3.50

Procedure and Fluoroscopy Duration

Procedure duration for the ZERO AF Study was defined as the time from first catheter inserted to last catheter removed in order to reduce variability in data reported due to procedure preparations and pre-ablation activities. As shown in Table 21, the mean procedure duration and mean fluoroscopy duration was similar for the Control and Investigational groups.

Table 21. Procedure Duration and Fluoroscopy Duration

Procedure Parameter	Measurement	Control	Investigational
Procedure duration (minutes)	N	164	156
	Mean ± SD	162 ± 66	168 ± 63
	Range	62–469	73–401
Fluoroscopy duration (minutes)	N	163	156
	Mean ± SD	25 ± 17	28 ± 18
	Range	0–90	3–85

Ablation Locations for All Randomized Treatment Subjects

Table 22 shows a summary of the number of PVs ablated and the acute success of the Pulmonary Vein Isolation (PVI). For the Investigational group, 141 subjects had four or more PVs ablated with 140 of those cases resulting in all PVs isolated.

Eleven subjects in the Investigational group had three PVs ablated resulting in all PVs isolated.

For 147 subjects in the Control group, four or more PVs were ablated resulting in all PVs isolated. Fifteen subjects in the Control group had three PVs ablated, with all cases achieving acute success for PVI.

Table 22. Pulmonary Vein Isolation

	Control		Investigational	
PV Locations Ablated	Ablated	Acute PVI Success	Ablated	Acute PVI Success
4+ PV Locations	147	147	141	140
3 PV Locations	15	15	11	11
2 PV Locations	2	1	4	4
1 PV Location	0	0	1	0

The majority of the Randomized subjects in the study underwent only ablation of the PVs N = 197) with 98 such cases in the Control group and 99 cases in the Investigational group. For the next two largest categories of procedure, 57 subjects (30 Control, 27 Investigational) underwent pulmonary vein isolation and ablation of the cavo-tricuspid isthmus and 46 subjects (25 Control, 21 Investigational) underwent PV ablation and additional non-PV Foci in the right or left atria. Table 23 shows the full breakdown for all Randomized subjects by assigned group.

Table 23. Ablation Locations for All Randomized Subjects

Ablation Locations	Control N (%)	Investigational N (%)
PV Only	98 (59.8)	99 (63.1)
PV + CTI	30 (18.3)	27 (17.2)
PV + RA/LA	24 (14.6)	20 (12.7)
PV + Additional Induced	0 (0.0	4 (2.5)
PV + CTI + RA/LA	11 (6.7	6 (3.8
PV + RA/LA + Additional Induced	1 (0.6	1 (0.6

Safety and Effectiveness Results

The tables in this section include data from all Randomized Treatment subjects (N = 321).

Primary Safety Endpoint

The objective of the Primary Safety Endpoint was to demonstrate that the proportion of subjects free from Primary Safety events in the Investigational group is non-inferior to that in the Control group. The Primary Safety Endpoint analysis includes all Randomized Treatment subjects (164 Control and 157 Investigational). Based on the Modified Intention-to-Treat analysis, the Primary Safety event-free rate was 90.24 % in the Control group and 89.17 % in the Investigational group. The difference in the rates between the Control and the Investigational groups was 1.07 %. The upper 95 % confidence bound of 6.93 % was less than the non-inferiority margin of 9 %, demonstrating non-inferiority between the two groups.

The results of the Primary Safety Endpoint are shown in Table 24. The Primary Safety Endpoint results were consistent between the two analysis cohorts (mITT and PP) and support the safety of the BLAZER OI Catheter for the treatment of PAF.

Table 24. Primary Safety Endpoint Results

Endpoint	Analysis	Study Group	Successful Procedures	Total Procedures	% Success	Difference (One-Sided Upper 95 % Bound)	Endpoint Result
Primary Safety Endpoint Non-Inferiority Margin: 9 %	mITT	Control	148	164	90.24 %	1.07 % (6.93 %)	Pass
		Investigational	140	157	89.17 %		
	PP	Control	145	160	90.63 %	1.45 % (7.35 %)	Pass
		Investigational	140	157	89.17 %		

Of the 321 Randomized Treatment subjects, 33 subjects (16 Control and 17 Investigational) had Safety Endpoint events as detailed in Table 25.

Table 25. Primary Safety Endpoint Events by Group

Adverse Event	Control Events (Subjects)	Investigational Events (Subjects)
AV fistula	1 (1)	0 (0)
Arrhythmia (severe bradycardia)	0 (0)	1 (1)
Arterial/venous thromboembolic events	0 (0)	1 (1)
Atypical atrial flutter	1 (1)	0 (0)
Cardiac arrest	0 (0)	1 (1)
Cardiac tamponade/perforation	3 (3)	4 (4)
Dizziness	0 (0)	1 (1)
Dyspnea	1 (1)	0 (0)
Fluid volume overload (i.e., diuresis, electrolyte imbalance) (ablation procedure)	0 (0)	1 (1)
Gastrointestinal	1 (1)	2 (2)
Genitourinary	0 (0)	1 (1)
Head, Eyes, Ears, Nose, Throat (HEENT)	2 (2)	0 (0)
Heart failure/pulmonary edema	0 (0)	2 (2)
Hematoma (ablation procedure)	0 (0)	1 (1)
Hypotension	0 (0)	1 (1)
Multiple symptoms	0 (0)	1 (1)
Myocardial infarction	0 (0)	1 (1)
Pulmonary	4 (4)	3 (3)
Pulmonary vein stenosis—significant (> 70 %)	2 (2)	1 (1)
Rectus sheath hematoma	0 (0)	1 (1)
Sanguineous drainage	1 (1)	0 (0)
Total	**16 (16)**	**23 (17)**

Two Randomized Treatment subjects (one Control subject and one Investigational subject) died during the course of the clinical study. Both deaths were adjudicated by the Clinical Events Committee as not Procedure-related.

Adverse Effects That Occurred in the Clinical Study

Adverse effects are defined in Table 26 and reported in Table 27.

Table 26. Definitions of Adverse Effects

Term	Definition
Complication	A clinical complication is a clinical event that required an invasive intervention, injury, or death (e.g., surgical evacuation of a hematoma, lead dislodgment requiring lead repositioning, generator replacement, loss or abandonment of therapy).
Observation	A clinical observation is a clinical event that did not result in invasive intervention, injury, or death, and is not an unanticipated adverse event. Corrective actions were simple adjustments such as reprogramming of the pulse generator or antibiotic treatment of a pocket infection.

Table 27. Ablation Related Adverse Effects

	Control N = 167				Investigational N = 159			
	Complications		Observations		Complications		Observations	
Adverse Events	N Events	N Patients (%)	N Events	N Patients (%)	N Events	N Patients (%)	N Events	N Patients (%)
Ablation Related Events	13	13 (7.8	30	21 (12.6)	20	14 (8.8	48	36 (22.6)
AV fistula	1	1 (0.6	0	0 (0.0	0	0 (0.0	1	1 (0.6
Allergic reaction (ablation procedure)	0	0 (0.0	1	1 (0.6	0	0 (0.0	1	1 (0.6
Anesthesia/sedation related complication (ablation procedure)	0	0 (0.0	0	0 (0.0	0	0 (0.0	3	1 (0.6
Arrhythmia (ablation procedure)	1	1 (0.6	1	1 (0.6	3	3 (1.9)	1	1 (0.6
Atrial tachycardia	0	0 (0.0	0	0 (0.0	0	0 (0.0	1	1 (0.6
Atypical atrial flutter	1	1 (0.6	0	0 (0.0	1	1 (0.6	0	0 (0.0
Back discomfort	1	1 (0.6	0	0 (0.0	0	0 (0.0	0	0 (0.0
Breathing difficulties	0	0 (0.0	1	1 (0.6	0	0 (0.0	0	0 (0.0
Cardiac arrest	0	0 (0.0	0	0 (0.0	1	1 (0.6	0	0 (0.0
Cardiac tamponade/perforation	3	3 (1.8)	0	0 (0.0	4	4 (2.5)	0	0 (0.0
Chest pain	0	0 (0.0	1	1 (0.6	0	0 (0.0	3	3 (1.9)
Dyspnea on exertion	0	0 (0.0	0	0 (0.0	0	0 (0.0	1	1 (0.6
Edema (ablation procedure)	0	0 (0.0	0	0 (0.0	0	0 (0.0	2	2 (1.3)
Fever	0	0 (0.0	1	1 (0.6	0	0 (0.0	1	1 (0.6
Fluid volume overload (i.e., diuresis, electrolyte imbalance) (ablation procedure)	0	0 (0.0	0	0 (0.0	2	2 (1.3)	0	0 (0.0
Gastroparesis (ablation procedure)	0	0 (0.0	0	0 (0.0	0	0 (0.0	1	1 (0.6
Genitourinary	0	0 (0.0	3	3 (1.8)	2	2 (1.3)	4	3 (1.9)
Groin pain	0	0 (0.0	0	0 (0.0	0	0 (0.0	1	1 (0.6
Heart failure	0	0 (0.0	0	0 (0.0	1	1 (0.6	0	0 (0.0
Hematoma (ablation procedure)	0	0 (0.0	5	5 (3.0	1	1 (0.6	8	7 (4.4)
Hemorrhage (ablation procedure)	0	0 (0.0	1	1 (0.6	0	0 (0.0	2	2 (1.3)
Hypotension (ablation procedure)	0	0 (0.0	1	1 (0.6	0	0 (0.0	0	0 (0.0
Long QT	0	0 (0.0	1	1 (0.6	0	0 (0.0	0	0 (0.0
Multiple symptoms	0	0 (0.0	0	0 (0.0	0	0 (0.0	1	1 (0.6
Non-toxic LLE cellulitis	0	0 (0.0	1	1 (0.6	0	0 (0.0	0	0 (0.0
Pain neuromuscular/non-cardiovascular (ablation procedure)	0	0 (0.0	0	0 (0.0	0	0 (0.0	2	2 (1.3)
Pericardial effusion (ablation procedure)*	1	1 (0.6	3	3 (1.8)	0	0 (0.0	5@	5 (3.1
Pericarditis (ablation procedure)	0	0 (0.0	0	0 (0.0	1	1 (0.6	0	0 (0.0
Peripheral neuropathy	0	0 (0.0	1	1 (0.6	0	0 (0.0	0	0 (0.0
Pleuritis (ablation procedure)	0	0 (0.0	1	1 (0.6	0	0 (0.0	0	0 (0.0
Pulmonary	2	2 (1.2)	3	3 (1.8)	2	2 (1.3)	1	1 (0.6
Pulmonary vein stenosis—mild or moderate (< 70 %)	0	0 (0.0	0	0 (0.0	0	0 (0.0	4	4 (2.5)

	Control N = 167				Investigational N = 159			
	Complications		Observations		Complications		Observations	
Adverse Events	N Events	N Patients (%)	N Events	N Patients (%)	N Events	N Patients (%)	N Events	N Patients (%)
Pulmonary vein stenosis—significant (> 70 %)	2	2 (1.2)	0	0 (0.0	1	1 (0.6	0	0 (0.0
Rectus sheath hematoma	0	0 (0.0	0	0 (0.0	1	1 (0.6	0	0 (0.0
Sanguineous drainage	1	1 (0.6	0	0 (0.0	0	0 (0.0	0	0 (0.0
Sore throat	0	0 (0.0	3	3 (1.8)	0	0 (0.0	0	0 (0.0
Swollen groin	0	0 (0.0	0	0 (0.0	0	0 (0.0	2	2 (1.3)
Tachycardia (ablation procedure)	0	0 (0.0	0	0 (0.0	0	0 (0.0	1	1 (0.6
Typical atrial flutter	0	0 (0.0	1	1 (0.6	0	0 (0.0	1	1 (0.6
Vagal denervation symptoms	0	0 (0.0	1	1 (0.6	0	0 (0.0	0	0 (0.0
Visual blurring/disturbances (ablation procedure)	0	0 (0.0	0	0 (0.0	0	0 (0.0	1	1 (0.6

* Non-significant pericardial effusion, no hemodynamic compromise, no action taken
@ One subject experienced a perforation/tamponade both reported as an initial primary adverse event and also reported as a pericardial effusion without any intervention 19 days post procedure.

Primary Effectiveness Endpoint

Chronic success was defined as freedom from recurrence of atrial arrhythmias at 12 months post procedure. Recurrences included being an acute procedure failure, having more than one repeat procedure within 90 days, prescribed a new AAD or higher dose of a previously failed AAD after 90 days, or a documented symptomatic AF, AT, or AFL episode after 90 days. The objective of the Primary Effectiveness Endpoint was to demonstrate that the proportion of subjects with chronic success in the Investigational group was non-inferior to that in the Control group.

The Modified Intention-to-Treat analysis of the Primary Effectiveness Endpoint included all 321 Randomized Treatment subjects (164 Control and 157 Investigational). Subjects that withdrew or died with no primary effectiveness event or met pre-defined criteria for incomplete follow-up data were classified as having incomplete data. Multiple imputation methods were used to determine primary effectiveness endpoint outcomes for these subjects in the mITT analysis. Among the 321 Randomized Treatment subjects, outcomes were imputed for 23 subjects (12 Control and 11 Investigational).

Based on the mITT analysis, the chronic success rate was 65.85 % in the Control group and 64.97 % in the Investigational group. The difference in the chronic success rates between the Control group and the Investigational group was 0.89 %. The upper 95 % confidence bound of 9.54 % was less than the non-inferiority margin of 15 %, demonstrating non-inferiority between the two groups.

The results of the Primary Effectiveness Endpoint are shown in Table 28. The results of the Per- Protocol analyses were consistent with the mITT analysis and support the effectiveness of the BLAZER OI Catheter for the treatment of PAF.

Table 28. Primary Effectiveness Endpoint Results

Endpoint	Analysis	Study Group	Successful Procedures	Total Procedures	% Success	Difference (One-Sided Upper 95 % Bound)	Endpoint Result
Chronic Success Non-Inferiority Margin: 15 %	mITT	Control	108	164	65.85 %	0.89 % (9.54 %)	Pass
		Investigational	102	157	64.97 %		
	PP	Control	95	148	64.19 %	-0.19 % (8.92 %)	Pass
		Investigational	94	146	64.38 %		

Secondary Effectiveness Endpoint

An acute success was defined as subject that successfully had all clinically relevant PVs electrically isolated, by demonstration of entrance block at a minimum and no evidence of exit conduction with the Investigational or Control catheter only. The objective of the Secondary Effectiveness Endpoint was to demonstrate that the proportion of subjects with acute success in the Investigational group was non-inferior to that in the Control group.

The Modified Intention-to-Treat analysis of the Secondary Effectiveness Endpoint included all 321 Randomized Treatment subjects (164 Control and 157 Investigational). Based on the Modified Intention-to-Treat analysis, the acute success rate was 89.39 % in the Control group and 98.73 % in the Investigational group. The difference in the acute success rates between the Control group and the Investigational group was 0.66 %. The upper 95 % confidence bound of 4.75 % was less than the non-inferiority margin of 10 %, demonstrating non-inferiority between the two groups.

The results of the Secondary Effectiveness Endpoint are shown in Table 29. The results of the Per-Protocol were consistent with the mITT analysis and support the effectiveness of the BLAZER Open-Irrigated Ablation Catheter for the treatment of PAF.

Table 29. Secondary Effectiveness Endpoint Results

Endpoint	Analysis	Study Group	Successful Procedures	Total Procedures	% Success	Difference (One-Sided Upper 95 % Bound)	Endpoint Result
Acute Procedural Success Non-Inferiority Margin: 10 %	mITT	Control	163	164	99.39 %	0.66 % (4.75 %)	Pass
		Investigational	155	157	98.73 %		
	PP	Control	159	160	99.38 %	0.65 % (4.78 %)	Pass
		Investigational	155	157	98.73 %		

Study Conclusion

All Primary and Secondary Endpoints for the ZERO AF study were met. The study results indicate that the overall safety and effectiveness profile of the BLAZER OI Catheters is similar to that of the Control catheters for the treatment of drug refractory, symptomatic paroxysmal atrial fibrillation. Taken together, the study results support a reasonable assurance of safety and effectiveness of the BLAZER OI Catheter when used in accordance with the Indications for Use.

NEwTON AF

Clinical Summary

Study title: Clinical Evaluation of the INTELLANAV STABLEPOINT Catheter and Force-Sensing System for Paroxysmal Atrial Fibrillation (NEwTON-AF study)

Number of centers: 45 sites in the United States (23), Europe (12), Canada (3), and Asia-Pacific (7)

Number of subjects: 299 subjects treated with the INTELLANAV STABLEPOINT Catheter and Force Sensing System

Objective

The purpose of the NEwTON AF clinical study was to demonstrate the INTELLANAV STABLEPOINT Catheter and Force Sensing System with DIRECTSENSE Technology is safe and effective for the treatment of drug refractory, recurrent symptomatic paroxysmal atrial fibrillation.

Design, Scope and Methods

The NEwTON AF study was a prospective, single arm, multi-center, global study conducted at 45 Investigational sites (23 sites in US, 12 sites in Europe, 3 sites in Canada and 7 sites in Asia-Pacific). A total of 321 subjects were enrolled between April 12, 2021 and June 3, 2022, with 299 subjects classified as Treatment undergoing an ablation procedure with the Investigational INTELLANAV STABLEPOINT Catheter. Subjects were followed at pre-discharge, 1 month, 3 months, 6 months, and 12 months post-Index Procedure for adverse events and recurrence of atrial tachyarrhythmias. The data set reflects data collected for the 12-month endpoint analyses which were prospectively planned and conducted after all 299 Treatment subjects completed their 12-month follow up.

Study Endpoints

Primary Safety Endpoint at 12 Months

The primary safety endpoint at 12 months was defined as the safety event-free rate at 12 months post-procedure. Primary safety events at 12 months consisted of a composite of the following serious procedure and/or device-related adverse events. The following events were counted through 7 days post index procedure or hospital discharge, whichever was later.

- 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
- Atrioventricular (AV) block*

The following events were counted through 30 days post index procedure:

- Cardiac tamponade/perforation

The following events were counted through 12 months post index procedure:

- Atrial esophageal fistula
- Severe pulmonary vein stenosis (≥70% reduction in the diameter of the PV or PV branch from baseline)
- Persistent phrenic nerve palsy**

* AV block not attributable to medication effect or vasovagal reaction.

** A non-recovered phrenic nerve palsy at 12 months post index procedure counted as a chronic primary endpoint. The study collected information on phrenic nerve palsy observed before the end of the index procedure and, in case it occurred, tracked information for potential recovery during the study visits.

Primary Effectiveness Endpoint - Acute Procedural Success

The primary effectiveness endpoint of acute procedural success was defined as successful pulmonary vein isolation of all PVs using the INTELLANAV STABLEPOINT Catheter only. Isolation was confirmed by demonstration of entrance block at a minimum after a 20-minute waiting period. If exit block testing was performed, the PV was only considered isolated if both entrance and exit block testing were successful.

Primary Effectiveness Endpoint at 12 Months

The primary effectiveness endpoint at 12 months was defined as the primary effectiveness event-free rate at 12 months (365 days) post-procedure. Primary effectiveness events are defined as:

- Acute procedural failure
- 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 365 days post-index 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 365 days post-index procedure:
    - Repeat procedure

- Electrical and/or pharmacological cardioversion
- Prescribed any anti-arrhythmic drug (AAD)*

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

Accountability of PMA Cohort

All subjects who signed and dated the Informed Consent Form were considered enrolled in the study. Of the 299 Treatment subjects, 291 completed the study, and 8 were withdrawn. There were no deaths reported in the NEwTON AF Clinical Trial. The following definitions were used to classify the study population:

- Consent Ineligible (N=14) - Refers to a subject who signed the informed consent but is later determined to not meet eligibility criteria before undergoing the study procedure.
- Intent (N=8) - Refers to a subject who was enrolled but did not have any study investigational devices inserted into the body.
- Treatment (N=299) - Refers to all enrolled subjects who had the study device inserted into the body and received at least one radiofrequency (RF) ablation with the INTELLANAV STABLEPOINT Catheter System.

Subject disposition is presented in Figure 4.

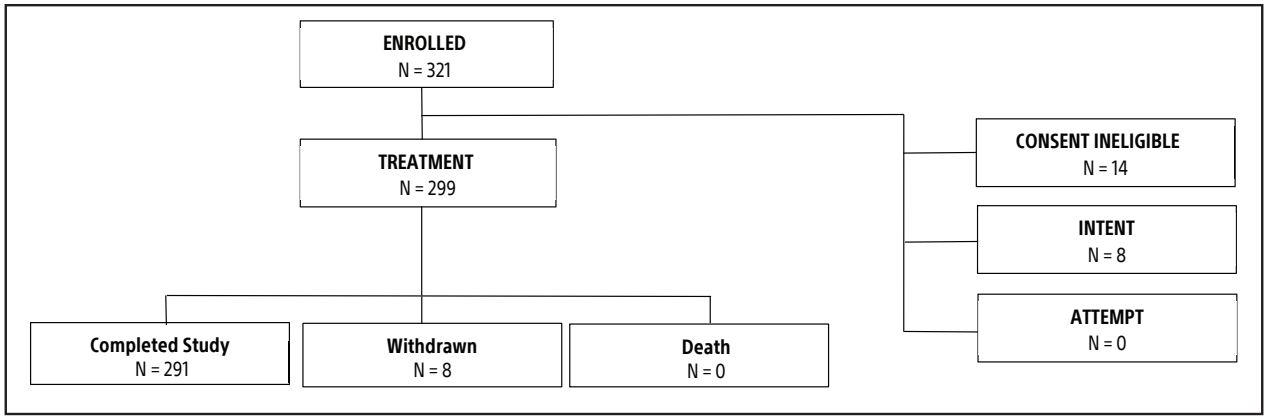

Figure 4. Subject Disposition

Study Population Demographics and Baseline Parameters

Table 30 and Table 31 summarize the demographics and baseline clinical characteristics of the Treatment subjects. The average age of subjects in the NEwTON AF study was 62 ± 12 years. The majority of subjects were male (60.5%). The gender representation was consistent with previous clinical studies for catheter ablation of paroxysmal atrial fibrillation (PAF).

Table 30. Subject Demographics

Characteristic	Measurement	Result
Age at Enrollment (years)	N	299
	Mean +/- SD	62 +/- 12
	Range	19 - 85
Gender [N (%)]	Male	181 (60.5)
	Female	118 (39.5)
Ethnicity Hispanic or Latino	Hispanic or Latino	5 (1.7)

Characteristic	Measurement	Result
Race*	Native American	0 (0.0
	Asian	48 (16.3)
	Black	3 (1.0)
	Pacific Islander	0 (0.0
	White	244 (83.0
	Lithuanian	1 (0.3)
	Race Undisclosed	5 (1.7)
*Subjects may contribute to more than one category		

Table 31. Cardiovascular Disease and Arrhythmia History

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
Non-Cardiac Comorbidities	Diabetes	--
	Type 1	2 (0.7
	Type 2	33 (11.0)
	Sleep Disordered Breathing	49 (16.4)
Neurological Medical History	None	287 (96.0
	Carotid Artery Disease	2 (0.7
	TIA	7 (2.3)
	CVA	3 (1.0)

Characteristic	Measurement	Result N (%)
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)
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)
	Typical	73 (24.4)
	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 cardiovascular procedures included: cardiac catheterization (5), cardioversion (3), stress test (1), and aortic repair (1)

***Other previous ablation included: Wolf-Parkinson White, SVT an one site report "CAG showed patent coronary arteries" and was queried

Subjects were required to be refractory, non-tolerant, or contraindicated to at least one Class I or Class III anti-arrhythmic drug (AAD). If subjects were previously prescribed amiodarone, they were required to have discontinued the medication for 60 days prior to enrollment. All subjects met the AAD eligibility requirements. Historical anti-arrhythmic medication status is summarized in Table 32.

Table 32. Historical Anti-Arrhythmic Medication Status

Characteristic	Measurement	Result N (%)
Contraindicated to Any Class I/III AADs [N (%)]	No	209 (70)
	Yes	90 (30)
Number of Refractory/Non-Tolerant AADs	N Subjects	253
	Mean Number of AADs +/- SD	1.1 +/- 0.3
	Range	1.0 - 3.0
Refractory/Non-Tolerant Class I/III AADs [N (%)][1]	Flecainide	134 (45)
	Sotalol	64 (21)
	Propafenone	27 (9)
	Dronedarone	22 (7)
	Amiodarone	13 (4)
	Dofetilide	8 (3)
	Pilsicainide	3 (1)
	Disopyramide	1 (0)
[1]Subjects may be refractory or non-tolerant to multiple AADs		

Procedural Data

A summary of the index procedure metrics collected for Treatment subjects is presented in Table 33.

Procedure duration for the study was defined as the time from first access sheath insertion to the time of final access sheath removed from the left atrium. Left atrial (LA) dwell time is defined as the time from the INTELLANAV STABLEPOINT Catheter exiting the sheath in the LA to the final access sheath removed from the left atrium.

Table 33. Index Procedure Ablation Summary

Procedure Time	N Subjects	Mean ± SD (Range)	Median (IQR) Times
Index procedure time (hrs:min)	299	2:45 ± 1:03 (1:09 - 7:16)	2:32 (1:59 - 3:24)
LA dwell time (hrs:min)	299	2:15 ± 0:55 (0:54 - 7:04)	2:05 (1:35 - 2:42)
Fluoroscopy time (min:sec)	299	0:15:26 ± 0:16:48 (0:00:00 - 1:47:34	0:09:49 (0:03:54 - 0:23:38)
RF Application Time in PVs (hrs:min:sec)	299	0:30:16 ± 0:24:24 (0:01:46 - 2:40:25)	0:21:37 (0:16:36 - 0:34:32)
Additional Ablation Procedure Time hh:mm)	151	0:37 ± 1:40 (0:00 - 16:24)	0:09 (0:04 - 0:25)
Total volume infused from ablation catheter (mL)	294	1095 +/- 507.9 (55.0 – 3850)	--
Total volume infused from all sources (mL)	287	2001 +/- 890.6 (500.0 – 7346)	--
Presence of char or coagulum formation [N (%)]	299	0 (0)	--
Steam Pops [N (%)]	299	0 (0)	--
Number of RF Applications in the PVs	725*	43.4 ± 27.8 (1 – 303)	--
*Number of treated PVs or PV pairs			

The use of point-by-point workflow was highly encouraged to accurately quantify the local impedance data. The RF application data in subjects that had PVI ablation only and utilized a point-by-point approach (164 subjects of

299 Treatment subjects, 54.8%) are summarized in Table 34. To ensure appropriate physiological ranges of the DIRECTSENSE parameters used in the analysis, individual RF applications were screened for artifact. Those that met the following criteria were included in the analysis: Local Impedance baseline must be <300 Ω and DIRECTSENSE must decrease during ablation.

Table 34. RHYTHMIA HDx Ablation Parameter Data

Characteristic	Measurement	Treatments with PVI and Point-by-Point Applications Only (N=163)
Mean power (W)	N	4,711
	Mean ± SD	43.61 ± 7.71
	Range	18.40 - 50.30
Max temp (°C)	N	4,711
	Mean ± SD	29.57 ± 2.69
	Range	22.90 - 41.70
RF Duration (sec)	N	16,254
	Mean ± SD	11.5 ± 6.3
	Range	3.0 - 67.1
Local impedance baseline (Ω)	N	16,086
	Mean ± SD	155.14 ± 20.64
	Range	74.80 - 297.10
DIRECTSENSE drop (Ω)	N	16,086
	Mean ± SD	21.34 ± 11.07
	Range	0.00 - 211.30
% DIRECTSENSE drop from baseline	N	16,086
	Mean ± SD	13.4% ± 5.9%
	Range	0.0% - 94.0%
Max raw force (g)	N	15,623
	Mean ± SD	28.51 ± 14.85
	Range	0.80 - 101.30
Min raw force (g)	N	15,623
	Mean ± SD	5.93 ± 4.92
	Range	0.00 - 44.10
Mean filtered force (g)	N	15,625
	Mean ± SD	14.19 ± 7.09
	Range	0.40 - 61.20

NOTE: The total number of data points available for each parameter may differ slightly due to the data available from the mapping system for each parameter.

Cavo-Tricuspid Isthmus (CTI) Ablation Summary

Pulmonary vein isolation (PVI) was the primary ablation strategy performed in all subjects. There were 129 Treatment subjects (43.1%) that had other protocol-allowed ablation in addition to PVI with the INTELLANAV STABLEPOINT Catheter, the majority of which were for cavo-tricuspid isthmus (CTI) ablation for typical atrial flutter (102/129, 79.1%). Bi-directional block across the isthmus was tested in 98/102 (96.1%) of subjects with CTI ablation and demonstrated in 100% (98/98) of subjects tested. Summarized data from the subjects with CTI ablation are provided below in Table 35.

Table 35. CTI Ablation Summary

Category	Classification	N (%) Treatment Subjects with CTI Ablations (N=102)
Bidirectional Block Assessment Performed	Yes	98 (96.1
	No	4 (3.9
Bidirectional Block Assessment Demonstrated	Yes	98 (100.0
Number of RF Applications for CTI Ablation	Mean ± SD	23.9 ± 18.9
	Median	20.5
	Range	3 - 152

Results

Primary Safety Endpoint

Primary Safety Endpoint at 12 Months

The results of the analysis for the primary safety endpoint at 12 months are presented in Figure 5.

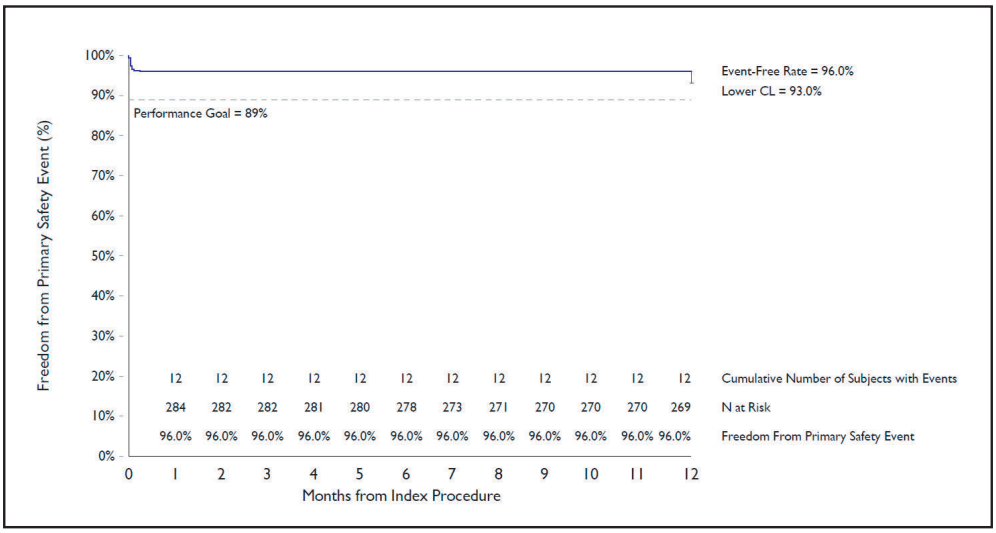

Figure 5. Primary Safety Event-Free Rate at 12 Months

The observed event-free rate at 12 months was 96.0% with a one-sided 97.5% lower confidence limit of 93.0%. The lower confidence limit was greater than the performance goal of 89%, resulting in a rejection of the null hypothesis, and the primary safety endpoint was passed.

Of the 299 Treatment subjects, a total of 13 primary safety events occurred through 12 months in 12 (4.0%) subjects. The primary safety events by event type are presented in Table 36.

Table 36. Clinical Events Committee (CEC) Adjudicated Primary Safety Events at 30 Days

Event Type	N (%)
Atrial esophageal fistula	0 (0)
AV block	0 (0)
Cardiac Tamponade or Perforation	1 (0.3)
Death	0 (0)
Major Vascular Access Complication	2 (0.7
Myocardial Infarction (MI)	0 (0)
Pericarditis	6 (2.0)
Pneumothorax	0 (0)
Pulmonary edema or heart failure	2 (0.7
Severe Pulmonary Vein Stenosis	0 (0)
Stroke/Cerebrovascular accident (CVA)	1 (0.3)
Pulmonary Thromboembolism	1 (0.3)
Transient ischemic attack (TIA)	0 (0)
Vagal Nerve Injury/Gastroparesis	0 (0)
NOTE: Subjects may experience multiple primary safety endpoint events within 30 days.	

Additional Safety Information

Adverse events (AEs) that occurred during the study were continuously monitored. There were no unanticipated adverse device effects or deaths that occurred during the study. Table 37 summarizes the adverse events reported by seriousness and relatedness. A total of 156 events were reported in 97 of the 299 Treatment subjects (32.4%).

Table 37. 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%)
Seriousness[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%)
Procedure Relatedness[2][4]	
Causal	33 (30, 10.0%)
Probable	25 (23, 7.7%)
Possible	26 (23, 7.7%)
Not related	72 (53, 17.7%)
Device Relatedness[2][4]	
Probable	3 (3, 1.0%)
Possible	33 (30, 10.0%)
Not related	120 (78, 26.1%)

[1] Primary safety events are based on CEC adjudication.
[2] Seriousness and Relatedness are based on sponsor assessment.
[3] Device and/or Procedure Relatedness- the strongest relationship with device or procedure is used in this category.
[4] A subject may count in more than one category.

All serious adverse events reported during the study are listed in Table 38.

Table 38. Serious Adverse Event Classification

Adverse Event Classification	By Event (N=72) n (%)	By Subject (N=299) n (%)
Total Subjects with at Least One SAE	NA	47 (15.7%)
Pericarditis	6 (8.3%)	6 (2.0%)
Gastrointestinal	5 (6.9%)	3 (1.0%)
Pulmonary	4 (5.6%)	4 (1.3%)
Atrial Fibrillation (AF)	4 (5.6%)	4 (1.3%)
Musculoskeletal	4 (5.6%)	4 (1.3%)
Pericardial effusion	3 (4.2%)	3 (1.0%)
Hematological	3 (4.2%)	2 (0.7%)
Cancer	2 (2.8%)	2 (0.7%)
Atrial tachycardia/Other supraventricular tachycardia (SVT) (e.g. AVRT, AVNRT, EAT)	2 (2.8%)	1 (0.3%)
Procedure related Anesthesia/Sedation	2 (2.8%)	2 (0.7%)
Procedure related Gastrointestinal	2 (2.8%)	2 (0.7%)
Neurological	2 (2.8%)	2 (0.7%)
Atrial flutter	2 (2.8%)	2 (0.7%)
Fever and/or virus	2 (2.8%)	2 (0.7%)
Pulmonary edema	2 (2.8%)	2 (0.7%)
Abnormal laboratory values	2 (2.8%)	2 (0.7%)
Coronary artery disease	2 (2.8%)	2 (0.7%)
Procedure related Genitourinary/Renal	1 (1.4%)	1 (0.3%)
Heart Failure symptoms - Unspecified	1 (1.4%)	1 (0.3%)
Procedure related Allergic reactions/Adverse drug reaction	1 (1.4%)	1 (0.3%)
Head, Eyes, Ears, Nose, Throat (HEENT)	1 (1.4%)	1 (0.3%)
Post procedure infection/sepsis	1 (1.4%)	1 (0.3%)
Physical trauma	1 (1.4%)	1 (0.3%)
Procedure related Abnormal labs	1 (1.4%)	1 (0.3%)
Fistula (Arterial/Venous)	1 (1.4%)	1 (0.3%)
Oozing/Bleeding	1 (1.4%)	1 (0.3%)
Atrial flutter, not specified	1 (1.4%)	1 (0.3%)
Myocardial perforation with tamponade	1 (1.4%)	1 (0.3%)
Ventricular Tachycardia (VT)/Monomorphic VT	1 (1.4%)	1 (0.3%)
Sinus bradycardia	1 (1.4%)	1 (0.3%)
Multiple symptoms	1 (1.4%)	1 (0.3%)
Right atrial (Typical) atrial flutter	1 (1.4%)	1 (0.3%)
Dyspnea - Heart Failure	1 (1.4%)	1 (0.3%)
Stroke	1 (1.4%)	1 (0.3%)
Infection - Unrelated procedure/device	1 (1.4%)	1 (0.3%)
Pulmonary Thromboembolism	1 (1.4%)	1 (0.3%)
Adverse reaction - Medication	1 (1.4%)	1 (0.3%)
Psychological	1 (1.4%)	1 (0.3%)

Adverse Event Classification	By Event (N=72) n (%)	By Subject (N=299) n (%)
Hemodynamic instability	1 (1.4%)	1 (0.3%)
Pseudoaneurysm	1 (1.4%)	1 (0.3%)

Primary Effectiveness Endpoint Results

Acute Procedural Success

The results of the primary effectiveness analysis for the acute procedural success endpoint are presented in Table 39.

Table 39. Primary Effectiveness Endpoint - Acute Procedural Success

N Total	N Success	Acute Success Rate (%)	95% Confidence Interval
299	294	98.3%	96.1%

Acute procedural success was observed in 294 (98.3%) of the 299 Treatment subjects that underwent an ablation procedure. The 97.5% one-sided Clopper-Pearson lower confidence limit of the observed rate of acute procedural success was calculated, and as the lower confidence limit of 96.1% was greater than the predefined performance goal of 92%, the endpoint was considered met.

Primary Effectiveness Endpoint at 12 Months

The freedom from primary effectiveness failure at 12-months was 60.3% with a one-sided 95% lower confidence limit of 54.5%. As the lower confidence limit was greater than the pre-specified performance goal of 50%, this objective was considered met. One hundred and eighteen (118) out of the 299 Treatment subjects experienced a primary effectiveness endpoint event.

The Kaplan-Meier curve for freedom from primary effectiveness failure through 12 months post-index procedure is presented below. Effectiveness failures within the blanking period reflect acute procedural failures, amiodarone usage, and repeat procedures with a non-study catheter.

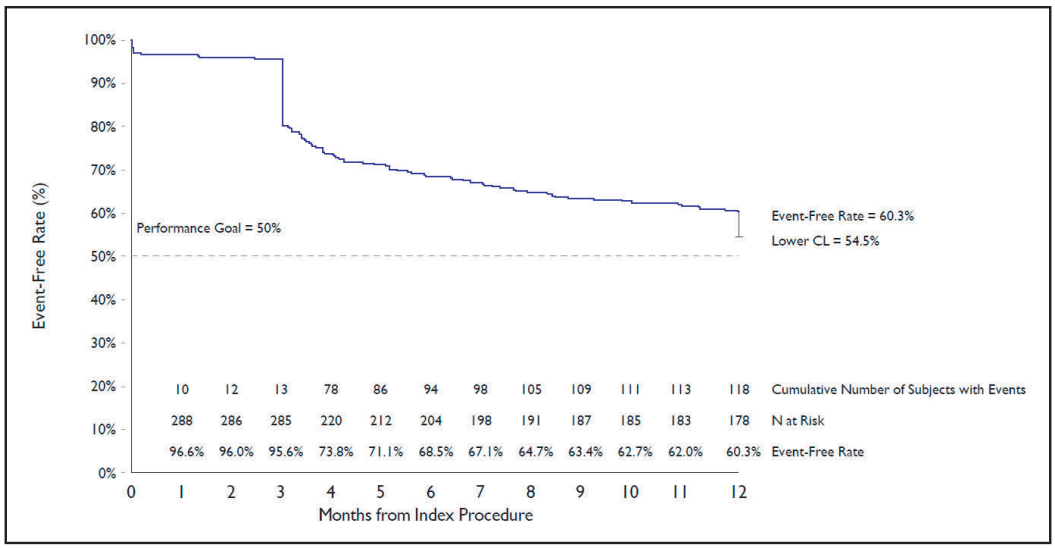

Figure 6. Freedom From Primary Effectiveness Failure at 12 Months

A summary of primary effectiveness failure at 12 months by first failure type is presented in Table 40. The most common reason for failure was documented AF/AT/AFL post-blanking period identified on the study event monitor or Holter monitor, followed by being actively prescribed an AAD other than amiodarone) beyond day 90 as defined per the protocol, and use of amiodarone post-index procedure.

Table 40. Primary Effectiveness Failure at 12 Months by Type

Primary Effectiveness Event Type	N (% Treatment Subjects)
Acute procedural failure	5 (1.7%)

Primary Effectiveness Event Type	N (% Treatment Subjects)
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%)
*Includes all Class I/III AADs, except amiodarone, and any Class II/IV AADs taken for control of AF, AFL, or AT recurrence.	

In consideration of the varying AAD definitions utilized across the PAF catheter ablation studies, a secondary effectiveness endpoint was pre-specified to assess the impact of AAD usage on the primary effectiveness outcome as presented in Figure 7.

When utilizing the same definition as used in ZERO AF, subjects were only counted as effectiveness failures if a new AAD or higher dose of a previously failed AAD continued after the blanking period. When this definition is applied, the event-free rate at 12-months was 65.4% with a 95% confidence interval of 59.7%-70.5%, as shown in Figure 6 below. Effectiveness failures within the blanking period reflect acute procedural failures, amiodarone usage, and repeat procedures with a non-study catheter. The steep drop in the Kaplan-Meier curve at day 91 is due to subjects continuing a new AAD or higher dose of previously prescribed AAD beyond the end of the blanking period.

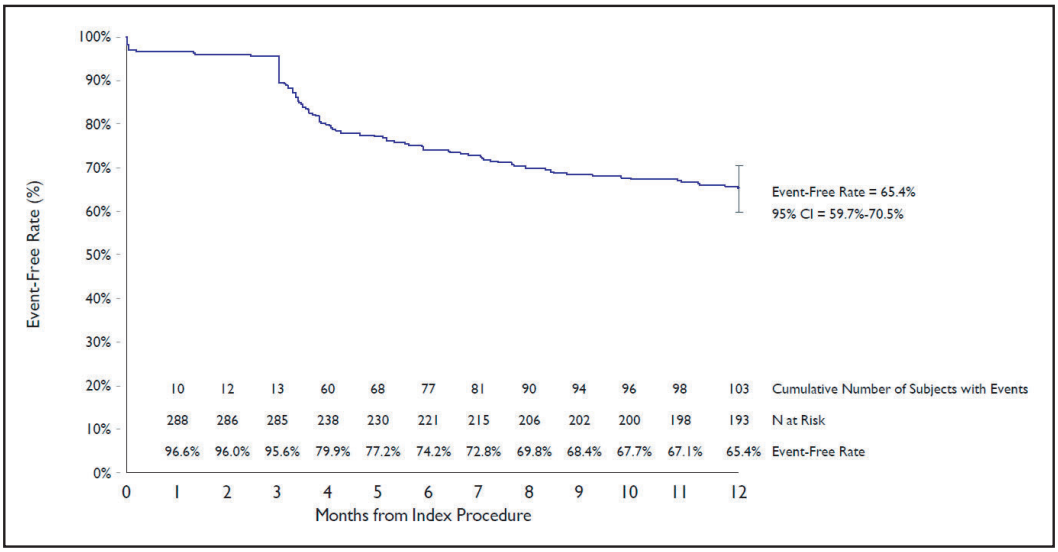

Figure 7. Freedom From Arrhythmia Recurrence – New or Increased Dose of Previously Prescribed AAD

Figure 8 shows recurrence free rates as documented on a rhythm monitoring device post- blanking period. Other protocol defined primary effectiveness failures (e.g., AAD failures, acute procedural failure) were not considered in this analysis. Overall, the freedom from documented arrhythmia recurrence, including atrial fibrillation (AF), atrial flutter (AFL), and atrial tachycardia (AT), was 71.9%.

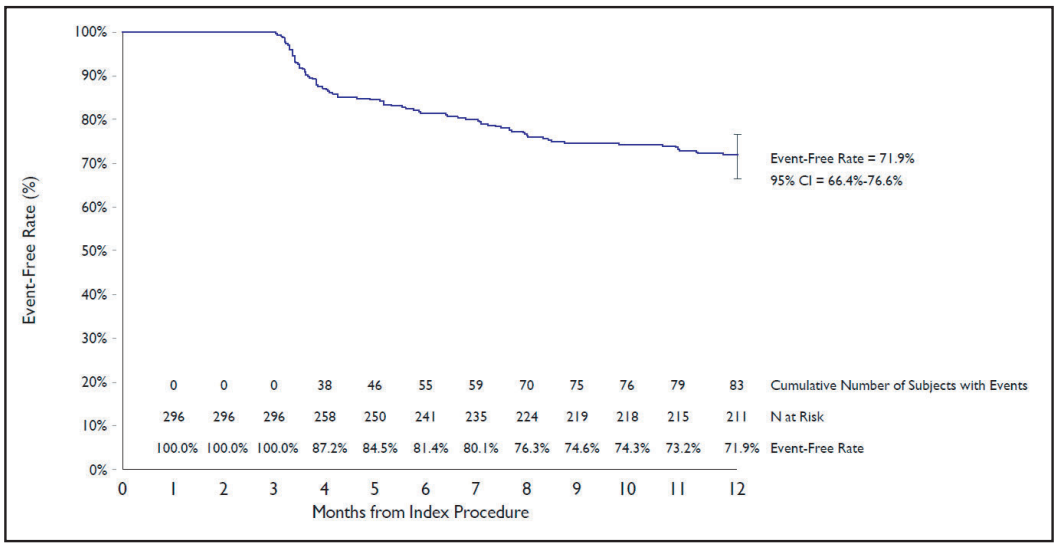

Figure 8. Freedom From Documented Arrythmia Recurrence on a Rhythm Monitoring Device

Rhythm Monitoring

Rhythm monitoring for the primary effectiveness endpoint required the collection of 12-lead ECGs at subjects' 3-, 6-, and 12-month follow-up visits, utilization of event monitors with a minimum of twice-per-month transmissions, and 24-hour holter monitors at the 6- and 12-month follow-up visits. Rhythm monitoring compliance in the NEwTON AF study was high across modalities. Total compliance for 12-lead ECGs was 97.5%, 93.3% for 24-hour holter monitoring and 75.1% for event monitoring.

Monthly rhythm monitoring compliance for event monitors is shown in Figure 9.

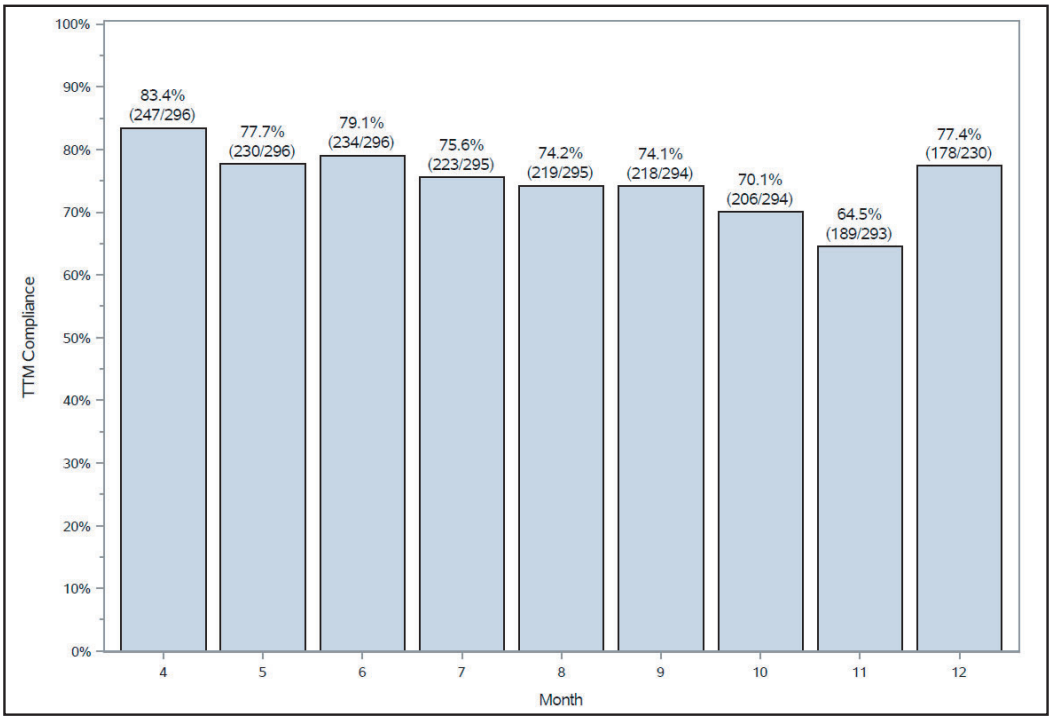

Figure 9. Monthly Event Monitoring Compliance

Study Conclusion

All primary endpoints in the NEwTON AF 12-month analysis were met. The study results support a reasonable assurance of safety and effectiveness of the INTELLANAV STABLEPOINT Catheter and Force Sensing System when used in accordance with the Indications for Use for the treatment of drug refractory, symptomatic paroxysmal atrial fibrillation.

HOW SUPPLIED

One (1) INTELLANAV STABLEPOINT Catheter is supplied sterile using an Ethylene Oxide (EO) process.

In addition to the INTELLANAV STABLEPOINT Catheter, please refer to the Additional Required Items section below for a detailed list of other materials typically required in an Electrophysiology (EP) procedure. (Refer to corresponding manufacturer's user manuals for specific material information).

Do not use if package is damaged or unintentionally opened before use.

Do not use if labeling is incomplete or illegible.

Do not use if device is past the "Use By" date.

Device Details

Report any serious incident that occurs in relation to this device to Boston Scientific and to the relevant local regulatory authority for medical devices in your country.

Handling and Storage

Do not use if the INTELLANAV STABLEPOINT Catheter is exposed to environmental conditions outside of the following ranges:

Operating Environment

Ambient Temperature: 10 °C to 40 °C

Relative Humidity: 30 % to 75 %

Atmospheric Pressure: 70 kPa to 106 kPa

Transport Environment

Temperature: -29 °C to 60 °C

Relative Humidity: 30 % to 85 %

Atmospheric Pressure: Uncontrolled

Storage Environment

Ambient Temperature: 15°C to 25 °C

Relative Humidity: Uncontrolled

Atmospheric Pressure: Uncontrolled

OPERATIONAL INSTRUCTIONS

Additional Required Items

Intracardiac electrophysiology and cardiac ablation procedures should be performed in a fully equipped clinical electrophysiology lab.

In addition to the INTELLANAV STABLEPOINT Catheter, the following devices and materials are required refer to corresponding manufacturer's operator's manuals for specific material information):

Note: The INTELLANAV STABLEPOINT Catheter is not designed to be compatible with the MAESTRO 3000 Cardiac Ablation system.

- Compatible Connection Box
- Compatible Catheter Cable
- Compatible RF Controller and accessories
- Compatible Irrigation Pump and accessories
- Irrigation Tubing Set

Note: The RF Controller and pump/tubing system must be capable of delivering flow rates of 2 mL/min (Standby), 17 mL/min (Low Ablation Flow Rate at ≤ 30 W), 30 mL/min (High Ablation Flow Rate at 31 W to 50 W).

Accessories

- Commercially available disposable Dispersive Pads which are in compliance with IEC 60601-2-2

Optional Additional Equipment

- Compatible Mapping System and accessories

Preparation

Caution: Before use, inspect the packaging for any violation of the sterile barrier and inspect the INTELLANAV STABLEPOINT Catheter for any defects. Do not use potentially contaminated or defective equipment.

Please refer to the operator's manuals and Instructions for Use for the Irrigation Pump, RF Controller, Mapping System, Connection Box, and the Irrigation Tubing Set for instructions on connecting and operating these systems in conjunction with the INTELLANAV STABLEPOINT Catheter. Use appropriate accessory cables to connect the catheter to the appropriate accessory equipment.

Procedure

1. Attach the Dispersive Pad to the patient and RF Controller per the manufacturer's instructions for use.
2. Attach the Location Reference Patch Kit to the patient per the IFU.
3. Connect the patient to an ECG recording system to facilitate arrhythmia monitoring per the standard operating procedure of the electrophysiology lab or manufacturer's operator's manual.

   Note: This should be done prior to introducing any intracardiac catheters.

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4. Open the INTELLANAV STABLEPOINT Catheter and Cable packages and the Irrigation Tubing Set package. Carefully transfer the package contents into the sterile field, maintaining sterile technique.
5. Obtain vascular access via a vein (e.g., a femoral vein) under aseptic conditions. Then place an introducer sheath into the vein using a standard percutaneous technique.
6. Connect the Connection Box to the RF Controller (and Mapping System if desired) according to the operator's manuals and/or IFUs.
7. Connect the RF Controller to the recording system (and the Mapping System if desired) with the appropriate interface cables according to the operator's manuals and/or IFUs.
8. Connect the INTELLANAV STABLEPOINT Catheter to the Connection Box using the INTELLANAV Cable. Ensure that the cable/catheter connection remains dry throughout the procedure. For connection information, refer to the IFU for additional connection instructions.
9. Turn ON the power to the RF Controller.
10. Set the RF Controller to Power Control mode. The RF Controller's temperature limit must not exceed 50 °C, but can be set lower at physician discretion.
11. Turn on the Irrigation Pump.
12. Make sure that the Irrigation Pump has the following flow rates: 2 mL/min (Standby), 17 mL/min (Low Ablation Flow—30 W or less), 30 mL/min (High Ablation Flow—above 30 W). Refer to the Irrigation Pump operator's manual for instructions on how to adjust the pump settings if required.
13. Refer to either the Irrigation Tubing Set or Irrigation Pump IFU for instructions to connect the Irrigation Tubing Set to irrigation fluid and Irrigation Pump.
14. Connect the INTELLANAV STABLEPOINT Catheter to the Irrigation Tubing Set via the luer fitting at the proximal end of the catheter handle. Care must be taken to ensure all luer fittings are secure to prevent leaking.
15. Purge the INTELLANAV STABLEPOINT Catheter and Irrigation Tubing Set. Fluid should exit all six (6) irrigation ports during the flushing process. Ensure that no air remains within the Irrigation Tubing Set or lumen and all irrigation ports are patent. Pre-condition the tip electrode if needed using programmed stimulation.
16. Set the pre-RF delay and post-RF delay on the Irrigation Pump (default is 2 seconds). Reference the Irrigation Pump operator's manual for instructions on how to change the pre-RF delay and post-RF delay.

17. Check the catheter steering by articulating the steering knob prior to inserting the catheter in the sheath.
18. Before placing the INTELLANAV STABLEPOINT Catheter in the sheath, begin continuous irrigation at a flow rate of 2 mL/min, i.e., standby flow. Check for any leaks at the tip of the catheter (other than normal saline flowing out of the distal ports), at the catheter handle, and at the luer connections and tubing joints.
19. To verify compatibility between the sheath and catheter, advance the catheter through sheath prior to insertion. Any sheath < 8.5F is contraindicated.

Warning: The use of excessive force to advance or withdraw the catheter may lead to catheter damage that may result in inaccurate force readings

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20. Under standard imaging guidance (e.g. fluoroscopy or echocardiography), insert the INTELLANAV STABLEPOINT Catheter into the sheath and advance through the vasculature into the heart.

Note: The degree of tip deflection of the INTELLANAV STABLEPOINT Catheter is controlled by the Steering Knob on the catheter handle (see Figure 1). If the Steering Knob is turned in a clockwise direction from its neutral position, the tip will curve proportionately in one direction depending upon the curve option selected. Turning the Steering Knob in the counter clockwise direction will cause the tip to deflect in the opposite direction. To prevent overstressing the tip, the Steering Knob movement is limited by the handle design. The tension adjust knob may be used when the desired catheter placement is achieved.

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21. In order to achieve optimal force reading accuracy and stability, allow the catheter to warm up after inserting into the patient and prior to the use of the force feature. Refer to instructions for use on compatible RHYTHMIA Mapping System for details on how to initiate warm-up.
22. If using the force feature, zero the contact force reading when the catheter is not in contact with the myocardial wall or other intracardiac devices. Ensure the tip and distal ring are outside the sheath prior to zero-ing. Ensure the catheter tip is not in contact by evaluating the location using standard imaging techniques and on the RHYTHMIA Mapping System. Refer to instructions for use on compatible RHYTHMIA Mapping System for details on how to re-zero catheter.
23. If using the force feature, confirm the non-contact state and re-zero as needed throughout procedure. Refer to Mapping System user manual for error messaging related to force accuracy.
24. If using the force feature, re-zero the force reading when moving the catheter from one chamber to another and upon re-insertion. Warm up is only needed upon first insertion to patient.
25. Determine the area of interest for ablation. Use both standard imaging techniques and intracardiac electrograms to aid in proper positioning. Ensure a stable position is achieved before delivering RF.

Note: If using the force and/or local impedance feature(s) to aid in positioning, be sure to use in the context of all available information including intracardiac electrograms, electroanatomic maps, generator information, fluoroscopy, etc.

Note: To ensure proper function of the force feature, ensure the tip electrode and distal ring electrode are outside of a sheath, if using a long sheath.

Note: To ensure correct use of electrograms, ensure the tip electrode and all ring electrodes are outside of a sheath, if using a long sheath.

Note: To ensure proper function of the local impedance feature, ensure the tip electrode and distal two ring electrodes are outside of a sheath, if using a long sheath.

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26. Set the initial power and irrigation flow rate based on the recommended ablation parameters in the table below.

RF Power	Minimum Irrigation Flow Rate
≤ 30W	17 mL/min
31-50W	30 mL/min

Note: Confirm the increased irrigation flow rate prior to onset of RF energy by observation of a decrease in tip electrode temperature of at least 2°C (default).

WARNING: Using the INTELLANAV STABLEPOINT Catheter at a lower than prescribed flow rate may increase the potential for thrombus, coagulum and char that may result in embolism.

WARNING: If using the force feature during RF delivery, contact forces greater than 70g may increase the incidence of steam pop occurrence, especially when used at RF powers greater than 30W.

Note: In some orientations a force >50 grams is only displayed as "High". Refer to Instructions for Use on compatible RHYTHMIA Mapping System for details.

27. Start RF energy delivery. Monitor the catheter tip temperature, generator impedance, fluoroscopy, catheter visualization, positional stability, intracardiac electrograms, force and local impedance changes to determine appropriate RF duration.

Note: Tip temperature should be used only as an indicator of adequate irrigation and not as a measure of tissue temperature.

WARNING: Carefully follow the power and the correlating flow rate procedures as specified above. Performing ablation with high power, insufficient flow rate, excessive contact force and/or excessive RF duration without moving the tip of the ablation catheter may lead to perforation, arrhythmias, damage to adjacent structures, and/or embolism.

Note: Proximity to the esophagus should be considered when ablating on the posterior atrial wall. Using high power, high contact, or long durations may increase the risk of esophageal injury.

WARNING: If using local impedance feature during RF delivery, a decrease in impedance greater than 65Ω from the pre-ablation baseline may not improve characteristics of lesion formation and may increase the risk of steam pop or perforation.

Note: If using the local impedance feature and a sudden rise in local impedance is noted during RF delivery, manually discontinue RF delivery, as this may be an indication of char or coagulum formation.

Note: If using the local impedance feature during RF delivery, a point by point workflow is recommended as the calculation of the impedance drop does not reset with changes in positional stability.

28. Do not ablate for greater than 60 seconds in duration without moving the tip of the INTELLANAV STABLEPOINT Catheter.
29. RF energy may be reapplied to the same or alternate sites using the same catheter.
30. To confirm effectiveness of ablation, user should use functional endpoints such as arrhythmia termination or demonstrated conduction block.

End of Procedure

1. Prior to removing the INTELLANAV STABLEPOINT Catheter, completely straighten the distal end of the catheter.
2. Withdraw the Catheter when the procedure is finished.
3. Turn off RF Controller and Irrigation Pump.
4. Carefully monitor patient while in recovery to ensure hemostasis is achieved and any complications are immediately treated.

Disposal

To minimize risk of infection or microbial hazards after use, dispose of device and packaging as follows:

After use, the catheter may contain biohazardous substances. The catheter and packaging should be treated and disposed of as biohazardous waste or have them treated and disposed of in accordance with any applicable hospital, administrative, and/or local government regulations. Use of a biohazardous container with biological hazard symbol is recommended. Untreated biohazardous waste should not be disposed of in the municipal waste system.

Post-Procedure

Any serious incident that occurs in relation to this device should be reported to Boston Scientific and the relevant local regulatory authority. Return any catheter related to a complaint, patient harm, injury, or death to Boston Scientific using a BSC Returned Product Kit.

- Returning products for analysis and providing product performance observations helps drive reliability higher on an ongoing basis.
- Be sure to follow the instructions with regard to packaging and shipping any biohazard devices taking care not to expose the handle or connector to fluid that may compromise the catheter and limit analysis.

PATIENT COUNSELING INFORMATION

The physician should consider the following points while counseling patients on the use of the INTELLANAV STABLEPOINT Catheter in association with the Electrophysiological cardiac interventional procedure:

- Discuss the risks and benefits including review of potential adverse events listed in this document.
- Discuss post procedure instructions, including any lifestyle changes, medications, when to call the Healthcare Provider (HCP) and any post procedure follow-up that might be needed.

TROUBLESHOOTING

See Instructions for Use for compatible RHYTHMIA Mapping System for troubleshooting related to Force and DIRECTSENSE Error Messaging.

If force inaccuracy is suspected, proceed through the following corrective actions:

1. Check the position of the sheath to ensure the tip and distal ring electrode are fully outside the sheath,
2. Reassess the unloaded state in the blood pool and re-zero if necessary,
3. Verify the connections between the catheter, cable, and connection box, or
4. Replace the INTELLANAV STABLEPOINT Catheter.

Problems	Probable Cause	Corrective Action Procedure
• Temperature not displayed	• Poor catheter/ cable connections	1. Verify that the Cable is plugged into the Connection Box and the INTELLANAV STABLEPOINT Catheter. 2. Verify that the Connection Box is connected to the RF Controller. 3. Replace cable and/or catheter. 4. If the RF Controller still does not display temperature, there may be a malfunction in the temperature sensing system. 5. Consult the operator's manual and correct this malfunction prior to reapplying RF energy.
• Impedance cutoff • Temperature cutoff	• Char/coagulum on tip electrode	1. Discontinue RF delivery. 2. Straighten the distal end and withdraw INTELLANAV STABLEPOINT Catheter. 3. Inspect tip electrode for any char/coagulum. 4. If present, gently wipe the tip section with a sterile gauze dampened with sterile saline (do not scrub or twist the tip electrode as damage to the tip electrode bond may occur and loosen the tip electrode). 5. Prior to reinsertion, ensure the irrigations ports are patent. If irrigation port occlusion occurs: a. Ensure INTELLANAV STABLEPOINT Catheter is removed from the patient. b. Fill a 1 mL or 2 mL syringe with sterile saline and attach to the stop-cock sidearm of the INTELLANAV STABLEPOINT Catheter. c. Carefully inject the saline from the syringe into the INTELLANAV STABLEPOINT Catheter. Fluid should exit all six (6) irrigation ports during the flushing process. d. Repeat steps b and c, if necessary. e. If the irrigation ports are cleared, the INTELLANAV STABLEPOINT Catheter can be reintroduced into the patient. **WARNING:** Do not continue using the INTELLANAV STABLEPOINT Catheter if the irrigation ports are occluded or the catheter is not functioning properly.
• Suspected failure of fluid flow integrity	• Leak in catheter and/or Irrigation Tubing Set • Irrigation Pump out of calibration	1. Discontinue RF delivery. 2. Straighten the distal end and withdraw catheter. 3. Replace INTELLANAV STABLEPOINT Catheter and Irrigation tubing set, prime outside of the patient. 4. Replace INTELLANAV STABLEPOINT Catheter and/or Irrigation tubing set if parameters do not appear normal or if there is any abnormality of the integrity of fluid flow. 5. Refer to the Irrigation Pump operator's manual to verify fluid flow is accurate. 6. Contact BSC representative to replace Irrigation pump.

WARRANTY

For device warranty information, visit (www.bostonscientific.com/warranty).

SYMBOL DEFINITIONS

Commonly used medical device symbols that appear on the labeling are defined at www.bostonscientific.com/SymbolsGlossary.

Additional symbols are defined at the end of this document.

BSC (MB eIFU Template 8.2677 x 11.6929 A4, 92524324F), eIFU, MB, INTELLANAV STABLEPOINT US, en, 51590762-01B

Contents

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