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Johnson & Johnson

Dual Energy THERMOCOOL SMARTTOUCH™ SF Bi-Directional Catheter

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Symbol Definitions

Following definitions are for reference only. Please refer to the product label for applicable usage.



Medical Device



Sterilized using ethylene oxide



Do not re-use



Caution



www.eifu.com

Consult instructions for use or consult electronic instructions for use



Do not use if package is damaged



Do not use if package is opened



Keep away from sunlight



Keep dry



Use-by date



Batch Code



Catalog Number



Unique Device Identifier



Packaging unit



Single sterile barrier system with protective packaging inside



Manufacturer



Date of manufacture



Authorized Representative in the European Union



The irrigation tubing contains substance N-methyl-2-pyrrolidone, CAS# 872-50-4, in concentration above 0.1% weight by weight. Refer to the ECHA website for more information: <https://echa.europa.eu/home>.



MR Unsafe



Pin connector

ELECTRODES EA

Electrodes

SPACING mm

Spacing



Temperature limit



Curve type. Refer to label for colored circle containing applicable curve type.

DE STSF

Dual Energy THERMOCOOL SMARTTOUCH™ SF Catheter

C3

Compatible with CARTO™ 3 EP Navigation System

R_x only

Caution: Federal (USA) law restricts this device to sale by or on the order of a licensed healthcare practitioner.

ASSEMBLED MEXICO

Assembled in Mexico

Dual Energy THERMOCOOL SMARTTOUCH™ SF Bi-Directional Catheter

Dual Energy THERMOCOOL SMARTTOUCH™ SF Bi-Directional Catheter

Caution: Federal (USA) law restricts this device to sale by or on the order of a licensed healthcare practitioner.

- **STERILE.** Sterilized using ethylene oxide.
- For single use only.
- Do not resterilize.
- Do not use if the package is opened or damaged.

DEVICE DESCRIPTION

The Dual Energy THERMOCOOL SMARTTOUCH™ SF Bi-Directional Catheter is a multi-electrode luminal catheter with a deflectable tip designed to facilitate electrophysiological mapping of the heart and to transmit energy to the catheter tip electrode for ablation purposes. The catheter shaft measures 7.5 F with 8 F ring electrodes. For ablation, the catheter is used in conjunction with a compatible generator, and dispersive pads (indifferent electrodes). The catheter has force -sensing technology that provides a real-time measurement of contact force between the catheter tip and the heart wall.

The catheter has a high -torque shaft with a bi-directional deflectable tip section containing an array of electrodes which includes a 3.5 mm tip dome. All of the electrodes may be used for recording and stimulation purposes. The tip electrode serves to deliver energy from the generator to the desired ablation site. The tip electrode and ring electrodes are made from noble metals. The catheter incorporates a thermocouple temperature sensor that is embedded in the 3.5 mm tip electrode. A Rocker Lever is used to deflect the tip. The high -torque shaft also allows the plane of the curved tip to be rotated to facilitate accurate positioning of the catheter tip at the desired site. Additionally, a variety of curve types are available in symmetric or asymmetric combinations, providing two 180° opposed, single planed curves.

At the proximal end of the catheter, a saline input port with a standard Luer fitting terminates from the open lumen. This saline port serves to permit the injection of normal saline to irrigate the tip electrode. During ablation, heparinized normal saline is passed through the internal lumen of the catheter and through the tip electrode, to irrigate and cool the ablation site as well as the tip electrode. A compatible irrigation pump is used to control the saline irrigation. The catheter interfaces with standard recording equipment and a compatible generator via accessory extension cables with the appropriate connectors.

The catheter features a location sensor embedded in the tip section that transmits location and contact force information to the CARTO™ System. An appropriate reference device is required for location reference position purposes. For information on using the catheter in mapping procedures and for information on appropriate reference devices, refer to the instructions for use for the compatible CARTO™ System. For further description of the operation of the irrigation pump, the generator, and the CARTO™ System, refer to the applicable instructions for use.

For details regarding the compatibility of the catheter with generators and CARTO™ Systems, refer to the "Matrix of Ablation Catheters and Compatible Devices."

INDICATIONS FOR USE

The Dual Energy THERMOCOOL SMARTTOUCH™ SF Bi-Directional Catheter and related accessory devices are indicated for catheter based cardiac electrophysiological mapping (stimulating and recording) and, when used with a compatible generator, for the treatment of:

When using Radiofrequency (RF) energy:

- Type I atrial flutter in patients age 18 or older.
- Drug refractory recurrent symptomatic paroxysmal atrial fibrillation, when used with compatible three-dimensional electroanatomic mapping systems.

Dual Energy THERMOCOOL SMARTTOUCH™ SF Bi-Directional Catheter

- Drug refractory recurrent symptomatic persistent atrial fibrillation (defined as continuous atrial fibrillation that is sustained beyond 7 days but less than 1 year), refractory or intolerant to at least one Class I or III antiarrhythmic medicine, when used with compatible three-dimensional electroanatomic mapping systems.

When using Pulsed Field (PF) energy:

- Drug refractory recurrent symptomatic paroxysmal atrial fibrillation, when used with compatible three-dimensional electroanatomic mapping systems.

The Dual Energy THERMOCOOL SMARTTOUCH™ SF Bi-Directional Catheter provides a real time measurement of contact force between the catheter tip and the heart wall, as well as location information when used with the CARTO™ System.

CONTRAINDICATIONS

Do not use the catheter:

1. If the patient has had a ventriculotomy or atriotomy within the preceding eight weeks because the recent surgery may increase the risk of perforation.
2. In patients with a myxoma or an intracardiac thrombus because the catheter could precipitate an embolus.
3. In patients with prosthetic valves because the catheter may damage the prosthesis.
4. In the coronary arterial vasculature because of the risk of damage to the coronary arterial vasculature.
5. In patients with an active systemic infection because this may increase the risk of cardiac infection.
6. Via the transseptal approach in a patient with an interatrial baffle or patch because the opening could persist and produce an iatrogenic atrial shunt.
7. Via the retrograde trans-aortic approach in patients who have had aortic valve replacement.
8. With a long sheath or short introducer < 8.5 F to avoid damage to the catheter shaft.

PATIENT TARGET GROUP

This catheter is targeted at patients who have been diagnosed with cardiac arrhythmias and are undergoing an electrophysiology procedure.

WARNINGS AND PRECAUTIONS

General

1. Only use the catheter in a fully equipped catheter or electrophysiological laboratory. It is recommended that the laboratory should have its corresponding equipment which may include but not limited to fluoroscopy, pacing, recording, defibrillator or intracardiac echocardiography units.
2. Do not use excessive force to advance or withdraw the catheter when resistance is encountered during catheter manipulation through the sheath.
3. Do not manually pre-shape the distal shaft of the catheter by applying external forces intended to bend or affect the intended shape or curve of the catheter.
4. Prior to use, the catheter must be warmed up as specified in the "Directions for Use" section of this document. If the catheter has not reached a steady state condition, there is potential for a zero -offset drift to occur which could result in an inaccurate contact force reading.
5. Always zero the contact force reading following insertion of the catheter into the patient or when moving the catheter from one chamber of the heart to another. Ensure the catheter is not in contact with heart tissue prior to zeroing. Refer to the instructions for use for the CARTO™ System for instructions on how to zero the contact force reading.

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6. The contact force reading might become inaccurate if the contact force sensor (located between the first and second ring electrode) comes into close proximity with a ferrous material, such as the braided shaft of another catheter. If extreme fluctuations in force are observed, ensure the catheter's contact force sensor is not in close proximity with another catheter's shaft, check zero on the catheter and, if necessary, remove and inspect the catheter.
7. The contact force reading is for information only and is not intended to replace standard handling precautions.
8. To ensure proper operation of the contact force sensor, the tip electrode and all four ring electrodes must protrude from the distal tip of the guiding sheath.
9. The catheter may damage the prosthetic tricuspid valve of a patient if the catheter is accidentally advanced through the valve.
10. In accordance with your hospital's protocol, monitor the patient's fluid balance throughout 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. Prior to the procedure, always identify the patient's risk of volume overload.
11. Minimize or eliminate X-ray exposure during the procedure. Catheter ablation procedures using fluoroscopic imaging may present the potential for significant X-ray exposure, which can result in acute radiation injury as well as increased risk for somatic and genetic effects to both patients and laboratory staff due to the X-ray beam intensity and duration of fluoroscopic imaging. Catheter ablation, when using fluoroscopic imaging, 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. Careful consideration must therefore be given for the use of the catheter in pregnant women.
12. Do not expose the catheter to volatile organic solvents such as alcohol. Doing so may compromise the structural integrity of the device and/or lead to device failure.
13. Do not immerse the proximal end of handle or cable connector in fluids; electrical performance could be affected.
14. Do not scrub or twist the distal tip electrode during cleaning.
15. Inspect the irrigation saline for air bubbles prior to its use in the procedure. Air bubbles in the irrigation saline may cause emboli.
16. Purge the catheter and the irrigation tubing with heparinized normal saline prior to insertion of the catheter into the patient.
17. Electrophysiology catheters and systems are intended for use only in X-ray shielded rooms due to electromagnetic compatibility requirements and other hospital safety guidelines.
18. Do not attempt to operate the catheter or the generator prior to completely reading and understanding the applicable instructions for use.
19. Cardiac ablation procedures should be performed by appropriately trained personnel in a fully equipped electrophysiology laboratory that meets the requirements of a medical room, as specific in IEC 60601-1. Appropriate clinical instruction in the use of the catheter should also be completed.
20. To prevent thromboembolism, intravenous heparin (target ACT of ≥ 300 s) should be administered prior to or immediately following transseptal puncture during AF ablation procedures. The 2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation recommends systemic anticoagulation with warfarin or a novel oral anticoagulant for at least 2 months following an AF ablation procedure (Calkins H, et al. 2017 HRS/EHRA/ECAS/APHRS/SOLAECE Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation, Heart Rhythm (2017), doi:10.1016/j.hrthm.2017.05.012).
21. When using the catheter with conventional systems (such as fluoroscopy or ultrasound imaging), or with the CARTO™ System, careful catheter manipulation must be performed in order to avoid cardiac damage, perforation, or tamponade. Catheter advancement should be done under direct imaging guidance. Do not use excessive force to advance or withdraw the catheter when resistance is encountered. The firmness of the braided tip dictates that care must be taken to prevent perforation of the heart.

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22. Always place the Rocker Lever in the neutral position to straighten the catheter tip before insertion or withdrawal of the catheter.
23. Always maintain a constant heparinized normal saline infusion to prevent coagulation within the lumen of the catheter. Do not use the catheter without irrigation flow.
24. Apparent low power output, high impedance reading, or failure of the equipment to function correctly at normal settings may indicate faulty application of the indifferent electrodes or failure of an electrical lead. Check for obvious defects or misapplication of the indifferent electrodes or other electrical leads prior to delivering energy.
25. Read and follow the indifferent electrode manufacturer's instructions for use. The use of indifferent electrodes that meet or exceed ANSI/AAMI requirements (AAMI IEC 60601-2-2) is recommended.
26. The catheter is intended for use only with a compatible generator, a compatible irrigation pump, a CARTO™ System, Biosense Webster cables, and other appropriate interface cables and connectors. Use of a compatible irrigation pump is recommended to ensure proper irrigation flow rate.
27. The sterile packaging and catheter should be inspected prior to use. Do not use if the packaging or catheter appears damaged.
28. The catheter was sterilized using ethylene oxide and should be used by the use-by date printed on the product label. Do not use the catheter after the date on the product label.
29. The catheter is intended for single patient use only.
30. Do not resterilize and reuse the catheter.
31. Do not use near MRI equipment since movement or heating of the catheter may occur and the image on the display may become distorted.
32. The catheter used in conjunction with a generator is capable of delivering significant electrical power. Patient or operator injury can result from improper handling of the catheter and indifferent electrodes, particularly when operating the catheter. During energy delivery, the patient should not be allowed to come in contact with grounded metal surfaces.
33. 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.
34. Electromagnetic interference (EMI) produced by the catheter, when used in conjunction with a compatible generator during normal operation, may adversely affect the performance of other equipment.
35. Electrodes and probes used for monitoring and stimulating devices can provide paths for high frequency current. The risk of burns can be reduced but not eliminated by placing the electrodes and probes as far away as possible from the ablation site and the indifferent electrodes. Protective impedances may reduce the risk of burns and permit continuous monitoring of the electrocardiogram during energy delivery.
36. Before use, verify that the irrigation ports are patent by infusing heparinized normal saline through the catheter and tubing.
37. When applying high lateral force during mapping and energy application, the user should monitor the contact force dashboard and vector display on the CARTO™ System screen to ensure that contact force measurements remain within the accurate range. Refer to the Error Messages and Alerts section of the instructions for use for the CARTO™ System for system -related alert messages and indications related to inaccurate force readings.
38. The catheter has not been shown to be safe at electrode temperatures above 40°C. To ensure that the maximum allowed temperature is 40°C, verify that the catheter selection on the generator is correct for the catheter.
39. The temperature sensor measures tip electrode temperature, not tissue temperature. The temperature displayed on the generator is for the cooled electrode only and does not represent tissue temperature. If the generator does not display temperature, verify that the appropriate cable is plugged into the generator. If the temperature is still not displayed, there may be a malfunction in the temperature sensing system that must be corrected prior to applying energy.
40. The temperature measurement accuracy of the catheter, as with any temperature measurement electrophysiology catheter, is largely determined by the temperature accuracy specification of the generator used. Consult the instructions for use for the generator to be used for the temperature accuracy specification.

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41. During energy delivery, ensure there is no metal guidewire in proximity to the catheter's active ablation electrode. Energy delivery near exposed metal on other electrophysiology (EP) devices, probes, or implants that can disrupt the electric field and potentially lead to injury.
42. Use both direct imaging guidance (such as fluoroscopy or ultrasound) and electrogram data to monitor catheter advancement and reduce risk of tissue injury.
43. During the transaortic approach, adequate fluoroscopic visualization is necessary to avoid placement of the catheter in the coronary vasculature. Intracoronary placement of the ablation catheter, energy application, or both have been associated with myocardial infarction.
44. The long-term risks of RF and PF induced lesions have not been established. Careful consideration must therefore be given for the use of the catheter in prepubescent children.
45. Presence of implantable pacemakers or implantable cardioverter defibrillators (ICDs), implanted LAAO device or other implanted metal cardiac device within cardiac space, may be adversely affected by RF and PF energy. ICDs should be deactivated during ablation. It is important to have temporary external sources for pacing and defibrillation available during ablation. Exercise extreme caution during ablation when the catheter is in close proximity to atrial or ventricular permanent leads. Perform a complete analysis of the implantable device after ablation. PF energy near or directly on metal implants has not been thoroughly studied, use caution when ablating near metal implants.

Warnings when Catheter is used with Generator in RF Mode

46. Do not use the temperature sensor to monitor tissue temperature or to guide power titration during ablation. The temperature sensor located within the tip section of the catheter does not reflect either electrode-tissue interface or tissue temperature due to the cooling effects of the saline irrigation of the electrode. The temperature displayed on the generator is the temperature of the cooled electrode, not tissue temperature. The temperature sensor is used to verify that the irrigation flow rate is adequate. Before initiating the application of RF energy, a decrease in electrode temperature confirms the onset of saline irrigation of the ablation electrode. Monitoring the temperature from the electrode during the application of RF energy ensures that the irrigation flow rate is being maintained. Using tip temperature to guide ablation could result in deeper lesions and increased risk for collateral damage.
47. When using RF on the posterior wall, Power and contact force should both be reduced, otherwise recommendations are to switch to PF.
48. Do not rely on electrode temperature rise to determine if tissue heating is occurring during RF energy delivery because bench, animal, and clinical studies showed no significant electrode temperature rise during RF ablations.
49. It is important to carefully follow the power titration procedure as specified in the "Directions for Use" section of this document. Too rapid an increase in RF power during ablation may lead to perforation caused by steam pop.
50. The safety of discontinuing anticoagulation therapy following catheter ablation of atrial fibrillation has not been established; anticoagulation therapy in such patients should be administered in accordance with the 2019 AHA/ACC/HRS Focused Update of the 2014 Guideline for Management of Patients with Atrial Fibrillation (January CT, Wann LS, Calkins H, et al. CITATION: 10.1016/j.jacc.2019.01.011.).
51. The safety and effectiveness of RF ablation for the treatment of atrial fibrillation in patients with significant left ventricular dysfunction (LV ejection fraction < 40%), NYHA class III or IV heart failure, substantial left atrial enlargement, and structural heart disease have not been established.
52. Patients undergoing septal accessory pathway ablations, ablations on the septal side of the isthmus, or in the treatment of AVNRT, are at risk for AV block which may require the implantation of a permanent pacemaker. Closely monitor AV conduction during energy delivery and immediately terminate energy delivery if partial or complete AV block is observed.
53. To prevent stenosis of the pulmonary veins, do not place the catheter in the pulmonary veins during the application of RF energy.
54. When ablating near the phrenic nerve, take precautions to avoid injuring the phrenic nerve, including appropriately reducing RF power and pacing to identify the proximity of the ablation electrode(s) to the nerve.

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- 55. When ablating near the esophagus (along the posterior wall of the left atrium), take precautions to avoid injuring the esophagus. These may include beginning the ablation with switching to PF energy, reduced RF power, reducing RF application time, increasing the time interval between ablations, esophageal visualization, and/or intraluminal esophageal temperature monitoring.
- 56. Cases of delayed onset of atrioesophageal fistula (AEF) in association with an RF catheter ablation procedure have been reported from postmarket experience. While rare, AEF is associated with significant morbidity and mortality. Prompt diagnosis and timely management may contribute to optimal patients' outcomes.
- 57. When RF energy is interrupted for either a temperature or an impedance rise (the set limit is exceeded), the catheter should be removed, and the tip cleaned of coagulum, if present. When cleaning the tip electrode, be careful not to twist the tip electrode with respect to the catheter shaft; twisting may damage the tip electrode bond and loosen the tip electrode or may damage the contact force sensor. A significant change in the baseline reading after cleaning might indicate a damaged contact force sensor. Make sure the irrigation holes are not plugged prior to reinsertion.
- 58. The catheter has been shown to create larger lesions than non-irrigated RF ablation catheters. Care should be taken when ablating near structures such as the sino-atrial and atrioventricular nodes.

Warnings when Catheter is used with Generator in PF Mode

- 59. Pulsed field ablation may result in an extended pause in cardiac rhythm. Prior to delivering PF energy, ensure adequate preparations are in place to commence emergency ventricular pacing, administer cardiopulmonary resuscitation, or apply other measures consistent with standard of care should the need arise.
- 60. Do not use the catheter in pregnant women because the effects of pulsed field energy on a fetus are unknown. The effects of pulsed field energy on children and newborns are unknown.
- 61. To prevent patient movement during PFA, patient comfort should be maintained through standards of care for pain management.
- 62. When ablating near the phrenic nerve, take precautions to avoid injuring the phrenic nerve, including appropriately pacing to identify the proximity of the ablation electrode(s) to the nerve and limiting stacking of PF ablations in this location to the maximum 24 applications allowed by the generator.
- 63. Prior to each application of energy, verify continuous irrigation flow by observing the dripping in the tubing drip chamber to confirm saline flow to the ablation electrode. If irrigation blockage is suspected, remove and inspect the catheter following the instructions in the "Directions for Use" section of this document.
- 64. Do not use PF energy in close proximity to structures such as the sino-atrial and atrioventricular nodes. Use extreme caution when delivering PF energy in close proximity to normal conduction system.
- 65. The long-term risks of the application of PF ablation in the heart have not been established.
- 66. PFA should not be used for type I CCW atrial flutter (CTI Dependent) due to proximity of ablation site to coronary arteries and reported risks associated with vasospasm and ischemia.
- 67. During PF energy delivery, contact with exposed metal could result in electrical arcing

MRI SAFETY INFORMATION

The catheter is MR Unsafe. Keep it outside the MRI scanner room. The MRI safety of the catheter has not been assessed. Do not use the catheter near MRI equipment because movement or heating of the catheter may occur and the image on the display may become distorted.

STORAGE

Refer to the product label for recommended storage conditions.

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STERILIZATION AND USE-BY DATE

The catheter was sterilized using ethylene oxide. Product and package testing have been conducted to support the use-by date printed on the product label. Do not use the catheter after the date on the product label.

The catheter was packaged and sterilized 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 that in turn may result in patient injury, illness, or death. Also, reprocessing or resterilization of single use devices may create a risk of contamination 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.

DISPOSAL

Recycle components, or dispose of the product and its residual elements or waste items in accordance with local laws and regulations.

COMPATIBLE EP NAVIGATION SYSTEM

The catheter provides location and contact force information only when used with the CARTO™ System. Compatibility with the CARTO™ System has been demonstrated via bench and animal testing to confirm that the catheter is capable of providing accurate location and contact force information when used in accordance with the instructions for use.

DIRECTIONS FOR USE

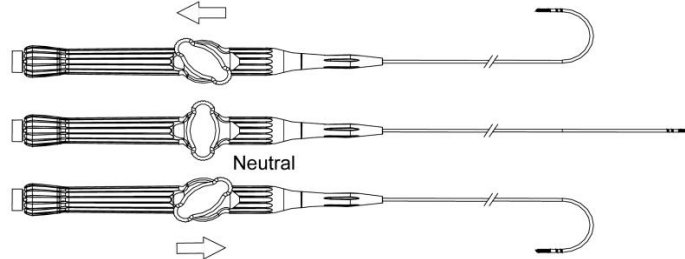
Refer to the instructions for use for the CARTO™ System, the irrigation pump, the generator, and the irrigation tubing for instructions on connecting and operating these systems in conjunction with the catheter. Use appropriate accessory cables to connect the catheter to the appropriate accessory equipment.

1. Using aseptic technique, remove the catheter from the package and place it in a sterile work area. Inspect the catheter carefully for electrode integrity and overall condition.
2. Create a vascular access in a large central vessel using aseptic techniques.
3. To prevent damage to the catheter tip, use the insertion tube supplied with the catheter to advance or retract the catheter through the hemostasis valve of the sheath. After insertion, slide the insertion tube back toward the handle.
4. To verify compatibility between the sheath and catheter, advance the catheter through the sheath prior to insertion. Any sheath < 8.5 F is contraindicated.
5. Use only Biosense Webster interface cables. To complete the electrical circuit, connect up to two indifferent electrodes to the indifferent electrode input on the generator. Connect the Patient Interface Unit (PIU) of the CARTO™ System to the generator to the appropriate recording and mapping systems with the appropriate interface cables. Connect the catheter to the compatible generator via the adapter cable. Connect the indifferent electrode to the indifferent electrode on the compatible generator.
6. Connect the irrigation tubing to a room temperature, heparinized (1 IU heparin/ml) normal saline bag using standard safe hospital practices. Open the stopcock on the end of the tubing set and fill the tubing set as slowly as possible. Remove any trapped air and then close the stopcock.
7. Load the irrigation tubing into the pump. Open the stopcock and flush the tubing per the pump instructions until the air is expelled through the open end of the tubing.
8. Connect the stopcock on the end of the irrigation tubing to the Luer fitting of the catheter.
9. Flush the catheter and tubing per standard technique to ensure purging of trapped air bubbles and to verify that the irrigation holes are patent.
10. Start continuous irrigation at a flow rate of 2 ml/min.
11. Insert the catheter via the entrance site using the insertion tube and an appropriately sized introducer sheath. Advance the catheter to the desired area. Use both direct imaging guidance (such as fluoroscopy or ultrasound) and electrograms (EGM) to aid in proper positioning.

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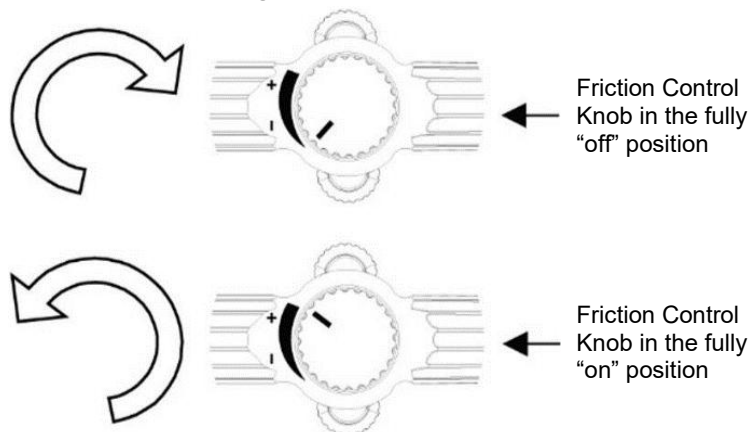
12. To achieve optimal force reading accuracy and stability, allow the catheter to warm up for 2 minutes after connection to the CARTO™ System prior to use of the force feedback feature.
13. Zero the contact force reading following insertion of the catheter into the patient. The tip electrode and all four ring electrodes on the catheter tip must be outside of the sheath so that the force sensor is inside the body. Ensure the catheter tip is not in contact with tissue by using both direct imaging guidance (such as fluoroscopy or ultrasound) and the CARTO™ System, the EGM amplitude, and catheter movement. Variations in the force reading at the same rate as the cardiac or respiration cycle may indicate contact with cardiac structures. When these markers indicate the catheter tip is not in contact, the reading can be zeroed. Refer to the instructions for use for the CARTO™ System for instructions on how to zero the contact force reading.
14. Zero the contact force reading when moving the catheter from one chamber of the heart to another or upon reinsertion.
15. Use the Rocker Lever to deflect the catheter tip (Figure 1). When the lever is turned out of the neutral position, the tip deflects in the same direction as the lever. The amount of deflection is relative to the amount of lever rotation. To straighten the tip, return the Rocker Lever to neutral position.

Figure 1 – Deflecting the Catheter Tip with the Rocker Lever



The handle has an adjustable friction control that allows the operator to use the Rocker Lever and deflecting tip in a “free” state or adjust the friction to where the Rocker Lever and tip curve are “locked” in place (Figure 2). This knob is located on the opposite side of the Rocker Lever. Out of the package, the knob will be in the “off” position, which allows the freest movement for the lever and deflecting tip. The amount of friction increases as the Friction Control Knob is rotated clockwise until it reaches the fully “on” position. Clockwise rotation from the “off” position increases the friction within the deflection mechanism. Counterclockwise rotation from the “on” position decreases the friction within the deflection mechanism.

Figure 2 – Friction Control Knob



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16. RF Energy Application

- a. Verify that the “Dual Energy THERMOCOOL SMARTTOUCH™ SF Catheter” option is selected on the generator. When this option is chosen, the generator defaults to the safety parameters established for the catheter. Do not use tip temperature to guide ablation.

Table 1 – RF and Flow Settings

RECOMMENDED RF APPLICATION PARAMETERS	
	ATRIAL ABLATION
Power Range	15 W to 45 W*
Temperature Monitoring	< 40°C**
Irrigation Flow Rate during RF Application	8 ml/min for power level up to 30 W
	15 ml/min for power levels between 31 W and 45 W
Application Time	Max 60 seconds***
* For power settings > 30 W, the recommended irrigation flow rate is 15 ml/min. ** The temperature displayed on the generator does not represent tissue temperature or electrode tissue interface temperature. *** The duration of ablation can be reduced in sensitive regions of the heart (close to the esophagus). It should be limited to 20 seconds per ablation location in the CS.	

- b. **Recommendation for irrigation:**

Increase the irrigation to the high flow rate starting up to 5 seconds before the onset of RF energy delivery and maintain the higher flow rate until 5 seconds after termination of the energy application. For power levels up to 30 W, a high flow rate of 8 ml/min should be used. For power levels between 31 W and 45 W a high flow rate of 15 ml/min should be used. Do not use the catheter without irrigation flow.

- c. The application of RF energy must not be initiated until the increase in irrigation flow rate is confirmed by a minimum of 2°C decrease in tip electrode temperature.
- d. Monitor the catheter tip temperature throughout the procedure to ensure adequate irrigation. If the temperature increases to 40°C during RF application, power delivery should be interrupted. Recheck the irrigation system prior to restarting RF application.
Note: The displayed temperature represents the temperature of the tip electrode only, not the temperature of the tissue.

- e. **Recommendation for RF power:**

For treatment of atrial flutter:

Start the procedure at 15 W to 20 W. After 15 seconds, power may be increased in 5 W to 10 W increments as needed, until a transmural lesion is achieved, defined by > 80% reduction in unipolar atrial electrogram amplitude, or emergence of double potentials of equal and low amplitude.

For treatment of atrial fibrillation:

- An RF power range of 15 W to 45 W is recommended for atrial ablation.
- Do not rely on the catheter tip temperature response to guide ablation. If temperature increases rapidly, stop RF application immediately.
- At anatomical locations not on the LA posterior wall or CS:
 - Maximum allowed power should not exceed 45 W.
 - Duration of ablation should not exceed 60 seconds of continuous ablation.

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- o Duration of ablation as well as decision to interrupt RF energy delivery at any time during ablation should be guided by clinical investigator judgment and monitoring of ablation effectiveness parameters commonly used such as EGM reduction and/or impedance changes.

f. **For Left Atrial posterior wall ablations close to the esophagus:**

It is recommended to use Pulsed field (PF) energy, refer to step 17, PFA energy application for appropriate guidance.

If using RF energy:

- Start ablation at ≤ 25 W.
- Move/drag the catheter to a new location if clinically effective ablation is achieved within 20 seconds (EGM reduction and/or impedance drop).
- Power can be increased if clinically effective ablation isn't achieved within 20 seconds (no electrogram reduction and/or no impedance drop). Maximum power used should not exceed 35 W.
- Duration of ablation, as well as decision to interrupt RF energy delivery at any time during ablation, should be guided by physician judgment and monitoring of ablation effectiveness parameters commonly used such as EGM reduction and/or impedance changes and esophageal temperature changes monitored by an endoluminal esophageal probe.
- Power should be limited to no more than 35 W if ablation is required in the CS and the duration of ablation should be limited to 20 seconds per ablation location.

g. **Contact Force (CF) ranges during ablation:**

A starting point minimum targeted CF of 5 to 10 grams is reasonable (Calkins H, et al. 2017 HRS/EHRA/ECAS/APHS/SOLAECE Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation, Heart Rhythm (2017), doi:10.1016/j.hrthm.2017.05.012).

In the PRECEPT study and SMART-SF study using the THERMOCOOL SMARTTOUCH™ SF Catheter, and the SMART-AF IDE study using the THERMOCOOL SMARTTOUCH™ Catheter, operators were instructed to monitor CF during initial cases using standard methods for evaluating effective RF applications.

In the PRECEPT study, operators most frequently chose a working range with a low of 5 grams and a high of 40 grams (37.5%, 130/347) as described in Section C.3: Contact Force Data. The overall average contact force recorded during a study ablation procedure for all subjects undergoing ablation was 15.23 ± 4.41 grams as described in Table 57: Average Contact Force Measurements Overall per Ablation Procedure. In the majority of procedures (239/283), the average contact force applied was less than 20 grams as described in Figure 1: Distribution of Average Contact Force per Ablation Procedure.

In the SMART-SF study, operators most frequently chose a working range with a low of 5 grams and a high of 40 grams (44.0%, 70/159) as described in Table 93: Working Ranges Configured by Investigators. The overall average contact force recorded during a study ablation procedure for all subjects undergoing ablation was 16.7 ± 6.14 grams as described in Table 79: Average Contact Force Measurements Overall per Ablation Procedure. In the majority of procedures (125/152), the average contact force applied during ablation was less than 20 grams. In the SMART-AF study, operators chose working ranges for RF applications that varied for both the low range (4 to 15 grams) and high range (20 to 60 grams) as described in Table 93: Working Ranges Configured by Investigators. During the study, investigators selected a working range of 5 to 40 grams for 67.4% of all study procedures. A low range of 5 grams was selected in more than 90% of the study subjects.

The average contact force applied to the endocardial heart surface during ablation procedures for all subjects undergoing ablation was 17.9 ± 9.42 grams. Results showed that when investigators stayed within their chosen working ranges $\geq 85\%$ of the time during RF applications, there was a significant improvement in the 12-month effectiveness outcome (87.1% vs. 65.7%).

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h. Esophageal monitoring:

An appropriate strategy to minimize risk of esophageal injury should be used to ensure the physician has accurate information about the location of the esophagus relative to intended sites of ablation. At least one of the following methods should be used for esophageal localization:

- Use of a multipolar esophageal temperature probe
- Esophageal visualization with CARTOSOUND™ Module and/or ICE
- Esophageal visualization using barium swallow

17. PFA energy application

- a. PFA energy is recommended for pulmonary vein isolation.
- b. Start the ablation without moving the catheter. A high flow rate of 4 ml/min should be used.
- c. Contact Force (CF) ranges during ablation:
 - A working range of 5 to 40 grams is recommended.

Table 2 – PF and Flow Settings

RECOMMENDED PF APPLICATION PARAMETERS	
	ATRIAL ABLATION (PF)
Number of applications	Up to 24
Temperature Monitoring	< 40°C*
Irrigation Flow Rate during PF Application	4 ml/min
Max Ablation Time	Up to 28 seconds**
* The temperature displayed on the generator does not represent tissue temperature or electrode tissue interface temperature.	
** 1 second intervals between applications.	

18. It is recommended that PF energy be delivered as follows for atrial ablation:

- On or near the posterior wall of the left atrium.
- When ablating near a location where pacing captures the phrenic nerve.
- Areas of touch up after PVI confirmation.

19. When using the catheter, operators should select individualized CF target ranges based on their case experience and the SMART-SF and SMART-AF IDE trial results.

20. In the event of a generator cutoff (impedance or temperature), the catheter must be withdrawn and the tip electrode inspected for coagulum before energy is reapplied. To remove any coagulum, if present, a sterile gauze pad dampened with sterile saline may be used to gently wipe the tip section clean. Do not scrub or twist the tip electrode as damage to the tip electrode bond may occur and loosen the tip electrode, or damage the contact force sensor and affect measurement accuracy. Prior to reinsertion, ensure that the irrigation holes are not plugged as follows:
 - a. Fill a 1 or 2 ml syringe with sterile saline and attach it to the stopcock on the end of the irrigation tubing or the sidearm on the catheter.
 - b. Carefully inject the saline from the syringe into the catheter. Uniform streams of fluid should be visible from the tip of the catheter.
 - c. Repeat steps a and b, if necessary.
 - d. Flush the catheter and tubing per standard technique to ensure purging of trapped air bubbles and to verify that the irrigation holes are patent.
 - e. The catheter can now be reintroduced into the patient.
 - f. Zero the catheter following reinsertion into the patient.

WARNING: Do not continue use of the catheter if it is still occluded or if it is not functioning properly.

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ADVERSE EVENTS

NOTE: The adverse events in the following summary were observed in clinical studies involving use of the Dual Energy THERMOCOOL SMARTTOUCH™ SF Catheter, THERMOCOOL SMARTTOUCH™ SF Catheter, THERMOCOOL SMARTTOUCH™ Catheter, and NAVISTAR™ THERMOCOOL™ Diagnostic/Ablation Catheter. The THERMOCOOL SMARTTOUCH™ SF and THERMOCOOL SMARTTOUCH™ Catheters are modified versions of the NAVISTAR™ THERMOCOOL™ Catheter with the added feature of a force sensor placed in the catheter tip used to measure the contact force between the catheter tip and endocardial tissue.

Clinical Trial for the Dual Energy THERMOCOOL SMARTTOUCH™ SF Catheter – SmartPulse PAF Study

Of the 231 patients in the Safety Population, 5 primary adverse events were reported in 5 subjects. See the “Summary of Clinical Studies Conducted for the Dual Energy THERMOCOOL SMARTTOUCH™ SF Catheter” section below for a complete description of the AEs encountered during the study.

Clinical Trial for the Dual Energy THERMOCOOL SMARTTOUCH™ SF Catheter – SmartFIRE Study

Of the 137 patients in Modified Intention to Treat (mITT) population, 6 primary adverse events were reported in 6 subjects. See the “Summary of Clinical Studies Conducted for the Dual Energy THERMOCOOL SMARTTOUCH™ SF Catheter” section below for a complete description of the AEs encountered during the study.

Clinical Trial for the THERMOCOOL SMARTTOUCH™ SF Catheter – PRECEPT Study

Of the 348 patients in the Safety Population, 17 primary adverse events were reported in 16 subjects. See the “Summary of Clinical Studies Conducted for the THERMOCOOL SMARTTOUCH™ SF Catheter” section below for a complete description of the AEs encountered during the study.

Clinical Trials for the THERMOCOOL SMARTTOUCH™ SF Catheter – Safety Study

Of the 159 patients in the Safety Cohort, 4 primary adverse events were reported in 4 subjects. See the “Summary of Clinical Studies Conducted for the THERMOCOOL SMARTTOUCH™ SF Catheter” section below for a complete description of the AEs encountered during the study.

Clinical Trials for the THERMOCOOL SMARTTOUCH™ Catheter – Pivotal Study

Of the 161 subjects in the Safety Analysis Cohort, 17 primary adverse events (AEs) were reported in 16 subjects. See the Pivotal Study in the “Summary of Clinical Studies Conducted for the THERMOCOOL SMARTTOUCH™ Catheter” section below for a complete description of the AEs encountered during the study.

Clinical Trials for the THERMOCOOL SMARTTOUCH™ Catheter – Continued Access Study

Of the 143 subjects in the Safety Analysis Cohort, 27 primary adverse events (AEs) were reported in 25 subjects. See the Continued Access Study in the “Summary of Clinical Studies Conducted for the THERMOCOOL SMARTTOUCH™ Catheter” section below for a complete description of the AEs encountered during the study.

Clinical Trials for Atrial Flutter Indication

Of the 190 subjects in the Safety Population in the pivotal study, 33 major adverse events were reported in 30 subjects. In the Post-Approval Study, 4 cardiovascular specific adverse events were reported in 4 of the 291 enrolled subjects. See the “Summary of Clinical Studies Conducted for Atrial Flutter Indication” section below for a complete description of the adverse events encountered during the studies.

Clinical Trials for Atrial Fibrillation Indication

Of the 139 subjects in the Primary Safety Analysis Cohort, 16 serious primary adverse events were reported in 15 subjects. See the “Summary of Clinical Studies Conducted for Atrial Fibrillation Indication” section below for a complete description of the AEs encountered during the study.

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SUMMARY OF CLINICAL STUDIES

The clinical testing described below was performed with the Dual Energy THERMOCOOL SMARTTOUCH™ SF Catheter, THERMOCOOL SMARTTOUCH™ SF Catheter, THERMOCOOL SMARTTOUCH™ Catheter, and NAVISTAR™ THERMOCOOL™ Catheter. The THERMOCOOL SMARTTOUCH™ SF Catheter meets the same performance specifications as the NAVISTAR™ THERMOCOOL™ and THERMOCOOL SMARTTOUCH™ Catheters using reduced saline flow rates.

SUMMARY OF CLINICAL STUDIES CONDUCTED FOR THE DUAL ENERGY THERMOCOOL SMARTTOUCH™ SF CATHETER

Study 1: Pivotal Study- Smartpulse PAF Study

A. Objective

The primary objective of the trial was to demonstrate safety and effectiveness of the BWI Pulsed Field (PF)/ Radiofrequency (RF) ablation system, consisting of Dual Energy THERMOCOOL SMARTTOUCH™ SF Catheter and TRUPULSE™ Generator when used in conjunction with CARTO™ 3 system V7.9 workstation with VISITAG SURPOINT™ module, in treatment of subjects with paroxysmal atrial fibrillation.

B. Study Design

The study was a prospective, interventional, single arm, multi-center and pre-market clinical evaluation conducted at 27 investigational sites in the US.

B.1 – Study Endpoints

The endpoints for the study were as follows:

Primary safety endpoint – the occurrence of early onset Primary Adverse Events (PAEs) within seven (7) days of an ablation procedure.

Primary Adverse Events included the following conditions:

- Esophageal perforating complications (Atrio-esophageal fistula¹, esophago-pericardial fistula)
- Cardiac Tamponade^{2,3} /perforation²
- Device or procedure related death⁴
- Major Vascular Access Complication/Bleeding
- Myocardial Infarction
- Pericarditis
- Pulmonary Edema (Respiratory Insufficiency)
- Phrenic Nerve Paralysis (permanent)⁵
- Pulmonary Vein Stenosis⁶
- Stroke/CVA^{7,8}
- Thromboembolism
- Transient Ischemic Attack (TIA)
- Heart Block
- Vagal Nerve Injury/Gastroparesis

¹ Atrio-esophageal fistula occurring up to 90 days post AF ablation process procedure will be considered a PAE.

² Cardiac Tamponade/Perforation occurring up to 30 days post AF ablation process procedure will be considered a PAE

³ Hemodynamic compromise or instability is defined as Systolic BP < 80 mm Hg.

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- ⁴ Device or procedure-related death anytime during or after the ablation procedure and any death reported within 30 days of ablation procedure where device and/or procedure relatedness cannot be determined via CEC adjudication
- ⁵ Absent phrenic nerve function as assessed by a sniff test at discharge.
- ⁶ Pulmonary Vein Stenosis occurring anytime during the 12 month follow up period will be considered a PAE.
- ⁷ Non-focal global encephalopathy requires unequivocal evidence based upon neuroimaging studies to be reported as a stroke
- ⁸ Modified Rankin score assessments should be made by certified individuals.

Primary Effectiveness Endpoint – Percent of subjects who had freedom from documented symptomatic and asymptomatic atrial tachyarrhythmia episodes based on electrocardiographic data during the effectiveness evaluation period from Day 91 to Day 365 and any of the following failure modes:

- Acute procedural failure: failure to achieve entrance block in all pulmonary veins using the investigational device (except those that are silent and/or cannot be cannulated post-procedure) by the end of the procedure
- Repeat ablation failure: more than 1 repeat ablation procedure for AF/AT/AFL (of unknown origin⁺) during the 3-Month Blanking Period or any repeat ablation procedure for AF/AT/AFL (of unknown origin⁺) during the evaluation period
- Non-study device failure: use of a non-study device to treat PV targets to achieve isolation of clinically relevant PVs during index or repeat procedure during the blanking period, or use of a non-study device for ablation in the left atrium during either index or repeat procedure within the blanking period
- AAD failure: taking a new AAD (Class I & III) for atrial tachyarrhythmia (AF, AT or AFL of unknown origin⁺), taking an increased dose of a previously failed Class I/III AAD for atrial tachyarrhythmia after the blanking period, or taking an increased dose of amiodarone at any time, post index procedure
- Continuous AF/AT/AFL of unknown origin⁺ (all AFL except those CTI dependent AFL as confirmed by 12-lead electrocardiogram and entrainment maneuvers in an EP study) on a standard 12-lead ECG during the effectiveness evaluation period
- Any DC cardioversion procedure during the evaluation period for documented atrial tachyarrhythmia (AF, AT or AFL of unknown origin⁺) recurrences ascertained through protocol specified arrhythmia monitoring methods (12-lead ECG, TTM and Holter)

⁺ AFL of unknown origin is defined as all AFL except those CTI dependent AFL as confirmed by 12-Lead electrocardiogram (ECG) and entrainment maneuvers in an EP study.

Secondary Endpoint – Change in quality of life (QOL) as measured by the total AFEQT score at 12 months post procedure in comparison to baseline assessment.

B.2 - Prespecified performance goal

Primary Safety Endpoint - Performance Goal = 12.0% of upper bound of exact one-sided 97.5% CI around the primary AE rate.

Primary Effectiveness Endpoint - Performance Goal = 50% of lower end of two-sided 99.5% CI around the 1-year rate of freedom from primary effectiveness endpoint.

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B.3 – Subject Disposition and Accountability

B.3.1 – Subject Disposition and Accountability

Table 3 – Subject Disposition and Accountability (Enrolled Subjects, N=250)

Subject Enrollment	n
Enrolled Subjects ¹	250
Excluded ²	19
Evaluable Subjects ³	231
Discontinued ⁴	0
Discontinued for study device-related reasons ⁵	0
RF/PF Energy Delivered	231
Death	2
Lost to Follow-up ⁶	2
Withdrawn/Early Termination ⁷	0
Completed ⁸	82
Ongoing	145
Other	0
CT/MRA Enrolled Subjects ¹	34

¹ **Enrolled Subjects:** Subjects who sign the Informed Consent Form (ICF).

² **Excluded Subjects:** Subjects who are enrolled but never undergo insertion of the study catheter.

³ **Evaluable Subjects:** All enrolled subjects who have the study catheter inserted.

⁴ **Discontinued:** Evaluable subjects who have the study catheter inserted, but do not undergo ablation (i.e., no PF/RF energy applied).

⁵ **Discontinued for study device-related reasons:** Subjects who have the study catheter inserted but do not undergo ablation due to Study Device (Dual Energy SMARTTOUCH™ SF (DE STSF), TRUPULSE™ Generator, and CARTO™ 3 v7.9 Workstation) related reasons will be discontinued and considered acute effectiveness failures.

⁶ **Lost to Follow-up:** Subjects who have study catheter inserted, but contact is lost after most recent follow-up visit (despite 3 documented attempts to contact the subject).

⁷ **Withdrawn/Early Termination:** Subjects who withdraw consent for study participation or are withdrawn by the investigator, are terminated from the study prior to completion of all follow-up visits.

⁸ **Completed Subjects:** Enrolled subjects who have not been excluded, discontinued, withdrawn, terminated early, or lost-to-follow-up from the study prior to the final study visit.

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B.3.2 - Study Analysis Set

Table 4 – Analysis Set (Safety Population Analysis Set, N=231)

Analysis Set	n
Safety Population (SP) Analysis Set¹	231
All Treated (AT) Analysis Set²	231
Did not meet eligibility	7
Modified Intent-To-Treat (mITT) Analysis Set³	224
Discontinued Subjects ⁴	0
Subjects with specified major PD ⁵	3
Per Protocol (PP) Analysis Set⁶	221
Discontinued subjects for study device-related reasons ⁷	0
Used non-study device to achieve PVI due to study-device related reason ⁸	2
Enrolled Subset Subjects	
Cardiac CT/MRA Subset	34

¹ **SP Analysis Set:** All enrolled subjects who have had the study catheter inserted, regardless of whether energy is delivered or not.

² **AT Analysis Set:** The AT analysis set will consist of all enrolled subjects who have undergone the insertion of the study catheter and energy delivery, regardless of whether they meet the eligibility criteria or not.

³ **mITT Analysis Set:** Enrolled subjects who meet eligibility criteria and have had insertion of the study catheter.

⁴ **Discontinued Subjects:** Evaluable subjects who have the study catheter inserted but do not undergo ablation.

⁵ Major protocol deviations that result in removal from Per Protocol analysis set as described in the SAP.

⁶ **PP Analysis Set:** Subjects who satisfy the following criteria: (1) undergone ablation using PF and/or RF energy via the investigational ablation system, (2) treated for study-related arrhythmia, (3) no specified major CIP deviations.

⁷ **Discontinued subjects for study device-related reasons:** subjects who have the study catheter inserted but do not undergo ablation (i.e., no energy is delivered with the study catheter) due to study device related reasons will be discontinued and considered as acute effectiveness failures and will be retained in this PP analysis set.

⁸ Subjects who have energy delivered with study catheter but switched to non-study device for PVI due to study-device related reasons will be considered as acute effectiveness failures and will be retained in the PP analysis set.

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B.4 – Subject Demographics

Table 5 – Demographics (Evaluable Subjects, N=231)

Variable	Safety Set (N=231)	mITT Set (N=224)	PP Set (N=221)	CT/MRA Analysis Set (N=34)
Age (years)¹				
N	231	224	221	34
Mean	63.1	63.2	63.2	61.8
Standard Deviation	9.67	9.54	9.59	8.32
Median	66.0	66.0	66.0	64.5
Sex, n/N (%)				
Male	138 / 231 (59.7%)	134 / 224 (59.8%)	133 / 221 (60.2%)	14 / 34 (41.2%)
Female	93 / 231 (40.3%)	90 / 224 (40.2%)	88 / 221 (39.8%)	20 / 34 (58.8%)
Ethnicity, n/N (%)				
Hispanic or Latino	10 / 231 (4.3%)	10 / 224 (4.5%)	10 / 221 (4.5%)	1 / 34 (2.9%)
Not Hispanic or Latino	214 / 231 (92.6%)	207 / 224 (92.4%)	204 / 221 (92.3%)	33 / 34 (97.1%)
Not Reported	7 / 231 (3.0%)	7 / 224 (3.1%)	7 / 221 (3.2%)	0 / 34 (0.0%)
Race, n/N (%)				
Asian	1 / 231 (0.4%)	1 / 224 (0.4%)	1 / 221 (0.5%)	0 / 34 (0.0%)
Black or African American	8 / 231 (3.5%)	6 / 224 (2.7%)	6 / 221 (2.7%)	0 / 34 (0.0%)
Race not reported	8 / 231 (3.5%)	8 / 224 (3.6%)	8 / 221 (3.6%)	2 / 34 (5.9%)
White	214 / 231 (92.6%)	209 / 224 (93.3%)	206 / 221 (93.2%)	32 / 34 (94.1%)
Weight (kg)				
n	231	224	221	34
Mean	94.50	93.93	94.06	94.40
Standard Deviation	21.218	20.952	21.043	21.803
Median	92.50	91.59	92.00	92.03
Height (cm)				
n	231	224	221	34
Mean	174.46	174.45	174.49	173.18
Standard Deviation	10.634	10.633	10.686	10.175
Median	175.26	175.26	175.30	173.99

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Variable	Safety Set (N=231)	mITT Set (N=224)	PP Set (N=221)	CT/MRA Analysis Set (N=34)
BMI (kg/m²)				
n	231	224	221	34
Mean	31.07	30.89	30.92	31.64
Standard Deviation	6.567	6.501	6.536	7.760
Median	29.70	29.45	29.50	29.20

¹ Age at informed consent.

B.5 – Baseline Characteristics

B.5.1 – Medical History

Table 6 – Medical History (Evaluable Subjects, N=231)

Variable	Safety Set n/N (%)	mITT Set n/N (%)	PP Set n/N (%)	CT/MRA Subset n/N (%)
Cardiovascular Medical History*	210 / 231 (90.9%)	204 / 224 (91.1%)	201 / 221 (91.0%)	31 / 34 (91.2%)
Congestive heart failure	38 / 231 (16.5%)	36 / 224 (16.1%)	35 / 221 (15.8%)	5 / 34 (14.7%)
NYHA Class				
Class I	7 / 231 (3.0%)	7 / 224 (3.1%)	6 / 221 (2.7%)	0 / 34 (0.0%)
Class II	31 / 231 (13.4%)	29 / 224 (12.9%)	29 / 221 (13.1%)	5 / 34 (14.7%)
Coronary disease	49 / 231 (21.2%)	45 / 224 (20.1%)	45 / 221 (20.4%)	4 / 34 (11.8%)
Vascular disease	34 / 231 (14.7%)	31 / 224 (13.8%)	30 / 221 (13.6%)	2 / 34 (5.9%)
Myocardial infarction	18 / 231 (7.8%)	16 / 224 (7.1%)	16 / 221 (7.2%)	1 / 34 (2.9%)
Hypertension (systemic)	165 / 231 (71.4%)	160 / 224 (71.4%)	158 / 221 (71.5%)	21 / 34 (61.8%)
Pulmonary hypertension	5 / 231 (2.2%)	5 / 224 (2.2%)	5 / 221 (2.3%)	0 / 34 (0.0%)
Cardiomyopathy	10 / 231 (4.3%)	9 / 224 (4.0%)	9 / 221 (4.1%)	2 / 34 (5.9%)
Ischemic	5 / 231 (2.2%)	4 / 224 (1.8%)	4 / 221 (1.8%)	0 / 34 (0.0%)
Non-Ischemic	5 / 231 (2.2%)	5 / 224 (2.2%)	5 / 221 (2.3%)	2 / 34 (5.9%)
Left ventricular hypertrophy	12 / 231 (5.2%)	10 / 224 (4.5%)	10 / 221 (4.5%)	1 / 34 (2.9%)
Significant valvular disease	3 / 231 (1.3%)	2 / 224 (0.9%)	2 / 221 (0.9%)	0 / 34 (0.0%)
Percutaneous coronary intervention (PCI)	23 / 231 (10.0%)	21 / 224 (9.4%)	21 / 221 (9.5%)	1 / 34 (2.9%)
Other cardiovascular procedure (e.g. CABG, pacemaker, ICD, LAAO, stent, implantable loop recorder, etc.)	30 / 231 (13.0%)	28 / 224 (12.5%)	26 / 221 (11.8%)	3 / 34 (8.8%)
Carotid stenting or endarterectomy	1 / 231 (0.4%)	1 / 224 (0.4%)	1 / 221 (0.5%)	0 / 34 (0.0%)
Unstable angina	1 / 231 (0.4%)	0 / 224 (0.0%)	0 / 221 (0.0%)	0 / 34 (0.0%)
Prior LA atrial appendage closure	1 / 231 (0.4%)	1 / 224 (0.4%)	1 / 221 (0.5%)	0 / 34 (0.0%)
Hypercholesterolemia	95 / 231 (41.1%)	90 / 224 (40.2%)	90 / 221 (40.7%)	16 / 34 (47.1%)

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Variable	Safety Set n/N (%)	mITT Set n/N (%)	PP Set n/N (%)	CT/MRA Subset n/N (%)
Other cardiovascular medical condition	78 / 231 (33.8%)	76 / 224 (33.9%)	74 / 221 (33.5%)	7 / 34 (20.6%)
Documented Thromboembolic Events*	11 / 231 (4.8%)	10 / 224 (4.5%)	10 / 221 (4.5%)	0 / 34 (0.0%)
Transient ischemic attack (TIA)	2 / 231 (0.9%)	2 / 224 (0.9%)	2 / 221 (0.9%)	0 / 34 (0.0%)
Stroke	6 / 231 (2.6%)	6 / 224 (2.7%)	6 / 221 (2.7%)	0 / 34 (0.0%)
Hemorrhagic	1 / 231 (0.4%)	1 / 224 (0.4%)	1 / 221 (0.5%)	0 / 34 (0.0%)
Ischemic	5 / 231 (2.2%)	5 / 224 (2.2%)	5 / 221 (2.3%)	0 / 34 (0.0%)
Pulmonary embolus	1 / 231 (0.4%)	1 / 224 (0.4%)	1 / 221 (0.5%)	0 / 34 (0.0%)
Other thromboembolic events	2 / 231 (0.9%)	1 / 224 (0.4%)	1 / 221 (0.5%)	0 / 34 (0.0%)

* Allow for multiple selections.

B.5.2 – Atrial Fibrillation History

Table 7 – Atrial Fibrillation History (Evaluable Population, n=231)

Variable	Safety Set (N=231)	mITT Set (N=224)	PP Set (N=221)	CT/MRA Subset (N=34)
Duration of symptomatic paroxysmal AF (months)				
n	231	224	221	34
Mean	47.48	47.46	46.50	36.94
Standard Deviation	60.171	60.929	59.857	51.457
Median	24.00	24.00	24.00	18.65
Number of symptomatic paroxysmal AF episodes in the past 6 months				
n	231	224	221	34
Mean	22.5	20.7	19.9	22.5
Standard Deviation	40.90	36.81	35.39	30.99
Median	7.0	6.0	6.0	7.5
Frequency of symptomatic paroxysmal AF episode in the past 6 months, n/N (%)				
Daily	28 / 231 (12.1%)	27 / 224 (12.1%)	26 / 221 (11.8%)	4 / 34 (11.8%)
Weekly	51 / 231 (22.1%)	50 / 224 (22.3%)	50 / 221 (22.6%)	13 / 34 (38.2%)
Bi-weekly	19 / 231 (8.2%)	19 / 224 (8.5%)	19 / 221 (8.6%)	1 / 34 (2.9%)
Monthly	32 / 231 (13.9%)	30 / 224 (13.4%)	29 / 221 (13.1%)	2 / 34 (5.9%)
Irregular	86 / 231 (37.2%)	83 / 224 (37.1%)	82 / 221 (37.1%)	10 / 34 (29.4%)
Unknown	15 / 231 (6.5%)	15 / 224 (6.7%)	15 / 221 (6.8%)	4 / 34 (11.8%)

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Variable	Safety Set (N=231)	mITT Set (N=224)	PP Set (N=221)	CT/MRA Subset (N=34)
Direct current cardioversion (DCCV) in the past 12 months for paroxysmal AF, n/N (%)	37 / 231 (16.0%)	36 / 224 (16.1%)	36 / 221 (16.3%)	7 / 34 (20.6%)
Number of previous DCCV				
1	29 / 37 (78.4%)	28 / 36 (77.8%)	28 / 36 (77.8%)	6 / 7 (85.7%)
2	7 / 36 (19.4%)	7 / 35 (20.0%)	7 / 35 (20.0%)	0 / 7 (0.0%)
3	0 / 36 (0.0%)	0 / 35 (0.0%)	0 / 35 (0.0%)	0 / 7 (0.0%)
≥ 4	1 / 36 (2.8%)	1 / 35 (2.9%)	1 / 35 (2.9%)	1 / 7 (14.3%)

B.5.3 – Cardiovascular Hospitalization and Cardioversion History

**Table 8 – Cardiovascular Hospitalization and Cardioversion History
(Evaluable Population, N=231)**

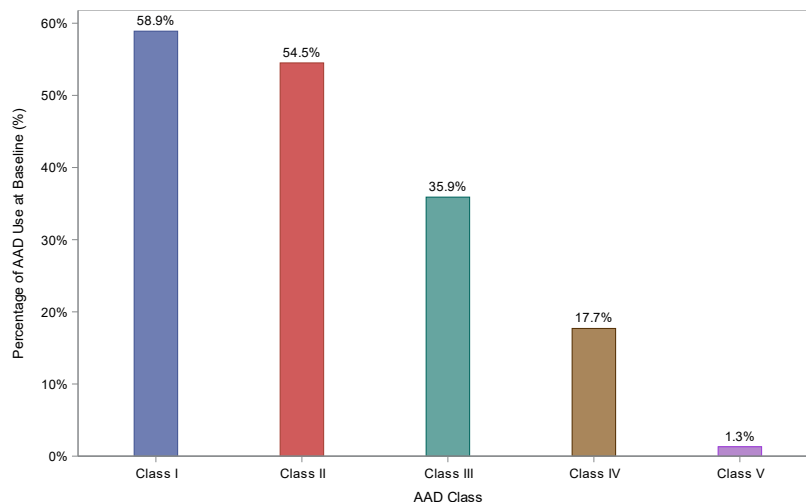
Variable	Safety Set (N=231)	mITT Set (N=224)	PP Set (N=221)	CT/MRA Subset (N=34)
Cardiovascular related hospital visits, n/N (%)¹	122/231 (52.8%)	118/224 (52.7%)	118/221 (53.4%)	19/34 (55.9%)
Type of Visit, n/N (%)¹				
Emergency room	53 / 122 (43.4%)	52 / 118 (44.1%)	52 / 118 (44.1%)	10 / 19 (52.6%)
Hospitalization	43 / 122 (35.2%)	40 / 118 (33.9%)	40 / 118 (33.9%)	4 / 19 (21.1%)
Outpatient	26 / 122 (21.3%)	26 / 118 (22.0%)	26 / 118 (22.0%)	5 / 19 (26.3%)
Reason, n/N (%)¹				
Ablation procedure	1 / 122 (0.8%)	1 / 118 (0.8%)	1 / 118 (0.8%)	1 / 19 (5.3%)
Angio/PCI	1 / 122 (0.8%)	1 / 118 (0.8%)	1 / 118 (0.8%)	10 / 19 (52.6%)
Electrical Cardioversion	42 / 122 (34.4%)	41 / 118 (34.7%)	41 / 118 (34.7%)	3 / 19 (15.8%)
Heart Failure	1 / 122 (0.8%)	1 / 118 (0.8%)	1 / 118 (0.8%)	5 / 19 (26.3%)
Pharmacological Cardioversion	22 / 122 (18.0%)	22 / 118 (18.6%)	22 / 118 (18.6%)	1 / 19 (5.3%)
Other	55 / 122 (45.1%)	52 / 118 (44.1%)	52 / 118 (44.1%)	10 / 19 (52.6%)

¹n represents the number of visits/reasons per category, and N represents the total number of cardiovascular hospitalizations/cardioversions within 12 months prior to study enrollment.

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B.5.4 – AAD Use at Baseline

Figure 3 – AAD Use at Baseline (Safety Population Set, N=231)



B.5.5 – Baseline CHADS₂ and CHA₂DS₂-VASc Score

Table 9 – CHADS₂ and CHA₂DS₂-VASc Score (Evaluable Population, N=231)

Variable	Safet Set (N=231)	mITT Set (N=224)	PP Set (N=221)	CT/MRA Subset (N=34)
CHADS₂ Score¹				
N	231	224	221	34
Mean	1.2	1.2	1.2	1.0
Standard Deviation	0.98	0.94	0.94	0.92
Median	1.0	1.0	1.0	1.0
CHA₂DS₂-VASc Score²				
N	231	224	221	34
Mean	2.3	2.3	2.3	2.1
Standard Deviation	1.41	1.37	1.37	1.31
Median	2.0	2.0	2.0	2.0

¹ The score for each subject is calculated as a sum of points given for each of the following conditions: 1 for congestive heart failure, 1 for hypertension, 1 for age ≥ 75 years, 1 for diabetes mellitus, and 2 for prior stroke or TIA or thromboembolism.

² The score for each subject is calculated as a sum of points given for each of the following conditions: 1 for congestive heart failure (or left ventricular systolic dysfunction), 1 for hypertension, 2 for age ≥ 75 years, 1 for diabetes mellitus, 2 for prior stroke or TIA or thromboembolism, 1 for vascular disease (e.g. peripheral artery disease, myocardial infarction, aortic plaque), 1 for age 65-74 years, and 1 for sex category (i.e. female).

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C. Results

C.1 – Procedural Data

C.1.1 – Index Procedure Data

Table 10 – Procedural Data of Index Procedure (Evaluable Population, N=231)

Variable	Safety Set (N=231)	mITT Set (N=224)	PP Set (N=221)	CT/MRA Subset (N=34)
Anesthesia Type, n/N (%)				
Conscious sedation	1 / 231 (0.4%)	1 / 224 (0.4%)	1 / 221 (0.5%)	0 / 34 (0.0%)
General (unconscious sedation)	230 / 231 (99.6%)	223 / 224 (99.6%)	220 / 221 (99.5%)	34 / 34 (100.0%)
Was a paralytic used, n/N (%) ⁺	187 / 231 (81.0%)	183 / 224 (81.7%)	180 / 221 (81.4%)	29 / 34 (85.3%)
Overall Ablation Details:				
PF energy applied via the study catheter, n/N (%)	231 / 231 (100.0%)	224 / 224 (100.0%)	221 / 221 (100.0%)	34 / 34 (100.0%)
RF energy applied via the study catheter, n/N (%)	230 / 231 (99.6%)	223 / 224 (99.6%)	220 / 221 (99.5%)	34 / 34 (100.0%)
Pre-Ablation Mapping:				
Total LA mapping time (min)				
n	231	224	221	34
Mean	7.09	7.04	7.03	7.53
Standard Deviation	4.954	4.953	4.968	5.118
Median	6.00	6.00	6.00	6.00
Ablation to Achieve PV Isolation:				
Total PVI Ablation time with THERMOCOOL SMARTTOUCH™ SF study catheter (min)				
n	231	224	221	34
Mean	52.65	52.05	52.21	50.09
Standard Deviation	23.889	23.589	23.591	20.499
Median	47.00	46.00	46.00	45.00
Total procedure time (min)				
n	231	224	221	34
Mean	105.49	104.00	104.14	99.79
Standard Deviation	38.819	37.449	37.149	26.341
Median	100.00	99.00	99.00	98.50

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Variable	Safety Set (N=231)	mITT Set (N=224)	PP Set (N=221)	CT/MRA Subset (N=34)
Total duration of fluoroscopy at end of procedure (min)				
n	231	224	221	34
Mean	4.07	4.10	4.06	2.22
Standard Deviation	6.553	6.627	6.588	3.206
Median	0.30	0.30	0.30	0.00
Ablation Procedure Information: Fluid Intake and Output [I & O]				
Fluid delivered via the study catheter(s) (mL)				
n	224	218	216	33
Mean	425.4	424.4	424.8	408.3
Standard Deviation	232.36	235.04	234.18	173.96
Median	400.0	400.0	400.0	400.0
Fluid delivered via intravenous fluids (mL)				
n	230	223	220	34
Mean	862.7	849.9	850.1	839.0
Standard Deviation	504.73	496.33	499.50	399.95
Median	800.0	800.0	800.0	900.0
Ablation Procedure Details:				
Heart rhythm at the beginning of the procedure, n/N (%)				
Atrial Fibrillation	28 / 231 (12.1%)	28 / 224 (12.5%)	28 / 221 (12.7%)	4 / 34 (11.8%)
Atrial Flutter Typical Right	6 / 231 (2.6%)	6 / 224 (2.7%)	6 / 221 (2.7%)	2 / 34 (5.9%)
Atrial Tachycardia Left Atrium	1 / 231 (0.4%)	1 / 224 (0.4%)	1 / 221 (0.5%)	0/34 (0.0%)
Sinus Rhythm	187 / 231 (81.0%)	180 / 224 (80.4%)	177 / 221 (80.1%)	26 / 34 (76.5%)
Other	9 / 231 (3.9%)	9 / 224 (4.0%)	9 / 221 (4.1%)	2 / 34 (5.9%)
Highest Esophageal temperature reached throughout the procedure (Centigrade)				
n	117	114	112	12
Mean	36.77	36.73	36.74	36.88
Standard Deviation	1.139	1.120	1.124	0.959
Median	36.40	36.40	36.40	36.50

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Variable	Safety Set (N=231)	mITT Set (N=224)	PP Set (N=221)	CT/MRA Subset (N=34)
Energy mode switched to PF if the phrenic nerve was located near the intended ablation line, n/N(%)				
Yes	18 / 231 (7.8%)	17 / 224 (7.6%)	17 / 221 (7.7%)	4 / 34 (11.8%)
No	8 / 231 (3.5%)	8 / 224 (3.6%)	8 / 221 (3.6%)	5 / 34 (14.7%)
Not applicable	205 / 231 (88.7%)	199 / 224 (88.8%)	196 / 221 (88.7%)	25 / 34 (73.5%)
If No, ablation line altered to avoid the phrenic location	8 / 8 (100.0%)	8 / 8 (100.0%)	8 / 8 (100.0%)	5 / 5 (100.0%)
Predominant heart rhythm at the end of the procedure, n/N (%)				
Atrial Fibrillation	9 / 231 (3.9%)	9 / 224 (4.0%)	9 / 221 (4.1%)	0/34 (0.0%)
Atrial Flutter Atypical Right	1 / 231 (0.4%)	1 / 224 (0.4%)	1 / 221 (0.5%)	0/34 (0.0%)
Sinus Rhythm	219 / 231 (94.8%)	212 / 224 (94.6%)	209 / 221 (94.6%)	34 / 34 (100.0%)
Other	2 / 231 (0.9%)	2 / 224 (0.9%)	2 / 221 (0.9%)	0/34 (0.0%)

* Allow for multiple selections

C.1.2 – Use of Ablation Energy by Ablation Targets at Subject Level

**Table 11 – Use of Ablation Energy by Ablation Targets at Subject Level
(Safety Population Analysis Set, N=231)**

Variable	Overall	PV Targets	Non-PV Targets
Number of PF/RF Ablations			
n	231	231	67
Mean	79.9	75.7	14.4
Standard Deviation	23.87	21.42	9.04
Median	76.0	73.0	12.0
Number of PF Ablations			
n	231	231	2
Mean	37.3	37.2	10.0
Standard Deviation	12.40	12.30	11.31
Median	36.0	36.0	10.0
Number of RF Ablations			
n	229	229	67
Mean	42.9	38.8	14.1
Standard Deviation	16.04	13.17	9.06
Median	40.0	37.0	12.0

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C.1.3 – Use of Ablation Energy by PV Targets

Table 12 – Number of Ablation per Ablation Target (Safety Population Analysis Set, N=231)

Variable	Overall	Number of PF Ablations	Number of RF Ablations
PV Target			
LPV			
n	230	230	229
Mean	37.5	17.6	20.0
Standard Deviation	12.12	6.91	8.18
Median	35.0	16.0	18.0
RPV			
n	229	229	226
Mean	38.7	19.9	19.1
Standard Deviation	12.42	8.19	7.77
Median	36.0	18.0	18.0
Non-PV Targets			
CTI Line			
n	62	-	62
Mean	14.0	-	14.0
Standard Deviation	8.75	-	8.75
Median	12.0	-	12.0

C.2 – Primary Endpoints

C.2.1 – Primary Safety Endpoints – Incidence of primary adverse events

Primary Adverse Events occurred in 5 subjects with 2.2% (5/224) incidence rate in mITT analysis set (Table 13). The upper bound of exact one-sided 97.5% confidence interval (CI), 5.1%, was lower than the pre-defined performance goal of 12%.

Table 13 – Primary Safety Endpoint Analysis (mITT Analysis Set, N=224)

Variable	Number of Subjects with Events	Event Rate n/N (%) ¹	Exact One-Sided 97.5% Upper Confidence Bound
Primary adverse event ¹	5	5/224 (2.2%)	5.1%

¹ Subjects without at least 3 months of follow-up are excluded from the primary safety analysis unless they experienced a PAE.

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The Primary Adverse events included two (2) events of cardiac tamponade/perforation, two (2) events of transient ischemic attack (TIA) and one (1) event of death (Table 14).

**Table 14 – Decomposition of Primary Safety Endpoint,
Primary Adverse Events (mITT Analysis Set, N=224)**

Variable	Number of Subjects with Events	Number of Events
Primary Adverse Event¹	5	5
Type of Primary Adverse Event		
Cardiac Tamponade/Perforation	2	2
Death	1	1
Device or procedure related death ²	0	0
Atrio-Esophageal Fistula ³	0	0
Cardiac Tamponade ^{4, 5} /perforation ⁴	0	0
Major Vascular Access Complication/ Bleeding	0	0
Myocardial Infarction	0	0
Pericarditis	0	0
Heart Block	0	0
Phrenic Nerve Paralysis (Permanent) ⁶	0	0
Pulmonary Vein Stenosis ⁷	0	0
Stroke/Cerebrovascular Accident ^{8, 9}	0	0
Thromboembolism	0	0
Transient Ischemic Attack	2	2
Pulmonary Edema (Respiratory Insufficiency)	0	0
Vagal Nerve Injury/ Gastroparesis	0	0

¹ Subjects without at least 3 months of follow-up are excluded from the primary safety analysis unless they experienced a PAE.

² Device or procedure-related death anytime during or after the ablation procedure and any death reported within 30 days of ablation procedure where device and/or procedure relatedness cannot be determined via CEC adjudication.

³ Atrio-esophageal fistula occurring up to 90 days post AF ablation process procedure is considered a PAE.

⁴ Cardiac Tamponade/Perforation occurring up to 30 days post AF ablation process procedure is considered a PAE.

⁵ Hemodynamic compromise or instability is defined as Systolic BP < 80 mm Hg.

⁶ Absent phrenic nerve function as assessed by a sniff test at discharge.

⁷ Pulmonary Vein Stenosis occurring anytime during the 12-month follow up period is considered a PAE.

⁸ Non-focal global encephalopathy requires unequivocal evidence based upon neuroimaging studies to be reported as a stroke.

⁹ Modified Rankin score assessments should be made by certified individuals.

Death – One subject died of cardiac arrest at 13 days post-procedure. The subject's death was considered possibly related to Dual Energy THERMOCOOL SMARTTOUCH™ SF Catheter, TRUPULSE™ Generator or ablation procedure. The subject was a 75-year-old male with a relevant medical history of drug refractory symptomatic paroxysmal atrial fibrillation, hypertension, hyperlipidemia, cerebrovascular accident (CVA), and type 2 diabetes. The subject presented to the lab in normal sinus rhythm. Pre-procedural examinations (TEE, ECG, and Chest X-ray) did not show any

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contraindications. The subject had a successful PVI ablation without complication and was awake and hemodynamically stable. The subject was discharged the next day after the procedure. There were no complaints during the 7-day post procedure follow-up via telehealth visit. On Day 13 post procedure, the subject displayed shortness of breath while on a phone with the medical provider and was advised to call 911. The subject was reported dead on the same day.

C.2.2 Primary Safety Endpoint– Primary Adverse Events – Safety Population Analysis Set

In addition to the primary safety endpoint results, the safety population includes all subjects where the catheter was inserted, which includes 7 additional subjects. The safety population also represents all treated subjects in the investigation. The seven additional subjects are not represented in the mITT population as they were found to have not met the inclusion and/or exclusion criteria of the investigation after the initial procedure.

Primary Adverse Events occurred in 6 subjects with 2.6% (6/231) incidence rate in Safety Population analysis set (Table X). The upper bound of exact one-sided 97.5% confidence interval (CI), 5.6%, was lower than the pre-defined performance goal of 12%.

Table 14-1. Snap-Shot Binomial Analysis of Primary Safety Endpoint (Safety Population Analysis Set, N=231)

Variable	Number of Subjects	Success Rate n/N (%) [1]	Exact One-Sided 97.5% Upper Confidence Bound
Primary adverse event	6	6 / 231 (2.6%)	5.6%

[1] Subjects without at least 3 months of follow-up are excluded from the primary safety analysis unless they experienced a PAE.

Table 14-2. Decomposition of Primary Safety Endpoint - Primary Adverse Events (Safety Population Analysis Set, N=231)

Variable	Number of Subjects with Events	Number of Events
Primary Adverse Event [1]	6	6
Type of Primary Adverse Event		
Cardiac Tamponade/Perforation	3	3
Death	1	1
Transient Ischemic Attack	2	2

[1] Subjects without at least 3 months of follow-up are excluded from the primary safety analysis unless they experienced a PAE.

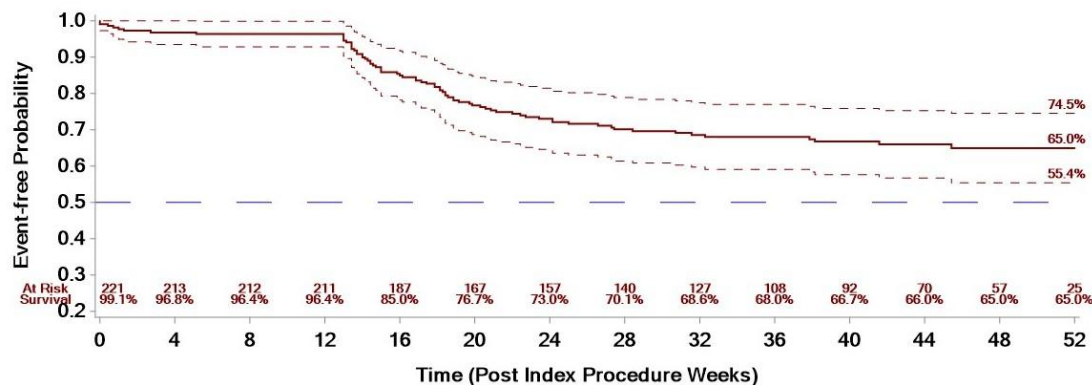
C2.3 – Primary Effectiveness Endpoints

The percentage of subjects who had freedom from documented atrial tachyarrhythmia episodes during effectiveness evaluation period and pre-defined failure modes.

The 1-year rate of freedom from primary effectiveness endpoint based on Kaplan-Meier analysis was 65.0%, with a two-sided 99.5% confidence interval (CI) of 55.4% and 74.5% (Figure 4). The lower end of the 99.5% CI, 55.4%, was higher than the predefined performance goal (55.4% vs 50%).

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**Figure 4 – Kaplan-Meier Analysis of Time to Primary Effectiveness Failure
(Per Protocol Analysis Set, N=221)**

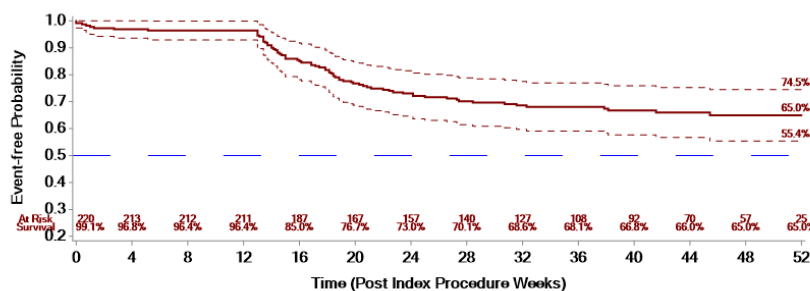


C2.4 – Primary Effectiveness Endpoints – mITT Analysis Set

The mITT analysis set includes 3 additional subjects (224 vs 221) whom were not included in the Per Protocol analysis sets due major protocol deviations in the index procedure. The following analysis includes the percentage of these subjects who had freedom from documented atrial tachyarrhythmia episodes during effectiveness evaluation period and pre-defined failure modes.

The 1-year rate of freedom from primary effectiveness endpoint based on Kaplan-Meier analysis was 65.0%, with a two-sided 99.5% confidence interval (CI) of 55.4% and 74.5% (**Error! Reference source not found.**). The lower end of the 99.5% CI, 55.4%, was higher than the predefined performance goal (55.4% vs 50%).

**Figure 4-1- Kaplan-Meier Analysis of Time to Primary Effectiveness Failure
(mITT Analysis Set, N=224)**



C.3 – Secondary Effectiveness Endpoint – Improvement in Quality of Life

Change in quality of life (QOL) as measured by increase of the total AFEQT score at 12 months post procedure from baseline in Per Protocol (PP) analysis set was 30.88 (p<0.0001) (Table 15).

Table 15 – Overall AFEQT Score by Visit (Per Protocol Analysis Set, N=221)

AFEQT Questionnaire	Statistics ¹	P-value ²
Change from Baseline based on PP Set, N=221		
Mean	30.88	<.0001

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AFEQT Questionnaire	Statistics ¹	P-value ²
95.5% Confidence Interval	(25.49, 36.27)	

¹With available data

²By paired t-test

C.4 – Additional Safety Endpoints

C.4.1 – Serious Adverse Events

The study reported 49 serious adverse events in 36 subjects (15.6%), 9 occurred during the initial 7 days, 4 during the first month after 7 days, and 24 after the first month (Table 16).

Table 15 – Serious Adverse Events by Timing of Onset (Safety Population Analysis Set, N=231)

Timing ¹	Number of Events	Number of Subjects with Event	Event Rate ² n/N (%)
Total	49	36	
Prior to Procedure	0	0	0 / 231 (0.0%)
0 - 7 Days	11	9	9 / 231 (3.9%)
8 - 30 Days	9	4	4 / 231 (1.7%)
≥ 31 Days	29	24	24 / 230 (10.4%)

¹Timing of AE based on onset in days post the procedure (index or repeat).

²N denotes the number of subjects with follow-up duration surpassing the left bound of the time interval.

Table 17 presents serious adverse events by System Organ Class (SOC) and Preferred Term (PT). Cardiac disorders were the most common SAEs with an incidence rate of 6.5% (15/231).

Table 16 – Serious Adverse Events by SOC and PT (Safety Population Analysis Set, N=231)

System Organ Class (SOC) Preferred Term (PT)	Number of Events	Number of Subjects with Event	Event Rate ¹ n/N (%)
Overall	49	36	36 / 231 (15.6%)
Cardiac disorders	18	15	15 / 231 (6.5%)
Atrial flutter	5	4	4 / 231 (1.7%)
Pericardial effusion	3	3	3 / 231 (1.3%)
Bradycardia	2	2	2 / 231 (0.9%)
Arteriosclerosis coronary artery	1	1	1 / 231 (0.4%)
Atrial fibrillation	1	1	1 / 231 (0.4%)
Atrioventricular block	1	1	1 / 231 (0.4%)
Cardiac arrest	1	1	1 / 231 (0.4%)
Cardiac tamponade	1	1	1 / 231 (0.4%)
Coronary artery disease	1	1	1 / 231 (0.4%)
Palpitations	1	1	1 / 231 (0.4%)
Supraventricular tachycardia	1	1	1 / 231 (0.4%)
Gastrointestinal disorders	5	5	5 / 231 (2.2%)
Abdominal pain	1	1	1 / 231 (0.4%)
Abdominal pain upper	1	1	1 / 231 (0.4%)

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System Organ Class (SOC) Preferred Term (PT)	Number of Events	Number of Subjects with Event	Event Rate ¹ n/N (%)
Diarrhea	1	1	1 / 231 (0.4%)
Gastrointestinal hemorrhage	1	1	1 / 231 (0.4%)
Hematemesis	1	1	1 / 231 (0.4%)
Musculoskeletal and connective tissue disorders	4	4	4 / 231 (1.7%)
Osteoarthritis	2	2	2 / 231 (0.9%)
Arthritis	1	1	1 / 231 (0.4%)
Rotator cuff syndrome	1	1	1 / 231 (0.4%)
Nervous system disorders	4	4	4 / 231 (1.7%)
Headache	1	1	1 / 231 (0.4%)
Migraine	1	1	1 / 231 (0.4%)
Syncope	1	1	1 / 231 (0.4%)
Transient ischemic attack	1	1	1 / 231 (0.4%)
Respiratory, thoracic and mediastinal disorders	4	3	3 / 231 (1.3%)
Acute pulmonary oedema	1	1	1 / 231 (0.4%)
Dyspnoea	1	1	1 / 231 (0.4%)
Hypoxia	1	1	1 / 231 (0.4%)
Pulmonary embolism	1	1	1 / 231 (0.4%)
Vascular disorders	4	4	4 / 231 (1.7%)
Hypotension	1	1	1 / 231 (0.4%)
Orthostatic hypotension	1	1	1 / 231 (0.4%)
Peripheral artery aneurysm	1	1	1 / 231 (0.4%)
Thrombophlebitis superficial	1	1	1 / 231 (0.4%)
Renal and urinary disorders	3	2	2 / 231 (0.9%)
Acute kidney injury	1	1	1 / 231 (0.4%)
Nephrolithiasis	1	1	1 / 231 (0.4%)
Renal artery stenosis	1	1	1 / 231 (0.4%)
Injury, poisoning and procedural complications	2	2	2 / 231 (0.9%)
Fractured sacrum	1	1	1 / 231 (0.4%)
Tendon rupture	1	1	1 / 231 (0.4%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	2	2	2 / 231 (0.9%)
Basal cell carcinoma	1	1	1 / 231 (0.4%)
Prostate cancer	1	1	1 / 231 (0.4%)

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System Organ Class (SOC) Preferred Term (PT)	Number of Events	Number of Subjects with Event	Event Rate ¹ n/N (%)
Blood and lymphatic system disorders	1	1	1 / 231 (0.4%)
Lymphadenopathy	1	1	1 / 231 (0.4%)
General disorders and administration site conditions	1	1	1 / 231 (0.4%)
Chest discomfort	1	1	1 / 231 (0.4%)
Immune system disorders	1	1	1 / 231 (0.4%)
Drug hypersensitivity	1	1	1 / 231 (0.4%)

¹ Event rate is the percentage of subjects with the event.

Most of the SAEs were not related to Dual Energy THERMOCOOL SMARTTOUCH™ SF (DE STSF) Catheter, TRUPULSE™ Generator or study procedure (Table 18). Only one (1) subject with SAEs had causal relationship to THERMOCOOL SMARTTOUCH™ SF (STSF) Catheter and another one (1) had possible relationship to the device.

Table 18 – Serious Adverse Events by Causality (Safety Population Analysis Set, N=231)

Relationship to the Device and Procedure	Number of Events	Number of Subjects with Event	Event Rate ¹ n/N (%)
Overall	49	36	36 / 231 (15.6%)
THERMOCOOL SMARTTOUCH™ SF (STSF) Catheter			
Not Device Related	47	35	35 / 231 (15.2%)
Possible Device Related	1	1	1 / 231 (0.4%)
Causal Relationship to Device	1	1	1 / 231 (0.4%)
TRUPULSE™ Generator			
Not Device Related	49	36	36 / 231 (15.6%)
CARTO™ 3 v7.9 Workstation			
Not Device Related	48	36	36 / 231 (15.6%)
Probable Device Related	1	1	1 / 231 (0.4%)
Primary Procedure			
Not Procedure Related	40	30	30 / 231 (13.0%)
Possible Procedure Related	4	4	4 / 231 (1.7%)
Probable Procedure Related	2	2	2 / 231 (0.9%)
Causal Relationship to Procedure	3	3	3 / 231 (1.3%)

¹ Event rate is the percentage of subjects with the event.

C.4.2 – Unanticipated Serious Adverse Device Effect (UADE)

Unanticipated Serious Adverse Device Effect did not occur to any of the study subjects.

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C.4.3 – Non-Serious Adverse Events

The study reported 249 events of non-serious adverse event (NSAE) in 125 subjects (54.1%), 65 occurred during the initial 7 days, 21 during the first month after 7 days, and 73 after the first month (Table 19).

**Table 19 – Non-Serious Adverse Events by Timing of Onset
(Safety Population Analysis Set, N=231)**

Timing ¹	Number of Events	Number of Subjects with Event	Event Rate ² n/N (%)
Total	249	125	125/231 (54.1%)
Prior to Procedure	3	3	3 / 231 (1.3%)
0 - 7 Days	89	65	65 / 231 (28.1%)
8 - 30 Days	26	21	21 / 231 (9.1%)
≥ 31 Days	131	73	73 / 230 (31.7%)

¹ Timing of AE based on onset in days post the procedure (index or repeat).

² N denotes the number of subjects with follow-up duration surpassing the left bound of the time interval.

The most common NSAEs by SOC were cardiac disorders, 19.0% (44/231). The others were related to infectious disease (10.8%), respiratory, thoracic and mediastinal disorders (10.8%), gastrointestinal disorders (7.4%), nervous system disorders (6.9%), vascular disorders (7.4%), injury, poisoning and procedural complications (6.1%) and etc. (Table 20).

Table 17 – Non-serious Adverse Events by SOC and PT (Safety Population Analysis Set, N=231)

System Organ Class (SOC) Preferred Term (PT)	Number of Events	Number of Subjects with Event	Event Rate ¹ n/N (%)
Overall	249	125	125 / 231 (54.1%)
Cardiac disorders	51	44	44 / 231 (19.0%)
Pericardial effusion	17	17	17 / 231 (7.4%)
Atrial flutter	9	8	8 / 231 (3.5%)
Pericarditis	4	2	2 / 231 (0.9%)
Tachycardia	4	4	4 / 231 (1.7%)
Bradycardia	3	3	3 / 231 (1.3%)
Angina pectoris	2	2	2 / 231 (0.9%)
Palpitations	2	2	2 / 231 (0.9%)
Atrial tachycardia	1	1	1 / 231 (0.4%)
Atrioventricular block first degree	1	1	1 / 231 (0.4%)
Cardiac perfusion defect	1	1	1 / 231 (0.4%)
Coronary artery disease	1	1	1 / 231 (0.4%)
Mitral valve incompetence	1	1	1 / 231 (0.4%)
Nodal arrhythmia	1	1	1 / 231 (0.4%)
Sinus tachycardia	1	1	1 / 231 (0.4%)
Supraventricular extrasystoles	1	1	1 / 231 (0.4%)
Ventricular extrasystoles	1	1	1 / 231 (0.4%)
Ventricular tachycardia	1	1	1 / 231 (0.4%)

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System Organ Class (SOC) Preferred Term (PT)	Number of Events	Number of Subjects with Event	Event Rate ¹ n/N (%)
Infections and infestations	30	25	25 / 231 (10.8%)
COVID-19	5	5	5 / 231 (2.2%)
Bronchitis	3	3	3 / 231 (1.3%)
Cellulitis	3	3	3 / 231 (1.3%)
Cystitis	2	2	2 / 231 (0.9%)
Influenza	2	2	2 / 231 (0.9%)
Sinusitis	2	2	2 / 231 (0.9%)
Upper respiratory tract infection	2	2	2 / 231 (0.9%)
Acute sinusitis	1	1	1 / 231 (0.4%)
Breast cellulitis	1	1	1 / 231 (0.4%)
Campylobacter gastroenteritis	1	1	1 / 231 (0.4%)
Ear infection	1	1	1 / 231 (0.4%)
Fungal infection	1	1	1 / 231 (0.4%)
Fungal skin infection	1	1	1 / 231 (0.4%)
Furuncle	1	1	1 / 231 (0.4%)
Lower respiratory tract infection	1	1	1 / 231 (0.4%)
Nasal abscess	1	1	1 / 231 (0.4%)
Tinea cruris	1	1	1 / 231 (0.4%)
Vascular access site infection	1	1	1 / 231 (0.4%)
Respiratory, thoracic and mediastinal disorders	29	25	25 / 231 (10.8%)
Sleep apnoea syndrome	6	6	6 / 231 (2.6%)
Dyspnoea	4	4	4 / 231 (1.7%)
Cough	2	2	2 / 231 (0.9%)
Epistaxis	2	2	2 / 231 (0.9%)
Hypoxia	2	2	2 / 231 (0.9%)
Pulmonary mass	2	2	2 / 231 (0.9%)
Asthma	1	1	1 / 231 (0.4%)
Chronic obstructive pulmonary disease	1	1	1 / 231 (0.4%)
Dysphonia	1	1	1 / 231 (0.4%)
Dyspnoea exertional	1	1	1 / 231 (0.4%)
Pharyngeal swelling	1	1	1 / 231 (0.4%)
Productive cough	1	1	1 / 231 (0.4%)
Pulmonary embolism	1	1	1 / 231 (0.4%)
Pulmonary vein stenosis	1	1	1 / 231 (0.4%)
Throat irritation	1	1	1 / 231 (0.4%)
Upper respiratory tract congestion	1	1	1 / 231 (0.4%)
Wheezing	1	1	1 / 231 (0.4%)

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System Organ Class (SOC) Preferred Term (PT)	Number of Events	Number of Subjects with Event	Event Rate ¹ n/N (%)
Gastrointestinal disorders	19	17	17 / 231 (7.4%)
Diarrhea	2	2	2 / 231 (0.9%)
Uvulitis	2	2	2 / 231 (0.9%)
Vomiting	2	1	1 / 231 (0.4%)
Abdominal distension	1	1	1 / 231 (0.4%)
Ascites	1	1	1 / 231 (0.4%)
Colitis	1	1	1 / 231 (0.4%)
Dyspepsia	1	1	1 / 231 (0.4%)
Flatulence	1	1	1 / 231 (0.4%)
Gastritis	1	1	1 / 231 (0.4%)
Gastroesophageal reflux disease	1	1	1 / 231 (0.4%)
Haematemesis	1	1	1 / 231 (0.4%)
Inguinal hernia	1	1	1 / 231 (0.4%)
Large intestine polyp	1	1	1 / 231 (0.4%)
Lip swelling	1	1	1 / 231 (0.4%)
Mouth hemorrhage	1	1	1 / 231 (0.4%)
Oral mucosal blistering	1	1	1 / 231 (0.4%)
Nervous system disorders	19	16	16 / 231 (6.9%)
Dizziness	4	4	4 / 231 (1.7%)
Paraesthesia	3	3	3 / 231 (1.3%)
Headache	2	2	2 / 231 (0.9%)
Hypoaesthesia	2	2	2 / 231 (0.9%)
Syncope	2	2	2 / 231 (0.9%)
Dysarthria	1	1	1 / 231 (0.4%)
Facial paralysis	1	1	1 / 231 (0.4%)
Memory impairment	1	1	1 / 231 (0.4%)
Migraine	1	1	1 / 231 (0.4%)
Migraine with aura	1	1	1 / 231 (0.4%)
Presyncope	1	1	1 / 231 (0.4%)
Vascular disorders	18	17	17 / 231 (7.4%)
Hypertension	6	6	6 / 231 (2.6%)
Hypotension	5	5	5 / 231 (2.2%)
Haematoma	4	4	4 / 231 (1.7%)
Orthostatic hypotension	3	3	3 / 231 (1.3%)

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System Organ Class (SOC) Preferred Term (PT)	Number of Events	Number of Subjects with Event	Event Rate ¹ n/N (%)
Injury, poisoning and procedural complications	17	14	14 / 231 (6.1%)
Ligament sprain	3	1	1 / 231 (0.4%)
Vascular access site bruising	3	3	3 / 231 (1.3%)
Foot fracture	2	2	2 / 231 (0.9%)
Hand fracture	1	1	1 / 231 (0.4%)
Muscle strain	1	1	1 / 231 (0.4%)
Periorbital hemorrhage	1	1	1 / 231 (0.4%)
Post procedural contusion	1	1	1 / 231 (0.4%)
Post procedural haematoma	1	1	1 / 231 (0.4%)
Procedural pain	1	1	1 / 231 (0.4%)
Urinary retention postoperative	1	1	1 / 231 (0.4%)
Vascular access site hemorrhage	1	1	1 / 231 (0.4%)
Wound	1	1	1 / 231 (0.4%)
General disorders and administration site conditions	16	16	16 / 231 (6.9%)
Chest pain	4	4	4 / 231 (1.7%)
Chest discomfort	3	3	3 / 231 (1.3%)
Oedema peripheral	3	3	3 / 231 (1.3%)
Adverse drug reaction	1	1	1 / 231 (0.4%)
Fatigue	1	1	1 / 231 (0.4%)
Influenza like illness	1	1	1 / 231 (0.4%)
Non-cardiac chest pain	1	1	1 / 231 (0.4%)
Peripheral swelling	1	1	1 / 231 (0.4%)
Pyrexia	1	1	1 / 231 (0.4%)
Musculoskeletal and connective tissue disorders	12	12	12 / 231 (5.2%)
Musculoskeletal chest pain	4	4	4 / 231 (1.7%)
Back pain	2	2	2 / 231 (0.9%)
Osteoarthritis	2	2	2 / 231 (0.9%)
Arthralgia	1	1	1 / 231 (0.4%)
Groin pain	1	1	1 / 231 (0.4%)
Joint effusion	1	1	1 / 231 (0.4%)
Pain in extremity	1	1	1 / 231 (0.4%)
Metabolism and nutrition disorders	8	8	8 / 231 (3.5%)
Fluid overload	3	3	3 / 231 (1.3%)
Gout	2	2	2 / 231 (0.9%)
Hyperlipidaemia	2	2	2 / 231 (0.9%)
Diabetes mellitus	1	1	1 / 231 (0.4%)

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System Organ Class (SOC) Preferred Term (PT)	Number of Events	Number of Subjects with Event	Event Rate ¹ n/N (%)
Investigations	7	7	7 / 231 (3.0%)
Ejection fraction decreased	2	2	2 / 231 (0.9%)
Body temperature increased	1	1	1 / 231 (0.4%)
Human metapneumovirus test	1	1	1 / 231 (0.4%)
Influenza A virus test positive	1	1	1 / 231 (0.4%)
Influenza virus test positive	1	1	1 / 231 (0.4%)
Oesophagogastroduodenoscopy	1	1	1 / 231 (0.4%)
Renal and urinary disorders	7	6	6 / 231 (2.6%)
Haematuria	2	2	2 / 231 (0.9%)
Nephrolithiasis	2	2	2 / 231 (0.9%)
Chronic kidney disease	1	1	1 / 231 (0.4%)
Renal cyst	1	1	1 / 231 (0.4%)
Urinary retention	1	1	1 / 231 (0.4%)
Skin and subcutaneous tissue disorders	4	4	4 / 231 (1.7%)
Cutaneous amyloidosis	1	1	1 / 231 (0.4%)
Dermal cyst	1	1	1 / 231 (0.4%)
Dermatitis contact	1	1	1 / 231 (0.4%)
Ecchymosis	1	1	1 / 231 (0.4%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	3	3	3 / 231 (1.3%)
Breast cancer	1	1	1 / 231 (0.4%)
Colon adenoma	1	1	1 / 231 (0.4%)
Skin cancer	1	1	1 / 231 (0.4%)
Eye disorders	2	2	2 / 231 (0.9%)
Conjunctival cyst	1	1	1 / 231 (0.4%)
Visual field defect	1	1	1 / 231 (0.4%)
Reproductive system and breast disorders	2	2	2 / 231 (0.9%)
Erectile dysfunction	2	2	2 / 231 (0.9%)
Blood and lymphatic system disorders	1	1	1 / 231 (0.4%)
Hilar lymphadenopathy	1	1	1 / 231 (0.4%)
Ear and labyrinth disorders	1	1	1 / 231 (0.4%)
Hypoacusis	1	1	1 / 231 (0.4%)

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System Organ Class (SOC) Preferred Term (PT)	Number of Events	Number of Subjects with Event	Event Rate ¹ n/N (%)
Endocrine disorders	1	1	1 / 231 (0.4%)
Thyroid mass	1	1	1 / 231 (0.4%)
Hepatobiliary disorders	1	1	1 / 231 (0.4%)
Hyperbilirubinaemia	1	1	1 / 231 (0.4%)
Psychiatric disorders	1	1	1 / 231 (0.4%)

¹ Event rate is the percentage of subjects with the event.

The majority of the NSAEs were not related to study devices or procedures. Two (2) of them were probably related and seven (7) were possibly related to the Dual Energy THERMOCOOL SMARTTOUCH™ SF Catheter (Table 21).

Table 18 – Non-Serious Adverse Events by Causality (Safety Population Analysis Set, N=231)

Relationship to the Device and Procedure	Number of Events	Number of Subjects with Event	Event Rate ¹ n/N (%)
Overall	249	125	125 / 231 (54.1%)
THERMOCOOL SMARTTOUCH™ SF (STSF) Catheter			
Not Device Related	240	121	121 / 231 (52.4%)
Possible Device Related	7	7	7 / 231 (3.0%)
Probable Device Related	2	2	2 / 231 (0.9%)
TRUPULSE™ Generator			
Not Device Related	244	123	123 / 231 (53.2%)
Possible Device Related	5	5	5 / 231 (2.2%)
CARTO™ 3 v7.9 Workstation			
Not Device Related	245	123	123 / 231 (53.2%)
Possible Device Related	4	4	4 / 231 (1.7%)
Primary Procedure			
Not Procedure Related	182	98	98 / 231 (42.4%)
Possible Procedure Related	34	29	29 / 231 (12.6%)
Probable Procedure Related	22	20	20 / 231 (8.7%)
Causal Relationship to Procedure	11	11	11 / 231 (4.8%)

¹ Event rate is the percentage of subjects with the event.

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C.4.4 – PV Narrowing Post Ablation in CT/MRA Subset (N=34)

The subjects in Cardiac CT/MRA subset were assessed for PV narrowing after 3 months post ablation. None of the subjects had PV narrowing greater than 50% (Table 22). Only 17.6% (6/34) of the subjects in this subset had PV narrowing between > 25% and 50%.

**Table 19 – PV Narrowing Post Ablation by PV Targets - Subject Level
(Cardiac CT/MRA Analysis Set, N=34)**

	PV Narrowing ¹				
Pulmonary Vein	None 0%	Minimum >0-25%	Mild >25-50%	Moderate >50-70%	Severe >70%
Subject-Level Summary, n/N (%)	2 / 34 (5.9%)	26 / 34 (76.5%)	6 / 34 (17.6%)	0 / 34 (0.0%)	0 / 34 (0.0%)

¹ Subject-Level Summary of PV Narrowing (%) = (number of subjects whose maximum percent of PV narrowing in a specific level of narrowing / number of subjects with available CT/MRA data).

C.4.5 Assessment of Cerebral Embolic Lesions in Neurological Assessment Subset

The SmartPulse PAF study enrolled nine (9) subjects into the NAE sub-study. Seven subjects completed baseline and pre-discharge MRIs. An independent core lab evaluated the MRIs and no cerebral lesions were observed.

A separate NAE Subset Analysis Report (G230170/S010) was submitted on October 24, 2024 to the FDA to assess the potential neurological impact on subjects utilizing the Biosense Webster ablation system from a similar investigational study conducted in Europe. This report included 30 subjects enrolled into an NAE subset evaluation from the SmartfIRE study (NCT05752487) which utilized the same Biosense Webster ablation system and included a generalizable population to the SmartPulse study.

Cerebral MRI data from SmartfIRE showed cerebral lesions (FLAIR+) post-ablation in two (2) out of 30 subjects (6.7%) of the Neurological Assessment (NAE) Analysis Set. One (1) lesion was symptomatic and one (1) was asymptomatic. All lesions were resolved at the next follow-up scan, one to three months after the procedure. None of the subjects presented with a decreased neurological status based on MMSE-2, mRS and NIHSS score pre-and post-ablation.

C.5 – Additional Effectiveness Endpoints

C.5.1 – Acute Procedural Success

All subjects achieved acute procedure success of PVI that was confirmed by entrance block (Table 23).

Table 20 – Acute Procedure Success - Entrance Block Confirmation

Variable	Number of Subjects Undergone Ablation Procedure ²	Number of Successful Subjects	Success Rate n/N (%)
PP Analysis Set, N=221			
Acute Procedural Success ¹	220	220	220/220 (100.0%)
mITT Analysis Set, N=224			
Acute Procedural Success ¹	220	220	220/220 (100.0%)
All Treated Analysis Set, N=231			
Acute Procedural Success ¹	227	227	227/227 (100.00)

¹ Acute procedural success is defined as confirmation of entrance block in all PVs after

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adenosine/isoproterenol challenge.

²Number of subjects who have energy delivered with study catheter. Subjects without adenosine/isoproterenol challenge will be considered as missingness and excluded from the analysis.

C.5.2 – Acute PV Reconnection at Subject Level

After the initial completion of PV ablation and confirmation of isolation by entrance block, 23.2% of subjects displayed acute PV reconnection following adenosine or isoproterenol challenge (Table 24).

Table 21 – Acute PV Reconnection - Subject Level

Endpoint	Number of Subjects ¹	Number of Subjects with Reconnection ²	Reconnection Rate
PP Analysis Set (N=221)			
Acute Reconnection	220	51	51 / 220 (23.2%)
mITT Analysis Set (N=224)			
Acute Reconnection	220	51	51 / 220 (23.2%)

¹Subjects not undergone adenosine/isoproterenol challenge are excluded.

²Subjects with at least one vein with reconnection identified after adenosine/isoproterenol challenge.

C.5.3 – First Pass Isolation at Subject Level

The first pass isolation, achievement of PVI as confirmed by entrance block after closure of ablation lesions encircling the ipsilateral PV pairs before administration of adenosine/ isoproterenol to induce dormant connections, was achieved in 95.4% of subjects in PP analysis set (Table 25).

Table 22 – First Pass Isolation - Subject Level

Endpoint	Number of Subjects	Number of Subjects with FPI	FPI Rate n/N (%)
PP Set (N=221)			
First Pass Isolation (FPI)	219	209	209 / 219 (95.4%)
mITT Set (N=224)			
First Pass Isolation (FPI)	221	210	210 / 221 (95.0%)

C.5.4 – Repeat ablation Procedures

Repeat ablations were performed in 10.9% (24/221) of subjects in PP analysis set. None of the subjects performed more than one repeat ablations (Table 26). Repeat ablation performed during the blanking period accounted for 8.3% (2/24) of procedures. The remaining 91.7% (22/24) were performed during the evaluation period.

Table 23 – Repeat Ablation Procedures (mITT Analysis Set, N=224 and PP Analysis Set, N=221)

Variable	PP Set (N=221) n/N (%)	mITT Set (N=224) n/N (%)
Subjects Underwent Repeat Ablation Procedures	24/221 (10.9%)	25/224 (11.2%)
Number of Repeat Ablations a Subject Underwent¹		
1	24/24 (100%)	25/25 (100%)
2	0/24 (0.0%)	0/25 (0.0%)

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Variable	PP Set (N=221) n/N (%)	mITT Set (N=224) n/N (%)
> 2	0/24 (0.0%)	0/25 (0.0%)
By Timing of Repeat Procedure - Days after Initial Procedure²		
During blanking period (Day 1-90)	2/24 (8.3%)	3/25 (12.0%)
During evaluation period (Day 91-365)	22/24 (91.7%)	22/25 (88.0%)
Arrhythmia Treated^{+, 1}		
Atrial Fibrillation	19/24 (79.2%)	20/25 (80.0%)
Atrial Flutter Typical Right	7/24 (29.2%)	7/25 (28.0%)
Atrial Flutter Atypical Right	5/24 (20.8%)	5/25 (20.0%)
Atrial Flutter Atypical Left	4/24 (16.7%)	4/25 (16.0%)
Atrial Tachycardia Right Atrium	3/24 (12.5%)	3/25 (12.0%)
Atrial Tachycardia Left Atrium	1/24 (4.2%)	1/25 (4.0%)
AVNRT	0/24 (0.0%)	0/25 (0.0%)
Other	1/24 (4.2%)	1/25 (4.0%)

⁺ Allows for multiple selection.

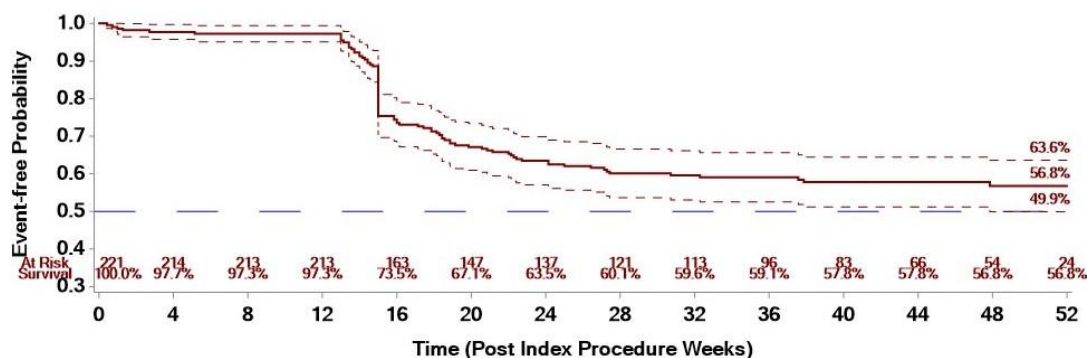
¹ N denotes the number of subjects who underwent repeat ablation procedure.

² N denotes the total number of repeat ablations.

C.5.5 – Freedom from Documented Atrial Tachyarrhythmia of Any AAD

The 12-months rate of freedom from documented symptomatic and asymptomatic atrial tachyarrhythmia off any AAD after 3-month blanking period in PP analysis set was 56.8% by Kaplan Meier analysis with 95% CI of 49.9% and 63.6% (Figure 5).

Figure 5 – Freedom from Documented Atrial Tachyarrhythmia off Any AAD (Class I or III) (PP Analysis Set, N=221)

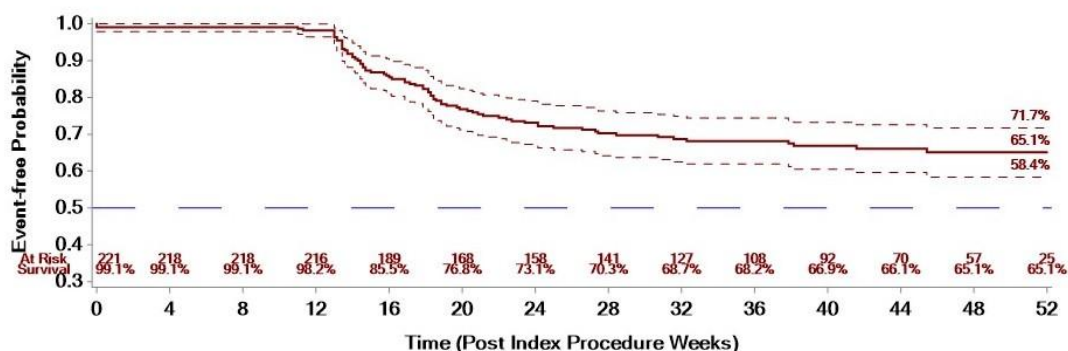


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C.5.6 – Kaplan-Meier analysis of Single Procedural Success

The 12-month rate of freedom from documented symptomatic atrial tachyarrhythmia following a single index ablation procedure after 3-month blanking period in PP analysis set was 65.1% with 95% CI of 58.4% and 71.7% (Figure 6).

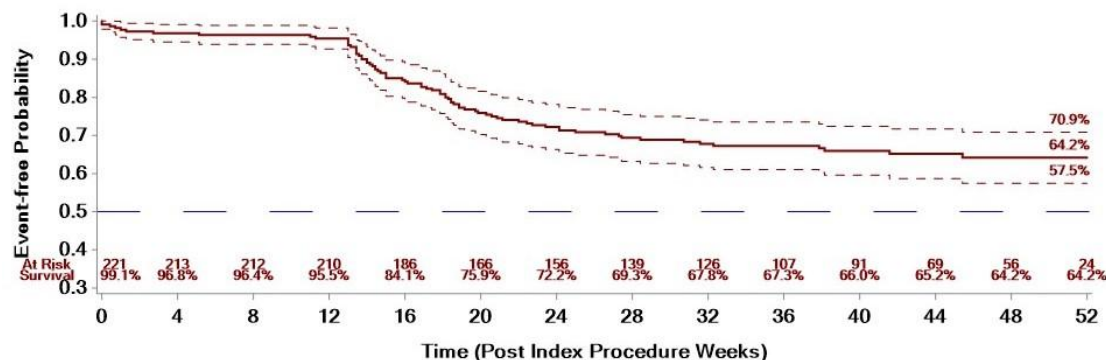
**Figure 6 – Kaplan-Meier Analysis of Single Procedural Success
(Per Protocol Analysis Set, N=221)**



C.5.7 – Kaplan-Meier Analysis of Single Procedure Success off Class I/III AAD

The 12-month rate of freedom from documented symptomatic atrial tachyarrhythmia following a single index ablation procedure off Class I/III AAD after 3-month blanking period in PP analysis set was 64.2% with 95% confidence CI of 57.5% and 70.9% (Figure 7).

**Figure 7 – Kaplan-Meier Analysis of Single Procedure Success off Class I/III AAD
(PP Analysis Set, N=221)**

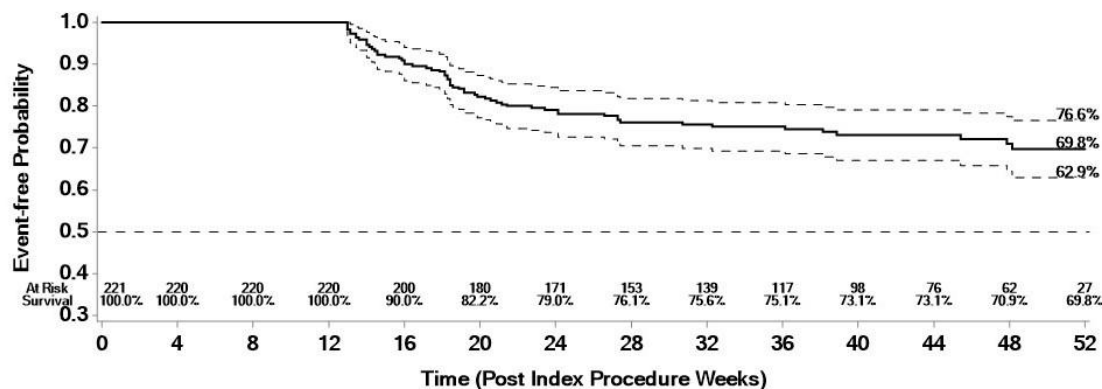


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C.5.8 – Kaplan-Meier Analysis of Time to Documented symptomatic Recurrence

The 12-month rate of freedom from documented symptomatic atrial tachyarrhythmia recurrence after 3-month blanking period in PP analysis set was 69.8% with 95% CI of 62.9% and 76.6% (Figure 8).

**Figure 8 – Kaplan-Meier Analysis of Time to Documented Symptomatic Recurrence¹
(PP Analysis Set, N=221)**

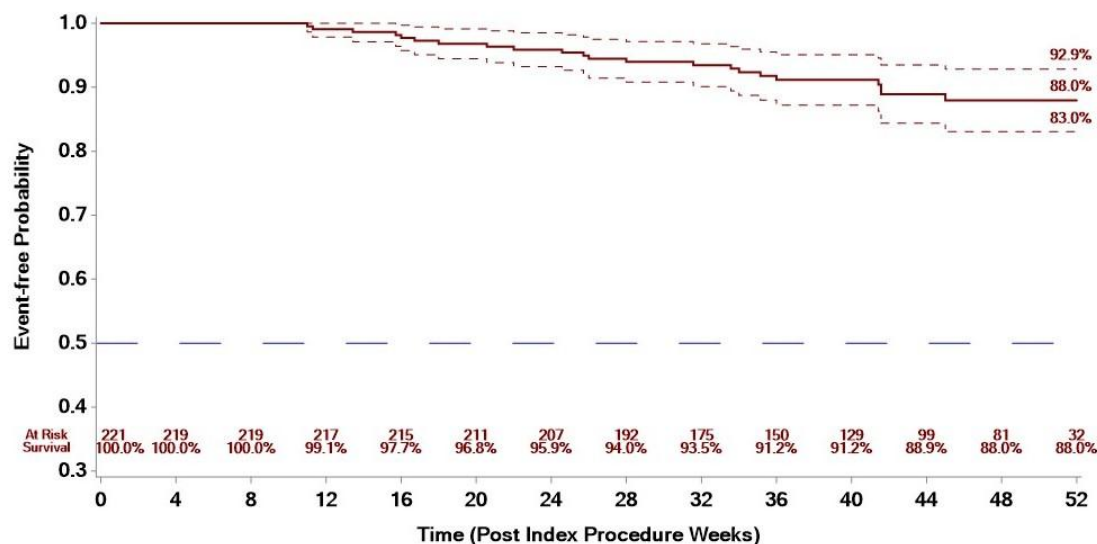


¹ The endpoint is defined as freedom from acute procedural failure and documented symptomatic atrial arrhythmia (AF/AT/AFL of unknown origin) episodes based on electrocardiographic data ($\geq$ 30 seconds on arrhythmia monitoring device) during the evaluation period.

C.5.9 – Kaplan-Meier Analysis of Time to Repeat ablation

The 12-month rate of freedom from repeat ablation in the PP analysis set at the end of the evaluation period was 88.0% with 95% CI of 83.0% and 92.9% (Figure 9).

Figure 9 – Kaplan-Meier Analysis of Time to Repeat Ablation Per Protocol Analysis Set (N=221)



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C.5.10 – Change of AAD Use from Baseline

At the end of the first 3 months, second 3 months, and last 6 months post ablation, the rate of AAD use was reduced by 36.1%, 44.0%, and 62.7%, respectively (Table 27).

Table 24 – AAD Utilization by Timing (PP Analysis Set, N=221)

Time Interval	Rate of AAD Use ² n/N (%)	Rate Change ³ %
Baseline¹		
AAD Used for AF/AT/AFL, n/N (%)	75 / 84 (89.3%)	
Class I/III AAD Used, n/N (%)	72 / 84 (85.7%)	
Class II/IV AAD Used, n/N (%)	28 / 84 (33.3%)	
> 0 - 3 months		
AAD Used for AF/AT/AFL, n/N (%)	48 / 84 (57.1%)	-36.1%
Class I/III AAD Used, n/N (%)	43 / 84 (51.2%)	-40.3%
Class II/IV AAD Used, n/N (%)	20 / 84 (23.8%)	-28.5%
>3 - 6 months		
AAD Used for AF/AT/AFL, n/N (%)	42 / 84 (50.0%)	-44.0%
Class I/III AAD Used, n/N (%)	31 / 84 (36.9%)	-56.9%
Class II/IV AAD Used, n/N (%)	23 / 84 (27.4%)	-17.7%
>6 - 12 months		
AAD Used for AF/AT/AFL, n/N (%)	28 / 84 (33.3%)	-62.7%
Class I/III AAD Used, n/N (%)	11 / 84 (13.1%)	-84.7%
Class II/IV AAD Used, n/N (%)	21 / 84 (25.0%)	-24.9%

¹ Baseline is defined as time of enrollment up to date of ablation procedure.

² N represents the number of subjects with data available at both baseline and the entire duration of the follow-up interval. n represents the number of subjects with AAD use at any point within the time interval.

³ Rate change is calculated as (follow-up rate - baseline rate)/(baseline rate) x 100.

C.5.11 – Change in Cardiovascular Hospitalization Rate

The 12-month cardiovascular hospitalization rate before and after ablation procedure was reduced by 63.4% (Table 28).

Table 28 – Change in Cardiovascular Hospitalization Rate (PP Analysis Set, N=221)

Time Interval	Number of Events	Number of Subjects with Events	CV Hospitalization Rate ² n/N (%)	Rate Change ³ %
Baseline ¹	11	11	11 / 84 (13.1%)	
>0-12 months post procedure	4	4	4 / 84 (4.8%)	-63.4%

¹ Baseline is defined as > 0-12 months pre-procedure.

² N represents the number of subjects with data available at both baseline and the entire duration of the follow-up interval. n represents the number of subjects with at least 1 CV hospitalization in the time interval.

³ Rate change is calculated as follow-up rate - baseline rate

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C.5.12 – Reduction in DCCV

The DCCV was reduced from 16.7% at baseline to 10.7% during the 12 months after the ablation procedure, a reduction of 35.9% (Table 29).

Table 29 – Reduction in DCCV (PP Analysis Set, N=221)

Time Interval	Number of Events	Number of Subjects with Events	DCCV Rate ² n/N (%)	Rate Change ³ %
Baseline ¹	14	14	14 / 84 (16.7%)	
>0-12 months post procedure	9	9	9 / 84 (10.7%)	-35.9%

¹ Baseline is defined as > 0-12 months pre-procedure.

² N represents the number of subjects with data available at both baseline and had completed the 12 month follow-up visit. n represents the number of subjects with at least 1 DCCV in the time interval.

³ Rate change is calculated as (follow-up rate – baseline rate)/baseline rate.

D. Study Conclusion

The study met the primary safety and primary effectiveness performance goals of the Dual Energy THERMOCOOL SMARTTOUCH™ SF Catheter with the TRUPULSE™ Generator for treatment of drug refractory symptomatic paroxysmal atrial fibrillation. In addition, clinical benefits were observed in increased quality of life during the effectiveness monitoring period.

STUDY 2: Pivotal Study – SmartFIRE Study

A. Objective

The primary objective of this clinical investigation was to demonstrate safety and acute effectiveness of the Dual Energy THERMOCOOL SMARTTOUCH™ SF Bi-Directional Navigation Catheter (DE STSF) when used in conjunction with the TRUPULSE™ Generator for isolation of the PVs in treatment of subjects with PAF.

B. Study Design

The study was an interventional, prospective, multicenter, single-arm safety and effectiveness clinical evaluation of PAF subjects at 9 investigational sites in Europe.

B.1 – Study Endpoints

The endpoints for the study were as follows:

Primary safety endpoint – the incidence of Primary Adverse Events (PAEs) within seven (7) days of the index ablation procedure.

Primary Adverse Events included the following conditions:

- Atrio-esophageal fistula*
- Cardiac Tamponade /perforation**
- Device or procedure related death*
- Major Vascular Access Complication/Bleeding
- Myocardial Infarction
- Pericarditis
- Pulmonary Edema (Respiratory Insufficiency)
- Phrenic Nerve Paralysis (permanent)***
- Pulmonary Vein Stenosis*
- Stroke/ Cerebrovascular Accident (CVA)

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- Thromboembolism
- Transient Ischemic Attack (TIA)
- Heart Block
- Vagal Nerve Injury/Gastroparesis

* Device or procedure related death, pulmonary vein stenosis and atrio-esophageal fistula that occur greater than 1 week (7 days) and less than or equal to 90 days post-procedure are considered and analyzed as PAEs.

** Cardiac Tamponade/Perforation occurring up to 30 days post AF ablation process procedure will be considered a PAE

*** A phrenic nerve paralysis is considered to be permanent when it is documented to be present 12 months or longer following ablation. Under this CIP, diaphragmatic paralysis/phrenic nerve palsy will be considered a Primary AE if specified symptoms have not improved at the 3-month visit.

Primary Effectiveness Endpoint – the percentage of subjects with acute procedural success, defined as electrical isolation of targeted PVs (confirmed by final entrance block) after adenosine/isoproterenol challenge at the end of the index ablation procedure. Use of a non-study device to achieve PVI was considered an acute procedural failure.

Secondary Endpoint – freedom from documented symptomatic and asymptomatic atrial arrhythmia episodes based on electrocardiographic data during the effectiveness evaluation period (Day 91- Day 365) on or off antiarrhythmic therapy. Acute procedural failures were also considered failures for this endpoint.

B.2 – Prespecified Performance Goal

Primary Safety Endpoint – performance Goal = 12.0% of upper bound of two-sided 95% CI around the PAE rate.

Primary Effectiveness Endpoint – Performance Goal = 90% of lower bound of two-sided 95% CI around the acute procedural success rate.

Secondary Endpoint – Performance Goal = 50% of lower bound of two-sided 95% CI around 1-year rate of freedom from secondary effectiveness endpoint.

B.3 – Subject Disposition and Accountability

B.3.1 – Subject Disposition and Accountability

Table 25 – Subject Enrollment and Accountability (Enrolled Subjects, N=149)

Subject Enrollment	n
Enrolled Subjects ¹	149
Excluded Subjects ²	9
Study Catheter Inserted ³	140
Discontinued Subjects ⁴	1
Death	0
Withdrawn/Early Termination Subjects ⁵	2
Lost to Follow-up Subjects ⁶	0
Completed Subjects ⁷	137
PVI Durability Subset	30
Neurological Analysis Subset	30
CT/MRA Subset	30
Esophageal Endoscopy Subset	30

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- ¹ Enrolled Subjects: Subjects who sign the Informed Consent Form (ICF).
- ² Excluded Subjects: Subjects who are enrolled but never undergo insertion of the study catheter.
- ³ Includes all enrolled subjects who have the investigational device inserted, regardless of whether energy is delivered or not.
- ⁴ Discontinued Subjects: Subjects who have the study catheter inserted but do not undergo ablation (i.e., no PF/RF energy applied).
- ⁵ Withdrawn/Early Termination Subjects: Subjects who withdraw consent for study participation prior to completion of all follow-up visits or are terminated by the site prior to completion of all follow-up visits.
- ⁶ Lost to Follow-up Subjects: Subjects who have study catheter inserted, but contact is lost after most recent follow-up visit (despite 3 documented attempts to contact the subject).
- ⁷ Completed Subjects: Enrolled subjects who have not been excluded, discontinued, withdrawn, terminated early, or lost-to-follow-up from the study prior to the final study visit.

B.3.2 – Study Analysis Set

Table 26 – Analysis Set (Safety Population Analysis Set, N=140)

Analysis Set	n
Safety Population (SP) Analysis Set¹	140
Did not meet eligibility*	3
Modified Intent-To-Treat (mITT) Analysis Set²	137
Subjects excluded from Per Protocol Analysis (PP) Set	1
Per-Protocol (PP) Analysis Set³	136
PVI Durability Subset	30
Neurological Analysis Subset	30
CT/MRA Subset	30
Esophageal Endoscopy Subset	30

* After sponsor assessment based on all information available during the trial.

¹ SP Analysis Set: Enrolled subjects who have had the study catheter inserted, regardless of whether energy is delivered or not.

² mITT Analysis Set: Enrolled subjects who meet eligibility criteria and have had insertion of the study catheter.

³ PP Analysis Set: Subjects who satisfy the following criteria: (1) undergone ablation (PF/RF) with the study catheter, (2) treated for study-related arrhythmia, (3) no specified major CIP deviations.

B.4 – Subject Demographics

Table 32 – Demographics (Safety Population Analysis Set, N=140)

Variable	Statistics
Age (years) ¹	61.6 ± 7.79
Sex, n/N (%)	
Male	80 / 140 (57.1%)
Female	60 / 140 (42.9%)
Of Childbearing Potential	2 / 60 (3.3%)
Permanently Sterilized (or infertile)	1 / 60 (1.7%)
Postmenopausal	57 / 60 (95.0%)
Weight (kg)	85.97 ± 16.052

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Variable	Statistics
Height (cm)	173.9 ± 9.07
BMI (kg/m ²)	28.38 ± 4.467

¹ Age at informed consent.

BMI = Body mass index.

B.5 – Baseline Characteristics

B.5.1 – Medical History

Table 27 – Medical History (Safety Population Analysis Set, N=140)

Variable	n/N (%)
Cardiovascular Medical History[†]	103 / 140 (73.6%)
Congestive heart failure	18 / 140 (12.9%)
Ongoing	18 / 140 (12.9%)
NYHA Class	
Class I	9 / 140 (6.4%)
Class II	6 / 140 (4.3%)
Coronary disease	22 / 140 (15.7%)
Ongoing	15 / 140 (10.7%)
Resolved	7 / 140 (5.0%)
Vascular disease	7 / 140 (5.0%)
Ongoing	4 / 140 (2.9%)
Resolved	3 / 140 (2.1%)
Myocardial infarction	4 / 140 (2.9%)
Hypertension (systemic)	78 / 140 (55.7%)
Ongoing	77 / 140 (55.0%)
Resolved	1 / 140 (0.7%)
Pulmonary hypertension	4 / 140 (2.9%)
Ongoing	4 / 140 (2.9%)
Cardiomyopathy	4 / 140 (2.9%)
Ongoing	3 / 140 (2.1%)
Resolved	1 / 140 (0.7%)
Hypertrophic	1 / 140 (0.7%)
Ischemic	1 / 140 (0.7%)
Non-Ischemic	2 / 140 (1.4%)
Left ventricular hypertrophy	8 / 140 (5.7%)
Ongoing	7 / 140 (5.0%)
Resolved	1 / 140 (0.7%)
Significant valvular disease	2 / 140 (1.4%)
Ongoing	2 / 140 (1.4%)
Percutaneous coronary intervention (PCI)	10 / 140 (7.1%)
Other cardiovascular procedure (e.g. CABG, etc.)	4 / 140 (2.9%)
Carotid stenting or endarterectomy	1 / 140 (0.7%)

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Variable	n/N (%)
Unstable angina	1 / 140 (0.7%)
Hypercholesterolemia	72 / 140 (51.4%)
Ongoing	71 / 140 (50.7%)
Resolved	1 / 140 (0.7%)
Other cardiovascular medical condition	5 / 140 (3.6%)
Documented Thromboembolic Events*	7 / 140 (5.0%)
Transient ischemic attack (TIA)	3 / 140 (2.1%)
Stroke	3 / 140 (2.1%)
Ischemic	2 / 140 (1.4%)
Pulmonary embolus	1 / 140 (0.7%)
Other thromboembolic events	1 / 140 (0.7%)
Other Medical History*	65 / 140 (46.4%)
Any significant pulmonary disease	1 / 140 (0.7%)
Diabetes Mellitus	10 / 140 (7.1%)
Type II	10 / 140 (7.1%)
Obstructive sleep apnea (OSA)	6 / 140 (4.3%)
OSA Type	
Mild	1 / 140 (0.7%)
Moderate	2 / 140 (1.4%)
Severe	3 / 140 (2.1%)
OSA Effective Treatment	3 / 140 (2.1%)
Hyperthyroidism	2 / 140 (1.4%)
Effective Treatment	1 / 140 (0.7%)
Any cardiovascular hospitalizations 12 months prior to index procedure	55 / 140 (39.3%)

* Allows for multiple selection.

*NYHA class unknown

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B.5.2 – Atrial Fibrillation History

Table 28 – Atrial Fibrillation History (Safety Population Analysis Set, N=140)

Variable	Statistics ¹
Duration of symptomatic paroxysmal AF (months)	53.07 ± 61.802
Number of symptomatic paroxysmal AF episodes in the past 12 months	45.6 ± 81.06
Average length of each of the paroxysmal AF episode in the past 12 months (hours)	12.193 ± 20.4869
Average frequency of symptomatic paroxysmal AF in the past 12 months, n/N (%)	**
Daily	10 / 140 (7.1%)
Weekly	31 / 140 (22.1%)
Bi-weekly	11 / 140 (7.9%)
Monthly	15 / 140 (10.7%)
Irregular	65 / 140 (46.4%)
Unknown	8 / 140 (5.7%)
Direct current cardioversion (DCCV) in the past 12 months for paroxysmal AF, n/N (%)	34 / 140 (24.3%)
1	18 / 34 (52.9%)
2	9 / 34 (26.5%)
3	2 / 34 (5.9%)
≥ 4	5 / 34 (14.7%)

¹ With available data.

Note:

*For “Number of symptomatic paroxysmal AF episodes in the past 12 months” and “Average length of each of the paroxysmal AF episode in the past 12 months (hours)” also non-documented episodes are reported. In case the information was unknown, the information was not completed, this was the case for 10 and 12 subjects respectively.

**For “Average frequency of symptomatic paroxysmal AF in the past 12 months”, also non-documented episodes are taken into account.

B.5.3 – AAD Failed at Baseline

Table 29 – AAD Failed at Baseline Per Subject (Safety Population Analysis Set, N=140)

AAD Drug Failed	Statistics
Number of AADs Failed per subject ¹	1.7 ± 0.80
Number of Class I/III AADs Failed per subject ^{1, 2}	1.3 ± 0.53
Number of Class II/IV AADs Failed per subject ^{1, 2}	1.1 ± 0.28

¹ For subjects who fail a specific AAD as indicated by a Generic Drug Class and Name.

² Class I/III and Class II/IV AAD are not mutually exclusive. Subjects who take both Class I/III and Class II/IV AAD drugs will be counted in both summaries.

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B.5.4 – Baseline CHADS₂ and CHA₂DS₂-VASc Score

Table 30 – CHADS₂ and CHA₂DS₂-VASc Score (Safety Population Analysis Set, N=140)

Variable	Statistics
CHADS ₂ Score ¹	0.9 ± 0.84
CHA ₂ DS ₂ -VASc Score ²	1.8 ± 1.30

¹ The score for each subject is calculated as a sum of points given for each of the following conditions: 1 for congestive heart failure, 1 for hypertension, 1 for age ≥ 75 years, 1 for diabetes mellitus, and 2 for prior stroke or TIA or thromboembolism.

² The score for each subject is calculated as a sum of points given for each of the following conditions: 1 for congestive heart failure (or left ventricular systolic dysfunction), 1 for hypertension, 2 for age ≥ 75 years, 1 for diabetes mellitus, 2 for prior stroke or TIA or thromboembolism, 1 for vascular disease (e.g. peripheral artery disease, myocardial infarction, aortic plaque), 1 for age 65-74 years, and 1 for sex category (i.e. female).

C. Results

C.1 – Procedural Data

C.1.1 – Procedural Data

Table 31 – Procedural Data of the Index Procedure (PP Analysis Set, N=136)

Variable	Statistics
Anesthesia Type, n/N (%)	
Conscious sedation	20 / 136 (14.7%)
General (unconscious sedation)	116 / 136 (85.3%)
Total procedure time (min)	109.19 ± 28.470
Transseptal Access, n/N (%)	
Double	77 / 136 (56.6%)
Single	59 / 136 (43.4%)
Pre-Ablation Mapping:	
Left atrial map acquired prior to ablation, n/N (%)	136 / 136 (100.0%)
Total LA mapping time (min)	9.52 ± 4.077
PV Ablation to Achieve PV Isolation:	
Total PV Ablation time with STSF study catheter (min)	57.87 ± 22.085
Total STSF study catheter LA dwell time (min)	80.86 ± 25.464
Total fluoroscopy duration at the end of all application (min)	6.44 ± 6.412
Fluid delivered via the study catheter(s) (mL)	456.7 ± 254.16
Heart rhythm at the beginning of the procedure, n/N (%)	

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Variable	Statistics
Atrial Fibrillation	12 / 136 (8.8%)
Sinus rhythm	122 / 136 (89.7%)
Other	2 / 136 (1.5%)
Predominant heart rhythm at the end of the procedure, n/N (%)	
Atrial Fibrillation	18 / 136 (13.2%)
Sinus Rhythm	118 / 136 (86.8%)
If not in sinus rhythm, cardioversion performed , n/N (%)	18 / 18 (100.0%)
Type of cardioversion, n/N (%)	
Electrical	18 / 18 (100.0%)

C.1.2 – Use of Ablation Energy at Subject Level

Table 32 – Use of Ablation Energy at Subject Level (PP analysis Set, N=136)

Variable	Overall
Number of Valid PF/RF Applications ¹	74.4 ± 22.07
Number of RF Applications	32.3 ± 10.55
Number of Valid PF Applications ¹	42.5 ± 17.51
Total Valid PF/RF Application Time (sec) ¹	879.96 ± 363.630
Total RF Application Time (sec)	790.11 ± 339.959
Total Valid PF Application Time (sec) ¹	95.66 ± 61.735
Total Ablation Duration (min)	62.29 ± 25.046

¹ The PF ablations with all applications less than 100% status are excluded and considered as invalid.

C.1.3 – Number of Applications per Ablation Target

Table 33 – Number of Applications per ablation Target (PP Analysis Set, N=136)

Variable	Overall ¹	Number of Valid PF Applications ¹	Number of RF Applications
LPV	35.2 ± 11.39	18.8 ± 7.92	16.6 ± 6.59
RPV	37.9 ± 12.93	22.8 ± 10.89	15.5 ± 5.73
CTI Line	13.9 ± 9.66	16.6 ± 9.76	8.5 ± 4.89

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C.2 – Primary Endpoints

C.2.1 – Primary Safety Endpoints

Primary adverse events occurred in 6 subjects with an incidence rate of 4.4% (6/137) in mITT analysis set. The upper bound of two-sided exact 95% confidence interval was 9.3%, which was lower than the performance goal of 12%. The study met the primary safety endpoint (Table 40).

The primary adverse events included pulmonary vein stenosis (2), cardiac tamponade/perforation (2), stroke/cerebrovascular accident (CVA) (1) and pericarditis (1).

Table 34 – Primary Safety Endpoint (mITT Analysis Set, N=137)

Variable	Number of Events	Number of Subjects with Events	Event Rate n/N (%) ¹	Upper Bound of Two-Sided Exact 95% Confidence Intervals
Primary Adverse Event*	6	6	6 / 137 (4.4%)	9.3%
Atrio-Esophageal Fistula ²	0	0	0 / 137 (0.0%)	
Phrenic Nerve Paralysis (permanent) ³	0	0	0 / 137 (0.0%)	
Pulmonary Vein Stenosis ²	2	2	2 / 137 (1.5%)	
Cardiac Tamponade/perforation ⁴	2	2	2 / 137 (1.5%)	
Stroke/Cerebrovascular Accident (CVA) ⁵	1	1	1 / 137 (0.7%)	
Transient Ischemic Attack (TIA)	0	0	0 / 137 (0.0%)	
Major Vascular Access Complication / Bleeding	0	0	0 / 137 (0.0%)	
Thromboembolism	0	0	0 / 137 (0.0%)	
Myocardial Infarction	0	0	0 / 137 (0.0%)	
Pericarditis	1	1	1 / 137 (0.7%)	
Heart Block	0	0	0 / 137 (0.0%)	
Pulmonary Edema (Respiratory Insufficiency)	0	0	0 / 137 (0.0%)	
Vagal Nerve injury/Gastroparesis	0	0	0 / 137 (0.0%)	
Death (Device or procedure related) ²	0	0	0 / 137 (0.0%)	

* Allow for multiple selection

¹ Subjects without at least 3 months of follow-up are excluded from the primary safety analysis unless they experienced a PAE.

² Device or procedure related death, pulmonary vein stenosis and atrio-esophageal fistula that occur greater than one week (7 days) and less than or equal to 90 days post-procedure are considered and analyzed as PAEs.

³ A phrenic nerve paralysis will be considered to be permanent when it is documented to be present 12 months or longer following ablation. It is considered as a PAE if specified symptoms have not improved at the 3-month visit.

⁴ Hemodynamic compromise or instability is defined as systolic BP < 80 mm Hg. The development of a significant pericardial effusion occurring within 30 days of undergone the index AF ablation process is considered as a PAE.

⁵ Subjects with non-focal global encephalopathy are not reported as a stroke without unequivocal evidence based upon neuroimaging studies. Modified Rankin score assessments should be made by qualified individuals according to a certification process.

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C.2.2 – Primary Effectiveness Endpoint

Acute procedural success was achieved in 100% of subjects. The lower bound of the exact two-sided 95% confidence interval was 97.3%, which was greater than the performance goal of 90% (Table 41).

Table 35 – Acute Procedural Success (mITT analysis Set, N=137)

Variable	Number of Subjects Undergone Ablation Procedure	Number of Successful Subjects	Success Rate n/N (%) ²	Lower Bound of Two-Sided Exact 95% Confidence Intervals
Acute Procedural Success ¹	137	137	137 / 137 (100.0%)	97.3

¹ Acute procedural success is defined as confirmation of entrance block in all PVs after adenosine/isoproterenol challenge. Subjects with use of a non-study catheter for PV isolation or failure to have energy delivery with the study catheter due to ablation system malfunctions are considered acute procedural failures.

² Success rate is the proportion of subjects with acute procedural success. N denotes the number of subjects in the analysis set with adenosine/isoproterenol challenge in all PVs.

C.3 – Secondary Effectiveness Endpoint

The secondary effectiveness endpoint, the 12-month success rate of freedom from recurrences of any documented atrial arrhythmia during the effectiveness follow-up period, was 71.6% (Table 42). The lower bound of the two-sided 95% confidence interval was 63.2%, which was higher than the performance goal of 50%.

Table 36 – Secondary Effectiveness Endpoint, 12-Month Effectiveness Success (PP analysis Set, N=136)

Outcome	Number of Subjects	Success Rate n/N (%) ¹	Exact One-Sided 97.5% Lower Confidence Bound
Success	96	96/134 (71.6%)	63.2%
Failure ²	38		
Missing ³	2		

¹ N denote number of subjects in the analysis set with secondary effectiveness outcomes (success or failure) identified prior to current data cut.

² First failure: if a subject has failed for more than one event, only count for the earliest failure.

³ Missing secondary effectiveness endpoint if a subject 1) did not experience any failure and 2) did not complete the 12M follow-up, or had no ECG, TTM, HM or Post Procedural Arrhythmia data beyond 335 days after index procedure in this analysis.

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C.4 – Additional Safety Endpoints

C.4.1 – Incidence of Serious Adverse Device Effects (SADEs)

Serious Adverse Device Effects occurred in 5 subjects (3.6%, 5/140), 3 of which were PAE and 2 non-PAEs. The PAEs included pericardial tamponade (2) and pulmonary vein stenosis evolving to occlusion (1). The non-PAEs included pulmonary vein stenosis (1) and anaphylactic shock (1). The details of SADEs by SOC and PT are presented in Table 43.

**Table 37 – Serious Adverse Device Effects by SOC and PT
(Safety Population Analysis Set, N=140)**

System Organ Class (SOC) Preferred Term (PT)	Number of Events	Number of Subjects with Event	Event Rate ¹ n/N (%)
Overall	5	5	5 / 140 (3.6%)
Cardiac disorders	2	2	2 / 140 (1.4%)
Cardiac tamponade	2	2	2 / 140 (1.4%)
Respiratory, thoracic and mediastinal disorders	2	2	2 / 140 (1.4%)
Pulmonary vein stenosis	2	2	2 / 140 (1.4%)
Immune system disorders	1	1	1 / 140 (0.7%)
Anaphylactic shock	1	1	1 / 140 (0.7%)

¹ Event rate is the percentage of subjects with the event.

C.4.2 – Incidence of unanticipated (serious) adverse device events (UADEs and USADEs)

No subjects had a UADE or USADE.

C.4.3 – Incidence of Serious Adverse Events (SAEs)

The study reported 26 SAEs in 23 (16.4%) subjects. By time of Onset, 10 SAEs occurred in 8 (5.7%) subjects during the initial 30 days post ablation (Table 44).

Table 38 – Serious Adverse Events by Timing of Onset (Safety Population analysis Set, N=140)

Timing ¹	Number of Events	Number of Subjects with Event	Event Rate n/N (%) ²
Total	26	23	
Prior to Procedure	0	0	0 / 140 (0.0%)
0 - 7 Days	7	6	6 / 140 (4.3%)
8 - 30 Days	3	2	2 / 140 (1.4%)
≥ 31 Days	16	15	15 / 139 (10.8%)

¹ Timing of AE based on onset in days post the procedure (index or repeat).

² N denotes the number of subjects with follow-up duration surpassing the left bound of the time interval.

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Table 45 presents SAEs by SOC and PT. The common SAEs by SOC included Cardiac disorders (5.0%), infections and infestations (2.9%), and nervous system disorders (2.9%).

Table 39 – SAEs by SOC and PT (Safety Population Analysis Set, N=140)

System Organ Class (SOC) Preferred Term (PT)	Number of Events	Number of Subjects with Event	Event Rate ¹ n/N (%)
Overall	26	23	23 / 140 (16.4%)
Cardiac disorders	7	7	7 / 140 (5.0%)
Atrial flutter	2	2	2 / 140 (1.4%)
Atrial tachycardia	2	2	2 / 140 (1.4%)
Cardiac tamponade	2	2	2 / 140 (1.4%)
Supraventricular tachycardia	1	1	1 / 140 (0.7%)
Infections and infestations	4	4	4 / 140 (2.9%)
Diverticulitis	2	2	2 / 140 (1.4%)
Pneumonia	1	1	1 / 140 (0.7%)
Postoperative wound infection	1	1	1 / 140 (0.7%)
Nervous system disorders	4	4	4 / 140 (2.9%)
Carpal tunnel syndrome	1	1	1 / 140 (0.7%)
Hemianaesthesia	1	1	1 / 140 (0.7%)
Migraine with aura	1	1	1 / 140 (0.7%)
Radiculopathy	1	1	1 / 140 (0.7%)
Injury, poisoning and procedural complications	2	2	2 / 140 (1.4%)
Radius fracture	1	1	1 / 140 (0.7%)
Rib fracture	1	1	1 / 140 (0.7%)
Musculoskeletal and connective tissue disorders	2	2	2 / 140 (1.4%)
Arthralgia	1	1	1 / 140 (0.7%)
Cervical spinal stenosis	1	1	1 / 140 (0.7%)
Respiratory, thoracic and mediastinal disorders	2	2	2 / 140 (1.4%)
Pulmonary vein stenosis	2	2	2 / 140 (1.4%)
Gastrointestinal disorders	1	1	1 / 140 (0.7%)
Large intestine polyp	1	1	1 / 140 (0.7%)
General disorders and administration site conditions	1	1	1 / 140 (0.7%)
Chest pain	1	1	1 / 140 (0.7%)

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System Organ Class (SOC) Preferred Term (PT)	Number of Events	Number of Subjects with Event	Event Rate ¹ n/N (%)
Immune system disorders	1	1	1 / 140 (0.7%)
Anaphylactic shock	1	1	1 / 140 (0.7%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1	1	1 / 140 (0.7%)
Adenocarcinoma	1	1	1 / 140 (0.7%)
Vascular disorders	1	1	1 / 140 (0.7%)
Hypotension	1	1	1 / 140 (0.7%)

¹ Event rate is the percentage of subjects with the event.

Most of the SAEs were not related to DE THERMOCOOL SMARTTOUCH™ SF (DE STSF) Catheter, TRUPULSE™ Generator or study procedure (Table 46). Only one (1) subject with an SAE was possibly related to THERMOCOOL SMARTTOUCH™ SF (STSF) Catheter.

Table 40 – SAEs by Causality (Safety Population Analysis Set, N=140)

Relationship to the Device and Procedure	Number of Events	Number of Subjects with Event	Event Rate ¹
Overall	26	23	23 / 140 (16.4%)
THERMOCOOL SMARTTOUCH™ SF Catheter			
Causal Relationship to Device	0	0	0 / 140 (0.0%)
Probable Device Related	0	0	0 / 140 (0.0%)
Possible Device Related	1	1	1 / 140 (0.7%)
Not Device Related	25	22	22 / 140 (15.7%)
Multi-Channel TRUPULSE™ Generator			
Causal Relationship to Device	0	0	0 / 140 (0.0%)
Probable Device Related	0	0	0 / 140 (0.0%)
Possible Device Related	1	1	1 / 140 (0.7%)
Not Device Related	25	22	22 / 140 (15.7%)
Procedure			
Causal Relationship to Procedure	3	3	3 / 140 (2.1%)
Probable Procedure Related	1	1	1 / 140 (0.7%)
Possible Procedure Related	1	1	1 / 140 (0.7%)
Not Procedure Related	21	19	19 / 140 (13.6%)

¹ Event rate is the percentage of subjects with the event.

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C.4.4 – Incidence of Non-serious Adverse Events

The study reported a total of 227 NSAEs in 90 (64.3%) subjects (Table 47). By timing of onset, 39 (27.9%) subjects reported NSAE during the initial 7 days after the procedure, 71 (51.1%) reported NSAEs after one month of the procedure.

Table 41 – NSAEs by Time of Onset (Safety Population Analysis Set, N=140)

Timing ¹	Number of Events	Number of Subjects with Event	Event Rate n/N (%) ²
Total	227	90	
Prior to Procedure	4	4	4 / 140 (2.9%)
0 - 7 Days	54	39	39 / 140 (27.9%)
8 - 30 Days	9	9	9 / 140 (6.4%)
≥ 31 Days	160	71	71 / 139 (51.1%)

¹ Timing of AE based on onset in days post the procedure (index or repeat).

² N denotes the number of subjects with follow-up duration surpassing the left bound of the time interval.

The majority of the NSAEs were not related to DE THERMOCOOL SMARTTOUCH™ SF (DE STSF) Catheter, TRUPULSE™ Generator or study procedure (Table 48). Only three (3) subjects with NSAEs were possibly related to THERMOCOOL SMARTTOUCH™ SF (STSF) Catheter.

Table 42 – NSAEs by Causality (Safety Population Analysis Set, N=140)

Relationship to the Device and Procedure	Number of Events	Number of Subjects with Event	Event Rate ¹
Overall	227	90	90 / 140 (64.3%)
THERMOCOOL SMARTTOUCH™ SF Catheter			
Causal Relationship to Device	0	0	0 / 140 (0.0%)
Probable Device Related	0	0	0 / 140 (0.0%)
Possible Device Related	3	3	3 / 140 (2.1%)
Not Device Related	224	88	88 / 140 (62.9%)
Multi-Channel TRUPULSE™ Generator			
Causal Relationship to Device	0	0	0 / 140 (0.0%)
Probable Device Related	0	0	0 / 140 (0.0%)
Possible Device Related	3	3	3 / 140 (2.1%)
Not Device Related	224	88	88 / 140 (62.9%)
Procedure			
Causal Relationship to Procedure	20	15	15 / 140 (10.7%)
Probable Procedure Related	3	3	3 / 140 (2.1%)
Possible Procedure Related	18	17	17 / 140 (12.1%)
Not Procedure Related	186	78	78 / 140 (55.7%)

¹ Event rate is the percentage of subjects with the event.

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C.5 – Additional Effectiveness Endpoints

C.5.1 – Acute Reconnection

Acute reconnections were detected in 11.0% of subjects or 3.2% of targeted PVs (Table 49).

Table 43 – Acute PV Reconnection – Subject Level (PP Analysis Set, N=136)

Variable	Number of Subjects ¹	Number of Subjects with Reconnection ²	Rate of Reconnection
Acute Reconnection	136	15	15 / 136 (11.0%)

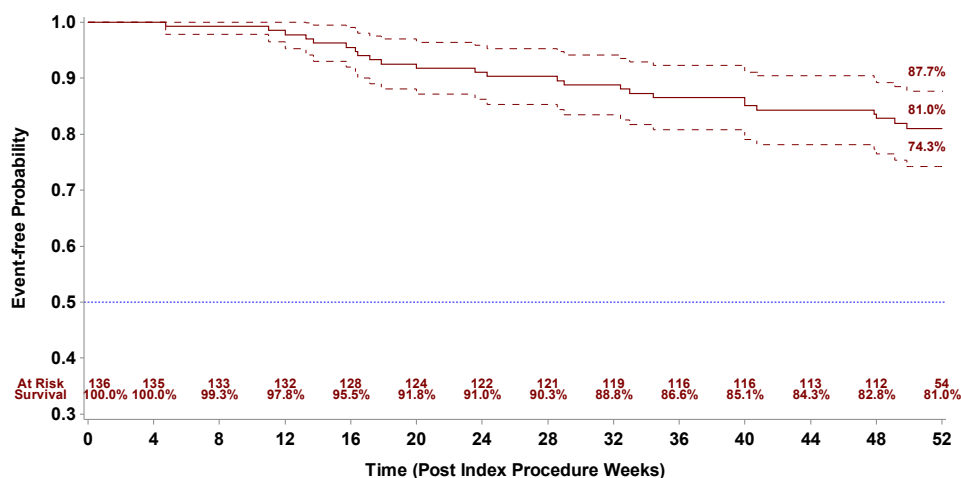
¹ Subjects undergone PV ablation procedure and adenosine/isoproterenol challenge.

² Subjects with at least one vein with reconnection identified after adenosine/isoproterenol challenge.

C.5.2 – Single Procedural Success

Kaplan-Meier (KM) estimates of the proportion of subjects who were free from symptomatic recurrences after single procedure at 12 months was 81.0%, with a two-sided 95% confidence interval of 74.3% to 87.7% in the PP analysis set (Figure 10).

Figure 10 – Kaplan-Meier Analysis of Single Procedure Success (PP Analysis Set, N=136)

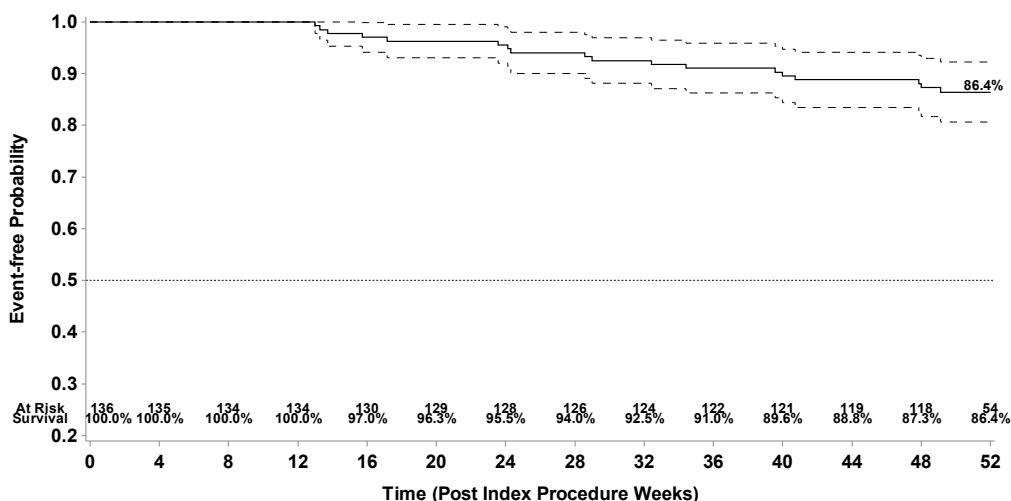


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C.5.3 – Freedom from Documented symptomatic Atrial Arrhythmia

Kaplan-Meier estimates of the proportion of subjects who were free from documented symptomatic atrial arrhythmia episodes based on electrocardiographic data during the effectiveness evaluation period was 86.4%, with a two-sided 95% confidence interval of 70.6% to 92.3% in the PP analysis set (Figure 11).

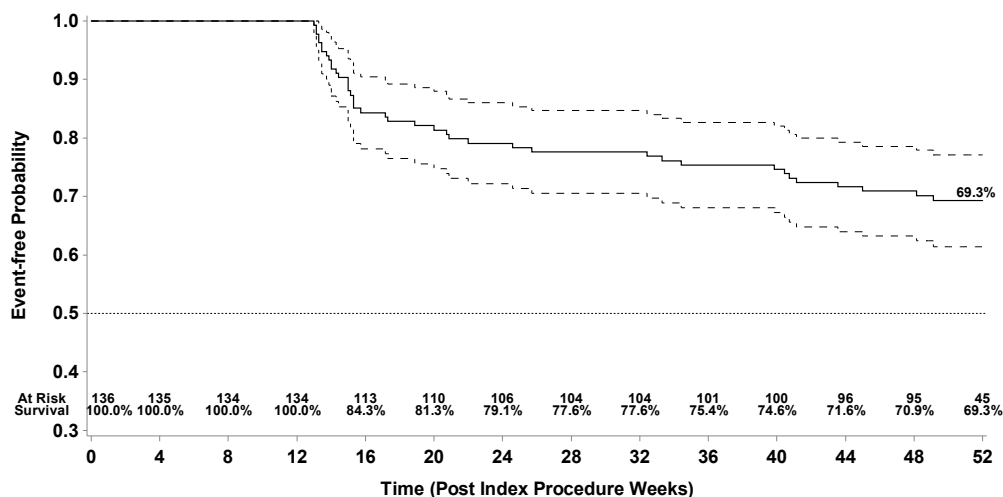
Figure 11 – Kaplan-Meier Analysis of time to Documented Symptomatic Recurrence (PP Analysis Set, N=136)



C.5.4 – Freedom from Documented Symptomatic and Asymptomatic Atrial Arrhythmia with Additional Failure Modes

Kaplan-Meier estimates of the proportion of subjects who were free from documented symptomatic and asymptomatic atrial arrhythmia during the effectiveness evaluation period and all additional failure modes was 69.3%, with a two-sided 95% confidence interval of 61.4% to 77.1% in the PP analysis set (Figure 12).

Figure 12 – Kaplan-Meier Analysis of Freedom from Documented Arrhythmia Recurrence with Additional Failure Modes (PP Analysis Set, N=136)

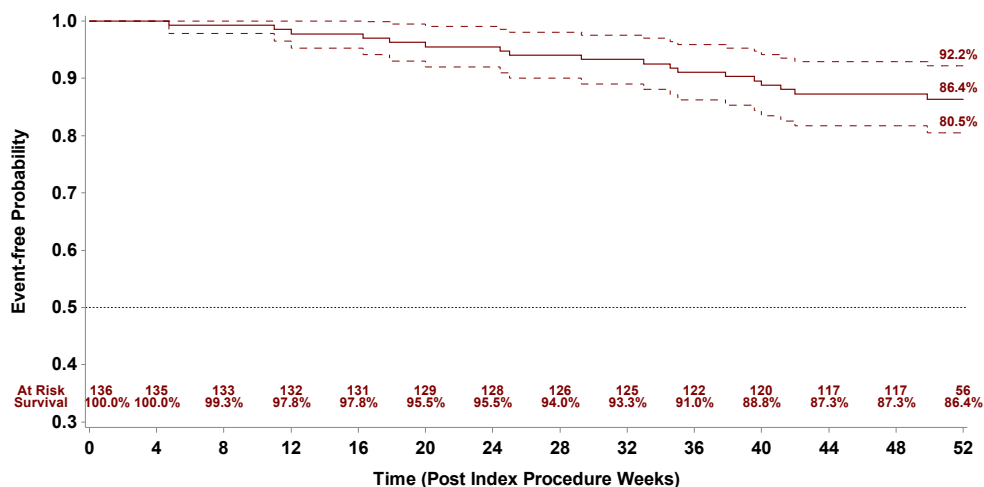


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C.5.5 – Freedom from Repeat Ablation

Kaplan-Meier estimates of the proportion of subjects who remained free from repeat ablation at 12 months was 86.4%, with two-sided 95% CI of 80.5% to 92.2% in the PP Population (Figure 13).

Figure 13 – Kaplan-Meier Analysis of Time to Repeat Ablation (PP Analysis Set, N=136)



C.5.6 – Quality of Life by AFEQT

In the PP analysis set, the overall AFEQT scores showed an average improvement of quality of life by 27.24 ± 21.463 at 12 months compared to baseline (Table 50). The average QOL improvements across the subscales were 23.82 ± 25.600 in AF-related symptoms, 29.36 ± 27.192 in daily activities, 26.66 ± 24.097 in treatment concerns, 29.89 ± 30.779 in satisfaction with current treatment control, and 29.20 ± 31.741 in satisfaction with relief of symptoms.

Table 44 – Quality of Life by AFEQT Questionnaire (PP Analysis Set, N=136)

Visit	Baseline	12 Month	Change from Baseline
Overall	59.3 ± 20.444	86.29 ± 16.176	27.24 ± 21.463
AF related symptoms	63.98 ± 23.151	87.58 ± 19.561	23.82 ± 25.600
Daily activities	55.07 ± 28.378	84.33 ± 20.691	29.36 ± 27.192
Treatment concerns	61.86 ± 22.587	88.02 ± 16.885	26.66 ± 24.097
Satisfaction Level –treatment controls	58.33 ± 26.977	87.58 ± 17.966	29.89 ± 30.779
Satisfaction Level –relief of symptoms	58.25 ± 26.795	86.76 ± 19.672	29.20 ± 31.741

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C.5.7 – Change in Cardiovascular Hospitalization Rate

Cardiovascular hospitalization rate changed from 20.1% during 12 months before ablation to 11.9% during 12 months after the ablation procedure (Table 51).

Table 45 – Change in Cardiovascular Hospitalization Rate (PP Analysis Set, N=136)

Time Interval	Number of Events	Number of Subjects with Events	CV Hospitalization Rate ² n/N (%)	Rate Change ³ %
Baseline ¹	46	27	27 / 134 (20.1%)	
>0-12 months	22	16	16 / 134 (11.9%)	-8.2%

¹ Baseline is defined > 0 - 12 months pre-procedure.

² N represents the number of subjects with data available at both baseline and the entire duration of the follow-up interval. n represents the number of subjects with at least 1 CV hospitalization in the time interval.

³ Rate change is calculated as (follow-up rate - baseline rate).

C.6 – Subset Analysis

C.6.1 – PVI Durability Rate

At a mean 79.3 ± 6.88 days post ablation, 60.0% of subjects showed that all PVs remained isolated (Table 52). The remaining 40% of subjects were found to have one or more non-isolated PVs.

Table 46 – Durability Assessment at Subject Level (PVI Durability Analysis Set, N=30)

Variable	Statistics
Subjects undergoing durability assessment	
Subjects with durable isolated veins	18/30 (60.0%)
Subjects with non-isolated veins	12/30 (40.0%)
Subjects with veins requiring re-isolation	12/30 (40.0%)*
Subjects with 1 non-isolated vein	10/30 (33.3%)
Subjects with 2 non-isolated veins	1/30 (3.3%)
Subjects with 3 non-isolated veins	1/30 (3.3%)
Days post index procedure	79.3 ±6.88

* Additional ablation following the 3D Electro Anatomical mapping was performed in 13 subjects.

C.6.2 – Neurological Deficits

At discharge, two subjects had neurological events (Table 53). In the next 12 months of follow-up, one subject reported a neurological event.

Table 47 – Incidence of New or Worsening Neurologic Deficits (NA Analysis Set, N=30)

Visit	Number of Subjects ¹	Number of Neurological Events	Number of Subjects with Neurological Events
Screening/ Baseline	30	4	4
Discharge	30	2	2
1 Month Follow-Up	8	0	0
3 Month Follow-Up	2	0	0
6 Month Follow-Up	0	0	0
12 Month Follow-Up	0	0	0
Unscheduled	1	1	1

¹ Subjects with neurological assessment performed.

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C.6.3 – PV narrowing

Three months after the procedure, 2 (6.7%) subjects had PV narrowing larger than 70% and 4 (13.3%) between > 50% and 70% (Table 54).

Table 48 – PV Narrowing Post Ablation Using Average Diameter, Subject Level (CT/MRA Analysis Set, N=30)

Pulmonary Vein	PV Narrowing ¹		
	Mild > 0-50%	Moderate > 50-70%	Severe > 70%
Subject-Level Summary, n/N (%)	24 / 30 (80.0%)	4 / 30 (13.3%)	2 / 30 (6.7%)

¹ Subject-Level Summary of PV Narrowing (%) = (number of subjects whose maximum percent of PV narrowing in a specific level of narrowing / number of subjects with available CT/MRA data).

C.6.4 – Esophageal Lesions

Based on esophageal endoscopy examination performed between 1 and 3 days post ablation, none of the subjects (0.0%) detected an esophageal lesion.

D. Study Conclusion

With the fulfillment of both the primary safety and effectiveness success criteria, the study is deemed successful. The Dual Energy THERMOCOOL SMARTTOUCH™ SF Catheter System has demonstrated both safety and effectiveness, meeting the study's success criteria. The outcomes affirm the conclusion that the investigational system has effectively showcased an acceptable safety and favorable effectiveness profile.

SUMMARY OF CLINICAL STUDIES CONDUCTED FOR THE THERMOCOOL SMARTTOUCH™ SF CATHETER

STUDY 1: PRECEPT Study

A. Objective

The purpose of this study was to demonstrate the safety and effectiveness of the THERMOCOOL SMARTTOUCH™ SF catheter in the treatment of drug refractory symptomatic persistent atrial fibrillation (PsAF) following standard electrophysiology mapping and RF ablation procedures.

B. Study Design

The study was a prospective, multicenter, non-randomized clinical evaluation compared to a predetermined performance goal. The study was conducted at investigational sites in the US and Canada.

B.1 - Study Endpoints

The Endpoints for the study were as follows:

Primary effectiveness endpoint – freedom from documented atrial fibrillation, atrial flutter, and atrial tachycardia (AF/AFL/AT, atrial tachyarrhythmias) recurrence (episodes ≥ 30 sec on Holter recordings/TTM or continuously recorded on the standard 12-leads ECG) during the evaluation period (Day 181-450).

Acute success – confirmation of entrance block in all pulmonary veins.

Primary safety endpoint – incidence primary adverse events (PAE) occurring within 7 days of the initial and repeat AF ablation procedures using the study catheter per protocol. Primary adverse events included the following conditions:

- Death
- Atrio-esophageal fistula¹
- Cardiac tamponade/Perforation
- Myocardial Infarction (MI)

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- Stroke/Cerebrovascular Accident (CVA)
- Thromboembolism
- Transient Ischemic Attack (TIA)
- Diaphragmatic paralysis
- Pneumothorax
- Heart block
- Pulmonary Vein (PV) stenosis¹
- Pulmonary edema (Respiratory insufficiency)
- Pericarditis
- Major vascular access complication/bleeding

¹ PV stenosis (PV) and atrio-esophageal fistula that occurs greater than one week (7 days) post-procedure shall be deemed Primary AEs.

Secondary safety endpoints included:

- Occurrence of early onset (within 7 days of initial ablation) Serious Adverse Event
- Occurrence of peri-procedural (> 7 to 30 days) Serious Adverse Event
- Occurrence of late onset (> 30 days) Serious Adverse Event

B.2 - Pre-determined Performance Goal

The performance goal was prospectively established.

- **Effectiveness** – Performance Goal = 40% lower bound of the of the 95% CI around the primary effectiveness success rate
- **Safety** – Performance Goal = 16.0% upper bound of the 95% CI around the primary AE rate

B.3. - Subject Accountability

Table 49 – Subject Accountability and Disposition

Disposition	N
Enrolled Subjects	381
Excluded Subjects	33
Safety Population	348
Not Meeting Eligibility Criteria	14
mITT Population	334
Undergone RF Ablation	334
Subjects Treated with Non-Study Catheter	1
Per-Protocol Population	333

The following definitions were used to classify subjects:

Safety Population (n = 348) was comprised of all enrolled subjects who underwent insertion of the THERMOCOOL SMARTTOUCH™ SF Catheter.

Per-Protocol Population (n = 333) consisted of subjects who satisfied the following criteria:

- Were enrolled and met all eligibility criteria
- Had undergone RF ablation
- Were treated with the study catheters, and had been treated for the study-related arrhythmia

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B.4 - Subject Demographics and Baseline Characteristics

Table 50– Subject Demographics
(Enrolled Subjects, N = 381; Safety, N = 348; Per-Protocol, N = 333)

Demographics	Enrolled n/381 (%)	Safety n/348 (%)	Per-Protocol n/333 (%)
Gender (%)			
Male	271 (71.1)	246 (70.7)	237 (71.2)
Female	110 (28.9)	102 (29.3)	96 (28.8)
Ethnicity (%)			
Hispanic or Latino	7 (1.8)	7 (2.0)	6 (1.8)
Race (%)			
Asian	3 (0.8)	3 (0.9)	3 (0.9)
Black or African American	6 (1.6)	6 (1.7)	6 (1.8)
White	349 (91.6)	319 (91.7)	307 (92.2)
Not reported	23 (6.0)	20 (5.7)	17 (5.1)
Age (years)	65.6 ± 8.72	65.4 ± 8.71	65.4 ± 8.79
AF History (months)	15.2 ± 29.2	15.5 ± 30.2	15.9 ± 30.8
LA Dimension (mm)	42.6 ± 5.20	42.4 ± 5.14	42.6 ± 5.06
LVEF (%)	56.0 ± 7.43	56.2 ± 7.23	56.2 ± 7.24

Table 51 – Baseline Characteristics
(Enrolled Subjects, N = 381; Safety, N = 348; Per-Protocol, N = 333)

Medical History	Enrolled n/381 (%)	Safety n/348 (%)	Per-Protocol n/333 (%)
Hypertension	260 (68.2)	238 (68.4)	227 (68.2)
Diabetes	69 (18.1)	62 (17.8)	61 (18.3)
Obstructive sleep apnea	145 (38.1)	134 (38.5)	132 (39.6)
AAD Failed			
Class I & III	1.3 ± 0.54	1.3 ± 0.55	1.3 ± 0.56
Heart Disease			
Coronary artery disease	86 (22.6)	77 (22.1)	74 (22.2)
Congestive heart failure	61 (16.0)	55 (15.8)	52 (15.6)
Prior myocardial infarction	23 (6.0)	19 (5.5)	19 (5.7)
Cardiomyopathy	43 (11.3)	42 (12.1)	39 (11.7)
Cardiac surgical procedures	41 (10.8)	36 (10.3)	34 (10.2)
Thromboembolic Event	27 (7.1)	25 (7.2)	24 (7.2)
Transient ischemic attack	10 (2.6)	10 (2.9)	9 (2.7)
Stroke	8 (2.1)	6 (1.7)	6 (1.8)
CHA2DS2-VASc score	2.3 ± 1.48	2.3 ± 1.48	2.3 ± 1.49
Other: Arrhythmia			
Atrial flutter	71 (18.6)	68 (19.5)	65 (19.5)
Atrial tachycardia	7 (1.8)	7 (2.0)	7 (2.1)

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C. Results

C.1 - Procedural Data

Table 58 and Table 59 present the index procedural data. There were 348 procedures in 348 subjects. All subjects underwent one (1) study ablation procedure.

Table 52 – Summary of Power, Temperature, and Impedance Data per Procedure (Safety Population, n = 348)

Description	Mean ± SD (n)
Mean Power (W)	30.02 ± 7.83 (291)
Mean Temperature (°C)	24.25 ± 2.49 (291)
Mean Impedance (ohms)	117.72 ± 13.73 (277)

Table 53 – Summary of Ablation Procedure Parameters (Safety Population, n = 348)

Procedure Parameters	Mean ± SD (n)
Total Procedure Time (min)	178.0 ± 70.97 (348)
Ablation Procedure Time (min)	107.7 ± 48.64 (348)
Total Fluoroscopy Time (min)	15.29 ± 16.61 (348)
Fluid Input (ml)	2115.9 ± 1016.54 (343)
Fluid via Catheter (ml)	886.3 ± 391.19 (339)
Fluid via IV (ml)	1247.2 ± 857.14 (341)
Fluid Output (ml)	1044.2 ± 835.18 (189)
Balance (input - output) (ml)	1493.6 ± 914.34 (187)

All AF ablation procedures began with circumferential lesions targeting all pulmonary veins, with additional atrial ablation lines created as clinically required.

Table 60 summarizes the lesion sets applied to the subjects undergoing ablation during the index ablation procedures. Table 61 presents a summary of non-PV targets in the 186 procedures in the SP and 179 procedures in the PP that involved ablation beyond PVI.

Table 54 – Outcomes by Ablation Targets per Procedure (Safety Population, n = 348; Per-Protocol, n = 333)

Ablation Targets	Safety n/348 (%)	Per-Protocol n/333 (%)
PVI only group	193 (55.5)	182 (54.7)
PVI+ CFAE group	60 (17.2)	59 (17.7)
PVI+ non-CFAE group	95 (27.3)	92 (27.6)

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Table 55 – Ablation Targets per Procedure
(Safety Population, n = 348; Per-Protocol, n = 333)

Ablation Target	Safety n/186 (%)	Per-Protocol n/179 (%)
Left Inferior PV Mitral	14 (7.5)	14 (7.8)
Roof Line	90 (48.4)	87 (48.6)
Other: Linear Lesion	16 (8.6)	16 (8.9)
SVC	10 (5.4)	10 (5.6)
CFAE	60 (32.3)	59 (33.0)
Other: AF Foci	75 (40.3)	72 (40.2)
Cavo-Tricuspid Isthmus	67 (36.0)	63 (35.2)
RAGP	1 (0.5)	1 (0.6)

C.2 - Acute Procedural Success

Acute success was defined as the confirmation of entrance block into all PVs. Any use of non-study catheters was considered acute procedural failures.

Acute procedural success results are presented in Table 62.

Table 56 – Acute Effectiveness Summary
(Per-Protocol Population, n = 333)

	Per Protocol
Number of Subjects with Success	330 / 333
Percentage of Subjects with Success	99.1%
One-Sided Exact 97.5% Lower Confidence Bound	97.4

C.3 - Contact Force Data

The graphical user interface (GUI) of the CARTO™ 3 workstation displays the pressure applied to the endocardial surface of the heart by the THERMOCOOL SMARTTOUCH™ SF in gram forces that the investigator can visualize during the procedure.

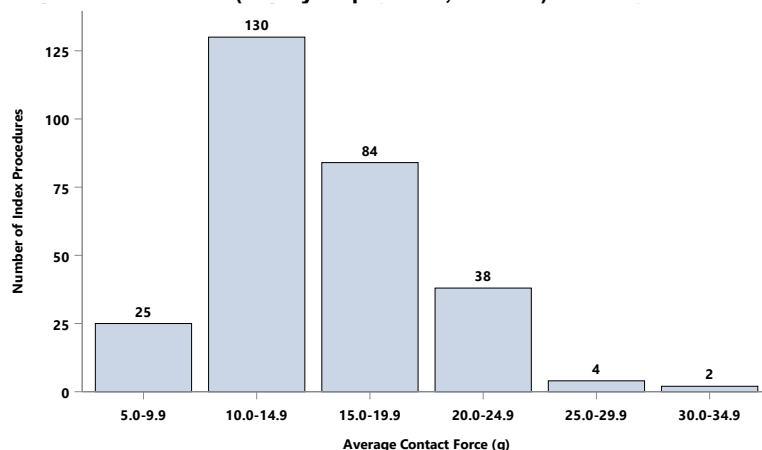
Table 63 presents the overall average contact force applied during the procedure for all subjects who underwent a study ablation procedure. As shown, the overall average CF applied during ablation procedures was 15.23 ± 4.41 grams. Figure 14 presents a distribution of average contact force in 5-gram increments. In the majority of procedures (239/283), the average contact force applied was less than 20 grams.

Table 57 – Average Contact Force Measurements Overall
per Ablation Procedure (Safety Population, n = 348)

	Average Contact Force (g)
n	298
Mean	15.23
Standard Deviation	4.41
Median	14.40
Q1 / Q3	12.10 / 18.13
Min / Max	6.6 / 33.7

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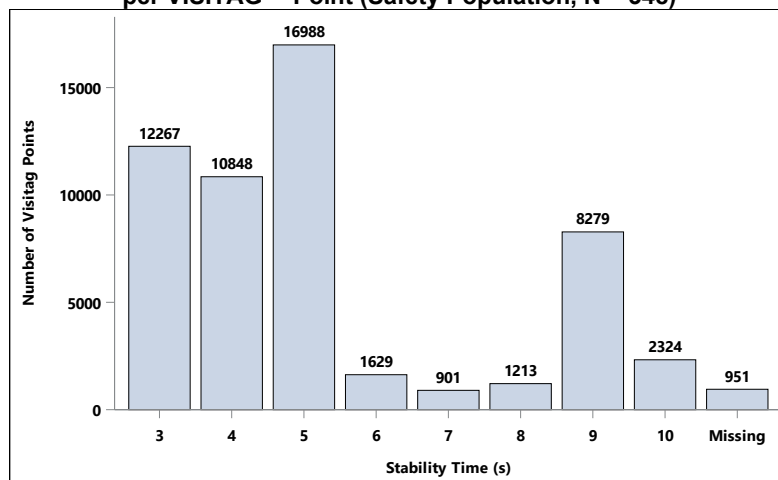
Figure 14 – Distribution of Average Contact Force per Ablation Procedure (Safety Population, n = 348)



The real-time rolling graph display with the working ranges acts as a visual aid providing real-time feedback of the pressure being applied by the operator in relationship to their pre-selected CF values. In this study, the most frequently selected working range of contact force was 5 to 40 g (37.5%, 130/347), which accounted for 37.5% of the procedures (130/347).

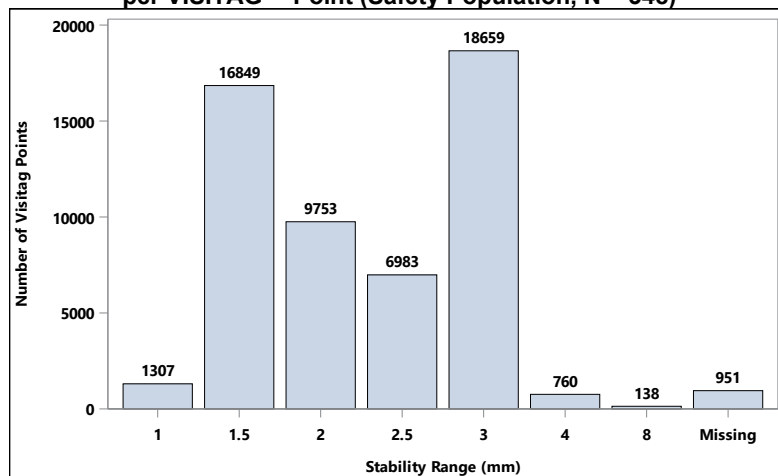
The CARTO VISITAG™ Module of the CARTO™ 3 System provides a marker for stability during an RF application. The CARTO™ 3 System produces an auto tag on the screen at the site of RF application that is dependent on the user's pre-defined settings. The auto tag appears when the RF application reaches a pre-determined time of application and the catheter has remained stable within a pre-determined range (mm) for the time. In this study the majority of operators chose a time to auto tag from 3-5 seconds with a stability of 1.5-3.0 mm.

Figure 15 – Operator-Configured VISITAG™ Stability Time per VISITAG™ Point (Safety Population, N = 348)



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Figure 16 – Operator-Configured VISITAG™ Stability Range per VISITAG™ Point (Safety Population, N = 348)



C.4 - Adverse Events (AE)

The primary safety endpoint for this study was defined as the incidence of early onset (within 7 days of ablation procedure) Primary AEs for subjects undergoing a study ablation procedure. The Safety Population (N = 348) was comprised of all enrolled subjects who had the study catheter inserted.

Primary Safety Endpoint – Primary Adverse Events

Table 64 presents the protocol-specified endpoint and safety results. There were 17 primary AEs reported in 16 subjects. Among 17 primary AEs, sixteen (16) were considered definitely procedure-related, and one (1) was considered possibly procedure-related. One (1) was considered definitely device-related, thirteen (13) were considered possibly device-related, and three (3) were considered not device-related. The overall percentage of subjects in the Safety Population who experienced a serious primary AE was 4.7% (16/344) with upper confidence at 7.4%, which is significantly less than the specified performance goal of 16.0%. Therefore, the results met the pre-specified performance goal for the safety endpoint.

Table 58 – Primary Safety Endpoint Outcome, Primary Adverse Events (Safety Population, n = 348)

Variable	Number of Subjects with Event	Number of Events	Event Rate n/N (%)	One-Sided Exact 97.5% Upper Confidence Bound
Primary Adverse Event	16	17	16 / 344 (4.7)	7.4%
Death	0	0	0 / 344 (0.0)	
Atrio-esophageal Fistula	0	0	0 / 344 (0.0)	
Cardiac Tamponade	5	5	5 / 344 (1.5)	
Myocardial Infarction	0	0	0 / 344 (0.0)	
Cerebrovascular Accident (CVA)/Stroke	1	1	1 / 344 (0.3)	
Thromboembolism	0	0	0 / 344 (0.0)	
Transient Ischemic Attack	0	0	0 / 344 (0.0)	
Diaphragmatic Paralysis	1	1	1 / 344 (0.3)	
Pneumothorax	0	0	0 / 344 (0.0)	
Heart Block	0	0	0 / 344 (0.0)	
Pulmonary Vein Stenosis	0	0	0 / 344 (0.0)	

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Variable	Number of Subjects with Event	Number of Events	Event Rate n/N (%)	One-Sided Exact 97.5% Upper Confidence Bound
Pulmonary Edema (Respiratory Insufficiency)	5	5	5 / 344 (1.5)	
Pericarditis	2	2	2 / 344 (0.6)	
Major Vascular Access Complication/Bleeding	3	3	3 / 344 (0.9)	

Table 65 summarizes the SAEs (by causality and body system) occurring within 30 days of a study ablation procedure that were not classified as Primary AEs by protocol definition.

Table 59 – Non Primary SAEs Occurring within 30 Days of the Ablation Procedure by Causality and Body System (Safety Population, n = 348)

Relationship to the Device/Procedure by Body System	Number of Subjects with Event	Number of Events
Occurring 0-7 Days Post Ablation Procedure		
Overall	20	20
Definitely device related	1	1
Esophageal ulcer	1	1
Possibly device related	1	1
Hypotension	1	1
Not device related	18	18
Atrial fibrillation	2	2
Hypotension	1	1
Complication associated with urinary catheter	3	3
Diplopia	1	1
Dyspnea	1	1
Fluid overload	2	2
Hypertensive crisis	1	1
Hypoxia	1	1
Pyrexia	1	1
Renal failure	1	1
Sepsis	1	1
Tachycardia	1	1
Torsade de pointes	1	1
Urinary tract infection	1	1
Definitely procedure related	9	9
Complication associated with urinary catheter	2	2
Hypotension	2	2
Fluid overload	2	2
Esophageal ulcer	1	1

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Relationship to the Device/Procedure by Body System	Number of Subjects with Event	Number of Events
Occurring 0-7 Days Post Ablation Procedure		
Sepsis	1	1
Torsade de pointes	1	1
Possibly procedure related	6	6
Complication associated with urinary catheter	1	1
Diplopia	1	1
Dyspnea	1	1
Hypoxia	1	1
Renal failure	1	1
Urinary tract infection	1	1
Not procedure related	5	5
Atrial fibrillation	2	2
Hypertensive crisis	1	1
Pyrexia	1	1
Tachycardia	1	1
Occurring 8-30 Days Post Ablation Procedure		
Overall	6	7
Not device related	6	7
Atrial flutter	1	1
Complication associated with device	1	1
Pleural effusion	1	1
Presyncope	1	1
Pulmonary embolism	1	1
Tachycardia	1	1
Tuberculosis	1	1
Definitely procedure related	1	1
Complication associated with urinary catheter	1	1
Possibly procedure related	2	2
Pleural effusion	1	1
Pulmonary embolism	1	1
Not procedure related	4	4
Atrial flutter	1	1
Presyncope	1	1
Tachycardia	1	1
Tuberculosis	1	1

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Two subjects died during the study. Neither death was reported to be device or procedure-related. No deaths occurred within 3 months following the study procedure. An 80-year-old woman with known coronary artery disease, type II DM, and hypertension underwent an uncomplicated study procedure for the treatment of persistent AF. The subject developed dyspnea and was hospitalized and treated for pneumonia and congestive heart failure at 452 days following the study procedure. She was discharged with home oxygen and died shortly after on day 464 following the index ablation. The second death occurred in an 83-year-old man who was hospitalized on day 164 for management of non-ST-elevation myocardial infarction, atrial fibrillation, and COPD exacerbation. The hospital course was complicated by respiratory decompensation and multifactorial neurologic dysfunction requiring intubation and mechanical ventilation support. The family subsequently withdrew care, and the patient died on day 166 following the index ablation.

Table 66 summarizes the primary safety outcome for the safety population by sex. There were no statistically significant differences in the Primary AE rates between males and females ($p > 0.15$).

Table 60 – Primary Safety Endpoint by Sex (Safety Population, N = 348)

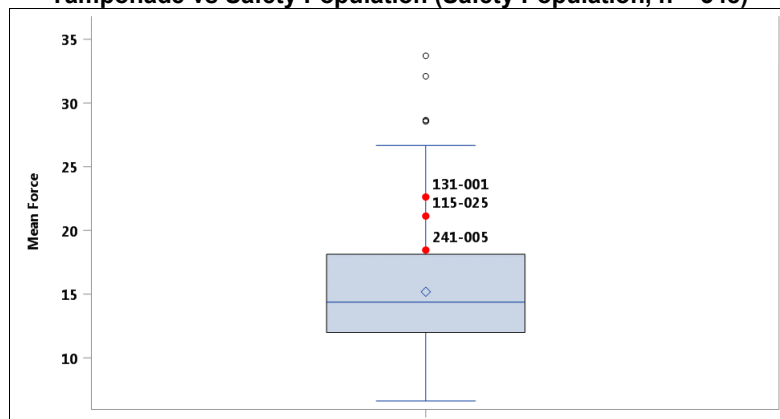
Primary Safety Endpoint	Male	Female	p-value ¹
Primary AE			1.000
n/N	12 / 244	4 / 100	
%	4.9%	4.0%	
One-Sided Exact 97.5% Upper Confidence Bound	8.4%	9.9%	

¹ Fisher's exact test

C.4.1 - Average CF and Primary AEs

Figure 17 compares the average CF during procedures in subjects experiencing Primary AEs with those who did not. Average contact force was recorded for three (3) subjects with tamponade. These are marked with solid dots in the box plot of average contact force for all subjects in the safety population. Average contact force of these 3 subjects are above the Q3 (75th percentile) of overall average contact force.

Figure 17 – Comparison of Average Contact Force in Subjects with Tamponade vs Safety Population (Safety Population, n = 348)



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C.5 - Primary Effectiveness Endpoint - Freedom from Atrial Tachyarrhythmias

Primary Effectiveness Analysis

The primary effectiveness endpoint was defined as freedom from documented symptomatic and asymptomatic AF/AFL/AT ("atrial tachyarrhythmias") based on electrocardiographic data and freedom from failure modes during the effectiveness evaluation period (day 181-450).

Approximately sixty percent (59.3%, 176/297) of the Per-Protocol population were free from documented atrial tachyarrhythmias and additional failure modes during their effectiveness evaluation period. The lower bound of the one-sided exact 97.5% lower confidence interval of the primary effectiveness rate was 53.4%, significantly higher than the pre-determined performance goal of 40%.

Primary effectiveness results are described in Table 67.

Table 61 – Primary Effectiveness Endpoint through 15 Month Follow-Up Visit (Per-Protocol Population, n = 333)

Variable	Number of Subjects	Event Rate n/N (%) ¹	One-sided Exact 97.5% Lower Confidence Bound
Success	176	176/297 (59.3%)	53.4%
Failures ²	121	121/297 (40.7%)	
Missing ³	36		

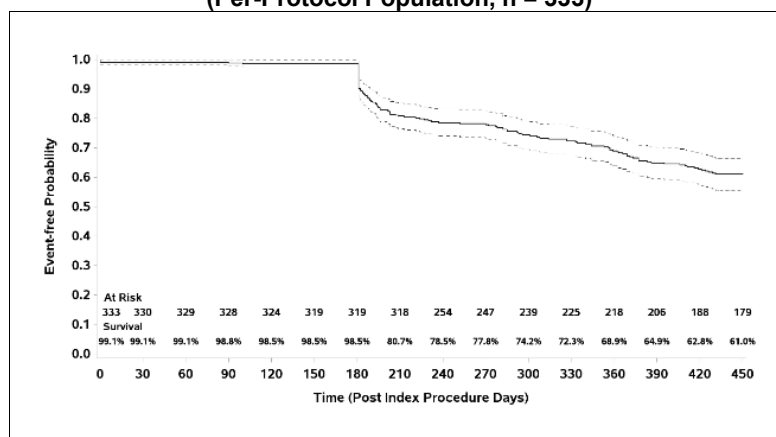
¹ N is the number of subjects with non-missing primary effectiveness endpoint.

² First failures: if a subject has more than one failure event, only the earliest failure event is considered.

³ Missing primary effectiveness endpoint: the endpoint is missing if a subject (1) did not experience any failure, (2) did not finish the 15-month follow-up, and (3) had no ECG, TTM, HM or Post Procedural Arrhythmia data beyond 422 days after index procedure.

Figure 18 shows the Kaplan-Meier survival curves for the per protocol population. The probability of freedom from primary effectiveness endpoint failure at 15 months post-blanking was 61.0%. The lower bound of the one-sided 97.5% CI for this KM graph (55.5%, as indicated by the lower dotted line) is greater than 40% of the pre-determined performance criterion. The primary effectiveness performance goal was met.

Figure 18 – Kaplan-Meier Analysis – Probability of Freedom from Chronic Effectiveness Failure through 15 Months Post-Procedure (Per-Protocol Population, n = 333)



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Comparison of Primary Effectiveness Endpoint by Sex

Table 68 presents the primary effectiveness outcome for the per-protocol population by sex. Males subjects had significantly higher success rates as compared to female subjects (64.3% vs 47.1%, nominal $p < 0.15$).

**Table 62 – Primary Effectiveness Endpoint by Sex
(Per-Protocol Population, N = 333)**

Variable	Male	Female	p-value ¹
Primary Effectiveness Endpoint			0.009
n/N	135 / 210	41 / 87	
%	64.3%	47.1%	
One-sided Exact 97.5% Lower Confidence Bound	57.4%	36.3%	

¹ Fisher's exact test used to test whether primary effectiveness success rate differed by sex

C.6 - Study Design

In this study, a 6-month blanking period was employed to allow investigators additional time to adjust treatment following the index procedure. In the therapy consolidation period (months 4-6) interventions such as CV, AAD adjustment, and repeat ablation procedures were allowed without a negative impact on the primary effectiveness outcome. 77 subjects received interventions during the therapy consolidation period. Of these subjects, only 27.3% (21/77) went on to successfully complete the 15-month follow-up without recurrence of disease (AF/AFL/AT). While effectiveness success was lower for these subjects, they did contribute to the overall success of the effectiveness at 15 months.

**Table 63 – Primary Effectiveness Endpoint by
Heart Rhythm Management in Therapy Consolidation Period (Day 91-180)
(Per-Protocol Population, N = 333)**

Therapy Consolidation Period	Primary Effectiveness Success with Intervention, n/N (%)	Primary Effectiveness Success without Intervention, n/N (%)
CV	3 / 15 (20.0)	173 / 282 (61.3)
AAD Adjustment	12 / 50 (24.0)	164 / 247 (66.4)
Repeat Procedure	5 / 15 (33.3)	171 / 282 (60.6)
Recurrence	8 / 25 (32.0)	168 / 272 (61.8)
Any Intervention	21 / 77 (27.3)	155 / 220 (70.5)

C.7 - Study Conclusion

The results demonstrate that the THERMOCOOL SMARTTOUCH™ Catheter met the pre-specified performance goals for safety and effectiveness.

STUDY 2: Safety Study

A. Objective

The primary objective of this trial was to demonstrate the safety of the THERMOCOOL SMARTTOUCH™ SF Catheter with Contact Force Sensing Capability in the treatment of drug refractory symptomatic paroxysmal AF during standard electrophysiology mapping and ablation procedures.

B. Study Design

The study was a prospective, single-arm, unblinded, multi-center, pivotal, clinical investigation conducted at 19 investigational sites in the US.

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B.1 - Study Endpoints

The endpoints for the study were as follows:

Primary safety endpoint – incidence of any primary adverse event occurring within 7 days of any AF ablation procedure

Primary adverse events include the following conditions:

- Death
- Atrio-esophageal fistula¹
- Cardiac tamponade²/Atrial perforation
- Myocardial Infarction (MI)
- Stroke/Cerebrovascular Accident (CVA)
- Thromboembolism
- Transient Ischemic Attack (TIA)
- Diaphragmatic paralysis
- Pneumothorax
- Heart block
- Pulmonary Vein (PV) stenosis¹
- Pulmonary edema (Respiratory Insufficiency)
- Pericarditis
- Major vascular access complication/Bleeding

¹ Pulmonary Vein (PV) stenosis and atrio-esophageal fistula that occurred greater than one week (7 days) post-procedure were deemed primary AEs.

² Hemodynamic compromise or instability was defined as Systolic BP < 80 mm Hg.

Secondary Endpoints

Acute success – confirmation of entrance block in all pulmonary veins

Secondary safety endpoints included:

Occurrence of early onset (within 7 days of initial ablation) serious adverse event

Occurrence of peri-procedural (> 7 to 30 days) serious adverse event

B.2 - Pre-Specified Performance Goal

The performance goal was prospectively established.

Safety – Performance Goal = 14.0% upper bound of the 95% CI around the primary AE rate

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B.3 - Subject Disposition and Accountability

Table 64 – Subject Accountability and Disposition

Disposition	N	%
Enrolled Subjects	165	100.0
Excluded Subjects	6	3.6
Safety Population	159	96.4
Not Meeting Eligibility Criteria	4	2.4
mITT Population	155	93.9
Undergone RF Ablation	155	93.9
Per-Protocol Population	155	93.9
Subjects Treated with Non-Study Catheter	0	0
Subjects Treated for Non-Study Arrhythmia	0	0

The following definitions were used to classify subjects:

Safety Population (n = 159) was comprised of enrolled subjects undergoing insertion of the THERMOCOOL SMARTTOUCH™ SF Catheter.

Modified Intent-To-Treat (mITT) Population (n = 155) consisted of enrolled subjects who met the eligibility criteria and had the study catheter inserted.

C. Subject Demographics and Baseline Characteristics

**Table 65 – Subject Demographics
(Enrolled Subjects, N = 165; mITT Population, N = 155)**

Demographics	Enrolled n/164	mITT n/155
Gender (%)		
Male	95 (57.9)	93 (60.0)
Female	69 (42.1)	62 (40.0)
Ethnicity – Hispanic or Latino (%)	2 (1.2)	1 (0.6)
Race (%)		
Asian	1 (0.6)	1 (0.6)
White	159 (97.0)	151 (97.4)
Pacific Islander	1 (0.6)	1 (0.6)
Black	2 (1.2)	2 (1.3)
Other	1 (0.6)	0
Age (Years)	62.7 ± 10.44	62.7 ± 10.13
AF History (months)	47.9 ± 67.45 (163)	46.0 ± 63.82 (155)
LA Dimension (mm)	38.8 ± 5.96 (154)	38.9 ± 5.87 (150)
LVEF (%)	60.1 ± 6.98 (155)	59.9 ± 6.74 (150)

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Table 66 – Baseline Characteristics
(Enrolled, N = 165; mITT Population, n = 155)

Medical History	Enrolled n/163 (%)	mITT n/155 (%)
Hypertension	93 (57.1%)	90 (58.1%)
Diabetes	23 (14.1%)	22 (14.2%)
AAD Failed		
Class I & III	116/161 (72.0)	110/155 (71.0)
Class II & IV Only	45/161 (28.0)	45/155 (29.0)
Heart Disease	44 (27.0%)	43 (27.7%)
Coronary artery disease	29 (17.8%)	28 (18.1%)
Congestive heart failure	6 (3.7%)	5 (3.2%)
Prior myocardial infarction	6 (3.7%)	6 (3.9%)
Cardiac surgical procedures	12 (7.4%)	12 (7.7%)
Thromboembolic Event	10 (6.1%)	10 (6.5%)
Transient ischemic attack	3 (1.8%)	3 (1.9%)
Stroke	4 (2.5%)	4 (2.6%)
Other Arrhythmia	68 (41.7%)	63 (40.6%)
Atrial flutter	51 (31.3%)	47 (30.3%)
Atrial tachycardia	8 (4.9%)	8 (5.2%)

D. Study Conclusion

C.1 - Procedural Data

Table 73, Table 74, and Table 75 present the procedural data. There were 159 procedures in 159 subjects. All subjects underwent one (1) study ablation procedure.

Table 67 – Summary of Power, Temperature, and Impedance Data
per Procedure (Safety Population, n =159)

Description	Mean ± SD (n)
Mean Maximum Power (W)	31.3 ± 3.98 (151)
Mean Temperature (°C)	27.8 ± 3.30 (151)
Mean Impedance (Ω)	127.2 ± 15.13 (151)

On average, less power was used on the posterior wall during RF applications.

Table 68 – Mean Max Power by Pulmonary Vein Anatomical Location
(Safety Population, n = 159)

Location	Mean ± SD	Median	Min / Max
Anterior	33.3 ± 4.24	35.0	12.0 / 45.8
Inferior	31.1 ± 5.30	30.9	15.3 / 45.4
Posterior	28.7 ± 5.84	30.0	10.0 / 45.5
Ridge	34.5 ± 4.64	35.5	15.4 / 45.9
Roof Line	32.2 ± 5.27	31.0	15.3 / 50.0

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**Table 69 – Summary of Ablation Procedure Parameters
(Safety Population, n = 159)**

Procedure Parameters	Mean ± SD (n)
Total Procedure Time (min)	181.1 ± 74.75 (159)
Ablation Procedure Time (min)	104.3 ± 51.48 (159)
Total Fluoroscopy Time (min)	18.5 ± 13.93 (159)
Fluid Input (ml)	2148.9 ± 1179.6 (158)
Fluid via Catheter (ml)	898.4 ± 586.33 (156)
Fluid via IV (ml)	1261.8 ± 901.76 (158)
Fluid Output (ml)	937.2 ± 962.98 (95)
Balance (input - output) (ml)	1443.0 ± 882.04 (95)

All AF ablation procedures began with circumferential lesions targeting all pulmonary veins, with additional atrial ablation lines created as clinically required.

Table 76 and Table 77 summarizes the lesion sets applied to the subjects undergoing ablation during the index ablation procedures.

**Table 70 – Outcomes by Ablation Targets per Procedure
(Safety Population, n = 159)**

Ablation Targets	n/159 (%)
PV Only	60 (37.7)
PV + Atrial Linear Lesions	78 (49.1)
PV + Foci	5 (3.1)
PV + Atrial Linear Lesions + Foci	16 (10.1)
Total	159 (100.0)

**Table 71 – Atrial Linear Lesions per Procedure
(Safety Population, n = 159)**

Linear Lesions	n/159 (%)
Left Inferior PV to Mitral	3 (1.9)
SVC	3 (1.9)
Cavo-Tricuspid Isthmus	72 (45.3)
Roof line	29 (18.2)
Other	7 (4.4)

C.2 - Acute Procedural Success

Acute success was defined as the confirmation of entrance block into all PVs. Any use of non-study catheters and >2 repeat ablations during the blanking period were considered acute procedural failures.

Acute procedural success results are presented in Table 78.

**Table 72 – Acute Effectiveness Summary
(Safety Population, n =159)**

	Safety
Number of Subjects with Success	153 / 159
Percentage of Subjects with Success	96.2%
95% Exact Binomial Confidence Interval	(92.0%, 98.6%)

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C.3 - Contact Force Data

The THERMOCOOL SMARTTOUCH™ SF Catheter for measuring the contact force (CF) applied to the endocardial wall of the heart is comprised of the THERMOCOOL SMARTTOUCH™ SF Catheter and CARTO™ 3 EP navigation workstation with the CARTO SMARTTOUCH™ Module installed. The graphical user interface (GUI) of the CARTO™ 3 workstation displays the pressure applied to the endocardial surface of the heart as gram forces that the investigator can visualize during the procedure.

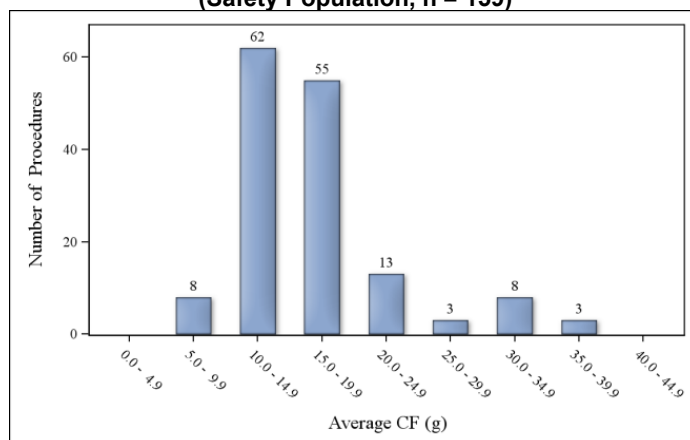
Table 79 presents the overall average contact force applied during the procedure for all subjects who underwent a study ablation procedure. As shown, the overall average CF applied during ablation procedures was 16.7 ± 6.14 grams. Figure 19 presents a distribution of average contact force in 5 gram increments. In the majority of procedures (125/152), the average contact force applied was less than 20 grams.

Table 73 – Average Contact Force Measurements Overall per Ablation Procedure (Safety Population, n = 159)

	Average Contact Force (g)
n ¹	152
Mean	16.7
Standard Deviation	6.14
Median	15.7
Q1 / Q3	12.9 / 18.7
Min / Max	7.4 / 38.3

¹ Contact force data available for 152 of 159 subjects.

Figure 19 – Distribution of Average Contact Force per Ablation Procedure (Safety Population, n = 159)



An integral part of the CARTO™ 3 graph display includes a real-time rolling graph of applied CF which includes a user configurable working range that is displayed on the graph as horizontal lines for a low and high range. The real-time rolling graph display with the working ranges acts as a visual aid providing real-time feedback of the pressure being applied by the operator in relationship to their pre-selected CF values.

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Table 80 presents the investigator-selected working ranges used during the study ablation procedures with the THERMOCOOL SMARTTOUCH™ SF Catheter.

**Table 74 – Working Ranges (g) Configured by Investigators
(Safety Population, n = 159¹)**

Lower	Upper	n / 159 (%)
0	38	1 (0.6%)
0	40	1 (0.6%)
2	23	1 (0.6%)
2	48	1 (0.6%)
3	50	5 (3.1%)
4	50	1 (0.6%)
5	20	6 (3.8%)
5	24	2 (1.3%)
5	25	8 (5.0%)
5	30	2 (1.3%)
5	35	16 (10.1%)
5	38	2 (1.3%)
5	40	70 (44.0%)
5	50	1 (0.6%)
5	60	1 (0.6%)
6	30	1 (0.6%)
6	40	1 (0.6%)
6	49	1 (0.6%)
7	46	1 (0.6%)
8	30	1 (0.6%)
9	58	1 (0.6%)
10	30	3 (1.9%)
10	40	28 (17.6%)
10	70	1 (0.6%)
15	20	1 (0.6%)
20	35	1 (0.6%)
20	40	1 (0.6%)

¹ Contact force data available for 152 of 159 subjects.

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C.3.1 - Average CF by Sex

Table 81 presents a comparison of average contact force by sex. There was no significant difference in the use of contact force between sexes.

Table 75 – Average Contact Force Measurements (g) by Sex per Ablation Procedure (Safety Population, n = 159¹)

	Male	Female	p-value
n	92	60	
Mean ± SD	16.6 ± 6.43	17.0 ± 5.73	0.3777
Median	15.5	15.8	
Min / Max	7.4 / 35.1	9.9 / 38.3	

¹ Contact force data available for 152 of 159 subjects.

C.4 - Adverse Events (AE)

The primary safety endpoint for this study was defined as the incidence of early-onset (within 7 days of ablation procedure) primary AEs for subjects undergoing a study ablation procedure. The Safety Population (n = 159) was comprised of all enrolled subjects who had the study catheter inserted.

Primary Safety Endpoint – Primary Adverse Events

Table 82 presents the protocol-specified endpoint and safety results. There were 4 primary AEs reported for 4 subjects. One primary AE was deemed related to the investigational catheter. Three (3) were deemed possibly device-related. The overall percentage of subjects in the Safety Population who experienced a serious primary AE was 2.5% (4/159) with upper confidence at 6.3%. The safety endpoint specified in the protocol was 7.0% (upper confidence bound of 14.0%). Therefore, the results met the pre-specified performance goal for the safety endpoint.

Table 76 – Primary Safety Endpoint Outcome – Primary Adverse Events (Safety Population, n = 159)

	Protocol Established Endpoint	n
Number of Subjects in Safety Cohort		159
Number of Subjects with Primary AEs		4
% Primary AEs	7.0	2.5
Upper Bound of 95% Exact CI	14.0	6.3

Table 83 summarizes the primary AEs. Of the two subjects who experienced cardiac tamponade/perforation, one underwent emergent open chest surgical repair and the other was managed medically. All primary AEs improved or resolved by the 30 day follow-up visit.

Table 77 – Primary Safety Endpoint – Early-Onset (within (≤) 7 Days) Primary Adverse Events (Safety Population, n = 159)

Description	Number of Safety with Primary AEs n/159 (%)
Total Primary AEs	4 (2.5)
Death	0
Atrio-Esophageal Fistula	0
Cardiac Tamponade/Perforation ¹	2 (1.3)
Myocardial Infarction	0
Stroke	0
Cerebrovascular Accident	0

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Description	Number of Safety with Primary AEs n/159 (%)
Thromboembolism (Ischemic Colitis)	1 (0.6)
Transient Ischemic Attack	1 (0.6)
Diaphragmatic Paralysis	0
Pneumothorax	0
Heart Block	0
Pulmonary Vein Stenosis	0
Pulmonary Edema (Respiratory Insufficiency)	0
Pericarditis	0
Major Vascular Access Complication/Bleeding	0

¹The Cardiac Tamponades/Perforation for subject 106-002 was adjudicated as both definitely device and definitely procedure related; the second for subject 265-003 was adjudicated as possible device related and definitely procedure related.

Table 84 summarizes the SAEs occurring within 30 days of a study ablation procedure that were not classified as primary AEs by protocol definition.

Table 78 – SAEs Occurring within 30 Days of the Ablation Procedure by Causality and Category (Safety Population, n = 159)

Description	Total Number of Subjects with SAEs	Total Number of SAEs
SAEs	6	6
Device-Related	0	0
Possibly Device-Related	0	0
Procedure-Related	2	2
Sepsis due to UTI	1	1
Aspiration Pneumonia	1	1
Possibly Procedure-Related	3	3
Hospitalization due to Transient Neurological Symptoms	1	1
Gastrointestinal Disorder	1	1
Septic Shock due to Pneumonia with Abscess	1	1
Not Related to Device or Procedure	1	1
AF Recurrence with Rapid Ventricular Response	1	1

There were no deaths during the study.

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C.4.1 - Average CF and Primary AEs

Table 85 compares the average CF during procedures in subjects experiencing primary AEs with those who did not. Procedural average contact force used in subjects who experienced primary AEs was similar to those that did not.

**Table 79 – Average Contact Force (g) by Primary Adverse Event
(Safety Population, n = 159¹)**

Subject ID	Primary AE	Mean ± SD	Median	Min / Max
106-001	Thromboembolism	19.4 ± 7.37	18.3	9.2 / 38.6
106-002	Cardiac Tamponade	15.7 ± 6.17	14.0	6.9 / 27.4
131-003	TIA	14.7 ± 4.79	15.0	8.2 / 25.4
Subjects who did not experience a primary AE (n = 155)		16.7 ± 6.14	15.7	7.4 / 38.3

¹ Necessary procedural data for subject 265-003 (adjudicated as cardiac tamponade/perforation due to the size of the pericardial effusion [1.3 cm]) was unavailable for analysis.

C.5 - Study Conclusion

The results demonstrate that the THERMOCOOL SMARTTOUCH™ SF Catheter met the pre-specified performance goal for safety.

SUMMARY OF CLINICAL STUDIES CONDUCTED FOR THE THERMOCOOL SMARTTOUCH™ CATHETER

STUDY 1: Pivotal Study

A. Objective

The primary objective of this trial was to demonstrate the safety and effectiveness of the THERMOCOOL SMARTTOUCH™ Catheter with Contact Force Sensing Capability for the radiofrequency ablation treatment of subjects with symptomatic Paroxysmal Atrial Fibrillation (PAF) who were refractory or intolerant to antiarrhythmic drug therapy.

B. Study Design

The study was a prospective, single-arm, unblinded, multi-center, pivotal clinical investigation conducted at 21 investigational sites in the US.

B.1 - Study Endpoints

The endpoints for the study were as follows:

Primary effectiveness endpoint – freedom from documented symptomatic atrial fibrillation (AF), atrial tachycardia (AT), or atrial flutter (AFL) episodes (hereinafter collectively referred to as “atrial tachyarrhythmias”) based on electrocardiographic data during the effectiveness evaluation period (Day 91-361) post a three-month blanking period

Acute success – confirmation of entrance block in all targeted pulmonary veins

Primary safety endpoint – incidence of early onset (within 7 days of an AF ablation procedure) primary adverse events. This included the following adverse events:

- Death
- Myocardial Infarction (MI)
- Pulmonary Vein (PV) stenosis¹
- Diaphragmatic paralysis
- Atrio-esophageal fistula¹
- Transient Ischemic Attack (TIA)
- Stroke/Cerebrovascular Accident (CVA)
- Thromboembolism

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- Pericarditis
- Cardiac tamponade
- Pericardial effusion
- Pneumothorax
- Atrial perforation
- Vascular access complications
- Pulmonary edema
- Hospitalization (initial and prolonged)
- Heart block

¹ PV stenosis and atrio-esophageal fistula that occur greater than one week (7 days) post-procedure were also classified as primary AEs

Secondary safety endpoints included:

Occurrence of peri-procedural serious adverse events > 7 but ≤30 days

Occurrence of late onset (> 30 days) serious adverse events excluding PV stenosis and atrio-esophageal fistula

Non-serious adverse events

B.2 - Objective Performance Criteria (OPC)

Objective performance goals were prospectively established.

Effectiveness – Performance Goal = 50% lower bound of the 95% CI around the primary success rate

Safety – Performance Goal = 16.6% upper bound of the 95% CI around the primary AE rate

B.3 - Subject Accountability

Table 80 – Subject Accountability and Disposition

Disposition	N	%
Enrolled Subjects	172	100.0
Subjects Not Meeting I/E Criteria	15	8.7
ITT Cohort	157	91.3
Enrolled Subjects	172	100.0
Excluded Subjects	11	6.4
Safety Cohort	161	93.6
Discontinued Subjects	1	0.6
Subjects Undergone RF Ablation	160	93.0
Roll-In Cases	38	22.1
Effectiveness Cohort	122	70.9
Subjects with Non-Study Arrhythmia	0	0
Subjects not meeting I/E Criteria	8	4.7
Primary Effectiveness Cohort	114	66.3

The following definitions were used to classify subjects:

Enrolled Subjects (n = 172) Patients who signed the informed consent.

Excluded Subjects (n = 11) Subjects that were enrolled but never underwent insertion of the study catheter. Excluded subjects were not included in either the effectiveness or safety evaluation of the study catheter.

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Discontinued Subjects (n = 1) Subjects that had the investigational catheter inserted but were not treated with the investigational device (i.e., no RF energy applied). Subjects were categorized as “discontinued” if ablation was not possible due to non-investigational equipment failure or if their arrhythmia was determined at the time of electrophysiologic study to be a non-study arrhythmia (e.g., atrial flutter). These discontinued subjects remained in follow-up for 7 days as part of the safety evaluation.

Intent-To-Treat (ITT) Cohort (n = 157) Enrolled subjects who met the inclusion/exclusion criteria.

Calibration Roll-In Subjects (n = 38) Enrolled subjects who underwent ablation with the study catheter during the calibration roll-in period were considered as part of the safety evaluation. Roll-in cases were prospectively identified prior to undergoing a study procedure.

Primary Effectiveness Cohort (n = 114) was comprised of subjects that received the treatment with the THERMOCOOL SMARTTOUCH™ Catheter and met the inclusion/exclusion criteria and did not meet the definitions of being excluded or discontinued. Roll-in cases were excluded from the primary effectiveness cohort.

Safety Cohort (n = 161) was comprised of enrolled subjects undergoing insertion of the THERMOCOOL SMARTTOUCH™ Catheter. The calibration roll-in subjects were included in this cohort.

B.4 - Subject Demographics

Table 81 – Subject Demographics (Enrolled Subjects, N = 172)

	Total n/172 (%)	Male n/124 (%)	Female n/48 (%)	p-value
Gender				
	172 (100.0)	124 (72.1)	48 (27.9)	
Ethnicity				
Hispanic	4 (2.3)	4 (3.2)	0 (0.0)	0.5772
Race				
Asian	0 (0)	0 (0)	0 (0.0)	0.8141
Other	3 (1.7)	3 (2.4)	0 (0.0)	
Black	4 (2.3)	3 (2.4)	1 (2.10)	
White	165 (95.9)	118 (95.2)	47 (97.9)	
Age (years)				
Mean	58.8 ± 11.00	57.3 ± 10.86	62.5 ± 10.60	0.0026
Median	60.0	58.0	65.0	
Min / Max	23 / 79	23 / 79	27 / 78	

The age in the above table was when the subject signed the informed consent. The p-value listed compares the ethnicity, race and age by gender.

C. Results

C.1 - Procedural Data

Table 88 and Table 89 present the procedural data. There were 175 procedures in 160 subjects. One hundred and forty-five (145) underwent one ablation procedure, 15 subjects (3 roll-in subjects and 12 in the effectiveness cohort) underwent a second ablation procedure. Of the 12 in the effectiveness cohort, 6 repeat ablations were during the blanking period and the remaining 6 were post-blanking due to effectiveness failure.

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**Table 82 – Summary of Power, Temperature and Impedance Data
(Subjects Undergoing Ablation, n = 160¹)**

Description	Roll-In Subjects Mean ± SD (n)	Effectiveness Cohort Mean ± SD (n)	Total Mean ± SD (n)
Mean power (W)/procedure (n = 135 procedures)	31.2 ± 5.2 (29)	31.0 ± 3.7 (106)	31.1 ± 4.1 (135)
Mean temperature (°C)/procedure (n = 136 procedures)	36.3 ± 1.31 (29)	35.9 ± 1.9 (107)	36.0 ± 1.8 (136)
Mean impedance (Ω)/procedure (n = 136 procedures)	112.7 ± 11.6 (29)	120.4 ± 14.9 (107)	118.8 ± 14.5 (136)

¹ Complete procedural data were not reported for all subjects.

Note: Table 88 reflects available data from index procedures for roll-in subjects and effectiveness cohort subjects.

**Table 83 – Summary of Ablation Procedure Parameters – All Ablation Procedures
(Subjects Undergoing Ablation, n = 160¹)**

Procedure Parameters	Roll-In Subjects Mean ± SD (n)	Effectiveness Cohort Mean ± SD (n)	Total Mean ± SD (n)
Number of RF applications (n = 175 procedures)	59.0 ± 38.8 (41)	59.6 ± 44.2 (134)	59.5 ± 42.9 (175)
Mean saline infused (ml) by THERMOCOOL SMARTTOUCH™ Catheter (n = 173 procedures)	1725.7 ± 860.8 (39)	1803.6 ± 910.5 (134)	1786.0 ± 897.6 (173)
Total procedure time (min)	236.4 ± 89.1 (41)	211.6 ± 86.0 (134)	217.4 ± 87.1 (175)
Ablation procedure time (min)	116.3 ± 46.3 (39)	117.6 ± 62.6 (127)	117.3 ± 59.1 (166)
Total fluoroscopy duration (min)	47.2 ± 28.1 (39)	38.6 ± 24.6 (134)	40.5 ± 25.6 (173)
Total fluid input (ml)	3071.0 ± 1378.6 (40)	3541.6 ± 1606.6 (134)	3433.4 ± 1565.9 (174)
Total fluid output (ml)	986.8 ± 738.9 (37)	1079.3 ± 919.4 (116)	1056.9 ± 877.8 (153)
Balance (input-output) (ml)	2145.3 ± 1314.1 (36)	2689.6 ± 1511.6 (116)	2560.7 ± 1481.4 (152)

¹ Data parameters not available for all ablation procedures.

All AF ablation procedures began with circumferential lesions targeting all pulmonary veins, with additional atrial ablation lines created as clinically required.

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Table 90 summarizes the lesion sets applied to the subjects undergoing ablation during the index ablation procedures.

**Table 84 – Outcomes by Ablation Targets per Subject – 1st Ablation Procedure
(Subjects Undergoing Ablation, n = 160)**

Ablation Targets	Roll-In Subjects n ¹ /38 (%)	Effectiveness Cohort n ¹ /122 (%)	All n ¹ /160 (%)
PV Only	19 (50.0)	61 (50.0)	80 (50.0)
PV + Atrial Lines	14 (36.8)	52 (42.6)	66 (41.3)
PV + Foci	1 (2.6)	2 (1.6)	3 (1.9)
PV + Atrial Lines + Foci	4 (10.5)	7 (5.7)	11 (6.9)
Total	38 (100.0)	122 (100.0)	160 (100.0)

¹n represents number of subjects.

C.2 - Acute Procedural Success

Acute success was defined as the confirmation of entrance block into all targeted PVs. Any use of non-study catheters and > 2 repeat ablations during the blanking period were considered acute procedural failures.

Acute procedural success results are presented in Table 91.

Table 85 – Acute Effectiveness Summary (Primary Effectiveness Cohort, n = 114)

	Number of Subjects n / n	Percentage of Subjects with Acute Success (%)	95% Exact Binomial Confidence Interval
Subjects Undergoing Ablation	158/160	98.8	(95.6, 99.8)
Roll-In	36/38	94.7	(82.3, 99.4)
Effectiveness Cohort	122/122	100.0	(97.0, 100.0)
Primary Effectiveness Cohort	114/114	100.0	(96.8, 100.0)

C.3 - Primary Effectiveness Endpoint - Freedom from Symptomatic Atrial Tachyarrhythmia

Primary Effectiveness Analysis

The primary effectiveness endpoint was defined as freedom from documented symptomatic AF/AT/AFL ("atrial tachyarrhythmias") based on electrocardiographic data and freedom from failure modes during the effectiveness evaluation period (Day 91-361). Any AF recurrence or repeat ablation procedure occurring greater than Day-361 post index procedure was deemed primary effectiveness successes at 12 months.

In the worst-case scenario analysis, over seventy-percent (70.2%, 80/114) of the primary effectiveness cohort were free from documented symptomatic atrial tachyarrhythmias during their effectiveness evaluation period. This includes 2 subjects who were protocol-adjudicated failures at 12 months follow-up who did not have documented symptomatic AF/AFL/AT recurrence. The lower bound of the 95% confidence interval of the primary effectiveness rate was 60.9%, significantly higher than the pre-determined performance goal of 50% ($p < 0.0001$).

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Primary effectiveness results are described in Table 92.

**Table 86 – Primary Effectiveness Endpoint through 12 Month Follow-Up Visit
(Primary Effectiveness Cohort, n = 114)**

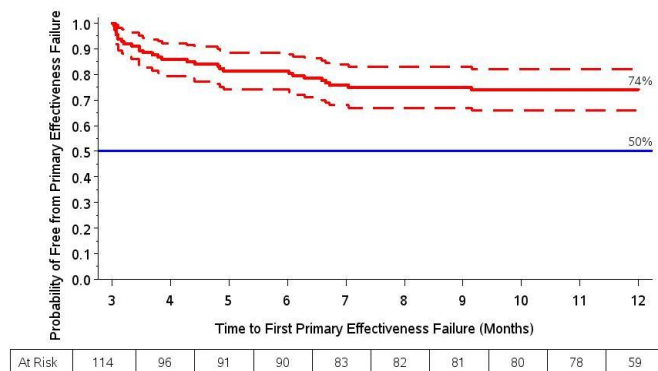
	Number of Subjects (n)	Percentage of Subjects (%)	95% Exact Binomial Confidence Interval	p-value
Freedom from Documented Symptomatic AF/AT/AFL	80	70.2	(60.9%, 78.4%)	< 0.0001
Primary Effectiveness Failures	29 ¹	25.4		
Missing Outcomes	5 ²	4.4		

¹ Two subjects were protocol adjudicated failures without documented symptomatic AF/AFL/AT recurrence.

² Five LTFU subjects were included in the denominator of the binomial exact analysis.

Figure 20 shows the Kaplan-Meier survival curves for the primary effectiveness cohort. The probability of freedom from primary effectiveness endpoint failure at 12 months post-blanking was 75.8% with a protocol-adjudicated success for this cohort of 74.0% (95% CI, 65.9%-82.2%). The lower bound of the 95% CI for this KM graph (as indicated by the lower dotted line) is greater than 50% pre-determined performance criterion. The primary effectiveness performance goal was met.

**Figure 20 – Kaplan-Meier Analysis – Probability of Freedom from Chronic Effectiveness Failure through 12 Months Post-Procedure
(Primary Effectiveness Cohort = 114)**



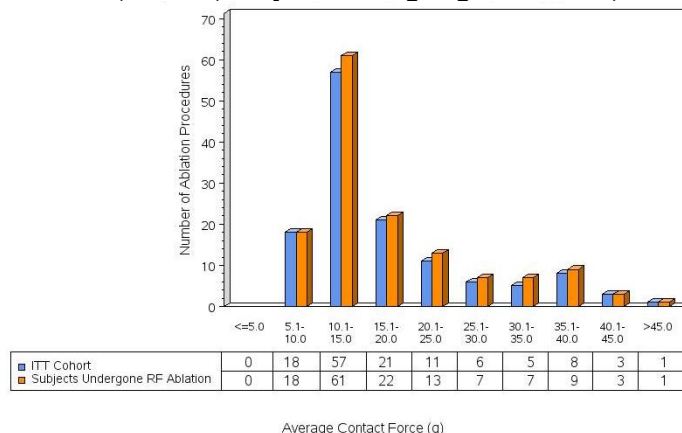
C.4 - Contact Force Data

The THERMOCOOL SMARTTOUCH™ system for measuring the contact force (CF) applied to the endocardial wall of the heart is comprised of the THERMOCOOL SMARTTOUCH™ Catheter and CARTO™ 3 EP navigation workstation with the CARTO SMARTTOUCH™ Module installed. The graphical user interface (GUI) of the CARTO™ 3 workstation displays the pressure applied to the endocardial surface of the heart as gram forces that the investigator can visualize during the procedure.

Figure 21 presents the distribution of average contact force (CF) per ablation procedure. Overall, the average CF applied during the trial was 17.9 g ± 9.42 g.

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Figure 21 – Distribution of Average Contact Force per Ablation Procedure (ITT Cohort, n = 157; Subjects Undergoing RF Ablation, n = 160)



An integral part of the CARTO™ 3 System graph display includes a real-time rolling graph of applied CF which includes a user configurable working range that is displayed on the graph as horizontal lines for a low and high range. The real-time rolling graph display with the working ranges acts as a visual aid providing real-time feedback of the pressure being applied by the operator in relationship to their pre-selected CF values.

Table 93 presents the investigator-selected working ranges used during the study ablation procedures with the THERMOCOOL SMARTTOUCH™ Catheter.

Table 87 – Working Ranges Configured by Investigators (Subjects Undergoing an Ablation Procedure, n = 160)

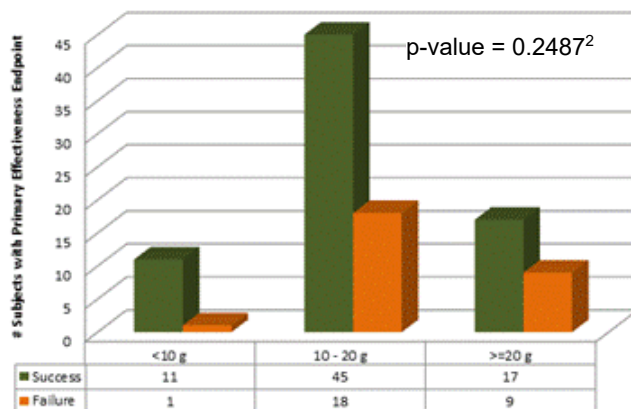
Investigator Range (g)		n / 141 (%)
Lower	Upper	
4	40	2 (1.4)
5	20	1 (0.7)
5	25	16 (11.3)
5	30	9 (6.4)
5	40	95 (67.4)
5	44	1 (0.7)
5	45	1 (0.7)
5	50	4 (2.8)
5	60	1 (0.7)
10	40	10 (7.1)
15	25	1 (0.7)

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C.4.1 - Correlation of Average CF and Primary Effectiveness

In this study the average CF during RF application for individual procedures did not correlate with the primary effectiveness endpoint. Figure 22 presents the analysis.

Figure 22 – Number of Subjects with Primary Effectiveness Endpoint by Average CF (Primary Effectiveness Cohort, n = 114¹)



¹ Subjects with censored primary effectiveness endpoint are not included in the analysis.

² Fisher's exact test

C.4.2 - Correlation of Average CF and Safety

Table 94 compares the average CF during procedures in subjects experiencing primary AEs with those who did not. Using CF as a continuous variable, there was no statistically significant difference in the average CF applied during procedures resulting in primary AEs and in those procedures that did not.

Table 88 – Average Contact Force by Primary Adverse Event (Primary Safety Cohort, n = 161)

Primary Adverse Event	Average Contact Force (g)			p-value
	Mean ± SD	Median	Min / Max	
Yes (n = 13)	18.2 ± 6.15	17.1	10.9 / 33.4	0.1995
No (n = 128)	17.8 ± 9.71	14.2	5.4 / 45.7	

C.4.3 - Correlation of CF and Tamponade

Table 95 presents the correlation of subjects experiencing cardiac tamponade AEs with the percentage of time with CF measurements were ≥ 40 grams and ≥ 50 grams. It was assumed that higher percentage of time with CF ≥ 40 grams and with CF ≥ 50 grams signified more excursions of CF applied during the procedure and that these excursions may possibly have resulted in more primary AEs and tamponades. On average 8.3% of the time was spent over 40 grams of CF with a median of 2.1% and on average only 4.8% of time was spent over 50 grams of CF, with a median of 0.8%. The data was skewed by one site where 23 cases had a mean of 35% of the time with CF ≥ 40 grams and 23% of the time with CF ≥ 50 grams. 2.1% of all cases were completed with average CF greater than or equal to 40 grams. In comparing procedures with CF ≥ 40 grams more than 2.1% of the time vs. those that were less than 2.1% of the time, there were no statistically significant differences exhibited in the comparisons presented in the table below. The four tamponade subjects all had percentage of time with CF ≥ 40 grams over 2.1%. Due to the sparse data of tamponade, the correlation was only borderline significant (p-value = 0.0581).

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**Table 89 – Correlation of Tamponade Cases with % of Time
CF Measurements $\geq$ 40 grams (Safety Cohort, n = 161¹)**

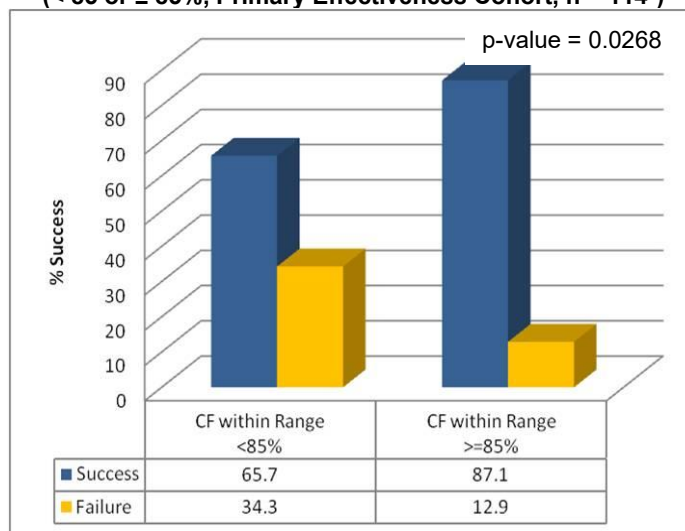
Tamponade Adverse Event	Percentage of Time with CF Measurements $\geq$ 40 Grams		p-value
	< 2.1% n / 71 (%)	$\geq$ 2.1% n / 70 (%)	
Yes	0	4 (5.7%)	0.0581
No	71 (100.0%)	66 (94.3%)	

¹ CF data were missing or not analyzable for 19 subjects.

C.4.4 - Percent of Time within Investigator-Selected Range and Primary Effectiveness and Safety

Sensitivity analysis showed that the percentage of time the investigator stayed within his selected working range (regardless of the range selected) correlated positively with primary effectiveness success. If the investigator maintained pressure on the heart endocardial surface within their selected working range 85% or more of the time during RF application, the success rate was greater than 87%. Figure 23 presents the results.

Figure 23 – Number of Subjects with Primary Effectiveness Endpoint by Percentage of Time with CF Measurements within Investigator-Selected Working Range (< 85 or $\geq$ 85%, Primary Effectiveness Cohort, n = 114¹)



¹ 101 subjects with non-missing data for primary effectiveness outcome and CF data were included in the analysis.

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Figure 24 – Time to Primary Effectiveness Failure through 12 Months Post-Procedure, by Percentage of Time in CF Working Range – Kaplan-Meier Curve (< 85% vs. ≥ 85%, Primary Effectiveness Cohort, n = 114)

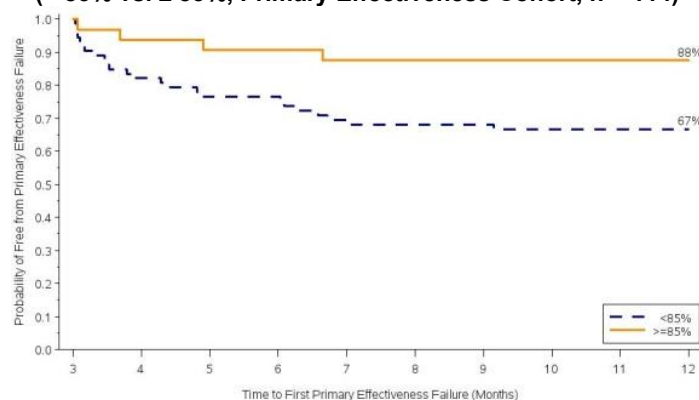


Table 90 – Primary AEs and Tamponade Adverse Event by Percentage of Time CF Measurements were within the Investigator-Selected Working Range (Primary Safety Cohort, n = 161)

Percent Time within Working Range (n)			Yes n (%)	No n (%)	p-value
Primary AE					
< 85% (100)		8 (8.0)		92 (92.0)	0.5229
≥ 85% (41)		5 (12.2)		36 (87.8)	
Cardiac Tamponade Events					
< 85% (100)		2 (2.0)		98 (98.0)	0.5798
≥ 85% (41)		2 (4.9)		39 (95.1)	

C.5 - Adverse Events (AE)

The primary safety endpoint for this study was defined as the incidence of early-onset (within 7 days of ablation procedure) primary AEs for subjects undergoing a study ablation procedure. The Safety Cohort (n = 161) was comprised of all enrolled subjects who had the study catheter inserted.

Primary Safety Endpoint – Primary Adverse Events

Table 97 presents the protocol-established endpoint and safety results. There were 17 primary AEs reported for 16 subjects. One primary AE was deemed related to the investigational catheter. Two were deemed possibly device-related. The remainder were deemed unrelated to the investigational catheter. The overall percentage of subjects who experienced a serious primary AE was 9.9% (16/161) and the upper confidence bound based on the Primary Safety Cohort was 15.6%. The safety endpoint specified in the protocol was 8.6% (upper confidence bound of 16.6%). Therefore, the results met the protocol-established performance criteria for the safety endpoint.

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**Table 91 – Primary Safety Endpoint Outcome – Primary Adverse Events
(Primary Safety Cohort, n = 161)**

	Protocol Established Endpoint	n
Number of Subjects in Safety Cohort		161
Number of Subjects with Primary AEs		16
% Primary AEs	8.6	9.9
Upper Bound of the Two-Sided 95% Confidence Interval ¹	16.6	15.6

¹ Exact binomial using a commercially available software package.

Table 98 summarizes the major primary AEs.

**Table 92 – Primary Safety Endpoint – Early-Onset (within (≤) 7 Days)
Primary Adverse Events (Primary Safety Cohort, n = 161)**

Description	Number of Subjects with Primary AEs n/161 (%)
Total Serious Primary AEs	16¹ (9.9%)
Death	0
Atrio-Esophageal Fistula	0
Atrial Perforation	0
Cardiac Tamponade	4 (2.48)
Myocardial Infarction	0
Stroke	0
Cerebrovascular Accident	0
Thromboembolism	0
Transient Ischemic Attack	0
Diaphragmatic Paralysis	0
Pneumothorax	0
Heart Block	1 (0.62)
Pulmonary Vein Stenosis	0
Pulmonary Edema	0
Pericarditis	3 (1.86)
Hospitalization (initial and prolonged)	6 (3.72)
Pericardial Effusion	0
Vascular Access Complication	3 (1.86)

¹ One subject appears in two categories.

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Table 99 summarizes the SAEs occurring within 30 days of a study ablation procedure that were not classified as primary AEs by protocol definition.

Table 93 – SAEs Occurring within 30 Days of the Ablation Procedure by Causality and Category (Safety Cohort, n = 161)

Description	Total Subjects with SAEs	Total Number of SAEs
Non-SAEs	8	8
Device-Related	0	0
Possibly Device-Related	0	0
Procedure-Related	1	1
Hospitalization: AF Recurrence	1	1
Possibly Procedure-Related	1	1
Loss of Consciousness	1	1
Not Related	6	6
Other: Dysphagia	1	1
Hospitalization:		
AF Recurrence	4	4
Rectal Bleed	1	1

There were no deaths during the study.

C.6 - Study Conclusion

The results demonstrate that the THERMOCOOL SMARTTOUCH™ Catheter met the objective criteria performance for safety and effectiveness.

STUDY 2: Continued Access Study

A. Objective

The purpose of this study was to allow continued access of the THERMOCOOL SMARTTOUCH™ Catheter for the ablation treatment of subjects with drug refractory symptomatic paroxysmal atrial fibrillation while the sponsor completed analysis of the pivotal study under the current IDE protocol and the FDA reviewed the pre-market application. This study provided additional corroborative safety and effectiveness data for the THERMOCOOL SMARTTOUCH™ Catheter system.

B. Study Design and Endpoints

The study design and endpoints were the same as those outlined above in the pivotal study.

B.1 - Subject Accountability

Table 94 – Subject Accountability (N = 148)

Subject Disposition	No. of Subjects
Enrolled Subjects	148
Excluded	3
ITT Cohort	145
Withdrawn	1
Data Not Available	1
Safety Analysis Cohort	143
Discontinued	2
Subjects Undergoing Ablation	141
Number of Subjects Currently in Follow-Up	141

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Enrolled Subjects (n = 148) Patients who sign the informed consent.

Excluded Subjects (n = 3) Subjects that are enrolled but never undergo insertion of the study catheter. Excluded subjects will not be included in either the effectiveness or safety evaluation of the study catheter.

Discontinued Subjects (n = 2) Subjects that have the investigational catheter inserted but are not treated with the investigational device (i.e., no RF energy applied). Subjects will be categorized as “discontinued” if ablation was not possible due to non-investigational equipment failure or if their arrhythmia was determined at the time of electrophysiologic study to be a non-study arrhythmia (e.g., atrial flutter). These discontinued subjects will remain in follow up for 7 days as part of the safety evaluation.

Intent To Treat (ITT) Cohort (n = 145) Enrolled subjects who meet the inclusion/exclusion criteria.

Subjects Undergoing Ablation/Effectiveness Cohort (n = 141) was comprised of subjects that received the treatment with the THERMOCOOL SMARTTOUCH™ Catheter and met the inclusion/exclusion criteria and did not meet the definitions of being excluded or discontinued. Roll in cases were excluded from the primary effectiveness cohort.

Safety Cohort (n = 143) was comprised of enrolled subjects undergoing insertion of the THERMOCOOL SMARTTOUCH™ Catheter. The calibration roll in subjects were included in this cohort.

B.2 - Subject Demographics

Table 95 – Subject Demographics (N = 148¹)

Characteristic	
Gender	n/147 (%)¹
Male	104 (70.7)
Female	43 (29.3)
Race	n/147 (%)¹
Caucasian	146 (99.3)
Black	1 (0.7)
Asian	0 (0.0)
Other	0 (0.0)
Ethnic Origin	n/147 (%)¹
Hispanic/Latino	2 (1.4)
Age (years)	
N	147 ¹
Mean	61
S.D.	10.44
Median	62
Min / Max	32 / 88

¹ At the time of publication, data was only available for 147 subjects.

C. Results

C.1 - Acute Procedural Success

Acute success was defined as the confirmation of entrance block into all targeted PVs. Any use of non-study catheters and > 2 repeat ablations were considered acute procedural failures.

At the time of publication, data analysis results for acute procedural success are not available for the Continued Access Study.

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C.2 - Primary Effectiveness Endpoint – Freedom from Symptomatic Atrial Tachyarrhythmia

Primary Effectiveness Analysis

The primary effectiveness endpoint was defined as freedom from documented symptomatic AF/AT/AFL (“atrial tachyarrhythmias”) based on electrocardiographic data and freedom from failure modes during the effectiveness evaluation period (Day 91-361). Any AF recurrence or repeat ablation procedure occurring greater than Day-361 post index procedure was deemed primary effectiveness successes at 12 months.

At the time of publication, the Continued Access Study data analysis is ongoing and 12 month follow-up data is not available.

C.3 - Primary Safety Endpoint

The primary safety endpoint for this study was defined as the incidence of early-onset (within 7 days of ablation procedure) primary AEs for subjects undergoing a study ablation procedure. The Safety Cohort (n = 143) was comprised of all enrolled subjects who had the study catheter inserted.

There were 27 primary AE in 25 subjects who had the investigational catheter inserted or underwent an ablation procedure. The percentage of subjects who experienced a primary AE in the safety cohort was 17.5% (25/143) and the upper bound of the two-sided 95% interval was 24.7%.

**Table 96 – Primary Safety Endpoint – Early-Onset (within (≤) 7 Days)
Primary Adverse Events (Primary Safety Cohort, n = 143)**

Description	# of Subjects with Primary AEs n/143 (%)
Total Serious Primary AEs	25¹ (17.5)
Death	0
Atrio-Esophageal Fistula	0
Atrial Perforation	0
Cardiac Tamponade	2 (1.40)
Myocardial Infarction	0
Stroke	0
Cerebrovascular Accident	1 (0.70)
Thromboembolism	0
Transient Ischemic Attack	0
Diaphragmatic Paralysis	0
Pneumothorax	0
Heart Block	2 (1.40)
Pulmonary Vein Stenosis	0
Pulmonary Edema	2 (1.40)
Pericarditis	1 (0.70)
Hospitalization (initial and prolonged)	10 (6.99)
Pericardial Effusion ²	1 (0.70)
Vascular Access Complication	8 (5.59)

¹Two subjects had events in two categories.

²Treated with pericardiocentesis.

No deaths have occurred during the reporting period, and there have been no unanticipated adverse effects.

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SUMMARY OF CLINICAL STUDIES CONDUCTED FOR ATRIAL FLUTTER INDICATION

STUDY 1: Pivotal Study

A. Objective

The objective of the study was to determine if the NAVISTAR™ THERMOCOOL™ Catheter, when used in conjunction with the CARTO™ EP/XP Navigation System, RF generator (Stockert 70), and related accessories, is safe and effective for the treatment of Type I atrial flutter in patients age 18 or older.

B. Study Design

The study was a prospective, non-randomized, unblinded, multi-center study conducted at 22 investigational sites (21 sites in US; 1 in Canada).

B.1 - Study Endpoints

The endpoints for the study were as follows:

- **Procedural safety** – defined by the absence of serious complication associated with the use of the investigational device within seven days of the ablation procedure; and
- **Acute procedural success** – defined as complete bi-directional conduction block (BDB) across the isthmus, and the inability to induce Type I atrial flutter post-procedure.

Long-term freedom from atrial flutter recurrence was not specifically identified as a study endpoint. Instead, acute procedural success was used as a surrogate endpoint for this parameter. Long-term (defined as 6 months post-treatment) freedom from atrial flutter recurrence information was also collected, in order to enable FDA to assess whether the surrogate endpoint was reasonable.

B.2 - Objective Performance Criteria (OPC)

Objective performance criteria (OPC) were prospectively established. The OPC for the safety endpoint used for this study was derived from the FDA guidance document "Cardiac Ablation Catheters Generic Arrhythmia Indications for Use; Guidance for Industry, July 2002 1998 NASPE Registry." The OPC for the effectiveness endpoint was based on an extensive literature search involving acute success rates associated with radiofrequency ablation of atrial flutter. The OPCs are defined below:

- **Safety** – major adverse events within 7 days of the procedure occur at a rate of 2.7% or less with a 7% one-sided 95% upper confidence bound;
- **Acute success** – 88% with an 80% one-sided 95% lower confidence bound.

B.3 - Subject Accountability

Table 103 documents the accountability and disposition of enrolled subjects.

Table 97 – Subject Accountability and Disposition

Subjects enrolled in study	198
Subjects not ablated with the NAVISTAR™ THERMOCOOL™ Catheter	8
Excluded subjects - enrolled but in whom the investigational catheter was not inserted	3
Discontinued subjects - either (1) in whom the investigational catheter was inserted but did not receive RF energy because of <u>non-investigational</u> equipment failure, or (2) for whom the arrhythmia was determined to be non-study arrhythmia at the time of electrophysiologic study (e.g., atypical atrial flutter)	5
Subjects ablated with NAVISTAR™ THERMOCOOL™ Catheter	190
Subjects ablated with NAVISTAR™ THERMOCOOL™ Catheter and non-investigational catheter ¹	19
Subjects ablated only with NAVISTAR™ THERMOCOOL™ Catheter	171
Subjects in whom BDB was not assessable	4

¹ This category includes enrolled subjects who received ablation therapy with the investigational catheter at the start of the procedure and for whom the investigator then

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switched to a non-protocol catheter to complete the procedure. Further subjects who could not receive ablation due to investigational device failure are included in this category. These subjects were considered acute effectiveness failures.

Effectiveness Analysis Population (n = 190) was defined as all subjects who received ablation therapy with the investigational catheter and for whom a valid assessment of BDB at the acute endpoint could be made OR if 6 month follow-up data were available.

Safety Analysis Population (n = 190) was defined as all enrolled subjects in whom the investigational catheter was inserted and received ablation therapy. Additionally, the rate of major adverse events is also reported for subjects in whom the investigational catheter was inserted and used for either mapping and/or ablation and for discontinued subjects. This additional category is referred to as the Inserted Patient Cohort (n = 195).

B.4 - Subject Demographics

Table 104 below summarizes the demographic information of all study subjects who received ablation therapy.

Table 98 – Subject Demographics
(All Subjects Who Received Ablation Therapy, n = 190)

Gender	N	%
Female	43	22.6
Male	147	77.4
Age (years)		
Mean ± standard deviation	59.8 ± 12.6	
Range	18 - 90	

Additionally, for the Inserted Patient Cohort of 195 subjects, 72 subjects (36.9%) did not have a concomitant arrhythmia reported in addition to Type I atrial flutter. One hundred and sixty-five (165) concomitant arrhythmias were reported for 123 subjects. The most common concomitant arrhythmias were atrial fibrillation (n = 104) and atypical atrial flutter (n = 27).

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C. Results

C.1 - Intraprocedural Data

Table 105 and Table 106 describes the procedural data.

Twenty-eight (28) subjects received ablation therapy for an arrhythmia other than Type I atrial flutter during the same index ablation procedure. The additional arrhythmias ablated were: 14 atrial fibrillation, 9 atrial tachycardia, 3 AVNRT, 1 intra-atrial tachycardia, 1 non-isthmus atrial flutter and 1 macro-reentry around the SVC eustachian ridge. One subject had more than one concomitant arrhythmia ablated.

Table 99 – Power, Temperature, and Impedance Data

Description	Mean ± Standard Deviation	Range
# RF applications/procedure ¹ (n = 188 procedures)	19 ± 16	1 - 86
Total saline infused by THERMOCOOL™ Catheter (ml) ² (n = 169 procedures)	999.7 ± 605.5	60 - 3750
Maximum power (W)/application ³ (n = 3502 RF applications)	35.0 ± 9.5	2 - 59
Maximum temperature (°C)/application ³ (n = 3476 RF applications)	39.6 ± 5.1	14 - 87
Maximum impedance (Ω)/application ³ (n = 3431 RF applications)	112.1 ± 21.0	13 - 251

¹ One subject had missing RF information; one subject did not undergo ablation with the NAVISTAR™ THERMOCOOL™ Catheter.

² Some procedural data are missing.

³ Power, temperature, and impedance not documented for several RF applications.

Table 100 – Overall Fluoroscopy/Procedure Time (minutes)

Description	Mean ± Standard Deviation	Range
Total fluoroscopy time/procedure ¹ (n = 189 procedures)	50.2 ± 32.4	8 - 174
Total procedure time ¹ (n = 190 procedures)	341.6 ± 166.9 (5.7 ± 2.8 hours)	96 - 925
Total fluoroscopy time/procedure for subjects with additional rhythms ablated during index procedure (n = 28 procedures)	58.8 ± 24.7	18 - 115
Total fluoroscopy time/procedure for subjects without concomitant ablation (n = 161 procedures)	48.7 ± 33.4	8 - 174
Total procedure time for subjects with additional rhythms ablated during index procedure (n = 28 procedures)	503.8 ± 193.0 (8.4 ± 3.2 hours)	158 - 804
Total procedure time for subjects without concomitant ablation (n = 162 procedures)	313.5 ± 145.2 (5.1 ± 2.4 hours)	96 - 925

¹ Incomplete fluoroscopy time was reported for one (1) subject and incomplete procedure time was reported for one (1) subject.

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C.2 - Acute Procedural Success

Acute success, defined as complete bi-directional conduction block across the isthmus at a minimum of 60 minutes following application of the last RF application, was analyzed. Acute success evaluation was based on the Efficacy Population, which was defined as all subjects who received ablation therapy with the investigational catheter and in whom a valid assessment of BDB could be made ($n = 190 - 4 = 186$).

Table 107 describes the acute ablation outcomes.

Table 101 – Acute Ablation Outcomes (n = 186)

	# Success/ # Subjects Ablated	% (One-Sided 95% Confidence Bound)
Acute study results	158/186	85% (80%)
OPC		88% (80%)

C.3 - Composite Assessment of Atrial Flutter Ablation Success

As noted in the above section, 158 subjects had BDB confirmed acutely after the ablation procedure.

In addition, of the four subjects in whom BDB was not measured acutely after the ablation procedure, 3 subjects were free of recurrence of atrial flutter at 6 months follow-up and one could not be validated. For the composite assessment, the 3 subjects were considered a success and the 1 subject a failure.

Table 108 summarizes the composite results.

Table 102 – Composite Assessment of Atrial Flutter Success

	# Success/ # Subjects Ablated	% (One-Sided 95% Confidence Bound)
Study results	161/190	85% (80%)
OPC		88% (80%)

C.4 - Freedom from Type I Atrial Flutter Recurrence at Six-Month Follow-Up

As indicated in section B.1 above, long-term freedom from atrial flutter recurrence was not a study endpoint. The long-term results are presented here in order to assess the suitability of the surrogate endpoint BDB.

Freedom from Type I atrial flutter recurrence was evaluated in subjects in whom BDB was achieved (as measured acutely) and for whom 6-month post-ablation information was available. Based on these criteria, information was available on a total of 147 subjects.

Results are described in Table 109 below.

**Table 103 – Freedom from Type I Atrial Flutter at 6 Months
(Results Based on 147 Subjects)**

Description	N	%
Subjects in whom BDB was achieved acutely and for whom 6-month information was available	147	100%
Subjects free from recurrence	136	93%
Subjects free from recurrence and anti-arrhythmic drug change	118	80%
Subjects with recurrence of atrial flutter	11	
Subjects with AAD changes to treat atrial fibrillation	15	
Subjects with AAD changes to treat atrial or supraventricular tachycardias	3	

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These results provide reasonable evidence that acute procedural success serves as an appropriate surrogate for long-term freedom from atrial flutter recurrence.

C.5 - Adverse Events

A major adverse event was defined as any clinical event that occurred within seven days post-ablation and which resulted in (1) death, (2) a life-threatening complication, or (3) a persistent or significant disability/incapacity that required inpatient hospitalization or prolonged hospitalization or required intervention to prevent a permanent impairment of a body function or damage to a body structure. A minor adverse event was defined as any adverse event resulting in minimal transient impairment of a body function or damage to a body structure, or which did not require any intervention other than monitoring or events occurring more than 7 days post-ablation.

Major Adverse Events

Of the 190 subjects who received ablation therapy with the investigational catheter, 33 major adverse events were reported in 30 subjects. The overall percentage of subjects who experienced a major adverse event was 15.8%. The one-sided 95% confidence bound rate was 20.9%. For subjects who had the investigational catheter inserted and used for mapping and/or ablation (n = 195), the major adverse event rate was 15.4%, and the one-sided 95% confidence bound rate was 20.4%.

Table 110 summarizes the major adverse events.

Table 104 – Major Adverse Events Observed within 7 Days Post-Ablation

Total Number Subjects with a Major AE (n = 30)	
Cardiovascular subjects	Total = 15
Arrhythmia complications = 5 subjects	
Complete atrio-ventricular block during procedure	
Bradycardia requiring pacemaker implant	
Ventricular tachycardia	
Atrial fibrillation	
Atrial fibrillation & atypical atrial flutter	
Pericardial effusion/tamponade = 4 subjects	
Pericardial tamponade	
Pericardial tamponade after mapping only	
Pericarditis with effusion	
RA thrombus, LV thrombus and pericardial effusion	
Intracardiac thrombus = 2 subjects	
RAA thrombus	
RA thrombus, LV thrombus and pericardial effusion	
Myocardial infarction = 1 subject	
Congestive heart failure = 4 subjects	
Pedal edema	
Dyspnea, rales requiring furosemide	
Dyspnea treated with one dose furosemide	
Pulmonary edema by PE treated with one dose furosemide	
Pulmonary subjects	Total = 8
Acute respiratory distress syndrome = 2 subjects	
Aspiration pneumonia = 2 subjects	
Pneumonia = 3 subjects	
Asthma = 1 subject	

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Total Number Subjects with a Major AE (n = 30)	
Anesthesia related subjects	Total = 2
Sedation induced apnea (intubation not required)	
Sedation induced CO ₂ retention with lethargy (intubation not required)	
Vascular subjects	Total = 2
Arteriovenous fistula/femoral artery-saphenous vein	
Pseudoaneurysm/right femoral artery	
Urologic subjects	Total = 2
Urinary tract infection	
Urinary retention	
Cholecystitis	Total = 1 Subject
Neurologic Subjects	Total = 2
Parkinson's disease	
Transient extremity numbness/possible TIA	

Note: Some subjects are listed more than once in the above table.

Three subjects died during the course of the study. One subject died due to cardiac arrest caused by cardiomyopathy and chronic obstructive pulmonary disease (COPD) complications 11 days post-ablation, one subject died following pulmonary valve replacement surgery 2 months post-ablation, and the third death was due to lung cancer more than 2 years following the ablation procedure. All deaths were determined to be unrelated to the procedure and device.

An overall risk/benefit evaluation of these adverse events was performed and a detailed review of each adverse event was completed. The adverse event rate described above was assessed to be specifically correlated to (1) the concomitant ablation procedures performed during the index procedure and (2) the increased number of co-morbid conditions present in the subject population enrolled relative to the patient population from which the OPCs were derived. See section C.1 for a list of concomitant ablation procedures.

C.6 - Statistical Analysis

Table 111 summarizes the safety and effectiveness of the device when compared to the control group OPC established for safety and acute success.

Table 105 – Comparison of Endpoints between NAVISTAR™ THERMOCOOL™ Study and OPC

Endpoint	OPC		NAVISTAR™ THERMOCOOL™ Study	
	%	One-Sided 95% Confidence Bound	% (n)	One-Sided 95% Confidence Bound
Acute success	88%	80%	85% (161/190)	80% (lower bound)
Major complications	2.7%	7%	15.8% (30/190)	20.9% (upper bound)

With comparison of the lower bounds of the acute success endpoints (80% vs. 80%), the results demonstrate that the NAVISTAR™ THERMOCOOL™ Catheter met the OPC for acute success. As previously explained in section C.5, although the device exceeded the upper bound of major complications, review of the specific events showed that they were related to the concomitant ablation procedures performed in addition to atrial flutter ablation and the subject population co-morbid conditions. Accordingly, study results demonstrate a reasonable assurance of the safety profile of the device.

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STUDY 2: Post-Approval Study

A. Objective

The primary objective was to provide additional, corroborative safety and efficacy data for the NAVISTAR™ THERMOCOOL™ Catheter for the treatment of subjects with typical atrial flutter (AFL).

B. Study Design

This study was a prospective, non-randomized, single-arm, multi-center post-approval evaluation.

B.1 - Study Endpoints

The endpoints for the study were as follows:

- **Primary safety endpoint** – the percentage of subjects experiencing Cardiovascular Specific Adverse Events (CSAE) within seven (7) days of the ablation procedure; and
- **Primary efficacy endpoint** – defined as complete bi-directional conduction block (BDB) across the sub-eustachian (cavo-tricuspid) isthmus at a minimum of 30 minutes following the last RF application.

B.2 - Objective Performance Criteria (OPC)

Objective performance criteria (OPC) were prospectively established. The OPCs are defined below:

- **Safety** – A CSAE rate below 2.7%, corresponding to a one-sided 95% upper confidence bound of 7%, was required to successfully achieve the safety endpoint.
- **Efficacy** – An efficacy success rate of 88% with a one-sided lower confidence bound of 80% was required for effectiveness success.

B.3 - Subject Accountability

Table 112 documents the accountability and disposition of enrolled subjects.

Table 106 – Subject Disposition (N = 291)

Category	N	%
Total Subjects Enrolled	291	100%
Excluded group	24	8.2%
Safety Cohort	267	91.8%
Discontinued group (no RF energy delivered via study catheter)	5	1.7%
Subject with typical AFL – non-evaluable ¹	1	0.3%
Subjects found to not have typical AFL	8	2.7%
Efficacy Cohort (evaluable subjects)	253	86.9%
Subjects with only typical AFL	236	81.1%
Subjects with typical AFL and other concomitant arrhythmia requiring ablation	17	5.8%

¹ Bidirectional block was not assessable in one subject due to an altered CS anatomy.

Safety Analysis Cohort (n = 267) The primary safety endpoint is the rate of occurrence of Cardiovascular Specific Adverse Events (CSAE), which is defined as “an event which occurs within the first week (7 days) following use of the device and is one of the following Cardiovascular Specific Adverse Events: cardiac perforation, pericardial effusion, pulmonary embolus, complete heart block, stroke, acute myocardial infarction, and death.” The protocol predetermined rate of CSAE was 2.7% with corresponding one-sided 95% upper confidence bound of 7%. The CSAE rate observed in the Safety Cohort (N = 267) was 1.5% (4/267). The one-sided 95% upper confidence bound for the Safety Cohort was 3.4%, which was below the cutoff rate of 7% required to achieve the safety endpoint.

Efficacy Analysis Cohort (n = 253) The primary efficacy endpoint of this study was defined as confirmation of complete bidirectional conduction block across the sub-eustachian (cavo-tricuspid) isthmus at a minimum of 30 minutes following the last RF application. An acute success rate of 88% was anticipated and the one-sided 95% lower confidence bound was compared to 80%. There was a total of

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253 subjects in the Efficacy Cohort. The overall acute efficacy success in the Efficacy Cohort was 93.3% (236/253), corresponding with a one-sided lower confidence bound of 90.1%. Acute efficacy success exceeded one-sided lower confidence bound of 80% as established in the protocol, thus the primary efficacy endpoint was met.

B.4 - Subject Demographics

Table 113 summarizes the demographic information of all study subjects enrolled in the study.

**Table 107 – Subject Demographics
(All Enrolled Subjects, n = 291)**

Gender	N	%
Female	48	16.5
Male	243	83.5
Age (years)		
Mean ± standard deviation	65.2 ± 12.1	
Range	19 - 92	

C. Results

C.1 - Intraprocedural Data

Table 114 and Table 115 describes the procedural data.

Seventeen (17) subjects received ablation therapy for an arrhythmia other than Type I atrial flutter during the same index ablation procedure. The additional arrhythmias ablated were: 10 right atrial tachycardia/non isthmus dependent flutter/scar flutter/ectopic, 4 left atrial tachycardia/flutter/scar flutter, 3 AVNRT, and 2 atrial fibrillation. One subject had multiple concomitant arrhythmias treated.

C.2 - Efficacy Success

Efficacy success, defined as complete bi-directional conduction block across the isthmus at a minimum of 30 minutes following application of the last RF application, was analyzed. If conduction across the isthmus was present at the end of the procedure or if another device (non-study catheter), in addition to the study catheter, was utilized for ablation, the procedure was considered to be an acute failure.

Table 114 describes the efficacy success.

Table 108 – Efficacy Success (n = 253)

	# Efficacy Success/ # Subjects Ablated	% (one-sided 95% confidence bound)
Efficacy success	236/253	93.3% (90.1%)
OPC		88% (80%)

C.3 - Adverse Events

A Cardiovascular Specific Adverse Event (CSAE) was defined as an event that occurred within the first week (7 days) following use of the device and was one of the following Cardiovascular Specific Adverse Events: cardiac perforation, pericardial effusion, pulmonary embolus, complete heart block, stroke, acute myocardial infarction, and death.

Of the 267 subjects who received ablation therapy with the study catheter, four (4) CSAEs were reported in four (4) subjects (1.5% of Safety Cohort). The one-sided 95% confidence bound rate was 3.4%.

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Table 115 summarizes the CSAEs observed.

**Table 109 – Cardiovascular Specific Adverse Events
Observed within 7 Days Post-Ablation**

Total Number Subjects Experiencing a CSAE (n = 4)
Pulmonary embolus = 1 subject, possibly procedure related
Complete heart block = 2 subjects, both unrelated to device or procedure
Myocardial infarction = 1 subject, unrelated to device or procedure

Three of the four CSAEs were determined by the investigators to be unrelated to the procedure or device and the remaining CSAE was deemed to be possibly procedure related.

There were three reported deaths during the course of the study, though no deaths occurred during the ablation procedure or during the study follow-up period. One subject died prior to the scheduled study procedure due to either pulmonary embolus or myocardial infarction. The other two subjects died after the completion of the study follow up period due to cancers (metastatic adenocarcinoma and lung cancer). All deaths were determined to be unrelated to the device or procedure.

An overall risk/benefit evaluation of these adverse events was performed and a detailed review of each adverse event was completed.

C.4 - Statistical Analysis

Table 116 summarizes the safety and effectiveness of the device compared to the OPC established for safety and efficacy.

**Table 110 – Endpoints Comparison between
NAVISTAR™ THERMOCOOL™ Catheter Post-Approval Study and OPC**

Primary Endpoints	OPC		NAVISTAR™ THERMOCOOL™ Study	
	%	One-Sided 95% Confidence Bound	% (N)	One-Sided 95% Confidence Bound
Safety (CSAEs)	2.7%	7%	1.5% (4/267)	3.4% (upper bound)
Efficacy	88%	80%	93.3% (236/253)	90.1% (lower bound)

The results demonstrate that the NAVISTAR™ THERMOCOOL™ Catheter met the OPC for safety and efficacy.

SUMMARY OF CLINICAL STUDIES CONDUCTED FOR ATRIAL FIBRILLATION INDICATION

The clinical testing described below was performed with the NAVISTAR™ THERMOCOOL™ Catheter.

A. Objective

The primary objective of this trial was to demonstrate the safety and efficacy of the NAVISTAR™ THERMOCOOL™ Catheter for the radiofrequency ablation treatment of subjects with symptomatic Paroxysmal Atrial Fibrillation (PAF) who were refractory or intolerant to antiarrhythmic drug therapy.

B. Study Design

The study was a prospective, randomized, unblinded, multi-center pivotal clinical investigation conducted at 19 investigational sites (15 in the US and 4 outside of the US).

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B.1 - Study Endpoints

The endpoints for the study were as follows:

The **primary effectiveness endpoint** was the chronic success rate of the NAVISTAR™ THERMOCOOL™ Catheter for the treatment of symptomatic PAF.

Acute success was defined as confirmation of entrance block in all targeted pulmonary veins.

Chronic success was defined as freedom of symptomatic AF based on electrocardiographic data and no changes in Anti-Arrhythmic Drug (AAD) regimen during comparable evaluation periods for the THERMOCOOL™ Catheter and AAD (Control) groups. AF status was evaluated by periodic transtelephonic monitoring and 24-hour Holter recordings.

Quality of life was evaluated using the AF frequency/severity checklist and SF-36 questionnaire.

The **primary safety endpoint** was the incidence of early onset (within 7 days of the ablation procedure) primary adverse events. This included the following adverse events:

- Death
- Myocardial Infarction (MI)
- Pulmonary Vein (PV) stenosis
- Diaphragmatic paralysis
- Atrio-esophageal fistula
- Transient Ischemic Attack (TIA)
- Stroke
- Cerebrovascular accident (CVA)
- Thromboembolism
- Pericarditis
- Cardiac tamponade
- Pericardial effusion
- Pneumothorax
- Atrial perforation
- Vascular access complications
- Pulmonary edema
- Hospitalization (initial and prolonged)
- Heart block

Secondary safety endpoints included comparisons between the THERMOCOOL™ Catheter and AAD (Control) groups on the following:

- Early onset (≤ 90 days post treatment) of serious adverse events
- Late onset (≥ 90 days post treatment) of serious adverse events

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B.2 - Subject Accountability

Table 111 – Subject Accountability and Disposition

Total Number of Subjects Enrolled	167
Subjects randomized to THERMOCOOL™ Catheter	106
Excluded subjects	3
Subjects who underwent ablation with the study catheter	103
Discontinued subjects	0
Subjects randomized to AAD (Control)	61
Excluded subjects	4
Subjects administered AAD therapy	57
Discontinued subjects	1
AAD (Control) subjects undergoing RF ablation	36

The following definitions were used to classify subjects:

Effectiveness Analysis Cohort (n = 159) was comprised of subjects that received the treatment that they were randomized to and also did not meet the definitions of being excluded or discontinued.

Primary Safety Analysis Cohort (n = 139) was comprised of subjects that underwent insertion of the THERMOCOOL™ Catheter, including subjects that were randomized to AAD (Control) group and became eligible for RF ablation with the THERMOCOOL™ Catheter.

Secondary Safety Analysis Cohort (n = 160) was comprised of subjects that received the treatment that they were randomized to, including subjects classified as discontinued.

B.3 - Subject Demographics

Table 118 summarizes the demographic information. Subjects were randomized 2:1 upon signing informed consent.

Table 112 – Subject Demographics

	THERMOCOOL™ Catheter n/N (%)	AAD (Control) n/N (%)	Total n/N (%)	p-value
	N = 106	N = 61	N = 167	
Gender				0.3997
Female	33/106 (31.1)	23/61 (37.7)	56/167 (33.5)	
Male	73/106 (68.9)	38/61 (62.3)	111/167 (66.5)	
Ethnicity				0.7031
Hispanic	1/106 (0.9)	0/61 (0.0)	1/167 (0.6)	
Other	2/106 (1.9)	0/61 (0.0)	2/167 (1.2)	
White	103/106 (97.2)	61/61 (100.0)	164/167 (98.2)	
Age (years)				0.3009
Mean	55.5 ± 9.34	56.1 ± 12.84	55.7 ± 10.72	
Median	56	58	57	
Min/Max	32/76	19/77	19/77	
Left atrial dimension (mm)¹				0.7118
Mean	40.0 ± 5.5	40.3 ± 5.3	40.1 ± 5.4	
Median	40	41	40	
Min/Max	27.0/50.0	26.5/49.0	26.5/50.0	

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	THERMOCOOL™ Catheter n/N (%)	AAD (Control) n/N (%)	Total n/N (%)	p-value
	N = 106	N = 61	N = 167	
Left ventricular ejection fraction (%)²				0.4670
Mean	62.3 ± 9.8	63.1 ± 7.4	62.6 ± 9.0	
Median	62	63	63	
Min/Max	30.0/86.0	44.0/80.0	30.0/86.0	

¹ Data are not available for 15 subjects (6 in THERMOCOOL™ Catheter group and 9 in AAD group).

² Data are not available for 14 subjects (7 in THERMOCOOL™ Catheter group and 7 in AAD group).

The age in the Table 118 was when the subject signed the informed consent. The p-value listed compares the randomized groups. There was one subject of Arab ethnicity and one subject that was Native American.

Subjects enrolled in the study reported a mean of 63.2 ± 92.4 atrial fibrillation episodes in the six months prior to baseline. Patients classified as New York Heart Association (NYHA) Class III and IV were excluded from the study. Approximately half of the enrolled subjects had a history of hypertension at baseline; 48.6% (51/105) in the THERMOCOOL™ Catheter group and 50.0% (30/60) in the AAD (Control) group. Less than a third of the enrolled subjects (27.7%; 44/159) had a history of atrial flutter at baseline. The overall mean number of AADs failed at baseline was 2.2 ± 1.2, with 27 of the 167 enrolled subjects having previously failed only a Class II/IV AAD.

C. Results

C.1 - Procedural Data

Table 119 and Table 120 presents the procedural data.

Table 113 – Summary of RF Applications, Saline Infused, Power, Temperature, and Impedance Data (THERMOCOOL™ Catheter Effectiveness Cohort, n = 103¹)

Description	Mean ± Standard Deviation
Number of RF applications (n = 125 procedures)	53.2 ± 36.6
Mean saline infused (ml) by NAVISTAR™ THERMOCOOL™ Catheter (n = 123 procedures)	1591.0 ± 752.7
Maximum power (W)/procedure (n = 125 procedures)	41.5 ± 7.1
Maximum temperature (°C)/procedure (n = 126 RF procedures)	43.9 ± 4.1
Maximum impedance (Ω)/procedure (n = 125 RF procedures)	135.4 ± 25.4

¹ Complete procedural data were not reported for all subjects.

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Table 114 – Summary of Ablation Procedure Parameters, All Ablation Procedures (THERMOCOOL™ Catheter Effectiveness Cohort, n = 103¹)

Procedure Parameters	THERMOCOOL™ Catheter Group Mean ± SD (n)
Total procedure time (min)	211.3 ± 86.1 (126)
Ablation procedure time (min)	111.0 ± 62.6 (127)
Total fluoroscopy duration (min)	47.9 ± 40.2 (127)
Total fluid input (ml)	2877.5 ± 1914.0 (125)
Total fluid output (ml)	783.8 ± 884.4 (126)
Balance (input-output) (ml)	2193.0 ± 1348.2 (121)

¹ Data parameters not available for all ablation procedures.

Note: Table 119 and Table 120 includes all ablation procedures for subjects randomized to the THERMOCOOL™ Catheter group, including 24 repeat ablation procedures (average of 1.2 ablation procedures per subject).

The overall fluoroscopy and procedure times reported include both the investigational (NAVISTAR™ THERMOCOOL™ Catheter) procedure time and all other procedures performed during the subject's stay in the electrophysiology (EP) lab. Therefore, the data do not solely reflect the actual use of the NAVISTAR™ THERMOCOOL™ Catheter.

All AF ablation procedures began with circumferential lesions targeting all pulmonary veins, with additional atrial ablation lines created as clinically required.

Table 121 summarizes the lesion sets applied to THERMOCOOL™ Catheter group subjects during the index ablation procedures.

Table 115 – Outcomes by Ablation Targets per Subject – 1st Ablation Procedure (THERMOCOOL™ Catheter Group Subjects, n = 103)¹

Ablation Targets	THERMOCOOL™ Catheter Group (n = 103)		
	Success n (%)	Fail n (%)	Total n (100%)
Pulmonary veins (PV) only	18 (41.9)	25 (58.1)	43 (100.0)
≥ 4 PV	17	24	
< 4 PV	1	1	
PV + atrial lines	28 (84.8)	5 (15.2)	33 (100.0)
+ Right atrial lines	11	3	
+ Left atrial lines	2	2	
+ Combination left and right	15	0	
PV + foci	3 (42.9)	4 (57.1)	7 (100.0)
PV + atrial lines + foci	4 (66.6)	2 (33.4)	6 (100.0)
TOTAL	53 (59.6)	36 (40.4)	89 (100.0)

¹ 14 subjects are still within the effectiveness evaluation period and were not included in this analysis.

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C.2 - Acute Procedural Success

Acute procedural success results are presented in Table 122.

**Table 116 – Acute Effectiveness Outcome
(NAVISTAR™ THERMOCOOL™ Catheter Group, n = 103¹)**

	NAVISTAR™ THERMOCOOL™ Catheter Group n
Underwent RF study procedure	103
Entrance block confirmed	102 ²
Ablation procedure > 80 days	2
Non-study catheter utilized for AF targets	0
> 2 repeat ablation procedures	0
Acute effectiveness success	100

¹ Includes all THERMOCOOL™ Catheter group subjects undergoing ablation with the study catheter.

² End of procedure information for one subject was not available.

C.3 - Chronic Success – Freedom from Chronic Effectiveness Failure

Primary Effectiveness Analysis

A pre-specified interim analysis was performed per the clinical trial protocol, and the results demonstrated sufficient statistical evidence of the study meeting the effectiveness endpoint. As a result, enrollment was stopped and the trial was declared an early success.

The critical results of the Bayesian analysis are the predictive probability of success for 230 patients and the posterior probability of superiority for the THERMOCOOL™ Catheter group. The posterior probability that the THERMOCOOL™ Catheter group is superior to the AAD (Control) group is essentially 1 (> 0.9999). The model estimates the probability of success for a subject in the THERMOCOOL™ Catheter group is 0.627 with a standard deviation of 0.048. For a subject in the AAD (Control) group, the posterior mean probability of success is 0.172 with a posterior standard deviation of 0.049. The predictive probability of success for the original maximum sample size of 230 subjects is also essentially 1 (> 0.9999). That is, if the full sample size of 230 had been enrolled, it is a virtual certainty that the final posterior probability would have been larger than 0.98 (protocol specified level needed for success).

Chronic success results are described in Table 123.

Table 117 – Summary of Data Available¹ – June 2008 Dataset

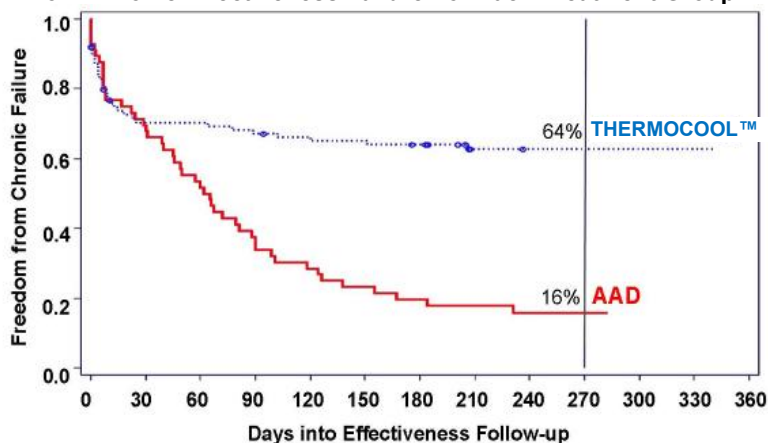
Group	0 < t ≤ 0.5			0.5 < t ≤ 2			2 < t ≤ 9		
	Expos	Fail	Rate	Expos	Fail	Rate	Expos	Fail	Rate
THERMOCOOL™ Catheter	40.21	26	0.647	104.17	3	0.029	413.09	7	0.017
AAD (Control)	23.27	13	0.559	54.21	14	0.258	90.46	20	0.221

¹ The exposure (Expos) time in months and number of failures (Fail) are reported for each of the three intervals in the time to event model.

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Figure 25 shows the Kaplan-Meier curves for each of the treatment groups for freedom from chronic effectiveness failure (n = 159) and shows superiority of the THERMOCOOL™ Catheter group (64%) compared to AAD group (16%) for the primary effectiveness endpoint.

Figure 25 – Kaplan-Meier Analysis – Probability of Freedom from Chronic Effectiveness Failure For Each Treatment Group



The June 2008 dataset status of each of the 159 subjects is reported in Table 124. At the time of this analysis, subjects were classified as “Success,” “Failure,” or “Censored” (i.e., those subjects that had not failed, but did not have complete 9-month follow-up).

Table 118 – Summary of the Status of Each of the Enrolled Subjects

Group	Success	Censored	Fail	n
THERMOCOOL™ Catheter	53	14	36	103
AAD (Control)	9	0	47	56

Site variation in primary effectiveness outcome was observed in this study. In particular, one investigational site located outside of the United States had a higher success rate than the remainder of the investigational sites. Various sensitivity analyses were performed which demonstrated that the study conclusions were robust to this site variation.

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Figure 26 shows that the 9-month failure-free rate in the THERMOCOOL™ Catheter group is superior to that of the AAD (Control) group. The 95% credible interval for the difference between the treatment and control probability of success is (0.313, 0.584) with a median difference of 0.457.

Figure 26 – The Posterior Distributions of the Probabilities of 9-Month Failure-Free Treatment Success for Each Treatment Group

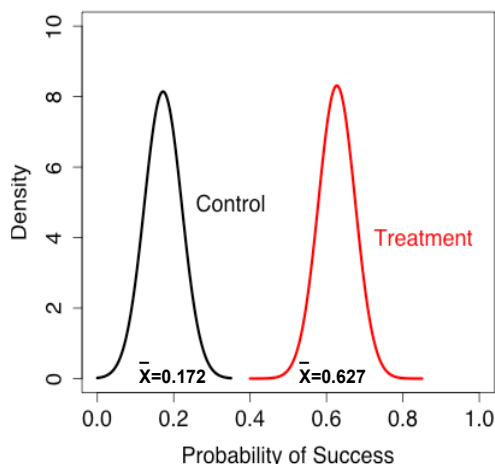
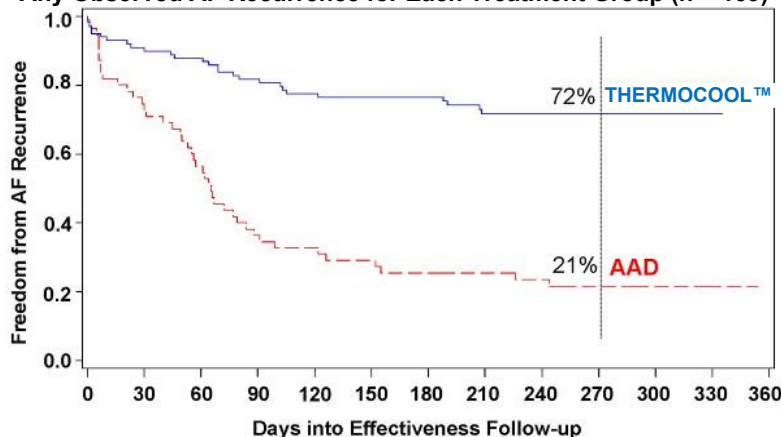


Figure 27 demonstrates that the THERMOCOOL™ Catheter group had a higher probability of freedom from any documented symptomatic or asymptomatic AF recurrence, subject to the monitoring provisions of the protocol, than the AAD (Control) subjects. The difference in likelihood of AF recurrence after 9 months of effectiveness evaluation was 51% (72% vs. 21%) in favor of the THERMOCOOL™ Catheter treatment group.

Figure 27 – Kaplan-Meier Analysis – Probability of Freedom from Any Observed AF Recurrence for Each Treatment Group (n = 159)



C.4 - Adverse Events (AE)

The primary safety endpoint for this study was defined as the incidence of early-onset (within 7 days of ablation procedure) primary AEs for subjects undergoing a study ablation procedure. The Primary Safety Cohort (n = 139) was comprised of THERMOCOOL™ Catheter group subjects (n = 103) and AAD (Control) group subjects undergoing an ablation procedure (n = 36).

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Primary Safety Endpoint – Primary Adverse Events

Table 125 presents the protocol-established endpoint and safety results based on the June 2008 dataset. There were 16 primary AEs reported for 15 subjects. The overall percentage of subjects who experienced a serious primary AE was 10.8% (15/139) and the upper confidence bounds based on the Primary Safety Cohort was 16.1%. The safety endpoint specified in the protocol was 7.0% (upper confidence bound of 16.0%). While the primary safety results exceeded the protocol-established primary safety endpoint for this study, the nature and types of adverse events experienced in this trial nonetheless represent an acceptable risk profile.

**Table 119 – Primary Safety Endpoint Outcome – Primary Adverse Events
(Primary Safety Cohort, n = 139)**

	Protocol Established Endpoint	n
Number of subjects in Safety Cohort		139
Number of subjects with primary AEs		15
% primary AEs	7.0	10.8
One-sided 95% confidence bound ¹	16.0	16.1

¹ Exact binomial using a commercially available software package.

Table 126 summarizes the major primary AEs.

**Table 120 – Primary Safety Endpoint –
Early-Onset (within (≤) 7 Days) Primary Adverse Events
(Primary Safety Cohort, n = 139)**

Description	Number of Subjects with Primary AEs n/139 (%)
Total Serious Primary AEs	15 (10.8%)
Death	0
Atrio-esophageal fistula	0
Atrial perforation	0
Cardiac tamponade	0
Myocardial infarction	0
Stroke	0
Cerebrovascular accident	0
Thromboembolism	0
Transient ischemic attack	0
Diaphragmatic paralysis	0
Pneumothorax	0
Heart block	0
Pulmonary vein stenosis	0
Pulmonary edema	1 (0.7%)
Pericarditis	1 (0.7%)
Hospitalization (initial and prolonged)	7 (5.0%)
Pericardial effusion	1 (0.7%)
Vascular access complication	5 (3.6%)

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Table 127 compares the incidence of early onset serious adverse events (SAE) between the two treatment groups occurring within the first 90 days of initial therapy.

**Table 121 – Percentage of Early Onset SAE by Randomization Group
(Overall Safety Cohort, n = 160)**

Randomization Group	Percent % of SAEs (n/N)	p-value
THERMOCOOL™ Catheter Group	18.4 (19/103)	0.022
AAD (Control) Group ¹	35.1 (20/57)	

¹ For AAD subjects undergoing an ablation procedure, only SAE prior to an ablation procedure were considered in this analysis.

One subject in the THERMOCOOL™ Catheter group expired during the effectiveness evaluation period. This event occurred 284 days after the ablation procedure and was considered to be unrelated to the investigational device and procedure.

C.5 - Study Conclusion

In conclusion, the results demonstrate that there is a reasonable assurance of safety and effectiveness to support the use of the NAVISTAR™ THERMOCOOL™ Catheter for the treatment of drug refractory recurrent symptomatic paroxysmal atrial fibrillation, when used with advanced three-dimensional electroanatomic mapping systems.

SUMMARY OF CLINICAL STUDIES CONDUCTED FOR ALTERNATIVE IMAGING TO DETERMINE CATHETER TIP LOCATION

STUDY 1: Zero/Low Fluoroscopy: A nested sub-study of REAL AF Registry

A. Objective

The objective of the study was to evaluate the safety and acute effectiveness of radiofrequency catheter ablation of paroxysmal atrial fibrillation (PAF) using a zero/low fluoroscopy workflow during standard of care practice.

B. Study Design

The study was a multicenter, prospective/retrospective, non-randomized, observational clinical investigation to evaluate the safety and acute effectiveness of radiofrequency ablation of PAF using a zero/low fluoroscopy workflow.

Consecutive eligible first-time drug refractory PAF catheter ablation patients from the REAL AF Registry treated in a zero/low fluoroscopy workflow were included. The REAL AF Registry consists of centers of private and academic institutions with the primary purpose of obtaining real-world clinical experience of atrial fibrillation (AF) ablation using contemporary radiofrequency technologies (e.g., THERMOCOOL SMARTTOUCH™, THERMOCOOL SMARTTOUCH™ SF). Only data from 16 sites in the United States (US) were used in this sub-study. All operators in the 16 sites have a target fluoroscopy time of less than 3 minutes for an AF ablation procedure. If the primary safety endpoint for the REAL AF Registry was met the following were to be performed:

- Secondary acute effectiveness endpoint from the REAL AF Registry tested by comparing the observed acute effectiveness against the performance goal of 90%.
- Descriptive comparison of the secondary safety endpoint between the zero/low fluoroscopy workflow group and the conventional fluoroscopy workflow group within the Mercy electronic health record (EHR) system database. Mercy is a large US integrated delivery network with hospitals and clinics in several states across the US. The secondary descriptive analysis from the Mercy EHR system database included all PAF patients who met the eligibility criteria similar to those of the REAL AF Registry. Patients treated using either THERMOCOOL SMARTTOUCH™ SF or THERMOCOOL SMARTTOUCH™ catheters were included from the Mercy EHR system database. The data were analyzed using both covariate-unadjusted and covariate-balanced data with point estimates for the cumulative incidence and within each group and for the risk difference between the groups provided.

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B.1 - Study Endpoints

The endpoints for the study were as follows:

The **primary safety endpoint** was the occurrence of procedure or device related primary adverse events (Table 128) within 7 days of the initial ablation procedures in the REAL AF Registry. Device or procedure related death, severe pulmonary vein stenosis, and atrio esophageal fistula up to 90 days and cardiac tamponade/perforation up to 30 days post-index procedure were also considered primary adverse events (Table 128).

Table 122 – REAL AF Zero/Low Fluoroscopy Sub-Study Primary Adverse Events

Primary Adverse Events (PAE)	
Atrio-Esophageal Fistula ¹	Phrenic Nerve Paralysis/injury
Cardiac Tamponade/Pericardial Effusion ¹	Severe Pulmonary Vein Stenosis (>70% reduction in the diameter of PV) ¹
Procedure or Device-Related Death ¹	Stroke/CVA
Major Vascular Access Complication/Bleeding including Hematoma, arteriovenous fistula, and pseudoaneurysm	Thromboembolism
Myocardial Infarction	Transient Ischemic Attack (TIA)
Pericarditis	Vagal nerve injury

¹ Procedure or device related death, severe pulmonary vein stenosis, and atrio-esophageal fistula that occurred greater than 1 week (7 days) post-procedure up to 90 days and cardiac tamponade/pericardial effusion that occurred greater than 1 week (7 days) post-procedure up to 30 days were considered and analyzed as PAEs.

The **secondary acute effectiveness endpoint** was acute effectiveness success which was defined as confirmation of pulmonary vein isolation in all targeted pulmonary veins, evaluated in the REAL AF Registry.

The **descriptive comparison of the secondary safety endpoint** between the group with fluoroscopy time of ≤ 2 minutes and the group with fluoroscopy time of ≥ 3 minutes within the Mercy EHR database based on the covariate-balanced data with point estimates for the cumulative incidence within each group and for the risk difference between the groups.

B.2 - Objective Performance Criteria (OPC)

Objective performance goals were prospectively established.

- **Safety** – Performance Goal = 10% upper bound of the 95% confidence interval around the primary adverse event rate
- **Acute Effectiveness** – Performance Goal = 90% lower bound of the 95% confidence interval around the isolation of all targeted pulmonary vein rate (effectiveness success)

B.3 - Subject Accountability

Table 123 – REAL AF Zero/Low Fluoroscopy Sub-Study Analysis Sets

Analysis Set	n
Full Analysis Set ¹	208
Retrospective Enrollment	48
Prospective Enrollment	160

¹Full Analysis Set: Includes all consecutive sub-study protocol eligible subjects in the REAL AF Registry who underwent their first-time catheter ablation procedure for PAF using the THERMOCOOL SMARTTOUCH™ or THERMOCOOL SMARTTOUCH™ SF catheter.

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Table 124 – REAL AF Zero/Low Fluoroscopy Sub-Study Subject Enrollment and Accountability

Subject Enrollment	n
Full Analysis Set ¹	208
Zero Fluoroscopy Subjects	104
Non-Zero Fluoroscopy Subjects	104
Lost to Follow-up Subjects ²	2
Death	1
Completed Subjects ³	10
Ongoing	195
Subjects with 3 Month Follow-up data	197

¹ Full Analysis Set: Includes all consecutive sub-study protocol eligible subjects in the REAL AF Registry who underwent their first-time catheter ablation procedure for PAF using the THERMOCOOL SMARTTOUCH™ or THERMOCOOL SMARTTOUCH™ SF catheter.

² Lost to Follow-up Subjects: Subjects with whom contact is lost after the index procedure or most recent follow-up visit.

³ Completed Subjects: Subjects who complete the 12-month follow-up visit.

Table 125 – Mercy EHR Database Patient Population Attrition

Attrition Criteria	No. of Patients	No. of Patients Lost	% Patients Lost
Inclusion criteria			
Patients who underwent an intracardial catheter ablation of AF since 2015	2,903	-	-
Patients with a primary or secondary diagnosis of PAF associated with the same intracardiac catheter ablation procedure encounter	1,392	1,511	52.05%
The first recorded intracardiac catheter ablation of AF with a primary or secondary diagnosis of PAF since 2015 was designated the index ablation procedure	1,392	0	0.00%
Index ablation procedure performed using either THERMOCOOL SMARTTOUCH™ SF or THERMOCOOL SMARTTOUCH™ catheters	1,107	285	20.47%
Had at least one class I or III antiarrhythmic drug prescription prior to the index ablation procedure	721	386	34.87%
18 years of age or older at the time of the index ablation procedure	721	0	0.00%
At least 6 months of encounter history prior to the index ablation procedure	629	92	12.76%
No recorded ablation prior to the index ablation procedure in the database	519	110	17.49%
Number of patients who met all inclusion criteria	519		
Exclusion criteria			
Did not have at least one class I or III antiarrhythmic drug prescription prior to the index ablation procedure	519	0	0.00%
Had a diagnosis of any primary safety events within 3 months prior to the index ablation procedure	503	16	3.08%
Missing fluoroscopy time of the index ablation procedure	349	154	30.62%

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Attrition Criteria	No. of Patients	No. of Patients Lost	% Patients Lost
Number of patients who met at least one exclusion criterion		170	
Number of patients who met all eligibility criteria	349		
Fluoroscopy time: ≤ 2 minutes	129		
Fluoroscopy time: ≥ 3 minutes	170		
Fluoroscopy time: > 2 minutes and < 3 minutes	50		

Primary Safety Analysis Cohort (n = 197 from the 208 REAL AF Zero/Low Fluoroscopy Sub-study full analysis set [FAS] subjects) was comprised of subjects with available endpoint data.

Secondary Acute Effectiveness Cohort (n = 202 from the 208 REAL AF Zero/Low Fluoroscopy Sub-study FAS subjects) was comprised of subjects with available endpoint data.

Descriptive Comparison of the Secondary Safety Cohort was comprised of 299 subjects for the comparison of the group with fluoroscopy time of ≤ 2 minutes and the group with fluoroscopy time of ≥ 3 minutes and 349 subjects for the sensitivity analysis using an alternative cutoff (i.e., fluoroscopy ≤ 2 minutes vs > 2 minutes).

B.4 - Subject Demographics and Baseline Characteristics

The tables below summarize the demographics and baseline characteristics information.

Table 126 – REAL AF Zero/Low Fluoroscopy Sub-Study Demographics

Analysis Variable	All (N=208)	Retrospective (N=48)	Prospective (N=160)
Age (year)¹			
N	208	48	160
Mean	65.1	62.5	65.8
Standard Deviation	10.63	11.84	10.15
Median	66.0	63.0	67.0
Q1/Q3	59.0/73.0	57.0/71.0	59.0/73.0
Min/Max	25/87	25/83	31/87
Sex, n/N (%)			
Male	106/208 (51.0%)	19/48 (39.6%)	87/160 (54.4%)
Female	102/208 (49.0%)	29/48 (60.4%)	73/160 (45.6%)
Ethnicity, n/N (%)			
Hispanic or Latino	3/208 (1.4%)	0	3/160 (1.9%)
Not Hispanic or Latino	196/208 (94.2%)	43/48 (89.6%)	153/160 (95.6%)
Declined/Unknown	6/208 (2.9%)	3/48 (6.3%)	3/160 (1.9%)

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Analysis Variable	All (N=208)	Retrospective (N=48)	Prospective (N=160)
Race, n/N (%)			
American Indian or Alaska Native	0	0	0
Asian	3/208 (1.4%)	0	3/160 (1.9%)
Black or African American	14/208 (6.7%)	3/48 (6.3%)	11/160 (6.9%)
Native Hawaiian or Other Pacific Islander	0	0	0
White	184/208 (88.5%)	43/48 (89.6%)	141/160 (88.1%)
Other	3/208 (1.4%)	0	3/160 (1.9%)
Declined or Unable to Disclose	1/208 (0.5%)	0	1/160 (0.6%)
Baseline BMI (kg/m²)			
N	207	48	159
Mean	29.77	28.95	30.01
Standard Deviation	5.988	5.445	6.137
Median	29.32	29.08	29.41
Q1/Q3	25.90 / 33.38	25.86 / 31.66	25.99 / 34.53
Min/Max	15.4 / 47.7	19.2 / 42.2	15.4 / 47.7
Current AAD, n/N (%)			
Class I	110/208 (52.9%)	24/48 (50.0%)	86/160 (53.8%)
Flecainide (Tambocar)	74/208 (35.6%)	20/48 (41.7%)	54/160 (33.8%)
Propafenone (Rythmol)	8/208 (3.8%)	1/48 (2.1%)	7/160 (4.4%)
Class III	53/208 (25.5%)	9/48 (18.8%)	44/160 (27.5%)
Amiodarone	36/208 (17.3%)	4/48 (8.3%)	32/160 (20.0%)
Dofetilide (Tikosyn)	1/208 (0.5%)	0	1/160 (0.6%)
Dronedarone (Multaq)	15/208 (7.2%)	4/48 (8.3%)	11/160 (6.9%)
Sotalol (Betapace)	29/208 (13.9%)	4/48 (8.3%)	25/160 (15.6%)
None	45/208 (21.6%)	15/48 (31.3%)	30/160 (18.8%)
Drug refractory (AAD Class I/III), n/N (%)	208/208 (100.0%)	48/48 (100.0%)	160/160 (100.0%)

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Analysis Variable	All (N=208)	Retrospective (N=48)	Prospective (N=160)
Pre-ablation OAC, n/N (%)			
None	17/208 (8.2%)	6/48 (12.5%)	11/160 (6.9%)
Coumadin	13/208 (6.3%)	0	13/160 (8.1%)
Eliquis	146/208 (70.2%)	33/48 (68.8%)	113/160 (70.6%)
Pradaxa	1/208 (0.5%)	0	1/160 (0.6%)
Savayesa	0	0	0
Xarelto	31/208 (14.9%)	9/48 (18.8%)	22/160 (13.8%)
Taking Aspirin, n/N (%)	56/208 (26.9%)	12/48 (25.0%)	44/160 (27.5%)
Sleep apnea			
Yes	54/208 (26.0%)	13/48 (27.1%)	41/160 (25.6%)
No	132/208 (63.5%)	32/48 (66.7%)	100/160 (62.5%)
Suspected	22/208 (10.6%)	3/48 (6.3%)	19/160 (11.9%)
HAS-BLED score²			
n	202	44	158
Mean	1.7	1.7	1.8
Standard Deviation	1.13	1.07	1.14
Median	2.0	1.5	2.0
Q1/Q3	1.0 / 3.0	1.0 / 2.5	1.0 / 3.0
Min/Max	0 / 5	0 / 4	0 / 5
CHA₂DS₂-VASc score³			
n	208	48	160
Mean	2.5	2.3	2.6
Standard Deviation	1.44	1.39	1.46
Median	2.0	2.0	2.0
Q1/Q3	2.0 / 3.0	1.0 / 3.0	2.0 / 3.0
Min/Max	0 / 8	0 / 6	0 / 8
Has an implantable device			
Implantable loop recorder	10/208 (4.8%)	2/48 (4.2%)	8/160 (5.0%)
Dual chamber or CRT Pacemaker	15/208 (7.2%)	2/48 (4.2%)	13/160 (8.1%)
Dual chamber or CRT ICD	15/208 (7.2%)	3/48 (6.3%)	12/160 (7.5%)

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Analysis Variable	All (N=208)	Retrospective (N=48)	Prospective (N=160)
Left Ventricle Ejection Fraction (%)			
n	125	26	99
Mean	56.32	54.89	56.70
Standard Deviation	8.815	8.294	8.948
Median	57.00	55.00	60.00
Q1/Q3	55.00/60.00	55.00/60.00	55.00/60.00
Min/Max	23.0/75.0	30.0/65.0	23.0/75.0
LA Diameter (cm)			
n	86	22	64
Mean	4.557	3.500	4.920
Standard Deviation	6.0996	0.8802	7.0296
Median	4.000	3.600	4.100
Q1/Q3	3.600/4.400	2.900/4.000	3.700/4.400
Min/Max	2.04/60.00	2.04/5.10	2.05/60.00
LA Volume (mL/m²)			
n	78	9	69
Mean	34.726	29.689	35.383
Standard Deviation	12.5605	7.4827	12.9717
Median	32.450	31.000	33.000
Q1/Q3	27.000/39.000	23.400/34.000	27.000/39.500
Min/Max	16.67/100.00	18.00/40.00	16.67/100.00

¹ Age at time of procedure

² The score for each subject is calculated as a sum of points given for each of the following conditions: 1 for hypertension, 1 for renal disease, 1 for liver disease, 1 for stroke history, 1 for prior major bleeding or predisposition to bleeding, 1 for labile INR, 1 for age > 65 years, 1 for medication usage predisposing to bleeding (e.g. aspirin, clopidogrel, NSAIDs), and 1 for alcohol use (≥ 8 drinks/week).

³ The score for each subject is calculated as a sum of points given for each of the following conditions: 1 for congestive heart failure (or left ventricular systolic dysfunction), 1 for hypertension, 2 for age ≥ 75 years, 1 for diabetes mellitus, 2 for prior stroke or TIA or thromboembolism, 1 for vascular disease (e.g. peripheral artery disease, myocardial infarction, aortic plaque), 1 for age 65-74 years, and 1 for sex category (i.e. female gender).

Abbreviations: AAD = antiarrhythmic drug; BMI = body mass index; CRT = cardiac resynchronization therapy; ICD = implantable cardioverter-defibrillator; LA = left atrial; OAC = oral anticoagulant.

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Table 127 – Mercy EHR Database Demographics and Baseline Characteristics

	Covariate-Unadjusted			Covariate-Balanced*		
Characteristic	Group with Fluoroscopy Time of ≤ 2 minutes	Group with Fluoroscopy Time of ≥ 3 minutes	ASD	Group with Fluoroscopy Time of ≤ 2 minutes	Group with Fluoroscopy Time of ≥ 3 minutes	ASD
	n (%)	n (%)		n (%)	n (%)	
Number of patients	129 (100.0)	170 (100.0)		129 (100.0)	121 (100.0)	
Age (years)			0.086			0.039
< 65	62 (48.1)	79 (46.5)		62 (48.1)	56 (46.1)	
65-74	46 (35.7)	67 (39.4)		46 (35.7)	45 (37.0)	
≥ 75	21 (16.3)	24 (14.1)		21 (16.3)	20 (16.9)	
Sex			0.036			0.033
Female	60 (46.5)	76 (44.7)		60 (46.5)	58 (48.2)	
Male	69 (53.5)	94 (55.3)		69 (53.5)	63 (51.8)	
Index year			0.562			0.129
2015/2016	22 (17.1)	38 (22.4)		22 (17.1)	20 (16.7)	
2017/2018	61 (47.3)	37 (21.8)		61 (47.3)	50 (41.6)	
2019/2020/2021	46 (35.7)	95 (55.9)		46 (35.7)	50 (41.6)	
Race			0.057			0.019
Black/Other	6 (4.7)	6 (3.5)		6 (4.7)	5 (4.3)	
White	123 (95.3)	164 (96.5)		123 (95.3)	116 (95.7)	
Ablation Catheter Type			0.132			0.048
THERMOCOOL SMARTTOUCH™	53 (41.1)	59 (34.7)		53 (41.1)	47 (38.7)	
THERMOCOOL SMARTTOUCH™ SF	76 (58.9)	111 (65.3)		76 (58.9)	74 (61.3)	
Medical history						
Anemia	9 (7.0)	12 (7.1)	0.003	9 (7.0)	8 (6.7)	0.013
Coagulopathy	9 (7.0)	7 (4.1)	0.125	9 (7.0)	8 (6.3)	0.026
Coronary artery disease	51 (39.5)	53 (31.2)	0.176	51 (39.5)	46 (38.1)	0.030
Chronic kidney disease	21 (16.3)	32 (18.8)	0.067	21 (16.3)	24 (19.9)	0.093
Chronic obstructive pulmonary disease	28 (21.7)	36 (21.2)	0.013	28 (21.7)	27 (22.5)	0.020
Congestive heart failure	24 (18.6)	45 (26.5)	0.189	24 (18.6)	27 (22.1)	0.087
Hypertension	95 (73.6)	131 (77.1)	0.079	95 (73.6)	89 (74.0)	0.007
Diabetes mellitus	28 (21.7)	50 (29.4)	0.177	28 (21.7)	27 (22.0)	0.008
Stroke or transient ischemic	8 (6.2)	9 (5.3)	0.039	8 (6.2)	8 (6.8)	0.026

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	Covariate-Unadjusted			Covariate-Balanced*		
Characteristic	Group with Fluoroscopy Time of ≤ 2 minutes	Group with Fluoroscopy Time of ≥ 3 minutes	ASD	Group with Fluoroscopy Time of ≤ 2 minutes	Group with Fluoroscopy Time of ≥ 3 minutes	ASD
attack or thromboembolism						
Vascular disease (peripheral arterial disease, previous myocardial infarction, or aortic atheroma)	57 (44.2)	57 (33.5)	0.220	57 (44.2)	49 (40.8)	0.069
	Mean (SD)	Mean (SD)		Mean (SD)	Mean (SD)	
HAS-BLED score prior to the index procedure	2.9 (1.4)	2.9 (1.5)	0.039	2.9 (1.4)	3.0 (1.4)	0.066
Body mass index† (kg/m²)	31.0 (6.5)	31.9 (7.4)	0.141	31.0 (6.5)	31.0 (6.8)	0.008
Atrial fibrillation history						
Time from first AF diagnosis recorded in database to the index procedure (years)	2.8 (2.1)	2.4 (2.3)	0.187	2.8 (2.1)	2.8 (2.5)	0.022
Number of AAD‡ prescriptions prior to the index procedure	7.4 (5.7)	7.2 (6.4)	0.023	7.4 (5.7)	7.7 (6.5)	0.051
Number of AF ablations performed by cardiac electrophysiologists (12 months prior to the index ablation)	111.7 (14.7)	105.4 (42.9)	0.196	111.7 (14.7)	114.9 (39.2)	0.107
	n (%)	n (%)		n (%)	n (%)	
Missing data for the number of AF ablations performed by cardiac electrophysiologists missing	3 (2.3)	9 (5.3)	0.156	3 (2.3)	4 (3.2)	0.053
Number of ASDs > 0.20			2			0
Average ASD			0.129			0.045

*Using the propensity score weighting method of the average treatment effect on the treated with weight trimming at the 99th percentile of the weight distribution in the comparator group

†Latest prior to the index procedure

‡Class I or III AAD

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Abbreviations: AAD: antiarrhythmic drug; ASD: absolute standardized difference; EHR: electronic health records; PAF: paroxysmal atrial fibrillation; SD: standard deviation

Left atrial size and left ventricular ejection fraction were available only among a subset of patients. These variables were not included in the propensity score model but were reported descriptively within each treatment group being compared, and both were similarly distributed between the group with fluoroscopy time of ≤ 2 minutes and the group with fluoroscopy time of ≥ 3 minutes.

Table 128 – Additional Baseline Characteristics of PAF Patients by Fluoroscopy Workflow Type in the Mercy EHR Database (Covariate-Unadjusted Data)

Characteristic	Group with Fluoroscopy Time of ≤ 2 minutes	Group with Fluoroscopy Time of ≥ 3 minutes	Absolute Standardized Difference
Number of patients	129	170	
Left atrial diameter (mm)			
N(%)	65 (50.39)	89 (52.35)	
Mean (SD)*	39.22 (6.11)	39.68 (6.83)	0.072
Missing, n (%)	64 (49.61)	81 (47.65)	0.039
Left Ventricular ejection fraction (%)			
≥ 50, n (%)*	90 (82.57)	102 (86.44)	0.107
< 50, n (%)*	19 (17.43)	16 (13.56)	
Missing, n (%)	20 (15.50)	52 (30.59)	0.364

*Based on non-missing data

Abbreviations: EHR: electronic health records; PAF: paroxysmal atrial fibrillation; SD: standard deviation

C. Results

The below tables summarize the results.

C.1 – REAL AF Zero/Low Fluoroscopy Sub-Study Procedure Counts and Device Utilization

Table 129 – REAL AF Zero/Low Fluoroscopy Sub-Study Procedure Type and Distribution of Device Utilization

Device	Frequency of Using, n/N (%) ¹
Index Procedure (N=208)	
THERMOCOOL SMARTTOUCH™ Catheter	1/208 (0.5%)
THERMOCOOL SMARTTOUCH™ SF Catheter	207/208 (99.5%)
Pentaray™ Nav eco High-Density Mapping Catheter	205/208 (98.6%)
Decanav™ Catheter	78/208 (37.5%)
Webster™ CS Catheter	94/208 (45.2%)
CARTO™ System	208/208 (100%)

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Device	Frequency of Using, n/N (%) ¹
Ablation Catheter Sheath	208/208 (100%)
Short	8/208 (3.8%)
Long Fixed	18/208 (8.7%)
Steerable	182/208 (87.5%)
CARTO VIZIGO™ Guiding Sheath	150/182 (82.4%)
Agilis	29/182 (15.9%)
Other	2/182 (1.1%)
Repeat Procedure (N=10)	
THERMOCOOL SMARTTOUCH™ Catheter	0/10 (0.0%)
THERMOCOOL SMARTTOUCH™ SF Catheter	10/10 (100%)
Pentaray™ Nav eco High-Density Mapping Catheter	8/10 (80.0%)
Decanav™ Catheter	6/10 (60.0%)
Webster™ CS Catheter	3/10 (30.0%)
CARTO™ System	10/10 (100%)
Ablation Catheter Sheath	10/10 (100%)
Short	0
Long Fixed	3/10 (30.0%)
Steerable	7/10 (70.0%)
CARTO VIZIGO™ Guiding Sheath	5/7 (71.4%)
Agilis	1/7 (14.3%)
Other	1/7 (14.3%)

¹ n and N Denotes number of catheters used in the index or repeat procedure.

C.2 – REAL AF Zero/Low Fluoroscopy Sub-Study Fluoroscopy Time Used During Procedure

Table 130 – REAL AF Zero/Low Fluoroscopy Sub-Study Total Fluoroscopy Time

Variable	All (N=208)	Non-Zero (N=104) ¹
Total Fluoroscopy Time (min)		
n	208	104
Mean	0.95	1.90
Standard Deviation	1.997	2.488
Median	0.05	1.00
Q1/Q3	0/1.0	0.3/2.5
Min/Max	0/15.6	0.1/15.6

¹ Subjects treated with any fluoroscopy.

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C.3 – REAL AF Zero/Low Fluoroscopy Sub-Study Total Procedure Time

Table 131 – REAL AF Zero/Low Fluoroscopy Sub-Study Procedure Time

Variable	Statistics
Total Procedure Time (min)	
n	208
Mean	97.3
Standard Deviation	44.42
Median	84.5
Q1/Q3	65.0/115.0
Min/Max	35/249

C.4 – REAL AF Zero/Low Fluoroscopy Sub-Study Anesthesia Agent

Table 132 – REAL AF Zero/Low Fluoroscopy Sub-Study Anesthesia Agent

Variable	Statistics
Anesthesia Agent, n/N (%) [+]	
Inhaled Anesthetics	149/208 (71.6%)
Paralytics	148/208 (71.2%)
Propofol	171/208 (82.2%)
Other	5/208 (2.4%)

C.5 – REAL AF Zero/Low Fluoroscopy Sub-Study Ventilation Mode

Table 133 – REAL AF Zero/Low Fluoroscopy Sub-Study Ventilation Mode

Variable	Statistics
Ventilation Mode, n/N (%) [+]	
Standard	135/208 (64.9%)
HFLV	91/208 (43.8%)
JET	6/208 (2.9%)
Intermittent Apnea	11/208 (5.3%)
Conscious sedation	5/208 (2.4%)

Abbreviations: HFLV = high frequency low volume.

C.6 – REAL AF Zero/Low Fluoroscopy Sub-Study Ablation Lesion Set

Table 134 – REAL AF Zero/Low Fluoroscopy Sub-Study Ablation Lesion Set

Variable	Statistics
Radiofrequency, n/N (%)	
PV only	63/208 (30.3%)
PV+CTI	96/208 (46.2%)
PV+CTI+SM	26/208 (12.5%)
PV+SM	23/208 (11.1%)
CTI+SM	0
SM only	0
CTI only	0

Dual Energy THERMOCOOL SMARTTOUCH™ SF Bi-Directional Catheter

Variable	Statistics
Substrate Modification, n/N (%)	
N/A	158/208 (76.0%)
Post Wall	26/208 (12.5%)
Mitral Isthmus	12/208 (5.8%)
Other	29/208 (13.9%)
Other Areas Ablated, n/N (%) [+]	
None	184/208 (88.5%)
SVC	3/208 (1.4%)
CS	4/208 (1.9%)
AVNRT Pathway	4/208 (1.9%)
Other	13/208 (6.3%)

Abbreviations: AVNRT = atrioventricular nodal reentrant tachycardia; CS = coronary sinus;
CTI = cavotricuspid isthmus; PV = pulmonary vein; SM = substrate modification;
SVC = superior vena cava.

C.7 – REAL AF Zero/Low Fluoroscopy Sub-Study Esophageal Monitoring

Table 135 – REAL AF Zero/Low Fluoroscopy Sub-Study Max Esophageal Temperature

Variable	Statistics
Max Esophageal Temp (C)	
n	166
Mean	36.56
Standard Deviation	6.487
Median	37.55
Q1/Q3	36.80/38.20
Min/Max	4.0/44.1

C.8 – REAL AF Zero/Low Fluoroscopy Sub-Study Same Day Discharge

Table 136 – REAL AF Zero/Low Fluoroscopy Sub-Study Same Day Discharge

Variable	Statistics
Plan to discharge same day, n/N (%)	173/208 (83.2%)
Patient discharged same day (confirmed), n/N (%)	153/208 (73.6%)

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C.9 - REAL AF Zero/Low Fluoroscopy Sub-Study Primary Safety Success

Complications were adjudicated by an independent clinical events committee. A total of 3 subjects reported 3 primary adverse events (1.5% rate). These primary adverse events included one of each: pseudoaneurysm (definitely procedure related), pulmonary vein stenosis (definitely related to study device and procedure), and hematoma (definitely procedure related). A total of 194 subjects did not have a primary adverse event.

Table 137 – REAL AF Zero/Low Fluoroscopy Sub-Study Primary Safety Endpoint

Variable	Number of Subjects with Event	Number of Events	PAE Rate ¹	One-sided 95% Upper Confidence Interval ²
Primary Adverse Event	3	3	3/197 (1.5%)	3.9%

¹ PAE rate is the percentage of subjects with PAEs. Subjects who did not have any documented encounter past post-index were excluded from the primary safety analysis.

² Exact test for binomial proportion. If the upper one-sided 95% CI of the primary safety endpoint is less than 10%, the primary endpoint will be met.

Note: Eleven subjects did not complete the 3-month visit and were excluded from analysis.

Two primary adverse events were observed in the zero fluoroscopy subgroup - pseudoaneurysm and pulmonary vein stenosis. One primary adverse event was observed in the non-zero fluoroscopy subgroup – hematoma.

Table 138 – REAL AF Zero/Low Fluoroscopy Sub-Study Primary Safety Endpoint by Zero vs Non-Zero Fluoroscopy

Subgroup	Number of Subjects with Event	Number of Events	PAE Rate ¹
Zero	2	2	2/94 (2.1%)
Non-Zero	1	1	1/103 (1.0%)

¹ The percentage of subjects with PAEs within each group. Subjects who do not have any documented encounter past post-index will be excluded from the primary safety analysis.

C.10 – REAL AF Zero/Low Fluoroscopy Sub-Study Secondary Acute Effectiveness Success

Table 139 – REAL AF Zero/Low Fluoroscopy Sub-Study Secondary Acute Effectiveness Endpoint

Variable	Number of Subjects	Number of Subjects Reaching PVI	Success Rate, n/N (%) ²	One-sided 95% Lower Confidence Interval ³
Acute Effectiveness ¹	202	202	202/202 (100%)	98.5%

¹ Acute effectiveness success is defined as confirmation of pulmonary vein isolation in all targeted pulmonary veins.

² Success rate is the proportion of subjects with acute effectiveness.

³ Exact test for binomial proportion. If the lower bound of the one-sided 95% CI is greater than 90%, the secondary endpoint will be met.

Abbreviations: PVI=pulmonary vein isolation.

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C.11 – Mercy EHR Database Procedural Information

Table 140 – Mercy EHR Database Count of Intracardiac Echocardiography

	Group with fluoroscopy time of ≤ 2 minutes	Group with fluoroscopy time of ≥ 3 minutes
Use of intracardiac echocardiography, n (%)	129 (100.00)	170 (100.00)

Table 141 – Mercy EHR Database Repeat Ablation Events by Fluoroscopy Workflow Type

	Group with fluoroscopy time of ≤ 2 minutes	Group with fluoroscopy time of ≥ 3 minutes
	129 (100.00)	170 (100.00)
Repeat Ablation Events	3 (2.33%)	6 (3.53%)
Within 12 months post index ablation procedure	3 (2.33%)	6 (3.53%)
Number of repeat ablations*	3 (2.33%)	6 (3.53%)
Number of patients who had a repeat ablation*	3 (2.33%)	6 (3.53%)
Number of repeat ablations a patient underwent		
1	3 (2.33%)	6 (3.53%)
2	0 (0.00%)	0 (0.00%)
≥ 3	0 (0.00%)	0 (0.00%)

* Percentages were based on patients meeting the eligibility criteria in the study group.

C.12 – Descriptive Comparison of the Secondary Safety Endpoint

One subject in the group with fluoroscopy time of ≤ 2 minutes had 1 event, pericarditis. Similarly in the group with fluoroscopy time of ≥ 3 minutes, one subject had 1 event, death. The cause of death was not available.

Table 142 – Cumulative Incidences of the Secondary Safety Endpoint by Fluoroscopy Workflow Type in the PAF Study Population in the Mercy EHR Database (Covariate-Unadjusted Data)

Study Group	No. of Patients	No. of Patients with Event	Cumulative Incidence (%)	Standard Error
Covariate-Unadjusted data				
Group with fluoroscopy time of ≤ 2 minutes	129	1	0.80%	0.008
Group with fluoroscopy time of ≥ 3 minutes	170	1	0.59%	0.006

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Table 143 –Cumulative Incidences of the Secondary Safety Endpoint by Fluoroscopy Workflow Type in the PAF Study Population in the Mercy EHR Database (Covariate-Balanced Data Using the Propensity Score Weighting Method*)

Study Group	No. of Patients	No. of Patients with Event	Cumulative Incidence (%)	Bootstrap Standard Error
Covariate-balanced data*				
Group with fluoroscopy time of ≤ 2 minutes	129	1	0.80%	0.008
Group with fluoroscopy time of ≥ 3 minutes	170	1	0.31%	0.003

*Using the propensity score weighting method of the average treatment effect on the treated with weight trimming at the 99th percentile of the weight distribution in the comparator group

D. Study Conclusion

The analysis of real-world data from the REAL AF Registry Sub-study supported the notion that the use of a zero/low fluoroscopy workflow in radiofrequency catheter ablation of paroxysmal atrial fibrillation is safe and does not compromise the acute effectiveness of pulmonary vein isolation.

COMPATIBLE EP NAVIGATION SYSTEM

The catheter provides location and contact force information only when used with the CARTO™ 3 System. Compatibility with the CARTO™ 3 System has been demonstrated via bench and animal testing to confirm that the catheter is capable of providing accurate location and contact force information when used in accordance with the instructions for use.

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ELECTRONIC INSTRUCTIONS FOR USE

This document is available at www.e-ifu.com.

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Symbol Definitions

Following definitions are for reference only. Please refer to the product label for applicable usage.



Medical Device



Sterilized using ethylene oxide



Do not re-use



Caution



www.eifu.com

Consult instructions for use or consult electronic instructions for use



Do not use if package is damaged



Do not use if package is opened



Keep away from sunlight



Keep dry



Use-by date



Batch Code



Catalog Number



Unique Device Identifier



Packaging unit



Single sterile barrier system with protective packaging inside



Manufacturer



Date of manufacture



Authorized Representative in the European Union



The irrigation tubing contains substance N-methyl-2-pyrrolidone, CAS# 872-50-4, in concentration above 0.1% weight by weight. Refer to the ECHA website for more information: <https://echa.europa.eu/home>.



MR Unsafe



Pin connector

ELECTRODES EA

Electrodes

SPACING mm

Spacing



Temperature limit



Curve type. Refer to label for colored circle containing applicable curve type.

DE STSF

Dual Energy THERMOCOOL SMARTTOUCH™ SF Catheter

C3

Compatible with CARTO™ 3 EP Navigation System

R_x only

Caution: Federal (USA) law restricts this device to sale by or on the order of a licensed healthcare practitioner.

ASSEMBLED MEXICO

Assembled in Mexico

Dual Energy THERMOCOOL SMARTTOUCH™ SF Uni-Directional Catheter

Dual Energy THERMOCOOL SMARTTOUCH™ SF Uni-Directional Catheter

Caution: Federal (USA) law restricts this device to sale by or on the order of a licensed healthcare practitioner.

- **STERILE.** Sterilized using ethylene oxide.
- For single use only. Do not resterilize.
- Do not use if the package is opened or damaged.

DEVICE DESCRIPTION

The Dual Energy THERMOCOOL SMARTTOUCH™ SF Uni-Directional Catheter is a multi-electrode luminal catheter with a deflectable tip designed to facilitate electrophysiological mapping of the heart and to transmit energy to the catheter tip electrode for ablation purposes. The catheter shaft measures 7.5 F with 8 F ring electrodes. For ablation, the catheter is used in conjunction with a compatible generator and dispersive pads (indifferent electrode). The catheter has force-sensing technology that provides a real-time measurement of contact force between the catheter tip and the heart wall.

The catheter has a high-torque shaft with a uni-directional deflectable tip section containing an array of electrodes which includes a 3.5 mm tip dome. All of the electrodes may be used for recording and stimulation purposes. The tip electrode serves to deliver energy from the generator to the desired ablation site. The tip electrode and ring electrodes are made from noble metals. The catheter incorporates a thermocouple temperature sensor that is embedded in the 3.5 mm tip electrode. Tip deflection is controlled at the proximal end by a handle in which a piston slides; a thumb knob on the piston controls piston travel. When the thumb knob is pushed forward, the tip deflects (curves). When the thumb knob is pulled back, the tip straightens. The high-torque shaft also allows the plane of the curved tip to be rotated to facilitate accurate positioning of the catheter tip at the desired site.

At the proximal end of the catheter, a saline input port with a standard Luer fitting terminates from the open lumen. This saline port serves to permit the injection of normal saline to irrigate the tip electrode. During ablation, heparinized normal saline is passed through the internal lumen of the catheter and through the tip electrode, to irrigate and cool the ablation site as well as the tip electrode. A compatible irrigation pump is used to control the saline irrigation. The catheter interfaces with standard recording equipment and a compatible generator via accessory extension cables with the appropriate connectors.

The catheter features a location sensor embedded in the tip section that transmits location and contact force information to the CARTO™ System. An appropriate reference device is required for location reference position purposes. For information on using the catheter in mapping procedures and for information on appropriate reference devices, refer to the instructions for use for the CARTO™ System. For further description of the operation of the irrigation pump, the generator, and the CARTO™ System, refer to the applicable instructions for use.

For details regarding the compatibility of the catheter with generators and CARTO™ Systems, refer to the "Matrix of Ablation Catheters and Compatible Devices."

INDICATIONS FOR USE

The Dual Energy THERMOCOOL SMARTTOUCH™ SF Uni-Directional Catheter and related accessory devices are indicated for catheter-based cardiac electrophysiological mapping (stimulating and recording) and, when used with a compatible generator, for the treatment of:

When using Radiofrequency (RF) energy:

- Type I atrial flutter in patients age 18 or older.
- Drug refractory recurrent symptomatic paroxysmal atrial fibrillation, when used with compatible three-dimensional electroanatomic mapping systems.

Dual Energy THERMOCOOL SMARTTOUCH™ SF Uni-Directional Catheter

- Drug refractory recurrent symptomatic persistent atrial fibrillation (defined as continuous atrial fibrillation that is sustained beyond 7 days but less than 1 year), refractory or intolerant to at least one Class I or III antiarrhythmic medicine, when used with compatible three-dimensional electroanatomic mapping systems.
- When using Pulsed Field (PF) energy:
- Drug refractory recurrent symptomatic paroxysmal atrial fibrillation, when used with compatible three-dimensional electroanatomic mapping systems.

The Dual Energy THERMOCOOL SMARTTOUCH™ SF Uni-Directional Catheter provides a real time measurement of contact force between the catheter tip and the heart wall, as well as location information when used with the CARTO™ System.

CONTRAINDICATIONS

Do not use the catheter:

1. If the patient has had a ventriculotomy or atriotomy within the preceding eight weeks because the recent surgery may increase the risk of perforation.
2. In patients with a myxoma or an intracardiac thrombus because the catheter could precipitate an embolus.
3. In patients with prosthetic valves because the catheter may damage the prosthesis.
4. In the coronary arterial vasculature because of the risk of damage to the coronary arterial vasculature.
5. In patients with an active systemic infection because this may increase the risk of cardiac infection.
6. Via the transseptal approach in a patient with an interatrial baffle or patch because the opening could persist and produce an iatrogenic atrial shunt.
7. Via the retrograde trans-aortic approach in patients who have had aortic valve replacement.
8. With a long sheath or short introducer < 8.5 F in order to avoid damage to the catheter shaft.

PATIENT TARGET GROUP

This catheter is targeted at patients who have been diagnosed with cardiac arrhythmias and are undergoing an electrophysiology procedure.

WARNINGS AND PRECAUTIONS

General

1. Only use the catheter in a fully equipped catheter or electrophysiological laboratory. It is recommended that the laboratory should have its corresponding equipment which may include but not limited to fluoroscopy, pacing, recording, defibrillator or intracardiac echocardiography units.
2. Do not use excessive force to advance or withdraw the catheter when resistance is encountered during catheter manipulation through the sheath.
3. Do not manually pre-shape the distal shaft of the catheter by applying external forces intended to bend or affect the intended shape or curve of the catheter.
4. Prior to use, the catheter must be warmed up as specified in the "Directions for Use" section of this document. If the catheter has not reached a steady state condition, there is potential for a zero-offset drift to occur which could result in an inaccurate contact force reading.
5. Always zero the contact force reading following insertion of the catheter into the patient or when moving the catheter from one chamber of the heart to another. Ensure the catheter is not in contact with heart tissue prior to zeroing. Refer to the instructions for use for the CARTO™ System for instructions on how to zero the contact force reading.

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6. The contact force reading might become inaccurate if the contact force sensor (located between the first and second ring electrode) comes into close proximity with a ferrous material, such as the braided shaft of another catheter. If extreme fluctuations in force are observed, ensure the catheter's contact force sensor is not in close proximity with another catheter's shaft, check zero on the catheter and, if necessary, remove and inspect the catheter.
7. The contact force reading is for information only and is not intended to replace standard handling precautions.
8. To ensure proper operation of the contact force sensor, the tip electrode and all four ring electrodes must protrude from the distal tip of the guiding sheath.
9. The catheter may damage the prosthetic tricuspid valve of a patient if the catheter is accidentally advanced through the valve.
10. In accordance with your hospital's protocol, monitor the patient's fluid balance throughout 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. Prior to the procedure, always identify the patient's risk of volume overload.
11. Minimize or eliminate X-ray exposure during the procedure. Catheter ablation procedures using fluoroscopic imaging may present the potential for significant X-ray exposure, which can result in acute radiation injury as well as increased risk for somatic and genetic effects to both patients and laboratory staff due to the X-ray beam intensity and duration of fluoroscopic imaging. Catheter ablation, when using fluoroscopic imaging, 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. Careful consideration must therefore be given for the use of the catheter in pregnant women.
12. Do not expose the catheter to volatile organic solvents such as alcohol. Doing so may compromise the structural integrity of the device and/or lead to device failure.
13. Do not immerse the proximal end of handle or cable connector in fluids; electrical performance could be affected.
14. Do not scrub or twist the distal tip electrode during cleaning.
15. Inspect the irrigation saline for air bubbles prior to its use in the procedure. Air bubbles in the irrigation saline may cause emboli.
16. Purge the catheter and the irrigation tubing with heparinized normal saline prior to insertion of the catheter into the patient.
17. Electrophysiology catheters and systems are intended for use only in X-ray shielded rooms due to electromagnetic compatibility requirements and other hospital safety guidelines.
18. Do not attempt to operate the catheter or the generator prior to completely reading and understanding the applicable instructions for use.
19. Cardiac ablation procedures should be performed by appropriately trained personnel in a fully equipped electrophysiology laboratory that meets the requirements of a medical room, as specific in IEC 60601-1. Appropriate clinical instruction in the use of the catheter should also be completed.
20. To prevent thromboembolism, intravenous heparin (target ACT of ≥ 300 s) should be administered prior to or immediately following transseptal puncture during AF ablation procedures. The 2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation recommends systemic anticoagulation with warfarin or a novel oral anticoagulant for at least 2 months following an AF ablation procedure (Calkins H, et al. 2017 HRS/EHRA/ECAS/APHRS/SOLAECE Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation, Heart Rhythm (2017), doi:10.1016/j.hrthm.2017.05.012).
21. When using the catheter with conventional systems (such as fluoroscopy or ultrasound imaging), or with the CARTO™ System, careful catheter manipulation must be performed in order to avoid cardiac damage, perforation, or tamponade. Catheter advancement should be done under direct imaging guidance. Do not use excessive force to advance or withdraw the catheter when resistance is encountered. The firmness of the braided tip dictates that care must be taken to prevent perforation of the heart.

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22. Always pull the thumb knob back to straighten the catheter tip before insertion or withdrawal of the catheter.
23. Always maintain a constant heparinized normal saline infusion to prevent coagulation within the lumen of the catheter. Do not use the catheter without irrigation flow.
24. Apparent low power output, high impedance reading, or failure of the equipment to function correctly at normal settings may indicate faulty application of the indifferent electrodes or failure of an electrical lead. Check for obvious defects or misapplication of the indifferent electrodes or other electrical leads prior to delivering energy.
25. Read and follow the indifferent electrode manufacturer's instructions for use. The use of indifferent electrodes that meet or exceed ANSI/AAMI requirements (AAMI IEC 60601-2-2) is recommended.
26. The catheter is intended for use only with a compatible generator, a compatible irrigation pump, a CARTO™ System, Biosense Webster cables, and other appropriate interface cables and connectors. Use of a compatible irrigation pump is recommended to assure proper irrigation flow rate.
27. The sterile packaging and catheter should be inspected prior to use. Do not use if the packaging or catheter appears damaged.
28. The catheter was sterilized using ethylene oxide and should be used by the use-by date printed on the product label. Do not use the catheter after the date on the product label.
29. The catheter is intended for single patient use only.
30. Do not resterilize and reuse the catheter.
31. Do not use near MRI equipment since movement or heating of the catheter may occur and the image on the display may become distorted.
32. The catheter used in conjunction with a generator is capable of delivering significant electrical power. Patient or operator injury can result from improper handling of the catheter and indifferent electrodes, particularly when operating the catheter. During energy delivery, the patient should not be allowed to come in contact with grounded metal surfaces.
33. 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.
34. Electromagnetic interference (EMI) produced by the catheter, when used in conjunction with a compatible generator during normal operation, may adversely affect the performance of other equipment.
35. Electrodes and probes used for monitoring and stimulating devices can provide paths for high frequency current. The risk of burns can be reduced but not eliminated by placing the electrodes and probes as far away as possible from the ablation site and the indifferent electrodes. Protective impedances may reduce the risk of burns and permit continuous monitoring of the electrocardiogram during energy delivery.
36. Before use, verify that the irrigation ports are patent by infusing heparinized normal saline through the catheter and tubing.
37. When applying high lateral force during mapping and energy application, the user should monitor the contact force dashboard and vector display on the CARTO™ System screen to ensure that contact force measurements remain within the accurate range. Refer to the Error Messages and Alerts section of the instructions for use for the CARTO™ System for system-related alert messages and indications related to inaccurate force readings.
38. The catheter has not been shown to be safe at electrode temperatures above 40°C. To ensure that the maximum allowed temperature is 40°C, verify that the catheter selection on the generator is correct for the catheter.
39. The temperature sensor measures tip electrode temperature, not tissue temperature. The temperature displayed on the generator is for the cooled electrode only and does not represent tissue temperature. If the generator does not display temperature, verify that the appropriate cable is plugged into the generator. If temperature still is not displayed, there may be a malfunction in the temperature sensing system that must be corrected prior to applying energy.
40. The temperature measurement accuracy of the catheter, as with any temperature measurement electrophysiology catheter, is largely determined by the temperature accuracy specification of the generator used. Consult the instructions for use for the generator to be used for the temperature accuracy specification.

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41. During energy delivery, ensure there is no metal guidewire in proximity to the catheter's active ablation electrode. Energy delivery near exposed metal on other electrophysiology (EP) devices, probes, or implants that can disrupt the electric field and potentially lead to injury.
42. Use both direct imaging guidance (such as fluoroscopy or ultrasound) and electrogram data to monitor catheter advancement and reduce risk of tissue injury.
43. During the transaortic approach, adequate fluoroscopic visualization is necessary to avoid placement of the catheter in the coronary vasculature. Intracoronary placement of the ablation catheter, energy application, or both have been associated with myocardial infarction.
44. The long term risks of RF and PF induced lesions have not been established. Careful consideration must therefore be given for the use of the catheter in prepubescent children.
45. Presence of implantable pacemakers or implantable cardioverter defibrillators (ICDs), implanted LAO device or other implanted metal cardiac device within cardiac space, may be adversely affected by RF and PF energy. ICDs should be deactivated during ablation. It is important to have temporary external sources for pacing and defibrillation available during ablation. Exercise extreme caution during ablation when the catheter is in close proximity to atrial or ventricular permanent leads. Perform a complete analysis of the implantable device after ablation. PF energy near or directly on metal implants has not been thoroughly studied, use caution when ablating near metal implants.

Warnings when Catheter is used with Generator in RF Mode

46. Do not use the temperature sensor to monitor tissue temperature or to guide power titration during ablation. The temperature sensor located within the tip section of the catheter does not reflect either electrode-tissue interface or tissue temperature due to the cooling effects of the saline irrigation of the electrode. The temperature displayed on the generator is the temperature of the cooled electrode, not tissue temperature. The temperature sensor is used to verify that the irrigation flow rate is adequate. Before initiating the application of RF energy, a decrease in electrode temperature confirms the onset of saline irrigation of the ablation electrode. Monitoring the temperature from the electrode during the application of RF energy ensures that the irrigation flow rate is being maintained. Using tip temperature to guide ablation could result in deeper lesions and increased risk for collateral damage.
47. When using RF on the posterior wall, Power and contact force should both be reduced, otherwise recommendations are to switch to PF.
48. Do not rely on electrode temperature rise to determine if tissue heating is occurring during RF energy delivery because bench, animal, and clinical studies showed no significant electrode temperature rise during RF ablations.
49. It is important to carefully follow the power titration procedure as specified in the "Directions for Use" section of this document. Too rapid an increase in RF power during ablation may lead to perforation caused by steam pop.
50. The safety of discontinuing anticoagulation therapy following catheter ablation of atrial fibrillation has not been established; anticoagulation therapy in such patients should be administered in accordance with the 2019 AHA/ACC/HRS Focused Update of the 2014 Guideline for Management of Patients with Atrial Fibrillation (January CT, Wann LS, Calkins H, et al. CITATION: 10.1016/j.jacc.2019.01.011.).
51. The safety and effectiveness of RF ablation for the treatment of atrial fibrillation in patients with significant left ventricular dysfunction (LV ejection fraction < 40%), NYHA class III or IV heart failure, substantial left atrial enlargement, and structural heart disease have not been established.
52. Patients undergoing septal accessory pathway ablations, ablations on the septal side of the isthmus, or in the treatment of AVNRT, are at risk for AV block which may require the implantation of a permanent pacemaker. Closely monitor AV conduction during energy delivery and immediately terminate energy delivery if partial or complete AV block is observed.
53. To prevent stenosis of the pulmonary veins, do not place the catheter in the pulmonary veins during the application of RF energy.

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54. When ablating near the phrenic nerve, take precautions to avoid injuring the phrenic nerve, including appropriately reducing RF power and pacing to identify the proximity of the ablation electrode(s) to the nerve.
55. When ablating near the esophagus (along the posterior wall of the left atrium), take precautions to avoid injuring the esophagus. These may include beginning the ablation with switching to PF energy, reduced RF power, reducing RF application time, increasing the time interval between ablations, esophageal visualization, and/or intraluminal esophageal temperature monitoring.
56. Cases of delayed onset of atrioesophageal fistula (AEF) in association with an RF catheter ablation procedure have been reported from postmarket experience. While rare, AEF is associated with significant morbidity and mortality. Prompt diagnosis and timely management may contribute to optimal patients' outcomes.
57. When RF energy is interrupted for either a temperature or an impedance rise (the set limit is exceeded), the catheter should be removed, and the tip cleaned of coagulum, if present. When cleaning the tip electrode, be careful not to twist the tip electrode with respect to the catheter shaft; twisting may damage the tip electrode bond and loosen the tip electrode, or may damage the contact force sensor. A significant change in the baseline reading after cleaning might indicate a damaged contact force sensor. Make sure the irrigation holes are not plugged prior to reinsertion.
58. The catheter has been shown to create larger lesions than non-irrigated RF ablation catheters. Care should be taken when ablating near structures such as the sino-atrial and atrioventricular nodes.

Warnings when Catheter is used with Generator in PF Mode

59. Pulsed field ablation may result in an extended pause in cardiac rhythm. Prior to delivering PF energy, ensure adequate preparations are in place to commence emergency ventricular pacing, administer cardiopulmonary resuscitation, or apply other measures consistent with standard of care should the need arise.
60. Do not use the catheter in pregnant women because the effects of pulsed field energy on a fetus are unknown. The effects of pulsed field energy on children and newborns are unknown.
61. To prevent patient movement during PFA, patient comfort should be maintained through standards of care for pain management.
62. When ablating near the phrenic nerve, take precautions to avoid injuring the phrenic nerve, including appropriately pacing to identify the proximity of the ablation electrode(s) to the nerve and limiting stacking of PF ablations in this location to the maximum 24 applications allowed by the generator.
63. Prior to each application of energy, verify continuous irrigation flow by observing the dripping in the tubing drip chamber to confirm saline flow to the ablation electrode. If irrigation blockage is suspected, remove and inspect the catheter following the instructions in the "Directions for Use" section of this document.
64. Do not use PF energy in close proximity to structures such as the sino-atrial and atrioventricular nodes. Use extreme caution when delivering PF energy in close proximity to normal conduction system.
65. The long-term risks of the application of PF ablation in the heart have not been established.
66. PFA should not be used for type I CCW atrial flutter (CTI Dependent) due to proximity of ablation site to coronary arteries and reported risks associated with vasospasm and ischemia.
67. During PF energy delivery, contact with exposed metal could result in electrical arcing.

MRI SAFETY INFORMATION

The catheter is MR Unsafe. Keep it outside the MRI scanner room. The MRI safety of the catheter has not been assessed. Do not use the catheter near MRI equipment because movement or heating of the catheter may occur and the image on the display may become distorted.

STORAGE

Refer to the product label for recommended storage conditions.

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STERILIZATION AND USE-BY DATE

The catheter was sterilized using ethylene oxide. Product and package testing have been conducted to support the use-by date printed on the product label. Do not use the catheter after the date on the product label.

The catheter was packaged and sterilized 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 that in turn may result in patient injury, illness, or death. Also, reprocessing or resterilization of single use devices may create a risk of contamination 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.

DISPOSAL

Recycle components, or dispose of the product and its residual elements or waste items in accordance with local laws and regulations.

COMPATIBLE EP NAVIGATION SYSTEM

The catheter provides location and contact force information only when used with the CARTO™ System. Compatibility with the CARTO™ System has been demonstrated via bench and animal testing to confirm that the catheter is capable of providing accurate location and contact force information when used in accordance with the instructions for use.

DIRECTIONS FOR USE

Refer to the instructions for use for the CARTO™ System, the irrigation pump, the RF generator, and the irrigation tubing for instructions on connecting and operating these systems in conjunction with the catheter. Use appropriate accessory cables to connect the catheter to the appropriate accessory equipment.

1. Using aseptic technique, remove the catheter from the package and place it in a sterile work area. Inspect the catheter carefully for electrode integrity and overall condition.
2. Create a vascular access in a large central vessel using aseptic techniques.
3. To prevent damage to the catheter tip, use the insertion tube supplied with the catheter to advance or retract the catheter through the hemostasis valve of the sheath. After insertion, slide the insertion tube back toward the handle.
4. To verify compatibility between the sheath and catheter, advance the catheter through the sheath prior to insertion. Any sheath < 8.5 F is contraindicated.
5. Use only Biosense Webster interface cables. To complete the electrical circuit, connect up to two indifferent electrodes to the indifferent electrode input on the generator. Connect the Patient Interface Unit (PIU) of the CARTO™ System to the generator to the appropriate recording and mapping systems with the appropriate interface cables. Connect the catheter to the compatible generator via the adapter cable. Connect the indifferent electrode to the indifferent electrode on the compatible generator.
6. Connect the irrigation tubing to a room temperature, heparinized (1 IU heparin/ml) normal saline bag using standard safe hospital practices. Open the stopcock on the end of the tubing set and fill the tubing set as slowly as possible. Remove any trapped air and then close the stopcock.
7. Load the irrigation tubing into the pump. Open the stopcock and flush the tubing per the instructions for use for the pump until the air is expelled through the open end of the tubing.
8. Connect the stopcock on the end of the irrigation tubing to the Luer fitting of the catheter.
9. Flush the catheter and tubing per standard technique to ensure purging of trapped air bubbles and to verify that the irrigation holes are patent.
10. Start continuous irrigation at a flow rate of 2 ml/min.
11. Insert the catheter via the entrance site using the insertion tube and an appropriately sized introducer sheath. Advance the catheter to the desired area. Use both fluoroscopy and electrograms (EGM) to aid in proper positioning.

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12. To achieve optimal force reading accuracy and stability, allow the catheter to warm up for 2 minutes after connection to the CARTO™ System prior to use of the force feedback feature.
13. Zero the contact force reading following insertion of the catheter into the patient. The tip electrode and all four ring electrodes on the catheter tip must be outside of the sheath so that the force sensor is inside the body. Ensure the catheter tip is not in contact with tissue by using both direct imaging guidance (such as fluoroscopy or ultrasound) and the CARTO™ System, the EGM amplitude, and catheter movement. Variations in the force reading at the same rate as the cardiac or respiration cycle may indicate contact with cardiac structures. When these markers indicate the catheter tip is not in contact, the reading can be zeroed. Refer to the instructions for use for the CARTO™ System for instructions on how to zero the contact force reading.
14. Zero the contact force reading when moving the catheter from one chamber of the heart to another or upon reinsertion.
15. The catheter tip can be deflected to facilitate positioning by using the thumb knob to vary tip curvature. Pushing the thumb knob forward causes the catheter tip to deflect; when the thumb knob is pulled back, the tip straightens.
16. **RF Energy Application**
 - a. Verify that the “Dual Energy THERMOCOOL SMARTTOUCH™ SF Catheter” option is selected on the generator. When this option is chosen, the generator defaults to the safety parameters established for the catheter. Do not use tip temperature to guide ablation.

Table 1 – RF and Flow Settings

RECOMMENDED RF APPLICATION PARAMETERS	
	ATRIAL ABLATION
Power Range	15 W to 45 W*
Temperature Monitoring	< 40°C**
Irrigation Flow Rate during RF Application	8 ml/min for power level up to 30 W
	15 ml/min for power levels between 31 W and 45 W
Application Time	Max 60 seconds***
* For power settings > 30 W, the recommended irrigation flow rate is 15 ml/min. ** The temperature displayed on the generator does not represent tissue temperature or electrode tissue interface temperature. *** The duration of ablation can be reduced in sensitive regions of the heart (close to the esophagus). It should be limited to 20 seconds per ablation location in the CS.	

- b. **Recommendation for irrigation:**

Increase the irrigation to the high flow rate starting up to 5 seconds before the onset of RF energy delivery and maintain the high flow rate until 5 seconds after termination of the RF energy application. For power levels up to 30 W, a high flow rate of 8 ml/min should be used. For power levels between 31 W and 45 W a high flow rate of 15 ml/min should be used. Do not use the catheter without irrigation flow.
- c. The application of RF energy must not be initiated until the increase in irrigation flow rate is confirmed by a minimum of 2°C decrease in tip electrode temperature.
- d. Monitor the catheter tip temperature throughout the procedure to ensure adequate irrigation. If the temperature increases to 40°C during RF application, power delivery should be interrupted. Recheck the irrigation system prior to restarting RF application.
Note: The displayed temperature represents the temperature of the tip electrode only, not the temperature of the tissue.

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e. Recommendation for RF power:

For treatment of atrial flutter:

Start the procedure at 15 W to 20 W. After 15 seconds, power may be increased in 5 W to 10 W increments as needed, until a transmural lesion is achieved, defined by > 80% reduction in unipolar atrial electrogram amplitude, or emergence of double potentials of equal and low amplitude.

For treatment of atrial fibrillation:

- An RF power range of 15 W to 45 W is recommended for atrial ablation.
- Do not rely on the catheter tip temperature response to guide ablation. If temperature increases rapidly, stop RF application immediately.
- At anatomical locations not on the LA posterior wall or CS:
 - Maximum allowed power should not exceed 45 W.
 - Duration of ablation should not exceed 60 seconds of continuous ablation.
 - Duration of ablation as well as decision to interrupt RF energy delivery at any time during ablation should be guided by clinical investigator judgment and monitoring of ablation effectiveness parameters commonly used such as EGM reduction and/or impedance changes.

f. For Left Atrial posterior wall ablations close to the esophagus:

It is recommended to use pulsed field (PF) energy, refer to step 17, PFA energy application for appropriate guidance.

If using RF energy is desired:

- Start ablation at ≤ 25 W.
- Move/drag the catheter to a new location if clinically effective ablation is achieved within 20 seconds (EGM reduction and/or impedance drop).
- Power can be increased if clinically effective ablation isn't achieved within 20 seconds (no electrogram reduction and/or no impedance drop). Maximum power used should not exceed 35 W.
- Duration of ablation, as well as decision to interrupt RF energy delivery at any time during ablation, should be guided by physician judgment and monitoring of ablation effectiveness parameters commonly used such as EGM reduction and/or impedance changes and esophageal temperature changes monitored by an endoluminal esophageal probe.
- Power should be limited to no more than 35 W if ablation is required in the CS and the duration of ablation should be limited to 20 seconds per ablation location.

g. Contact Force (CF) ranges during ablation:

A starting point minimum targeted CF of 5 to 10 grams is reasonable (Calkins H, et al. 2017 HRS/EHRA/ECAS/APHS/SOLAECE Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation, Heart Rhythm (2017), doi:10.1016/j.hrthm.2017.05.012).

In the PRECEPT study and the SMART-SF study using the THERMOCOOL SMARTTOUCH™ SF Catheter, and the SMART-AF IDE study using the THERMOCOOL SMARTTOUCH™ Catheter, operators were instructed to monitor CF during initial cases using standard methods for evaluating effective RF applications.

In the PRECEPT study, operators most frequently chose a working range with a low of 5 grams and a high of 40 grams (37.5%, 130/347) as described in Section C.3: Contact Force Data. The overall average contact force recorded during a study ablation procedure for all subjects undergoing ablation was 15.23 ± 4.41 grams as described in Table 63: Average Contact Force Measurements Overall per Ablation Procedure. In the majority of procedures (239/283), the average contact force applied was less than 20 grams as described in Figure 1: Distribution of Average Contact Force per Ablation Procedure.

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In the SMART-SF study, operators most frequently chose a working range with a low of 5 grams and a high of 40 grams (44.0%, 70/159) as described in Table 93: Working Ranges Configured by Investigators. The overall average contact force recorded during a study ablation procedure for all subjects undergoing ablation was 16.7 ± 6.14 grams as described in Table 79: Average Contact Force Measurements Overall per Ablation Procedure. In the majority of procedures (125/152), the average contact force applied during ablation was less than 20 grams.

In the SMART-AF study, operators chose working ranges for RF applications that varied for both the low range (4 to 15 grams) and high range (20 to 60 grams) as described in Table 39: Working Ranges Configured by Investigators. During the study, investigators selected a working range of 5 to 40 grams for 67.4% of all study procedures. A low range of 5 grams was selected in more than 90% of the study subjects.

The average contact force applied to the endocardial heart surface during ablation procedures for all subjects undergoing ablation was 17.9 ± 9.42 grams. Results showed that when investigators stayed within their chosen working ranges $\geq 85\%$ of the time during RF applications, there was a significant improvement in the 12-month effectiveness outcome (87.1% vs. 65.7%).

h. Esophageal monitoring:

An appropriate strategy to minimize risk of esophageal injury should be used to ensure the physician has accurate information about the location of the esophagus relative to intended sites of ablation. At least one of the following methods should be used for esophageal localization:

- Use of a multipolar esophageal temperature probe
- Esophageal visualization with CARTOSOUND™ Module and/or ICE
- Esophageal visualization using barium swallow

17. PFA energy application

- a. PFA energy is recommended for pulmonary vein isolation.
- b. Start the ablation without moving the catheter. A high flow rate of 4 ml/min should be used.
- c. Contact Force (CF) ranges during ablation:
 - A working range of 5 to 40 grams is recommended.

Table 2 – PF and Flow Settings

RECOMMENDED PF APPLICATION PARAMETERS	
	ATRIAL ABLATION (PF)
Number of applications	Up to 24
Temperature Monitoring	< 40°C*
Irrigation Flow Rate during PF Application	4 ml/min
Max Ablation Time	Up to 28 seconds**
* The temperature displayed on the generator does not represent tissue temperature or electrode tissue interface temperature.	
** 1 second intervals between applications	

18. It is recommended that PF energy be delivered as follows for atrial ablation:

- On or near the posterior wall of the left atrium.
- When ablating near a location where pacing captures the phrenic nerve.
- Areas of touch up after PVI confirmation.

19. When using the catheter, operators should select individualized CF target ranges based on their case experience and the SMART-SF and SMART-AF IDE trial results.

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20. In the event of a generator cutoff (impedance or temperature), the catheter must be withdrawn and the tip electrode inspected for coagulum before RF energy is reapplied. To remove any coagulum, if present, a sterile gauze pad dampened with sterile saline may be used to gently wipe the tip section clean. Do not scrub or twist the tip electrode as damage to the tip electrode bond may occur and loosen the tip electrode, or damage the contact force sensor and affect measurement accuracy. Prior to reinsertion, ensure that the irrigation holes are not plugged as follows:
- Fill a 1 or 2 ml syringe with sterile saline and attach it to the stopcock on the end of the irrigation tubing or the sidearm on the catheter.
 - Carefully inject the saline from the syringe into the catheter. Uniform streams of fluid should be visible from the tip of the catheter.
 - Repeat steps a and b, if necessary.
 - Flush the catheter and the tubing per standard technique to ensure purging of trapped air bubbles and to verify that the irrigation holes are patent.
 - The catheter can now be reintroduced into the patient.
 - Zero the catheter following reinsertion into the patient.

WARNING: Do not continue use of the catheter if it is still occluded or it is not functioning properly.

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ADVERSE EVENTS

NOTE: The adverse events in the following summary were observed in clinical studies involving use of the Dual Energy THERMOCOOL SMARTTOUCH™ SF Catheter, THERMOCOOL SMARTTOUCH™ SF Catheter, THERMOCOOL SMARTTOUCH™ Catheter, and NAVISTAR™ THERMOCOOL™ Diagnostic/Ablation Catheter. The THERMOCOOL SMARTTOUCH™ SF and THERMOCOOL SMARTTOUCH™ Catheters are modified versions of the NAVISTAR™ THERMOCOOL™ Catheter with the added feature of a force sensor placed in the catheter tip used to measure the contact force between the catheter tip and endocardial tissue.

Clinical Trial for the Dual Energy THERMOCOOL SMARTTOUCH™ SF Catheter – SmartPulse PAF Study

Of the 231 patients in the Safety Population, 5 primary adverse events were reported in 5 subjects. See the “Summary of Clinical Studies Conducted for the Dual Energy THERMOCOOL SMARTTOUCH™ SF Catheter” section below for a complete description of the AEs encountered during the study.

Clinical Trial for the THERMOCOOL SMARTTOUCH™ SF Catheter – PRECEPT Study

Of the 348 patients in the Safety Population, 17 primary adverse events were reported in 16 subjects. See the “Summary of Clinical Studies Conducted for the THERMOCOOL SMARTTOUCH™ SF Catheter” section below for a complete description of the AEs encountered during the study.

Clinical Trials for the THERMOCOOL SMARTTOUCH™ SF Catheter – Safety Study

Of the 159 patients in the Safety Cohort, 4 primary adverse events were reported in 4 subjects. See the “Summary of Clinical Studies Conducted for the THERMOCOOL SMARTTOUCH™ SF Catheter” section below for a complete description of the AEs encountered during the study.

Clinical Trials for the THERMOCOOL SMARTTOUCH™ Catheter – Pivotal Study

Of the 161 subjects in the Safety Analysis Cohort, 17 primary adverse events (AEs) were reported in 16 subjects. See the Pivotal Study in the “Summary of Clinical Studies Conducted for the THERMOCOOL SMARTTOUCH™ Catheter” section below for a complete description of the AEs encountered during the study.

Clinical Trials for the THERMOCOOL SMARTTOUCH™ Catheter – Continued Access Study

Of the 143 subjects in the Safety Analysis Cohort, 27 primary adverse events (AEs) were reported in 25 subjects. See the Continued Access Study in the “Summary of Clinical Studies Conducted for the THERMOCOOL SMARTTOUCH™ Catheter” section below for a complete description of the AEs encountered during the study.

Clinical Trials for Atrial Flutter Indication

Of the 190 subjects in the Safety Population in the pivotal study, 33 major adverse events were reported in 30 subjects. In the Post-Approval Study, 4 cardiovascular specific adverse events were reported in 4 of the 291 enrolled subjects. See the “Summary of Clinical Studies Conducted for Atrial Flutter Indication” section below for a complete description of the adverse events encountered during the studies.

Clinical Trials for Atrial Fibrillation Indication

Of the 139 subjects in the Primary Safety Analysis Cohort, 16 serious primary adverse events were reported in 15 subjects. See the “Summary of Clinical Studies Conducted for Atrial Fibrillation Indication” section below for a complete description of the AEs encountered during the study.

SUMMARY OF CLINICAL STUDIES

The clinical testing described below was performed with the Dual Energy THERMOCOOL SMARTTOUCH™ SF Catheter, THERMOCOOL SMARTTOUCH™ SF Catheter, THERMOCOOL SMARTTOUCH™ Catheter, and NAVISTAR™ THERMOCOOL™ Catheter. The THERMOCOOL SMARTTOUCH™ SF Catheter meets the same performance specifications as the NAVISTAR™ THERMOCOOL™ and THERMOCOOL SMARTTOUCH™ Catheters using reduced saline flow rates.

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SUMMARY OF CLINICAL STUDIES CONDUCTED FOR THE DUAL ENERGY THERMOCOOL SMARTTOUCH™ SF CATHETER

Study 1: Pivotal Study- SMARTPULSE PAF STUDY

A. Objective

The primary objective of the trial was to demonstrate safety and effectiveness of the BWI Pulsed Field (PF)/ Radiofrequency (RF) ablation system, consisting of Dual Energy THERMOCOOL SMARTTOUCH™ SF Catheter and TRUPULSE™ Generator when used in conjunction with CARTO™ 3 system V7.9 workstation with VISITAG SURPOINT™ module, in treatment of subjects with paroxysmal atrial fibrillation.

B. Study Design

The study was a prospective, interventional, single arm, multi-center and pre-market clinical evaluation conducted at 27 investigational sites in the US.

B.1 – Study Endpoints

The endpoints for the study were as follows:

Primary safety endpoint – the occurrence of early onset Primary Adverse Events (PAEs) within seven (7) days of an ablation procedure.

Primary Adverse Events included the following conditions:

- Esophageal perforating complications (Atrio-esophageal fistula¹, esophago-pericardial fistula)
- Cardiac Tamponade^{2,3} /perforation²
- Device or procedure related death⁴
- Major Vascular Access Complication/Bleeding
- Myocardial Infarction
- Pericarditis
- Pulmonary Edema (Respiratory Insufficiency)
- Phrenic Nerve Paralysis (permanent)⁵
- Pulmonary Vein Stenosis⁶
- Stroke/CVA^{7,8}
- Thromboembolism
- Transient Ischemic Attack (TIA)
- Heart Block
- Vagal Nerve Injury/Gastroparesis

¹ Atrio-esophageal fistula occurring up to 90 days post AF ablation process procedure will be considered a PAE.

² Cardiac Tamponade/Perforation occurring up to 30 days post AF ablation process procedure will be considered a PAE

³ Hemodynamic compromise or instability is defined as Systolic BP < 80 mm Hg.

⁴ Device or procedure-related death anytime during or after the ablation procedure and any death reported within 30 days of ablation procedure where device and/or procedure relatedness cannot be determined via CEC adjudication

⁵ Absent phrenic nerve function as assessed by a sniff test at discharge.

⁶ Pulmonary Vein Stenosis occurring anytime during the 12 month follow up period will be considered a PAE.

⁷ Non-focal global encephalopathy requires unequivocal evidence based upon neuroimaging studies to be reported as a stroke

⁸ Modified Rankin score assessments should be made by certified individuals.

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Primary Effectiveness Endpoint – Percent of subjects who had freedom from documented symptomatic and asymptomatic atrial tachyarrhythmia episodes based on electrocardiographic data during the effectiveness evaluation period from Day 91 to Day 365 and any of the following failure modes:

- Acute procedural failure: failure to achieve entrance block in all pulmonary veins using the investigational device (except those that are silent and/or cannot be cannulated post-procedure) by the end of the procedure
- Repeat ablation failure: more than 1 repeat ablation procedure for AF/AT/AFL (of unknown origin⁺) during the 3-Month Blanking Period or any repeat ablation procedure for AF/AT/AFL (of unknown origin⁺) during the evaluation period
- Non-study device failure: use of a non-study device to treat PV targets to achieve isolation of clinically relevant PVs during index or repeat procedure during the blanking period, or use of a non-study device for ablation in the left atrium during either index or repeat procedure within the blanking period
- AAD failure: taking a new AAD (Class I & III) for atrial tachyarrhythmia (AF, AT or AFL of unknown origin⁺), taking an increased dose of a previously failed Class I/III AAD for atrial tachyarrhythmia after the blanking period, or taking an increased dose of amiodarone at any time, post index procedure
- Continuous AF/AT/AFL of unknown origin⁺ (all AFL except those CTI dependent AFL as confirmed by 12-lead electrocardiogram and entrainment maneuvers in an EP study) on a standard 12-lead ECG during the effectiveness evaluation period
- Any DC cardioversion procedure during the evaluation period for documented atrial tachyarrhythmia (AF, AT or AFL of unknown origin⁺) recurrences ascertained through protocol specified arrhythmia monitoring methods (12-lead ECG, TTM and Holter)

⁺ AFL of unknown origin is defined as all AFL except those CTI dependent AFL as confirmed by 12-Lead electrocardiogram (ECG) and entrainment maneuvers in an EP study.

Secondary Endpoint – Change in quality of life (QOL) as measured by the total AFEQT score at 12 months post procedure in comparison to baseline assessment.

B.2 - Prespecified performance goal

Primary Safety Endpoint - Performance Goal = 12.0% of upper bound of exact one-sided 97.5% CI around the primary AE rate.

Primary Effectiveness Endpoint - Performance Goal = 50% of lower end of two-sided 99.5% CI around the 1-year rate of freedom from primary effectiveness endpoint.

B.3 – Subject Disposition and Accountability

B.3.1 – Subject Disposition and Accountability

Table 3 – Subject Disposition and Accountability (Enrolled Subjects, N=250)

Subject Enrollment	n
Enrolled Subjects ¹	250
Excluded ²	19
Evaluable Subjects ³	231
Discontinued ⁴	0
Discontinued for study device-related reasons ⁵	0
RF/PF Energy Delivered	231
Death	2
Lost to Follow-up ⁶	2
Withdrawn/Early Termination ⁷	0

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Subject Enrollment	n
Completed ⁸	82
Ongoing	145
Other	0
CT/MRA Enrolled Subjects ¹	34

¹ **Enrolled Subjects:** Subjects who sign the Informed Consent Form (ICF).

² **Excluded Subjects:** Subjects who are enrolled but never undergo insertion of the study catheter.

³ **Evaluable Subjects:** All enrolled subjects who have the study catheter inserted.

⁴ **Discontinued:** Evaluable subjects who have the study catheter inserted, but do not undergo ablation (i.e., no PF/RF energy applied).

⁵ **Discontinued for study device-related reasons:** Subjects who have the study catheter inserted but do not undergo ablation due to Study Device (Dual Energy SMARTTOUCH™ SF (DE STSF), TRUPULSE™ Generator, and CARTO™ 3 v7.9 Workstation) related reasons will be discontinued and considered acute effectiveness failures.

⁶ **Lost to Follow-up:** Subjects who have study catheter inserted, but contact is lost after most recent follow-up visit (despite 3 documented attempts to contact the subject).

⁷ **Withdrawn/Early Termination:** Subjects who withdraw consent for study participation or are withdrawn by the investigator, are terminated from the study prior to completion of all follow-up visits.

⁸ **Completed Subjects:** Enrolled subjects who have not been excluded, discontinued, withdrawn, terminated early, or lost-to-follow-up from the study prior to the final study visit.

B.3.2 - Study Analysis Set

Table 4 – Analysis Set (Safety Population Analysis Set, N=231)

Analysis Set	n
Safety Population (SP) Analysis Set¹	231
All Treated (AT) Analysis Set²	231
Did not meet eligibility	7
Modified Intent-To-Treat (mITT) Analysis Set³	224
Discontinued Subjects ⁴	0
Subjects with specified major PD ⁵	3
Per Protocol (PP) Analysis Set⁶	221
Discontinued subjects for study device-related reasons ⁷	0
Used non-study device to achieve PVI due to study-device related reason ⁸	2
Enrolled Subset Subjects	
Cardiac CT/MRA Subset	34

¹ **SP Analysis Set:** All enrolled subjects who have had the study catheter inserted, regardless of whether energy is delivered or not.

² **AT Analysis Set:** The AT analysis set will consist of all enrolled subjects who have undergone the insertion of the study catheter and energy delivery, regardless of whether they meet the eligibility criteria or not.

³ **mITT Analysis Set:** Enrolled subjects who meet eligibility criteria and have had insertion of the study catheter.

⁴ **Discontinued Subjects:** Evaluable subjects who have the study catheter inserted but do not undergo ablation.

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⁵ Major protocol deviations that result in removal from Per Protocol analysis set as described in the SAP.

⁶ **PP Analysis Set:** Subjects who satisfy the following criteria: (1) undergone ablation using PF and/or RF energy via the investigational ablation system, (2) treated for study-related arrhythmia, (3) no specified major CIP deviations.

⁷ **Discontinued subjects for study device-related reasons:** subjects who have the study catheter inserted but do not undergo ablation (i.e., no energy is delivered with the study catheter) due to study device related reasons will be discontinued and considered as acute effectiveness failures and will be retained in this PP analysis set.

⁸ Subjects who have energy delivered with study catheter but switched to non-study device for PVI due to study-device related reasons will be considered as acute effectiveness failures and will be retained in the PP analysis set.

B.4 – Subject Demographics

Table 5 – Demographics (Evaluable Subjects, N=231)

Variable	Safety Set (N=231)	mITT Set (N=224)	PP Set (N=221)	CT/MRA Analysis Set (N=34)
Age (years)¹				
n	231	224	221	34
Mean	63.1	63.2	63.2	61.8
Standard Deviation	9.67	9.54	9.59	8.32
Median	66.0	66.0	66.0	64.5
Sex, n/N (%)				
Male	138 / 231 (59.7%)	134 / 224 (59.8%)	133 / 221 (60.2%)	14 / 34 (41.2%)
Female	93 / 231 (40.3%)	90 / 224 (40.2%)	88 / 221 (39.8%)	20 / 34 (58.8%)
Ethnicity, n/N (%)				
Hispanic or Latino	10 / 231 (4.3%)	10 / 224 (4.5%)	10 / 221 (4.5%)	1 / 34 (2.9%)
Not Hispanic or Latino	214 / 231 (92.6%)	207 / 224 (92.4%)	204 / 221 (92.3%)	33 / 34 (97.1%)
Not Reported	7 / 231 (3.0%)	7 / 224 (3.1%)	7 / 221 (3.2%)	0 / 34 (0.0%)
Race, n/N (%)				
Asian	1 / 231 (0.4%)	1 / 224 (0.4%)	1 / 221 (0.5%)	0 / 34 (0.0%)
Black or African American	8 / 231 (3.5%)	6 / 224 (2.7%)	6 / 221 (2.7%)	0 / 34 (0.0%)
Race not reported	8 / 231 (3.5%)	8 / 224 (3.6%)	8 / 221 (3.6%)	2 / 34 (5.9%)
White	214 / 231 (92.6%)	209 / 224 (93.3%)	206 / 221 (93.2%)	32 / 34 (94.1%)
Weight (kg)				
n	231	224	221	34
Mean	94.50	93.93	94.06	94.40
Standard Deviation	21.218	20.952	21.043	21.803
Median	92.50	91.59	92.00	92.03

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Variable	Safety Set (N=231)	mITT Set (N=224)	PP Set (N=221)	CT/MRA Analysis Set (N=34)
Height (cm)				
n	231	224	221	34
Mean	174.46	174.45	174.49	173.18
Standard Deviation	10.634	10.633	10.686	10.175
Median	175.26	175.26	175.30	173.99
BMI (kg/m²)				
n	231	224	221	34
Mean	31.07	30.89	30.92	31.64
Standard Deviation	6.567	6.501	6.536	7.760
Median	29.70	29.45	29.50	29.20

¹ Age at informed consent.

B.5 – Baseline Characteristics

B.5.1 – Medical History

Table 6 – Medical History (Evaluable Subjects, N=231)

Variable	Safety Set n/N (%)	mITT Set n/N (%)	PP Set n/N (%)	CT/MRA Subset n/N (%)
Cardiovascular Medical History¹	210 / 231 (90.9%)	204 / 224 (91.1%)	201 / 221 (91.0%)	31 / 34 (91.2%)
Congestive heart failure	38 / 231 (16.5%)	36 / 224 (16.1%)	35 / 221 (15.8%)	5 / 34 (14.7%)
NYHA Class				
Class I	7 / 231 (3.0%)	7 / 224 (3.1%)	6 / 221 (2.7%)	0 / 34 (0.0%)
Class II	31 / 231 (13.4%)	29 / 224 (12.9%)	29 / 221 (13.1%)	5 / 34 (14.7%)
Coronary disease	49 / 231 (21.2%)	45 / 224 (20.1%)	45 / 221 (20.4%)	4 / 34 (11.8%)
Vascular disease	34 / 231 (14.7%)	31 / 224 (13.8%)	30 / 221 (13.6%)	2 / 34 (5.9%)
Myocardial infarction	18 / 231 (7.8%)	16 / 224 (7.1%)	16 / 221 (7.2%)	1 / 34 (2.9%)
Hypertension (systemic)	165 / 231 (71.4%)	160 / 224 (71.4%)	158 / 221 (71.5%)	21 / 34 (61.8%)
Pulmonary hypertension	5 / 231 (2.2%)	5 / 224 (2.2%)	5 / 221 (2.3%)	0 / 34 (0.0%)
Cardiomyopathy	10 / 231 (4.3%)	9 / 224 (4.0%)	9 / 221 (4.1%)	2 / 34 (5.9%)
Ischemic	5 / 231 (2.2%)	4 / 224 (1.8%)	4 / 221 (1.8%)	0 / 34 (0.0%)
Non-Ischemic	5 / 231 (2.2%)	5 / 224 (2.2%)	5 / 221 (2.3%)	2 / 34 (5.9%)
Left ventricular hypertrophy	12 / 231 (5.2%)	10 / 224 (4.5%)	10 / 221 (4.5%)	1 / 34 (2.9%)
Significant valvular disease	3 / 231 (1.3%)	2 / 224 (0.9%)	2 / 221 (0.9%)	0 / 34 (0.0%)
Percutaneous coronary intervention (PCI)	23 / 231 (10.0%)	21 / 224 (9.4%)	21 / 221 (9.5%)	1 / 34 (2.9%)
Other cardiovascular procedure (e.g. CABG, pacemaker, ICD, LAAO, stent, implantable loop recorder, etc.)	30 / 231 (13.0%)	28 / 224 (12.5%)	26 / 221 (11.8%)	3 / 34 (8.8%)

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Variable	Safety Set n/N (%)	mITT Set n/N (%)	PP Set n/N (%)	CT/MRA Subset n/N (%)
Carotid stenting or endarterectomy	1 / 231 (0.4%)	1 / 224 (0.4%)	1 / 221 (0.5%)	0 / 34 (0.0%)
Unstable angina	1 / 231 (0.4%)	0 / 224 (0.0%)	0 / 221 (0.0%)	0 / 34 (0.0%)
Prior LA atrial appendage closure	1 / 231 (0.4%)	1 / 224 (0.4%)	1 / 221 (0.5%)	0 / 34 (0.0%)
Hypercholesterolemia	95 / 231 (41.1%)	90 / 224 (40.2%)	90 / 221 (40.7%)	16 / 34 (47.1%)
Other cardiovascular medical condition	78 / 231 (33.8%)	76 / 224 (33.9%)	74 / 221 (33.5%)	7 / 34 (20.6%)
Documented Thromboembolic Events*	11 / 231 (4.8%)	10 / 224 (4.5%)	10 / 221 (4.5%)	0 / 34 (0.0%)
Transient ischemic attack (TIA)	2 / 231 (0.9%)	2 / 224 (0.9%)	2 / 221 (0.9%)	0 / 34 (0.0%)
Stroke	6 / 231 (2.6%)	6 / 224 (2.7%)	6 / 221 (2.7%)	0 / 34 (0.0%)
Hemorrhagic	1 / 231 (0.4%)	1 / 224 (0.4%)	1 / 221 (0.5%)	0 / 34 (0.0%)
Ischemic	5 / 231 (2.2%)	5 / 224 (2.2%)	5 / 221 (2.3%)	0 / 34 (0.0%)
Pulmonary embolus	1 / 231 (0.4%)	1 / 224 (0.4%)	1 / 221 (0.5%)	0 / 34 (0.0%)
Other thromboembolic events	2 / 231 (0.9%)	1 / 224 (0.4%)	1 / 221 (0.5%)	0 / 34 (0.0%)

* Allow for multiple selection.

B.5.2 – Atrial Fibrillation History

Table 7 – Atrial Fibrillation History (Evaluable Population, n=231)

Variable	Safety Set (N=231)	mITT Set (N=224)	PP Set (N=221)	CT/MRA Subset (N=34)
Duration of symptomatic paroxysmal AF (months)				
n	231	224	221	34
Mean	47.48	47.46	46.50	36.94
Standard Deviation	60.171	60.929	59.857	51.457
Median	24.00	24.00	24.00	18.65
Number of symptomatic paroxysmal AF episodes in the past 6 months				
n	231	224	221	34
Mean	22.5	20.7	19.9	22.5
Standard Deviation	40.90	36.81	35.39	30.99
Median	7.0	6.0	6.0	7.5

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Variable	Safety Set (N=231)	mITT Set (N=224)	PP Set (N=221)	CT/MRA Subset (N=34)
Frequency of symptomatic paroxysmal AF episode in the past 6 months, n/N (%)				
Daily	28 / 231 (12.1%)	27 / 224 (12.1%)	26 / 221 (11.8%)	4 / 34 (11.8%)
Weekly	51 / 231 (22.1%)	50 / 224 (22.3%)	50 / 221 (22.6%)	13 / 34 (38.2%)
Bi-weekly	19 / 231 (8.2%)	19 / 224 (8.5%)	19 / 221 (8.6%)	1 / 34 (2.9%)
Monthly	32 / 231 (13.9%)	30 / 224 (13.4%)	29 / 221 (13.1%)	2 / 34 (5.9%)
Irregular	86 / 231 (37.2%)	83 / 224 (37.1%)	82 / 221 (37.1%)	10 / 34 (29.4%)
Unknown	15 / 231 (6.5%)	15 / 224 (6.7%)	15 / 221 (6.8%)	4 / 34 (11.8%)
Direct current cardioversion (DCCV) in the past 12 months for paroxysmal AF, n/N (%)	37 / 231 (16.0%)	36 / 224 (16.1%)	36 / 221 (16.3%)	7 / 34 (20.6%)
Number of previous DCCV				
1	29 / 37 (78.4%)	28 / 36 (77.8%)	28 / 36 (77.8%)	6 / 7 (85.7%)
2	7 / 36 (19.4%)	7 / 35 (20.0%)	7 / 35 (20.0%)	0 / 7 (0.0%)
3	0 / 36 (0.0%)	0 / 35 (0.0%)	0 / 35 (0.0%)	0 / 7 (0.0%)
≥ 4	1 / 36 (2.8%)	1 / 35 (2.9%)	1 / 35 (2.9%)	1 / 7 (14.3%)

B.5.3 – Cardiovascular Hospitalization and Cardioversion History

**Table 8 – Cardiovascular Hospitalization and Cardioversion History
(Evaluable Population, N=231)**

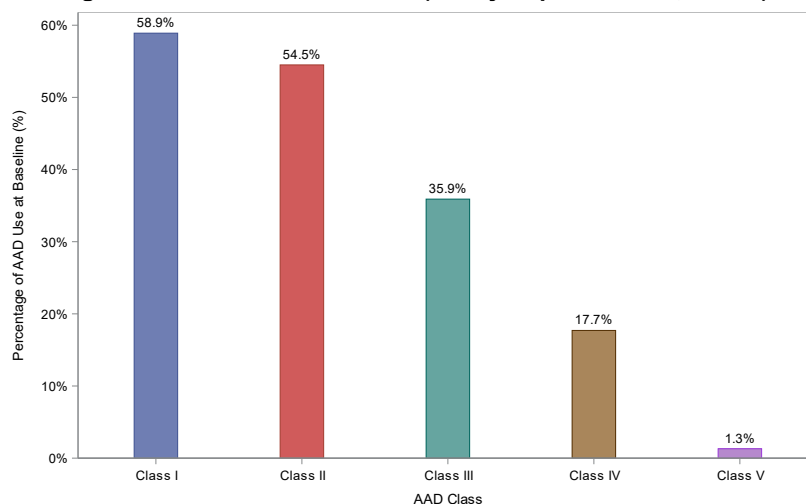
Variable	Safety Set (N=231)	mITT Set (N=224)	PP Set (N=221)	CT/MRA Subset (N=34)
Cardiovascular related hospital visits, n/N (%)¹	122/231 (52.8%)	118/224 (52.7%)	118/221 (53.4%)	19/34 (55.9%)
Type of Visit, n/N (%)¹				
Emergency room	53 / 122 (43.4%)	52 / 118 (44.1%)	52 / 118 (44.1%)	10 / 19 (52.6%)
Hospitalization	43 / 122 (35.2%)	40 / 118 (33.9%)	40 / 118 (33.9%)	4 / 19 (21.1%)
Outpatient	26 / 122 (21.3%)	26 / 118 (22.0%)	26 / 118 (22.0%)	5 / 19 (26.3%)
Reason, n/N (%)¹				
Ablation procedure	1 / 122 (0.8%)	1 / 118 (0.8%)	1 / 118 (0.8%)	1 / 19 (5.3%)
Angio/PCI	1 / 122 (0.8%)	1 / 118 (0.8%)	1 / 118 (0.8%)	10 / 19 (52.6%)
Electrical Cardioversion	42 / 122 (34.4%)	41 / 118 (34.7%)	41 / 118 (34.7%)	3 / 19 (15.8%)
Heart Failure	1 / 122 (0.8%)	1 / 118 (0.8%)	1 / 118 (0.8%)	5 / 19 (26.3%)
Pharmacological Cardioversion	22 / 122 (18.0%)	22 / 118 (18.6%)	22 / 118 (18.6%)	1 / 19 (5.3%)
Other	55 / 122 (45.1%)	52 / 118 (44.1%)	52 / 118 (44.1%)	10 / 19 (52.6%)

¹ n represents the number of visits/reasons per category and N represents the total number of cardiovascular hospitalizations/cardioversions within 12 months prior to study enrollment.

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B.5.4 – AAD Use at Baseline

Figure 1 – AAD Use at Baseline (Safety Population Set, N=231)



B.5.5 – Baseline CHADS₂ and CHA₂DS₂-VASc Score

Table 9 – CHADS₂ and CHA₂DS₂-VASc Score (Evaluable Population, N=231)

Variable	Safet Set (N=231)	mITT Set (N=224)	PP Set (N=221)	CT/MRA Subset (N=34)
CHADS₂ Score¹				
N	231	224	221	34
Mean	1.2	1.2	1.2	1.0
Standard Deviation	0.98	0.94	0.94	0.92
Median	1.0	1.0	1.0	1.0
CHA₂DS₂-VASc Score²				
N	231	224	221	34
Mean	2.3	2.3	2.3	2.1
Standard Deviation	1.41	1.37	1.37	1.31
Median	2.0	2.0	2.0	2.0

¹The score for each subject is calculated as a sum of points given for each of the following conditions: 1 for congestive heart failure, 1 for hypertension, 1 for age ≥ 75 years, 1 for diabetes mellitus, and 2 for prior stroke or TIA or thromboembolism.

²The score for each subject is calculated as a sum of points given for each of the following conditions: 1 for congestive heart failure (or left ventricular systolic dysfunction), 1 for hypertension, 2 for age ≥ 75 years, 1 for diabetes mellitus, 2 for prior stroke or TIA or thromboembolism, 1 for vascular disease (e.g. peripheral artery disease, myocardial infarction, aortic plaque), 1 for age 65-74 years, and 1 for sex category (i.e. female).

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C. Results

C.1 – Procedural Data

C.1.1 – Index Procedure Data

Table 10 – Procedural Data of Index Procedure (Evaluable Population, N=231)

Variable	Safety Set (N=231)	mITT Set (N=224)	PP Set (N=221)	CT/MRA Subset (N=34)
Anesthesia Type, n/N (%)				
Conscious sedation	1 / 231 (0.4%)	1 / 224 (0.4%)	1 / 221 (0.5%)	0 / 34 (0.0%)
General (unconscious sedation)	230 / 231 (99.6%)	223 / 224 (99.6%)	220 / 221 (99.5%)	34 / 34 (100.0%)
Was a paralytic used, n/N (%) ⁺	187 / 231 (81.0%)	183 / 224 (81.7%)	180 / 221 (81.4%)	29 / 34 (85.3%)
Overall Ablation Details:				
PF energy applied via the study catheter, n/N (%)	231 / 231 (100.0%)	224 / 224 (100.0%)	221 / 221 (100.0%)	34 / 34 (100.0%)
RF energy applied via the study catheter, n/N (%)	230 / 231 (99.6%)	223 / 224 (99.6%)	220 / 221 (99.5%)	34 / 34 (100.0%)
Pre-Ablation Mapping:				
Total LA mapping time (min)				
n	231	224	221	34
Mean	7.09	7.04	7.03	7.53
Standard Deviation	4.954	4.953	4.968	5.118
Median	6.00	6.00	6.00	6.00
Ablation to Achieve PV Isolation:				
Total PVI Ablation time with THERMOCOOL SMARTTOUCH™ SF study catheter (min)				
n	231	224	221	34
Mean	52.65	52.05	52.21	50.09
Standard Deviation	23.889	23.589	23.591	20.499
Median	47.00	46.00	46.00	45.00
Total procedure time (min)				
n	231	224	221	34
Mean	105.49	104.00	104.14	99.79
Standard Deviation	38.819	37.449	37.149	26.341
Median	100.00	99.00	99.00	98.50

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Variable	Safety Set (N=231)	mITT Set (N=224)	PP Set (N=221)	CT/MRA Subset (N=34)
Total duration of fluoroscopy at end of procedure (min)				
n	231	224	221	34
Mean	4.07	4.10	4.06	2.22
Standard Deviation	6.553	6.627	6.588	3.206
Median	0.30	0.30	0.30	0.00
Ablation Procedure Information: Fluid Intake and Output [I & O]				
Fluid delivered via the study catheter(s) (mL)				
n	224	218	216	33
Mean	425.4	424.4	424.8	408.3
Standard Deviation	232.36	235.04	234.18	173.96
Median	400.0	400.0	400.0	400.0
Fluid delivered via intravenous fluids (mL)				
n	230	223	220	34
Mean	862.7	849.9	850.1	839.0
Standard Deviation	504.73	496.33	499.50	399.95
Median	800.0	800.0	800.0	900.0
Ablation Procedure Details:				
Heart rhythm at the beginning of the procedure, n/N (%)				
Atrial Fibrillation	28 / 231 (12.1%)	28 / 224 (12.5%)	28 / 221 (12.7%)	4 / 34 (11.8%)
Atrial Flutter Typical Right	6 / 231 (2.6%)	6 / 224 (2.7%)	6 / 221 (2.7%)	2 / 34 (5.9%)
Atrial Tachycardia Left Atrium	1 / 231 (0.4%)	1 / 224 (0.4%)	1 / 221 (0.5%)	0/34 (0.0%)
Sinus Rhythm	187 / 231 (81.0%)	180 / 224 (80.4%)	177 / 221 (80.1%)	26 / 34 (76.5%)
Other	9 / 231 (3.9%)	9 / 224 (4.0%)	9 / 221 (4.1%)	2 / 34 (5.9%)
Highest Esophageal temperature reached throughout the procedure (Centigrade)				
n	117	114	112	12
Mean	36.77	36.73	36.74	36.88
Standard Deviation	1.139	1.120	1.124	0.959
Median	36.40	36.40	36.40	36.50

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Variable	Safety Set (N=231)	mITT Set (N=224)	PP Set (N=221)	CT/MRA Subset (N=34)
Energy mode switched to PF if the phrenic nerve was located near the intended ablation line, n/N(%)				
Yes	18 / 231 (7.8%)	17 / 224 (7.6%)	17 / 221 (7.7%)	4 / 34 (11.8%)
No	8 / 231 (3.5%)	8 / 224 (3.6%)	8 / 221 (3.6%)	5 / 34 (14.7%)
Not applicable	205 / 231 (88.7%)	199 / 224 (88.8%)	196 / 221 (88.7%)	25 / 34 (73.5%)
If No, ablation line altered to avoid the phrenic location	8 / 8 (100.0%)	8 / 8 (100.0%)	8 / 8 (100.0%)	5 / 5 (100.0%)
Predominant heart rhythm at the end of the procedure, n/N (%)				
Atrial Fibrillation	9 / 231 (3.9%)	9 / 224 (4.0%)	9 / 221 (4.1%)	0/34 (0.0%)
Atrial Flutter Atypical Right	1 / 231 (0.4%)	1 / 224 (0.4%)	1 / 221 (0.5%)	0/34 (0.0%)
Sinus Rhythm	219 / 231 (94.8%)	212 / 224 (94.6%)	209 / 221 (94.6%)	34 / 34 (100.0%)
Other	2 / 231 (0.9%)	2 / 224 (0.9%)	2 / 221 (0.9%)	0/34 (0.0%)

* Allow for multiple selections

C.1.2 – Use of Ablation Energy by Ablation Targets at Subject Level

**Table 11 – Use of Ablation Energy by Ablation Targets at Subject Level
(Safety Population Analysis Set, N=231)**

Variable	Overall	PV Targets	Non-PV Targets
Number of PF/RF Ablations			
n	231	231	67
Mean	79.9	75.7	14.4
Standard Deviation	23.87	21.42	9.04
Median	76.0	73.0	12.0
Number of PF Ablations			
n	231	231	2
Mean	37.3	37.2	10.0
Standard Deviation	12.40	12.30	11.31
Median	36.0	36.0	10.0
Number of RF Ablations			
n	229	229	67
Mean	42.9	38.8	14.1
Standard Deviation	16.04	13.17	9.06
Median	40.0	37.0	12.0

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C.1.3 – Use of Ablation Energy by PV Targets

Table 12 – Number of Ablation per Ablation Target (Safety Population Analysis Set, N=231)

Variable	Overall	Number of PF Ablations	Number of RF Ablations
PV Target			
LPV			
n	230	230	229
Mean	37.5	17.6	20.0
Standard Deviation	12.12	6.91	8.18
Median	35.0	16.0	18.0
RPV			
n	229	229	226
Mean	38.7	19.9	19.1
Standard Deviation	12.42	8.19	7.77
Median	36.0	18.0	18.0
Non-PV Targets			
CTI Line			
n	62	-	62
Mean	14.0	-	14.0
Standard Deviation	8.75	-	8.75
Median	12.0	-	12.0

C.2 – Primary Endpoints

C.2.1 – Primary Safety Endpoints – Incidence of primary adverse events

Primary Adverse Events occurred in 5 subjects with 2.2% (5/224) incidence rate in mITT analysis set (Table 13). The upper bound of exact one-sided 97.5% confidence interval (CI), 5.1%, was lower than the pre-defined performance goal of 12%.

Table 13 – Primary Safety Endpoint Analysis (mITT Analysis Set, N=224)

Variable	Number of Subjects with Events	Event Rate n/N (%) ¹	Exact One-Sided 97.5% Upper Confidence Bound
Primary adverse event ¹	5	5/224 (2.2%)	5.1%

¹Subjects without at least 3 months of follow-up are excluded from the primary safety analysis unless they experienced a PAE.

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The Primary Adverse events included two (2) events of cardiac tamponade/perforation, two (2) events of transient ischemic attack (TIA) and one (1) event of death (Table 14).

**Table 14 – Decomposition of Primary Safety Endpoint,
Primary Adverse Events (mITT Analysis Set, N=224)**

Variable	Number of Subjects with Events	Number of Events
Primary Adverse Event¹	5	5
Type of Primary Adverse Event		
Cardiac Tamponade/Perforation	2	2
Death	1	1
Device or procedure related death ²	0	0
Atrio-Esophageal Fistula ³	0	0
Cardiac Tamponade ^{4, 5} /perforation ⁴	0	0
Major Vascular Access Complication/ Bleeding	0	0
Myocardial Infarction	0	0
Pericarditis	0	0
Heart Block	0	0
Phrenic Nerve Paralysis (Permanent) ⁶	0	0
Pulmonary Vein Stenosis ⁷	0	0
Stroke/Cerebrovascular Accident ^{8, 9}	0	0
Thromboembolism	0	0
Transient Ischemic Attack	2	2
Pulmonary Edema (Respiratory Insufficiency)	0	0
Vagal Nerve Injury/ Gastroparesis	0	0

¹ Subjects without at least 3 months of follow-up are excluded from the primary safety analysis unless they experienced a PAE.

² Device or procedure-related death anytime during or after the ablation procedure and any death reported within 30 days of ablation procedure where device and/or procedure relatedness cannot be determined via CEC adjudication.

³ Atrio-esophageal fistula occurring up to 90 days post AF ablation process procedure is considered a PAE.

⁴ Cardiac Tamponade/Perforation occurring up to 30 days post AF ablation process procedure is considered a PAE.

⁵ Hemodynamic compromise or instability is defined as Systolic BP < 80 mm Hg.

⁶ Absent phrenic nerve function as assessed by a sniff test at discharge.

⁷ Pulmonary Vein Stenosis occurring anytime during the 12-month follow up period is considered a PAE.

⁸ Non-focal global encephalopathy requires unequivocal evidence based upon neuroimaging studies to be reported as a stroke.

⁹ Modified Rankin score assessments should be made by certified individuals.

Death – One subject died of cardiac arrest at 13 days post-procedure. The subject's death was considered possibly related to Dual Energy THERMOCOOL SMARTTOUCH™ SF Catheter, TRUPULSE™™ Generator or ablation procedure. The subject was a 75-year-old male with a relevant medical history of drug refractory symptomatic paroxysmal atrial fibrillation, hypertension, hyperlipidemia, cerebrovascular accident (CVA), and type 2 diabetes. The subject presented to the lab in normal sinus rhythm. Pre-procedural examinations (TEE, ECG, and Chest X-ray) did not show any

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contraindications. The subject had a successful PVI ablation without complication and was awake and hemodynamically stable. The subject was discharged the next day after the procedure. There were no complaints during the 7-day post procedure follow-up via telehealth visit. On Day 13 post procedure, the subject displayed shortness of breath while on a phone with the medical provider and was advised to call 911. The subject was reported dead on the same day.

C.2.2 Primary Safety Endpoint– Primary Adverse Events – Safety Population Analysis Set

In addition to the primary safety endpoint results, the safety population includes all subjects where the catheter was inserted, which includes 7 additional subjects. The safety population also represents all treated subjects in the investigation. The seven additional subjects are not represented in the mITT population as they were found to have not met the inclusion and/or exclusion criteria of the investigation after the initial procedure.

Primary Adverse Events occurred in 6 subjects with 2.6% (6/231) incidence rate in Safety Population analysis set (Table X). The upper bound of exact one-sided 97.5% confidence interval (CI), 5.6%, was lower than the pre-defined performance goal of 12%.

Table 14-1. Snap-Shot Binomial Analysis of Primary Safety Endpoint (Safety Population Analysis Set, N=231)

Variable	Number of Subjects	Success Rate n/N (%) [1]	Exact One-Sided 97.5% Upper Confidence Bound
Primary adverse event	6	6 / 231 (2.6%)	5.6%

[1] Subjects without at least 3 months of follow-up are excluded from the primary safety analysis unless they experienced a PAE.

Table 14-2. Decomposition of Primary Safety Endpoint - Primary Adverse Events (Safety Population Analysis Set, N=231)

Variable	Number of Subjects with Events	Number of Events
Primary Adverse Event [1]	6	6
Type of Primary Adverse Event		
Cardiac Tamponade/Perforation	3	3
Death	1	1
Transient Ischemic Attack	2	2

[1] Subjects without at least 3 months of follow-up are excluded from the primary safety analysis unless they experienced a PAE.

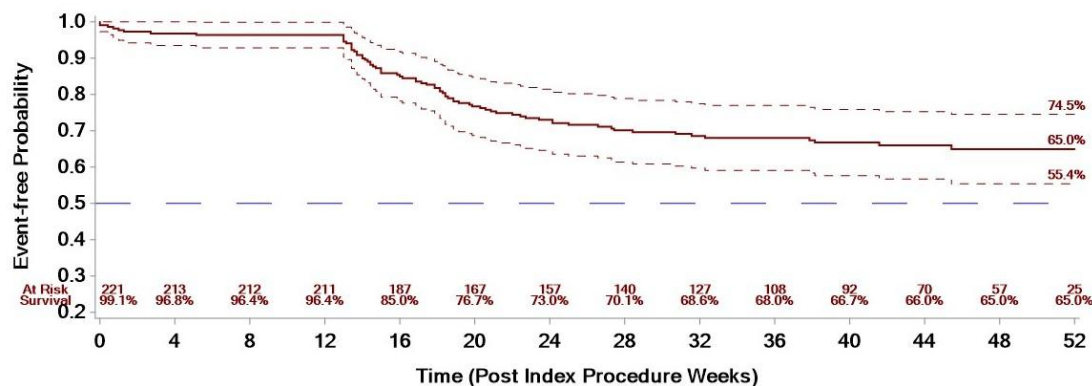
C2.3 – Primary Effectiveness Endpoints

The percentage of subjects who had freedom from documented atrial tachyarrhythmia episodes during effectiveness evaluation period and pre-defined failure modes.

The 1-year rate of freedom from primary effectiveness endpoint based on Kaplan-Meier analysis was 65.0%, with a two-sided 99.5% confidence interval (CI) of 55.4% and 74.5% (Figure 2). The lower end of the 99.5% CI, 55.4%, was higher than the predefined performance goal (55.4% vs 50%).

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Figure 2 – Kaplan-Meier Analysis of Time to Primary Effectiveness Failure (Per Protocol Analysis Set, N=221)

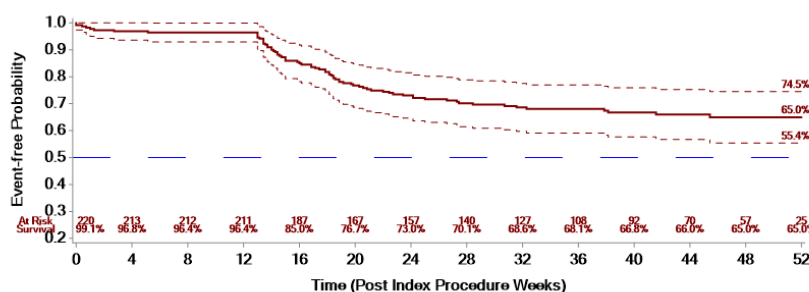


C2.4 – Primary Effectiveness Endpoints – mITT Analysis Set

The mITT analysis set includes 3 additional subjects (224 vs 221) whom were not included in the Per Protocol analysis sets due major protocol deviations in the index procedure. The following analysis includes the percentage of these subjects who had freedom from documented atrial tachyarrhythmia episodes during effectiveness evaluation period and pre-defined failure modes.

The 1-year rate of freedom from primary effectiveness endpoint based on Kaplan-Meier analysis was 65.0%, with a two-sided 99.5% confidence interval (CI) of 55.4% and 74.5% (Figure 2). The lower end of the 99.5% CI, 55.4%, was higher than the predefined performance goal (55.4% vs 50%).

Figure 2-1- Kaplan-Meier Analysis of Time to Primary Effectiveness Failure (mITT Analysis Set, N=224)



C.3 – Secondary Effectiveness Endpoint – Improvement in Quality of Life

Change in quality of life (QOL) as measured by increase of the total AFEQT score at 12 months post procedure from baseline in Per Protocol (PP) analysis set was 30.88 (p < 0.0001) (Table 15).

Table 15 – Overall AFEQT Score by Visit (Per Protocol Analysis Set, N=221)

AFEQT Questionnaire	Statistics ¹	P-value ²
Change from Baseline based on PP Set, N=221		
Mean	30.88	<.0001

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AFEQT Questionnaire	Statistics ¹	P-value ²
95.5% Confidence Interval	(25.49, 36.27)	

¹ With available data

² By paired t-test

C.4 – Additional Safety Endpoints

C.4.1 – Serious Adverse Events

The study reported 49 serious adverse events in 36 subjects (15.6%), 9 occurred during the initial 7 days, 4 during the first month after 7 days, and 24 after the first month (Table 16).

Table 16 – Serious Adverse Events by Timing of Onset (Safety Population Analysis Set, N=231)

Timing ¹	Number of Events	Number of Subjects with Event	Event Rate ² n/N (%)
Total	49	36	
Prior to Procedure	0	0	0 / 231 (0.0%)
0 - 7 Days	11	9	9 / 231 (3.9%)
8 - 30 Days	9	4	4 / 231 (1.7%)
≥ 31 Days	29	24	24 / 230 (10.4%)

¹ Timing of AE based on onset in days post the procedure (index or repeat).

² N denotes the number of subjects with follow-up duration surpassing the left bound of the time interval.

Table 17 presents serious adverse events by System Organ Class (SOC) and Preferred Term (PT). Cardiac disorders were the most common SAEs with an incidence rate of 6.5% (15/231).

Table 17 – Serious Adverse Events by SOC and PT (Safety Population Analysis Set, N=231)

System Organ Class (SOC) Preferred Term (PT)	Number of Events	Number of Subjects with Event	Event Rate ¹ n/N (%)
Overall	49	36	36 / 231 (15.6%)
Cardiac disorders	18	15	15 / 231 (6.5%)
Atrial flutter	5	4	4 / 231 (1.7%)
Pericardial effusion	3	3	3 / 231 (1.3%)
Bradycardia	2	2	2 / 231 (0.9%)
Arteriosclerosis coronary artery	1	1	1 / 231 (0.4%)
Atrial fibrillation	1	1	1 / 231 (0.4%)
Atrioventricular block	1	1	1 / 231 (0.4%)
Cardiac arrest	1	1	1 / 231 (0.4%)
Cardiac tamponade	1	1	1 / 231 (0.4%)
Coronary artery disease	1	1	1 / 231 (0.4%)
Palpitations	1	1	1 / 231 (0.4%)
Supraventricular tachycardia	1	1	1 / 231 (0.4%)
Gastrointestinal disorders	5	5	5 / 231 (2.2%)
Abdominal pain	1	1	1 / 231 (0.4%)
Abdominal pain upper	1	1	1 / 231 (0.4%)
Diarrhea	1	1	1 / 231 (0.4%)

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System Organ Class (SOC) Preferred Term (PT)	Number of Events	Number of Subjects with Event	Event Rate ¹ n/N (%)
Gastrointestinal hemorrhage	1	1	1 / 231 (0.4%)
Hematemesis	1	1	1 / 231 (0.4%)
Musculoskeletal and connective tissue disorders	4	4	4 / 231 (1.7%)
Osteoarthritis	2	2	2 / 231 (0.9%)
Arthritis	1	1	1 / 231 (0.4%)
Rotator cuff syndrome	1	1	1 / 231 (0.4%)
Nervous system disorders	4	4	4 / 231 (1.7%)
Headache	1	1	1 / 231 (0.4%)
Migraine	1	1	1 / 231 (0.4%)
Syncope	1	1	1 / 231 (0.4%)
Transient ischemic attack	1	1	1 / 231 (0.4%)
Respiratory, thoracic and mediastinal disorders	4	3	3 / 231 (1.3%)
Acute pulmonary oedema	1	1	1 / 231 (0.4%)
Dyspnoea	1	1	1 / 231 (0.4%)
Hypoxia	1	1	1 / 231 (0.4%)
Pulmonary embolism	1	1	1 / 231 (0.4%)
Vascular disorders	4	4	4 / 231 (1.7%)
Hypotension	1	1	1 / 231 (0.4%)
Orthostatic hypotension	1	1	1 / 231 (0.4%)
Peripheral artery aneurysm	1	1	1 / 231 (0.4%)
Thrombophlebitis superficial	1	1	1 / 231 (0.4%)
Renal and urinary disorders	3	2	2 / 231 (0.9%)
Acute kidney injury	1	1	1 / 231 (0.4%)
Nephrolithiasis	1	1	1 / 231 (0.4%)
Renal artery stenosis	1	1	1 / 231 (0.4%)
Injury, poisoning and procedural complications	2	2	2 / 231 (0.9%)
Fractured sacrum	1	1	1 / 231 (0.4%)
Tendon rupture	1	1	1 / 231 (0.4%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	2	2	2 / 231 (0.9%)
Basal cell carcinoma	1	1	1 / 231 (0.4%)
Prostate cancer	1	1	1 / 231 (0.4%)

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System Organ Class (SOC) Preferred Term (PT)	Number of Events	Number of Subjects with Event	Event Rate ¹ n/N (%)
Blood and lymphatic system disorders	1	1	1 / 231 (0.4%)
Lymphadenopathy	1	1	1 / 231 (0.4%)
General disorders and administration site conditions	1	1	1 / 231 (0.4%)
Chest discomfort	1	1	1 / 231 (0.4%)
Immune system disorders	1	1	1 / 231 (0.4%)
Drug hypersensitivity	1	1	1 / 231 (0.4%)

¹ Event rate is the percentage of subjects with the event.

Most of the SAEs were not related to Dual Energy THERMOCOOL SMARTTOUCH™ SF (DE STSF) Catheter, TRUPULSE™ Generator or study procedure (Table 18). Only one (1) subject with SAEs had causal relationship to THERMOCOOL SMARTTOUCH™ SF (STSF) Catheter and another one (1) had possible relationship to the device.

Table 18 – Serious Adverse Events by Causality (Safety Population Analysis Set, N=231)

Relationship to the Device and Procedure	Number of Events	Number of Subjects with Event	Event Rate ¹ n/N (%)
Overall	49	36	36 / 231 (15.6%)
THERMOCOOL SMARTTOUCH™ SF (STSF) Catheter			
Not Device Related	47	35	35 / 231 (15.2%)
Possible Device Related	1	1	1 / 231 (0.4%)
Causal Relationship to Device	1	1	1 / 231 (0.4%)
TRUPULSE™ Generator			
Not Device Related	49	36	36 / 231 (15.6%)
CARTO™ 3 v7.9 Workstation			
Not Device Related	48	36	36 / 231 (15.6%)
Probable Device Related	1	1	1 / 231 (0.4%)
Primary Procedure			
Not Procedure Related	40	30	30 / 231 (13.0%)
Possible Procedure Related	4	4	4 / 231 (1.7%)
Probable Procedure Related	2	2	2 / 231 (0.9%)
Causal Relationship to Procedure	3	3	3 / 231 (1.3%)

¹ Event rate is the percentage of subjects with the event.

C.4.2 – Unanticipated Serious Adverse Device Effect (UADE)

Unanticipated Serious Adverse Device Effect did not occur to any of the study subjects.

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C.4.3 – Non-Serious Adverse Events

The study reported 249 events of non-serious adverse event (NSAE) in 125 subjects (54.1%), 65 occurred during the initial 7 days, 21 during the first month after 7 days, and 73 after the first month (Table 19).

**Table 19 – Non-Serious Adverse Events by Timing of Onset
(Safety Population Analysis Set, N=231)**

Timing ¹	Number of Events	Number of Subjects with Event	Event Rate ² n/N (%)
Total	249	125	125/231 (54.1%)
Prior to Procedure	3	3	3 / 231 (1.3%)
0 - 7 Days	89	65	65 / 231 (28.1%)
8 - 30 Days	26	21	21 / 231 (9.1%)
≥ 31 Days	131	73	73 / 230 (31.7%)

¹ Timing of AE based on onset in days post the procedure (index or repeat).

² N denotes the number of subjects with follow-up duration surpassing the left bound of the time interval.

The most common NSAEs by SOC were cardiac disorders, 19.0% (44/231). The others were related to infectious disease (10.8%), respiratory, thoracic and mediastinal disorders (10.8%), gastrointestinal disorders (7.4%), nervous system disorders (6.9%), vascular disorders (7.4%), injury, poisoning and procedural complications (6.1%) and etc. (Table 20).

Table 20 – Non-serious Adverse Events by SOC and PT (Safety Population Analysis Set, N=231)

System Organ Class (SOC) Preferred Term (PT)	Number of Events	Number of Subjects with Event	Event Rate ¹ n/N (%)
Overall	249	125	125 / 231 (54.1%)
Cardiac disorders	51	44	44 / 231 (19.0%)
Pericardial effusion	17	17	17 / 231 (7.4%)
Atrial flutter	9	8	8 / 231 (3.5%)
Pericarditis	4	2	2 / 231 (0.9%)
Tachycardia	4	4	4 / 231 (1.7%)
Bradycardia	3	3	3 / 231 (1.3%)
Angina pectoris	2	2	2 / 231 (0.9%)
Palpitations	2	2	2 / 231 (0.9%)
Atrial tachycardia	1	1	1 / 231 (0.4%)
Atrioventricular block first degree	1	1	1 / 231 (0.4%)
Cardiac perfusion defect	1	1	1 / 231 (0.4%)
Coronary artery disease	1	1	1 / 231 (0.4%)
Mitral valve incompetence	1	1	1 / 231 (0.4%)
Nodal arrhythmia	1	1	1 / 231 (0.4%)
Sinus tachycardia	1	1	1 / 231 (0.4%)
Supraventricular extrasystoles	1	1	1 / 231 (0.4%)
Ventricular extrasystoles	1	1	1 / 231 (0.4%)
Ventricular tachycardia	1	1	1 / 231 (0.4%)

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System Organ Class (SOC) Preferred Term (PT)	Number of Events	Number of Subjects with Event	Event Rate ¹ n/N (%)
Infections and infestations	30	25	25 / 231 (10.8%)
COVID-19	5	5	5 / 231 (2.2%)
Bronchitis	3	3	3 / 231 (1.3%)
Cellulitis	3	3	3 / 231 (1.3%)
Cystitis	2	2	2 / 231 (0.9%)
Influenza	2	2	2 / 231 (0.9%)
Sinusitis	2	2	2 / 231 (0.9%)
Upper respiratory tract infection	2	2	2 / 231 (0.9%)
Acute sinusitis	1	1	1 / 231 (0.4%)
Breast cellulitis	1	1	1 / 231 (0.4%)
Campylobacter gastroenteritis	1	1	1 / 231 (0.4%)
Ear infection	1	1	1 / 231 (0.4%)
Fungal infection	1	1	1 / 231 (0.4%)
Fungal skin infection	1	1	1 / 231 (0.4%)
Furuncle	1	1	1 / 231 (0.4%)
Lower respiratory tract infection	1	1	1 / 231 (0.4%)
Nasal abscess	1	1	1 / 231 (0.4%)
Tinea cruris	1	1	1 / 231 (0.4%)
Vascular access site infection	1	1	1 / 231 (0.4%)
Respiratory, thoracic and mediastinal disorders	29	25	25 / 231 (10.8%)
Sleep apnoea syndrome	6	6	6 / 231 (2.6%)
Dyspnoea	4	4	4 / 231 (1.7%)
Cough	2	2	2 / 231 (0.9%)
Epistaxis	2	2	2 / 231 (0.9%)
Hypoxia	2	2	2 / 231 (0.9%)
Pulmonary mass	2	2	2 / 231 (0.9%)
Asthma	1	1	1 / 231 (0.4%)
Chronic obstructive pulmonary disease	1	1	1 / 231 (0.4%)
Dysphonia	1	1	1 / 231 (0.4%)
Dyspnoea exertional	1	1	1 / 231 (0.4%)
Pharyngeal swelling	1	1	1 / 231 (0.4%)
Productive cough	1	1	1 / 231 (0.4%)
Pulmonary embolism	1	1	1 / 231 (0.4%)
Pulmonary vein stenosis	1	1	1 / 231 (0.4%)
Throat irritation	1	1	1 / 231 (0.4%)
Upper respiratory tract congestion	1	1	1 / 231 (0.4%)
Wheezing	1	1	1 / 231 (0.4%)

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System Organ Class (SOC) Preferred Term (PT)	Number of Events	Number of Subjects with Event	Event Rate ¹ n/N (%)
Gastrointestinal disorders	19	17	17 / 231 (7.4%)
Diarrhea	2	2	2 / 231 (0.9%)
Uvulitis	2	2	2 / 231 (0.9%)
Vomiting	2	1	1 / 231 (0.4%)
Abdominal distension	1	1	1 / 231 (0.4%)
Ascites	1	1	1 / 231 (0.4%)
Colitis	1	1	1 / 231 (0.4%)
Dyspepsia	1	1	1 / 231 (0.4%)
Flatulence	1	1	1 / 231 (0.4%)
Gastritis	1	1	1 / 231 (0.4%)
Gastroesophageal reflux disease	1	1	1 / 231 (0.4%)
Hematemesis	1	1	1 / 231 (0.4%)
Inguinal hernia	1	1	1 / 231 (0.4%)
Large intestine polyp	1	1	1 / 231 (0.4%)
Lip swelling	1	1	1 / 231 (0.4%)
Mouth hemorrhage	1	1	1 / 231 (0.4%)
Oral mucosal blistering	1	1	1 / 231 (0.4%)
Nervous system disorders	19	16	16 / 231 (6.9%)
Dizziness	4	4	4 / 231 (1.7%)
Paraesthesia	3	3	3 / 231 (1.3%)
Headache	2	2	2 / 231 (0.9%)
Hypoaesthesia	2	2	2 / 231 (0.9%)
Syncope	2	2	2 / 231 (0.9%)
Dysarthria	1	1	1 / 231 (0.4%)
Facial paralysis	1	1	1 / 231 (0.4%)
Memory impairment	1	1	1 / 231 (0.4%)
Migraine	1	1	1 / 231 (0.4%)
Migraine with aura	1	1	1 / 231 (0.4%)
Presyncope	1	1	1 / 231 (0.4%)
Vascular disorders	18	17	17 / 231 (7.4%)
Hypertension	6	6	6 / 231 (2.6%)
Hypotension	5	5	5 / 231 (2.2%)
Hematoma	4	4	4 / 231 (1.7%)
Orthostatic hypotension	3	3	3 / 231 (1.3%)

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System Organ Class (SOC) Preferred Term (PT)	Number of Events	Number of Subjects with Event	Event Rate ¹ n/N (%)
Injury, poisoning and procedural complications	17	14	14 / 231 (6.1%)
Ligament sprain	3	1	1 / 231 (0.4%)
Vascular access site bruising	3	3	3 / 231 (1.3%)
Foot fracture	2	2	2 / 231 (0.9%)
Hand fracture	1	1	1 / 231 (0.4%)
Muscle strain	1	1	1 / 231 (0.4%)
Periorbital hemorrhage	1	1	1 / 231 (0.4%)
Post procedural contusion	1	1	1 / 231 (0.4%)
Post procedural hematoma	1	1	1 / 231 (0.4%)
Procedural pain	1	1	1 / 231 (0.4%)
Urinary retention postoperative	1	1	1 / 231 (0.4%)
Vascular access site hemorrhage	1	1	1 / 231 (0.4%)
Wound	1	1	1 / 231 (0.4%)
General disorders and administration site conditions	16	16	16 / 231 (6.9%)
Chest pain	4	4	4 / 231 (1.7%)
Chest discomfort	3	3	3 / 231 (1.3%)
Oedema peripheral	3	3	3 / 231 (1.3%)
Adverse drug reaction	1	1	1 / 231 (0.4%)
Fatigue	1	1	1 / 231 (0.4%)
Influenza like illness	1	1	1 / 231 (0.4%)
Non-cardiac chest pain	1	1	1 / 231 (0.4%)
Peripheral swelling	1	1	1 / 231 (0.4%)
Pyrexia	1	1	1 / 231 (0.4%)
Musculoskeletal and connective tissue disorders	12	12	12 / 231 (5.2%)
Musculoskeletal chest pain	4	4	4 / 231 (1.7%)
Back pain	2	2	2 / 231 (0.9%)
Osteoarthritis	2	2	2 / 231 (0.9%)
Arthralgia	1	1	1 / 231 (0.4%)
Groin pain	1	1	1 / 231 (0.4%)
Joint effusion	1	1	1 / 231 (0.4%)
Pain in extremity	1	1	1 / 231 (0.4%)
Metabolism and nutrition disorders	8	8	8 / 231 (3.5%)
Fluid overload	3	3	3 / 231 (1.3%)
Gout	2	2	2 / 231 (0.9%)
Hyperlipidaemia	2	2	2 / 231 (0.9%)
Diabetes mellitus	1	1	1 / 231 (0.4%)

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System Organ Class (SOC) Preferred Term (PT)	Number of Events	Number of Subjects with Event	Event Rate ¹ n/N (%)
Investigations	7	7	7 / 231 (3.0%)
Ejection fraction decreased	2	2	2 / 231 (0.9%)
Body temperature increased	1	1	1 / 231 (0.4%)
Human metapneumovirus test	1	1	1 / 231 (0.4%)
Influenza A virus test positive	1	1	1 / 231 (0.4%)
Influenza virus test positive	1	1	1 / 231 (0.4%)
Oesophagogastroduodenoscopy	1	1	1 / 231 (0.4%)
Renal and urinary disorders	7	6	6 / 231 (2.6%)
Haematuria	2	2	2 / 231 (0.9%)
Nephrolithiasis	2	2	2 / 231 (0.9%)
Chronic kidney disease	1	1	1 / 231 (0.4%)
Renal cyst	1	1	1 / 231 (0.4%)
Urinary retention	1	1	1 / 231 (0.4%)
Skin and subcutaneous tissue disorders	4	4	4 / 231 (1.7%)
Cutaneous amyloidosis	1	1	1 / 231 (0.4%)
Dermal cyst	1	1	1 / 231 (0.4%)
Dermatitis contact	1	1	1 / 231 (0.4%)
Ecchymosis	1	1	1 / 231 (0.4%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	3	3	3 / 231 (1.3%)
Breast cancer	1	1	1 / 231 (0.4%)
Colon adenoma	1	1	1 / 231 (0.4%)
Skin cancer	1	1	1 / 231 (0.4%)
Eye disorders	2	2	2 / 231 (0.9%)
Conjunctival cyst	1	1	1 / 231 (0.4%)
Visual field defect	1	1	1 / 231 (0.4%)
Reproductive system and breast disorders	2	2	2 / 231 (0.9%)
Erectile dysfunction	2	2	2 / 231 (0.9%)
Blood and lymphatic system disorders	1	1	1 / 231 (0.4%)
Hilar lymphadenopathy	1	1	1 / 231 (0.4%)
Ear and labyrinth disorders	1	1	1 / 231 (0.4%)
Hypoacusis	1	1	1 / 231 (0.4%)

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System Organ Class (SOC) Preferred Term (PT)	Number of Events	Number of Subjects with Event	Event Rate ¹ n/N (%)
Endocrine disorders	1	1	1 / 231 (0.4%)
Thyroid mass	1	1	1 / 231 (0.4%)
Hepatobiliary disorders	1	1	1 / 231 (0.4%)
Hyperbilirubinaemia	1	1	1 / 231 (0.4%)
Psychiatric disorders	1	1	1 / 231 (0.4%)

¹ Event rate is the percentage of subjects with the event.

The majority of the NSAEs were not related to study devices or procedures. Two (2) of them were probably related and seven (7) were possibly related to the Dual Energy THERMOCOOL SMARTTOUCH™ SF Catheter (Table 21).

Table 21 – Non-Serious Adverse Events by Causality (Safety Population Analysis Set, N=231)

Relationship to the Device and Procedure	Number of Events	Number of Subjects with Event	Event Rate ¹ n/N (%)
Overall	249	125	125 / 231 (54.1%)
THERMOCOOL SMARTTOUCH™ SF (STSF) Catheter			
Not Device Related	240	121	121 / 231 (52.4%)
Possible Device Related	7	7	7 / 231 (3.0%)
Probable Device Related	2	2	2 / 231 (0.9%)
TRUPULSE™ Generator			
Not Device Related	244	123	123 / 231 (53.2%)
Possible Device Related	5	5	5 / 231 (2.2%)
CARTO™ 3 v7.9 Workstation			
Not Device Related	245	123	123 / 231 (53.2%)
Possible Device Related	4	4	4 / 231 (1.7%)
Primary Procedure			
Not Procedure Related	182	98	98 / 231 (42.4%)
Possible Procedure Related	34	29	29 / 231 (12.6%)
Probable Procedure Related	22	20	20 / 231 (8.7%)
Causal Relationship to Procedure	11	11	11 / 231 (4.8%)

¹ Event rate is the percentage of subjects with the event.

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C.4.4 – PV Narrowing Post Ablation in CT/MRA Subset (N=34)

The subjects in Cardiac CT/MRA subset were assessed for PV narrowing after 3 months post ablation. None of the subjects had PV narrowing greater than 50% (Table 22). Only 17.6% (6/34) of the subjects in this subset had PV narrowing between >25% and 50%.

Table 22 – PV Narrowing Post Ablation by PV Targets, Subject Level (Cardiac CT/MRA Analysis Set, N=34)

Pulmonary Vein	PV Narrowing ¹				
	None 0%	Minimum >0-25%	Mild >25-50%	Moderate >50-70%	Severe >70%
Subject-Level Summary, n/N (%)	2 / 34 (5.9%)	26 / 34 (76.5%)	6 / 34 (17.6%)	0 / 34 (0.0%)	0 / 34 (0.0%)

¹ Subject-Level Summary of PV Narrowing (%) = (number of subjects whose maximum percent of PV narrowing in a specific level of narrowing / number of subjects with available CT/MRA data).

C.4.5 Assessment of Cerebral Embolic Lesions in Neurological Assessment Subset

The SmartPulse PAF study enrolled nine (9) subjects into the NAE sub-study. Seven subjects completed baseline and pre-discharge MRIs. An independent core lab evaluated the MRIs and no cerebral lesions were observed.

A separate NAE Subset Analysis Report (G230170/S010) was submitted on October 24, 2024 to the FDA to assess the potential neurological impact on subjects utilizing the Biosense Webster ablation system from a similar investigational study conducted in Europe. This report included 30 subjects enrolled into an NAE subset evaluation from the SmartfIRE study (NCT05752487) which utilized the same Biosense Webster ablation system and included a generalizable population to the SmartPulse study.

Cerebral MRI data from SmartfIRE showed cerebral lesions (FLAIR+) post-ablation in two (2) out of 30 subjects (6.7%) of the Neurological Assessment (NAE) Analysis Set. One (1) lesion was symptomatic and one (1) was asymptomatic. All lesions were resolved at the next follow-up scan, one to three months after the procedure. None of the subjects presented with a decreased neurological status based on MMSE-2, mRS and NIHSS score pre-and post-ablation.

C.5 – Additional Effectiveness Endpoints

C.5.1 – Acute Procedural Success

All subjects achieved acute procedure success of PVI that was confirmed by entrance block (Table 23).

Table 23 – Acute Procedure Success - Entrance Block Confirmation

Variable	Number of Subjects Undergone Ablation Procedure ²	Number of Successful Subjects	Success Rate n/N (%)
PP Analysis Set, N=221			
Acute Procedural Success ¹	220	220	220/220 (100.0%)
mITT Analysis Set, N=224			
Acute Procedural Success ¹	220	220	220/220 (100.0%)
All Treated Analysis Set, N=231			
Acute Procedural Success ¹	227	227	227/227 (100.00)

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¹ Acute procedural success is defined as confirmation of entrance block in all PVs after adenosine/isoproterenol challenge.

² Number of subjects who have energy delivered with study catheter. Subjects without adenosine/isoproterenol challenge will be considered as missingness and excluded from the analysis.

C.5.2 – Acute PV Reconnection at Subject Level

After the initial completion of PV ablation and confirmation of isolation by entrance block, 23.2% of subjects displayed acute PV reconnection following adenosine or isoproterenol challenge (Table 24).

Table 24 – Acute PV Reconnection - Subject Level

Endpoint	Number of Subjects ¹	Number of Subjects with Reconnection ²	Reconnection Rate
PP Analysis Set (N=221)			
Acute Reconnection	220	51	51 / 220 (23.2%)
mITT Analysis Set (N=224)			
Acute Reconnection	220	51	51 / 220 (23.2%)

¹ Subjects has not undergone adenosine/isoproterenol challenge are excluded.

² Subjects with at least one vein with reconnection identified after adenosine/isoproterenol challenge.

C.5.3 – First Pass Isolation at Subject Level

The first pass isolation, achievement of PVI as confirmed by entrance block after closure of ablation lesions encircling the ipsilateral PV pairs before administration of adenosine/ isoproterenol to induce dormant connections, was achieved in 95.4% of subjects in PP analysis set (Table 25).

Table 25 – First Pass Isolation - Subject Level

Endpoint	Number of Subjects	Number of Subjects with FPI	FPI Rate n/N (%)
PP Set (N=221)			
First Pass Isolation (FPI)	219	209	209 / 219 (95.4%)
mITT Set (N=224)			
First Pass Isolation (FPI)	221	210	210 / 221 (95.0%)

C.5.4 – Repeat ablation Procedures

Repeat ablations were performed in 10.9% (24/221) of subjects in PP analysis set. None of the subjects performed more than one repeat ablations (Table 26). Repeat ablation performed during the blanking period accounted for 8.3% (2/24) of procedures. The remaining 91.7% (22/24) were performed during the evaluation period.

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Table 26 – Repeat Ablation Procedures (mITT Analysis Set, N=224 and PP Analysis Set, N=221)

Variable	PP Set (N=221) n/N (%)	mITT Set (N=224) n/N (%)
Subjects Underwent Repeat Ablation Procedures	24/221 (10.9%)	25/224 (11.2%)
Number of Repeat Ablations a Subject Underwent¹		
1	24/24 (100%)	25/25 (100%)
2	0/24 (0.0%)	0/25 (0.0%)
> 2	0/24 (0.0%)	0/25 (0.0%)
By Timing of Repeat Procedure - Days after Initial Procedure²		
During blanking period (Day 1-90)	2/24 (8.3%)	3/25 (12.0%)
During evaluation period (Day 91-365)	22/24 (91.7%)	22/25 (88.0%)
Arrhythmia Treated^{1, +}		
Atrial Fibrillation	19/24 (79.2%)	20/25 (80.0%)
Atrial Flutter Typical Right	7/24 (29.2%)	7/25 (28.0%)
Atrial Flutter Atypical Right	5/24 (20.8%)	5/25 (20.0%)
Atrial Flutter Atypical Left	4/24 (16.7%)	4/25 (16.0%)
Atrial Tachycardia Right Atrium	3/24 (12.5%)	3/25 (12.0%)
Atrial Tachycardia Left Atrium	1/24 (4.2%)	1/25 (4.0%)
AVNRT	0/24 (0.0%)	0/25 (0.0%)
Other	1/24 (4.2%)	1/25 (4.0%)

⁺ Allows for multiple selection.

¹ N denotes the number of subjects who underwent repeat ablation procedure.

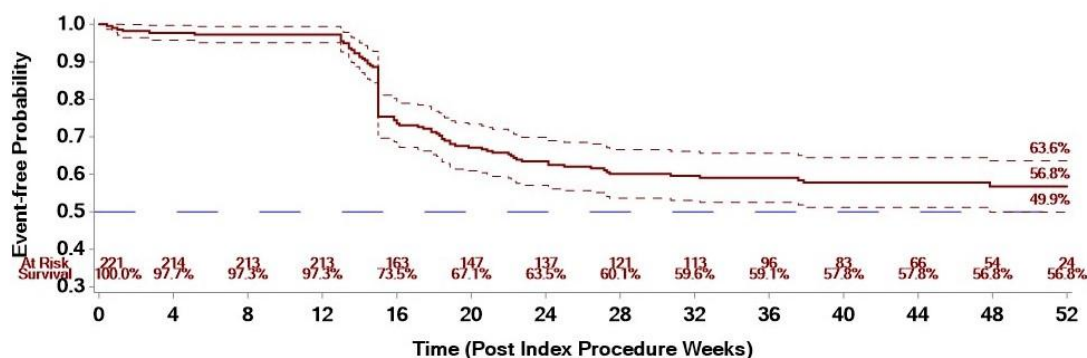
² N denotes the total number of repeat ablations.

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C.5.5 – Freedom from Documented Atrial Tachyarrhythmia of Any AAD

The 12-months rate of freedom from documented symptomatic and asymptomatic atrial tachyarrhythmia off any AAD after 3-month blanking period in PP analysis set was 56.8% by Kaplan Meier analysis with 95% CI of 49.9% and 63.6% (Figure 3).

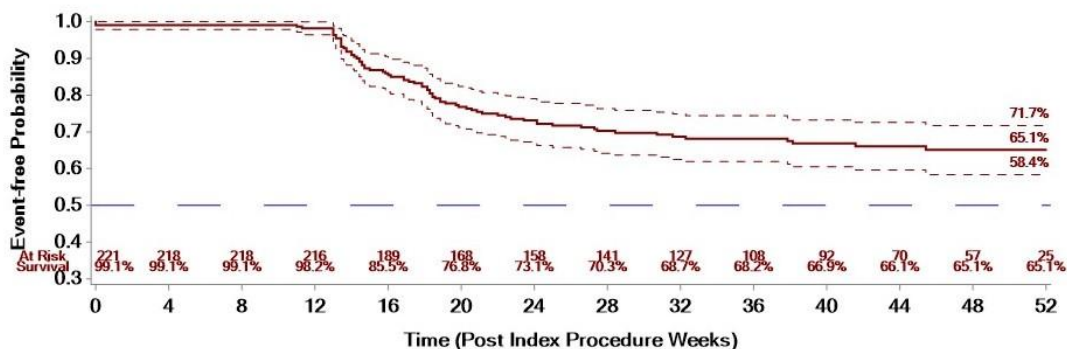
Figure 3 – Freedom from Documented Atrial Tachyarrhythmia off Any AAD (Class I or III) (PP Analysis Set, N=221)



C.5.6 – Kaplan-Meier analysis of Single Procedural Success

The 12-month rate of freedom from documented symptomatic atrial tachyarrhythmia following a single index ablation procedure after 3-month blanking period in PP analysis set was 65.1% with 95% CI of 58.4% and 71.7% (Figure 4).

Figure 4 – Kaplan-Meier Analysis of Single Procedural Success (Per Protocol Analysis Set, N=221)

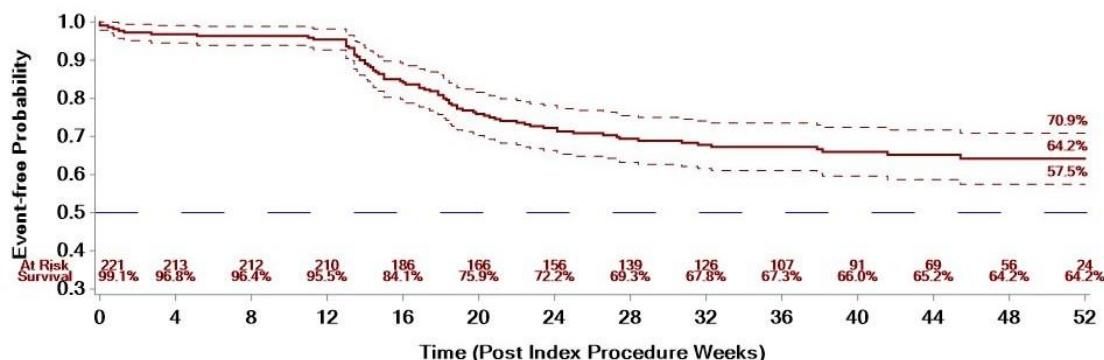


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C.5.7 – Kaplan-Meier Analysis of Single Procedure Success off Class I/III AAD

The 12-month rate of freedom from documented symptomatic atrial tachyarrhythmia following a single index ablation procedure off Class I/III AAD after 3-month blanking period in PP analysis set was 64.2% with 95% confidence CI of 57.5% and 70.9% (Figure 5).

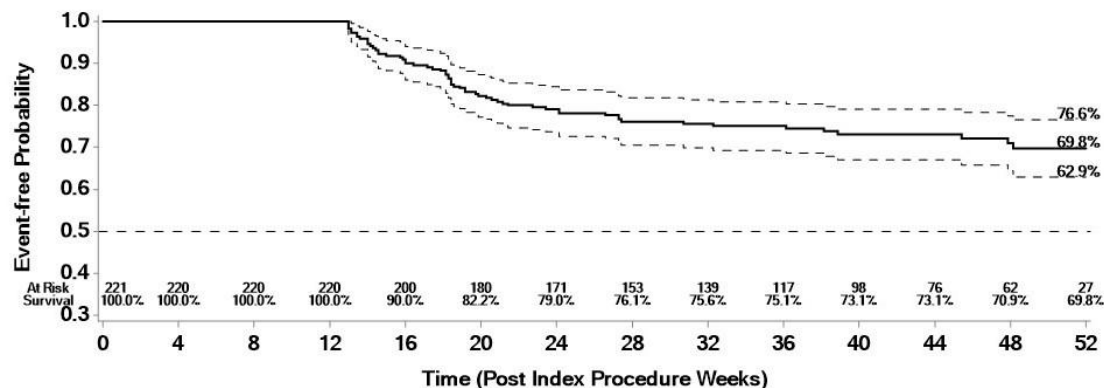
Figure 5 – Kaplan-Meier Analysis of Single Procedure Success off Class I/III AAD (PP Analysis Set, N=221)



C.5.8 – Kaplan-Meier Analysis of Time to Documented symptomatic Recurrence

The 12-month rate of freedom from documented symptomatic atrial tachyarrhythmia recurrence after 3-month blanking period in PP analysis set was 69.8% with 95% CI of 62.9% and 76.6% (Figure 6).

Figure 6 – Kaplan-Meier Analysis of Time to Documented Symptomatic Recurrence [1] (PP Analysis Set, N=221)

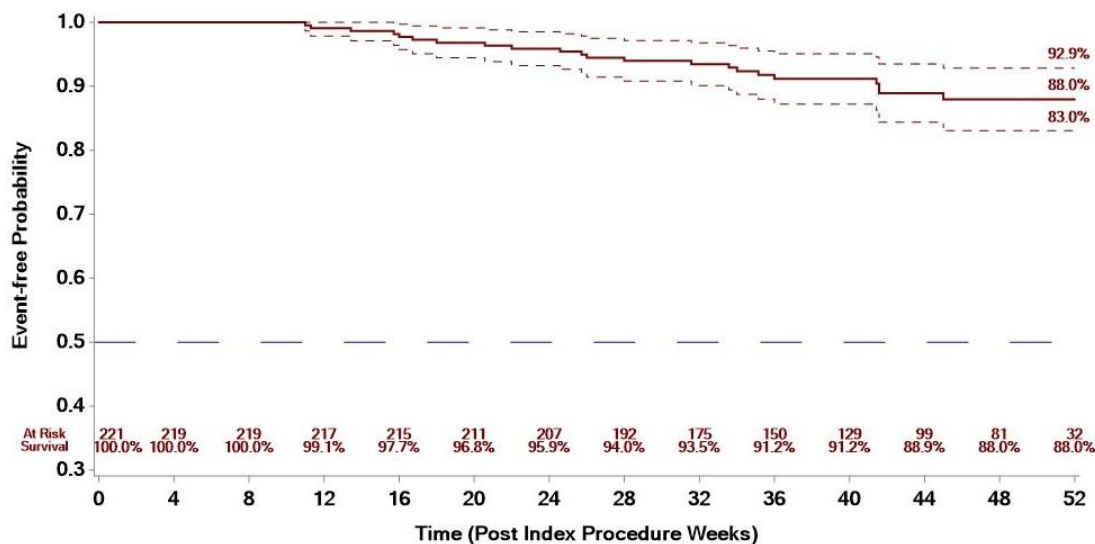


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C.5.9 – Kaplan-Meier Analysis of Time to Repeat ablation

The 12-month rate of freedom from repeat ablation in the PP analysis set at the end of the evaluation period was 88.0% with 95% CI of 83.0% and 92.9% (Figure 7)

**Figure 7 – Kaplan-Meier Analysis of Time to Repeat Ablation
Per Protocol Analysis Set (N=221)**



C.5.10 – Change of AAD Use from Baseline

At the end of the first 3 months, second 3 months, and last 6 months post ablation, the rate of AAD use was reduced by 36.1%, 44.0%, and 62.7%, respectively (Table 27).

Table 27 – AAD Utilization by Timing (PP Analysis Set, N=221)

Time Interval	Rate of AAD Use ² n/N (%)	Rate Change ³ %
Baseline¹		
AAD Used for AF/AT/AFL, n/N (%)	75 / 84 (89.3%)	
Class I/III AAD Used, n/N (%)	72 / 84 (85.7%)	
Class II/IV AAD Used, n/N (%)	28 / 84 (33.3%)	
>0 - 3 months		
AAD Used for AF/AT/AFL, n/N (%)	48 / 84 (57.1%)	-36.1%
Class I/III AAD Used, n/N (%)	43 / 84 (51.2%)	-40.3%
Class II/IV AAD Used, n/N (%)	20 / 84 (23.8%)	-28.5%
>3 - 6 months		
AAD Used for AF/AT/AFL, n/N (%)	42 / 84 (50.0%)	-44.0%
Class I/III AAD Used, n/N (%)	31 / 84 (36.9%)	-56.9%
Class II/IV AAD Used, n/N (%)	23 / 84 (27.4%)	-17.7%

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Time Interval	Rate of AAD Use ² n/N (%)	Rate Change ³ %
>6 - 12 months		
AAD Used for AF/AT/AFL, n/N (%)	28 / 84 (33.3%)	-62.7%
Class I/III AAD Used, n/N (%)	11 / 84 (13.1%)	-84.7%
Class II/IV AAD Used, n/N (%)	21 / 84 (25.0%)	-24.9%

¹ Baseline is defined as time of enrollment up to date of ablation procedure.

² N represents the number of subjects with data available at both baseline and the entire duration of the follow-up interval. n represents the number of subjects with AAD use at any point within the time interval.

³ Rate change is calculated as (follow-up rate - baseline rate)/(baseline rate) x 100.

C.5.11 – Change in Cardiovascular Hospitalization Rate

The 12-month cardiovascular hospitalization rate before and after ablation procedure was reduced by 63.4% (Table 28).

Table 28 – Change in Cardiovascular Hospitalization Rate (PP Analysis Set, N=221)

Time Interval	Number of Events	Number of Subjects with Events	CV Hospitalization Rate ² n/N (%)	Rate Change ³ %
Baseline ¹	11	11	11 / 84 (13.1%)	
> 0-12 months post procedure	4	4	4 / 84 (4.8%)	-63.4%

¹ Baseline is defined as >0-12 months pre-procedure.

² N represents the number of subjects with data available at both baseline and the entire duration of the follow-up interval. n represents the number of subjects with at least 1 CV hospitalization in the time interval.

³ Rate change is calculated as follow-up rate - baseline rate

C.5.12 – Reduction in DCCV

The DCCV was reduced from 16.7% at baseline to 10.7% during the 12 months after the ablation procedure, a reduction of 35.9% (Table 29).

Table 29 – Reduction in DCCV (PP Analysis Set, N=221)

Time Interval	Number of Events	Number of Subjects with Events	DCCV Rate ² n/N (%)	Rate Change ³ %
Baseline ¹	14	14	14 / 84 (16.7%)	
> 0-12 months post procedure	9	9	9 / 84 (10.7%)	-35.9%

¹ Baseline is defined as >0-12 months pre-procedure.

² N represents the number of subjects with data available at both baseline and had completed the 12 month follow-up visit. n represents the number of subjects with at least 1 DCCV in the time interval.

³ Rate change is calculated as (follow-up rate – baseline rate)/baseline rate.

D. Study Conclusion

The study met the primary safety and primary effectiveness performance goals of the Dual Energy THERMOCOOL SMARTTOUCH™ SF Catheter with the TRUPULSE™ Generator for treatment of drug refractory symptomatic paroxysmal atrial fibrillation. In addition, clinical benefits were observed in increased quality of life during the effectiveness monitoring period.

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STUDY 2: Pivotal Study – SmartfIRE Study

A. Objective

The primary objective of this clinical investigation was to demonstrate safety and acute effectiveness of the Dual Energy THERMOCOOL SMARTTOUCH™ SF Bi-directional Navigation (DE STSF) Catheter when used in conjunction with the TRUPULSE™ Generator for isolation of the PVs in treatment of subjects with PAF.

B. Study Design

The study was an interventional, prospective, multicenter, single-arm safety and effectiveness clinical evaluation of PAF subjects at 9 investigational sites in Europe.

B.1 – Study Endpoints

The endpoints for the study were as follows:

Primary safety endpoint – the incidence of Primary Adverse Events (PAEs) within seven (7) days of the index ablation procedure.

Primary Adverse Events included the following conditions:

- Atrio-esophageal fistula*
- Cardiac Tamponade /perforation**
- Device or procedure related death*
- Major Vascular Access Complication/Bleeding
- Myocardial Infarction
- Pericarditis
- Pulmonary Edema (Respiratory Insufficiency)
- Phrenic Nerve Paralysis (permanent)***
- Pulmonary Vein Stenosis*
- Stroke/ Cerebrovascular Accident (CVA)
- Thromboembolism
- Transient Ischemic Attack (TIA)
- Heart Block
- Vagal Nerve Injury/Gastroparesis

* Device or procedure related death, pulmonary vein stenosis and atrio-esophageal fistula that occur greater than 1 week (7 days) and less than or equal to 90 days post-procedure are considered and analyzed as PAEs.

** Cardiac Tamponade/Perforation occurring up to 30 days post AF ablation process procedure will be considered a PAE

*** A phrenic nerve paralysis is considered to be permanent when it is documented to be present 12 months or longer following ablation. Under this CIP, diaphragmatic paralysis/phrenic nerve palsy will be considered a Primary AE if specified symptoms have not improved at the 3-month visit.

Primary Effectiveness Endpoint – the percentage of subjects with acute procedural success, defined as electrical isolation of targeted PVs (confirmed by final entrance block) after adenosine/isoproterenol challenge at the end of the index ablation procedure. Use of a non-study device to achieve PVI was considered an acute procedural failure.

Secondary Endpoint – freedom from documented symptomatic and asymptomatic atrial arrhythmia episodes based on electrocardiographic data during the effectiveness evaluation period (Day 91-Day 365) on or off antiarrhythmic therapy. Acute procedural failures were also considered failures for this endpoint.

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B.2 – Prespecified Performance Goal

Primary Safety Endpoint – performance Goal = 12.0% of upper bound of two-sided 95% CI around the PAE rate.

Primary Effectiveness Endpoint – Performance Goal = 90% of lower bound of two-sided 95% CI around the acute procedural success rate.

Secondary Endpoint – Performance Goal = 50% of lower bound of two-sided 95% CI around 1-year rate of freedom from secondary effectiveness endpoint.

B.3 – Subject Disposition and Accountability

B.3.1 – Subject Disposition and Accountability

Table 30 – Subject Enrollment and Accountability (Enrolled Subjects, N=149)

Subject Enrollment	n
Enrolled Subjects ¹	149
Excluded Subjects ²	9
Study Catheter Inserted ³	140
Discontinued Subjects ⁴	1
Death	0
Withdrawn/Early Termination Subjects ⁵	2
Lost to Follow-up Subjects ⁶	0
Completed Subjects ⁷	137
PVI Durability Subset	30
Neurological Analysis Subset	30
CT/MRA Subset	30
Esophageal Endoscopy Subset	30

¹ Enrolled Subjects: Subjects who sign the Informed Consent Form (ICF).

² Excluded Subjects: Subjects who are enrolled but never undergo insertion of the study catheter.

³ Includes all enrolled subjects who have the investigational device inserted, regardless of whether energy is delivered or not.

⁴ Discontinued Subjects: Subjects who have the study catheter inserted but do not undergo ablation (i.e., no PF/RF energy applied).

⁵ Withdrawn/Early Termination Subjects: Subjects who withdraw consent for study participation prior to completion of all follow-up visits or are terminated by the site prior to completion of all follow-up visits.

⁶ Lost to Follow-up Subjects: Subjects who have study catheter inserted, but contact is lost after most recent follow-up visit (despite 3 documented attempts to contact the subject).

⁷ Completed Subjects: Enrolled subjects who have not been excluded, discontinued, withdrawn, terminated early, or lost-to-follow-up from the study prior to the final study visit.

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B.3.2 – Study Analysis Set

Table 31 – Analysis Set (Safety Population Analysis Set, N=140)

Analysis Set	n
Safety Population (SP) Analysis Set¹	140
Did not meet eligibility*	3
Modified Intent-To-Treat (mITT) Analysis Set²	137
Subjects excluded from Per Protocol Analysis (PP) Set	1
Per-Protocol (PP) Analysis Set³	136
PVI Durability Subset	30
Neurological Analysis Subset	30
CT/MRA Subset	30
Esophageal Endoscopy Subset	30

* After sponsor assessment based on all information available during the trial.

¹ SP Analysis Set: Enrolled subjects who have had the study catheter inserted, regardless of whether energy is delivered or not.

² mITT Analysis Set: Enrolled subjects who meet eligibility criteria and have had insertion of the study catheter.

³ PP Analysis Set: Subjects who satisfy the following criteria: (1) undergone ablation (PF/RF) with the study catheter, (2) treated for study-related arrhythmia, (3) no specified major CIP deviations.

B.4 – Subject Demographics

Table 32 – Demographics (Safety Population Analysis Set, N=140)

Variable	Statistics
Age (years) ¹	61.6 ± 7.79
Sex, n/N (%)	
Male	80 / 140 (57.1%)
Female	60 / 140 (42.9%)
Of Childbearing Potential	2 / 60 (3.3%)
Permanently Sterilized (or infertile)	1 / 60 (1.7%)
Postmenopausal	57 / 60 (95.0%)
Weight (kg)	85.97 ± 16.052
Height (cm)	173.9 ± 9.07
BMI (kg/m ²)	28.38 ± 4.467

¹Age at informed consent.

BMI = Body mass index.

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B.5 – Baseline Characteristics

B.5.1 – Medical History

Table 33 – Medical History (Safety Population Analysis Set, N=140)

Variable	n/N (%)
Cardiovascular Medical History*	103 / 140 (73.6%)
Congestive heart failure	18 / 140 (12.9%)
Ongoing	18 / 140 (12.9%)
NYHA Class	*
Class I	9 / 140 (6.4%)
Class II	6 / 140 (4.3%)
Coronary disease	22 / 140 (15.7%)
Ongoing	15 / 140 (10.7%)
Resolved	7 / 140 (5.0%)
Vascular disease	7 / 140 (5.0%)
Ongoing	4 / 140 (2.9%)
Resolved	3 / 140 (2.1%)
Myocardial infarction	4 / 140 (2.9%)
Hypertension (systemic)	78 / 140 (55.7%)
Ongoing	77 / 140 (55.0%)
Resolved	1 / 140 (0.7%)
Pulmonary hypertension	4 / 140 (2.9%)
Ongoing	4 / 140 (2.9%)
Cardiomyopathy	4 / 140 (2.9%)
Ongoing	3 / 140 (2.1%)
Resolved	1 / 140 (0.7%)
Hypertrophic	1 / 140 (0.7%)
Ischemic	1 / 140 (0.7%)
Non-Ischemic	2 / 140 (1.4%)
Left ventricular hypertrophy	8 / 140 (5.7%)
Ongoing	7 / 140 (5.0%)
Resolved	1 / 140 (0.7%)
Significant valvular disease	2 / 140 (1.4%)
Ongoing	2 / 140 (1.4%)
Percutaneous coronary intervention (PCI)	10 / 140 (7.1%)
Other cardiovascular procedure (e.g. CABG, etc.)	4 / 140 (2.9%)
Carotid stenting or endarterectomy	1 / 140 (0.7%)
Unstable angina	1 / 140 (0.7%)
Hypercholesterolemia	72 / 140 (51.4%)
Ongoing	71 / 140 (50.7%)
Resolved	1 / 140 (0.7%)
Other cardiovascular medical condition	5 / 140 (3.6%)

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Variable	n/N (%)
Documented Thromboembolic Events*	7 / 140 (5.0%)
Transient ischemic attack (TIA)	3 / 140 (2.1%)
Stroke	3 / 140 (2.1%) **
Ischemic	2 / 140 (1.4%)
Pulmonary embolus	1 / 140 (0.7%)
Other thromboembolic events	1 / 140 (0.7%)
Other Medical History*	65 / 140 (46.4%)
Any significant pulmonary disease	1 / 140 (0.7%)
Diabetes Mellitus	10 / 140 (7.1%)
Type II	10 / 140 (7.1%)
Obstructive sleep apnea (OSA)	6 / 140 (4.3%)
OSA Type	
Mild	1 / 140 (0.7%)
Moderate	2 / 140 (1.4%)
Severe	3 / 140 (2.1%)
OSA Effective Treatment	3 / 140 (2.1%)
Hyperthyroidism	2 / 140 (1.4%)
Effective Treatment	1 / 140 (0.7%)
Any cardiovascular hospitalizations 12 months prior to index procedure	55 / 140 (39.3%)

* Allow for multiple selection.

Note:

* subj 599-013, 1315-001, 1315-002: NYHA class unknown

** subj 501-007: stroke type unknown

B.5.2 – Atrial Fibrillation History

Table 34 – Atrial Fibrillation History (Safety Population Analysis Set, N=140)

Variable	Statistics ¹
Duration of symptomatic paroxysmal AF (months)	53.07 ± 61.802
Number of symptomatic paroxysmal AF episodes in the past 12 months	45.6 ± 81.06
Average length of each of the paroxysmal AF episode in the past 12 months (hours)	12.193 ± 20.4869
Average frequency of symptomatic paroxysmal AF in the past 12 months, n/N (%)	**
Daily	10 / 140 (7.1%)
Weekly	31 / 140 (22.1%)
Bi-weekly	11 / 140 (7.9%)
Monthly	15 / 140 (10.7%)

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Variable	Statistics ¹
Irregular	65 / 140 (46.4%)
Unknown	8 / 140 (5.7%)
Direct current cardioversion (DCCV) in the past 12 months for paroxysmal AF, n/N (%)	34 / 140 (24.3%)
1	18 / 34 (52.9%)
2	9 / 34 (26.5%)
3	2 / 34 (5.9%)
≥ 4	5 / 34 (14.7%)

¹ With available data.

Note:

* For “Number of symptomatic paroxysmal AF episodes in the past 12 months” and “Average length of each of the paroxysmal AF episode in the past 12 months (hours)” also non-documented episodes are reported. In case the information was unknown, the information was not completed, this was the case for 10 and 12 subjects respectively.

**For “Average frequency of symptomatic paroxysmal AF in the past 12 months”, also non-documented episodes are taken into account.

B.5.3 – AAD Failed at Baseline

Table 35 – AAD Failed at Baseline Per Subject (Safety Population Analysis Set, N=140)

AAD Drug Failed	Statistics
Number of AADs Failed per subject ¹	1.7 ± 0.80
Number of Class I/III AADs Failed per subject ^{1, 2}	1.3 ± 0.53
Number of Class II/IV AADs Failed per subject ^{1, 2}	1.1 ± 0.28

¹ For subjects who fail a specific AAD as indicated by a Generic Drug Class and Name.

² Class I/III and Class II/IV AAD are not mutually exclusive. Subjects who take both Class I/III and Class II/IV AAD drugs will be counted in both summaries.

B.5.4 – Baseline CHADS₂ and CHA₂DS₂-VASc Score

Table 36 – CHADS₂ and CHA₂DS₂-VASc Score (Safety Population Analysis Set, N=140)

Variable	Statistics
CHADS ₂ Score ¹	0.9±0.84
CHA ₂ DS ₂ -VASc Score ²	1.8±1.30

¹ The score for each subject is calculated as a sum of points given for each of the following conditions: 1 for congestive heart failure, 1 for hypertension, 1 for age ≥ 75 years, 1 for diabetes mellitus, and 2 for prior stroke or TIA or thromboembolism.

² The score for each subject is calculated as a sum of points given for each of the following conditions: 1 for congestive heart failure (or left ventricular systolic dysfunction), 1 for hypertension, 2 for age ≥ 75 years, 1 for diabetes mellitus, 2 for prior stroke or TIA or thromboembolism, 1 for vascular disease (e.g. peripheral artery disease, myocardial infarction, aortic plaque), 1 for age 65-74 years, and 1 for sex category (i.e. female).

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C. Results

C.1 – Procedural Data

C.1.1 – Procedural Data

Table 37 – Procedural Data of the Index Procedure (PP Analysis Set, N=136)

Variable	Statistics
Anesthesia Type, n/N (%)	
Conscious sedation	20 / 136 (14.7%)
General (unconscious sedation)	116 / 136 (85.3%)
Total procedure time (min)	109.19 ± 28.470
Transseptal Access, n/N (%)	
Double	77 / 136 (56.6%)
Single	59 / 136 (43.4%)
Pre-Ablation Mapping:	
Left atrial map acquired prior to ablation, n/N (%)	136 / 136 (100.0%)
Total LA mapping time (min)	9.52 ± 4.077
PV Ablation to Achieve PV Isolation:	
Total PV Ablation time with STSF study catheter (min)	57.87 ± 22.085
Total STSF study catheter LA dwell time (min)	80.86 ± 25.464
Total fluoroscopy duration at the end of all application (min)	6.44 ± 6.412
Fluid delivered via the study catheter(s) (mL)	456.7 ± 254.16
Heart rhythm at the beginning of the procedure, n/N (%)	
Atrial Fibrillation	12 / 136 (8.8%)
Sinus rhythm	122 / 136 (89.7%)
Other [✓]	2 / 136 (1.5%)
Predominant heart rhythm at the end of the procedure, n/N (%)	
Atrial Fibrillation	18 / 136 (13.2%)
Sinus Rhythm	118 / 136 (86.8%)
If not in sinus rhythm, cardioversion performed , n/N (%)	18 / 18 (100.0%)
Type of cardioversion, n/N (%)	
Electrical	18 / 18 (100.0%)

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C.1.2 – Use of Ablation Energy at Subject Level

Table 38 – Use of Ablation Energy at Subject Level (PP analysis Set, N=136)

Variable	Overall
Number of Valid PF/RF Applications ¹	74.4 ± 22.07
Number of RF Applications	32.3 ± 10.55
Number of Valid PF Applications ¹	42.5 ± 17.51
Total Valid PF/RF Application Time (sec) ¹	879.96 ± 363.630
Total RF Application Time (sec)	790.11 ± 339.959
Total Valid PF Application Time (sec) ¹	95.66 ± 61.735
Total Ablation Duration (min)	62.29 ± 25.046

¹ The PF ablations with all applications less than 100% status are excluded and considered as invalid.

C.1.3 – Number of Applications per Ablation Target

Table 39 – Number of Applications per ablation Target (PP Analysis Set, N=136)

Variable	Overall ¹	Number of Valid PF Applications ¹	Number of RF Applications
LPV	35.2 ± 11.39	18.8 ± 7.92	16.6 ± 6.59
RPV	37.9 ± 12.93	22.8 ± 10.89	15.5 ± 5.73
CTI Line	13.9 ± 9.66	16.6 ± 9.76	8.5 ± 4.89

C.2 – Primary Endpoints

C.2.1 – Primary Safety Endpoints

Primary adverse events occurred in 6 subjects with an incidence rate of 4.4% (6/137) in mITT analysis set. The upper bound of two-sided exact 95% confidence interval was 9.3%, which was lower than the performance goal of 12%. The study met the primary safety endpoint (Table 40).

The primary adverse events included pulmonary vein stenosis (2), cardiac tamponade/perforation (2), stroke/cerebrovascular accident (CVA) (1) and pericarditis (1).

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Table 40 – Primary Safety Endpoint (mITT Analysis Set, N=137)

Variable	Number of Events	Number of Subjects with Events	Event Rate n/N (%) ¹	Upper Bound of Two-Sided Exact 95% Confidence Intervals
Primary Adverse Event[†]	6	6	6 / 137 (4.4%)	9.3%
Atrio-Esophageal Fistula ²	0	0	0 / 137 (0.0%)	
Phrenic Nerve Paralysis (permanent) ³	0	0	0 / 137 (0.0%)	
Pulmonary Vein Stenosis ²	2	2	2 / 137 (1.5%)	
Cardiac Tamponade/perforation ⁴	2	2	2 / 137 (1.5%)	
Stroke / Cerebrovascular Accident (CVA) ⁵	1	1	1 / 137 (0.7%)	
Transient Ischemic Attack (TIA)	0	0	0 / 137 (0.0%)	
Major Vascular Access Complication / Bleeding	0	0	0 / 137 (0.0%)	
Thromboembolism	0	0	0 / 137 (0.0%)	
Myocardial Infarction	0	0	0 / 137 (0.0%)	
Pericarditis	1	1	1 / 137 (0.7%)	
Heart Block	0	0	0 / 137 (0.0%)	
Pulmonary Edema (Respiratory Insufficiency)	0	0	0 / 137 (0.0%)	
Vagal Nerve injury/Gastroparesis	0	0	0 / 137 (0.0%)	
Death (Device or procedure related) ²	0	0	0 / 137 (0.0%)	

[†] Allow for multiple selection

¹ Subjects without at least 3 months of follow-up are excluded from the primary safety analysis unless they experienced a PAE.

² Device or procedure related death, pulmonary vein stenosis and atrio-esophageal fistula that occur greater than one week (7 days) and less than or equal to 90 days post-procedure are considered and analyzed as PAEs.

³ A phrenic nerve paralysis will be considered to be permanent when it is documented to be present 12 months or longer following ablation. It is considered as a PAE if specified symptoms have not improved at the 3-month visit.

⁴ Hemodynamic compromise or instability is defined as systolic BP < 80 mm Hg. The development of a significant pericardial effusion occurring within 30 days of undergone the index AF ablation process is considered as a PAE.

⁵ Subjects with non-focal global encephalopathy are not reported as a stroke without unequivocal evidence based upon neuroimaging studies. Modified Rankin score assessments should be made by qualified individuals according to a certification process.

Note: Subject 599-014 withdrew from the trial 64 days after ablation procedure but experienced a PAE, so was included in the analysis. Subject 1472-017 withdrew from the trial 29 days after the ablation procedure in absence of any PAE, so she was treated as missing data for this analysis.

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C.2.2 – Primary Effectiveness Endpoint

Acute procedural success was achieved in 100% of subjects. The lower bound of the exact two-sided 95% confidence interval was 97.3%, which was greater than the performance goal of 90% (Table 41).

Table 41 – Acute Procedural Success (mITT analysis Set, N=137)

Variable	Number of Subjects Undergone Ablation Procedure	Number of Successful Subjects	Success Rate n/N (%) ²	Lower Bound of Two-Sided Exact 95% Confidence Intervals
Acute Procedural Success ¹	137	137	137 / 137 (100.0%)	97.3

¹ Acute procedural success is defined as confirmation of entrance block in all PVs after adenosine/isoproterenol challenge. Subjects with use of a non-study catheter for PV isolation or failure to have energy delivery with the study catheter due to ablation system malfunctions are considered acute procedural failures.

² Success rate is the proportion of subjects with acute procedural success. N denotes the number of subjects in the analysis set with adenosine/isoproterenol challenge in all PVs.

C.3 – Secondary Effectiveness Endpoint

The secondary effectiveness endpoint, the 12-month success rate of freedom from recurrences of any documented atrial arrhythmia during the effectiveness follow-up period, was 71.6% (Table 42). The lower bound of the two-sided 95% confidence interval was 63.2%, which was higher than the performance goal of 50%.

Table 42 – Secondary Effectiveness Endpoint, 12-Month Effectiveness Success (PP analysis Set, N=136)

Outcome	Number of Subjects	Success Rate n/N (%) ¹	Exact One-Sided 97.5% Lower Confidence Bound
Success	96	96/134 (71.6%)	63.2%
Failure ²	38		
Missing ³	2		

¹ N denote number of subjects in the analysis set with secondary effectiveness outcomes (success or failure) identified prior to current data cut.

² First failure: if a subject has failed for more than one event, only count for the earliest failure.

³ Missing secondary effectiveness endpoint if a subject 1) did not experience any failure and 2) did not complete the 12M follow-up, or had no ECG, TTM, HM or Post Procedural Arrhythmia data beyond 335 days after index procedure in this analysis.

Note: Subject 599-014 and 1472-017 withdrew consent prior to the effectiveness evaluation period and didn't experience an effectiveness failure.

C.4 – Additional Safety Endpoints

C.4.1 – Incidence of Serious Adverse Device Effects (SADEs)

Serious Adverse Device Effects occurred in 5 subjects (3.6%, 5/140), 3 of which were PAE and 2 non-PAEs. The PAEs included pericardial tamponade (2) and pulmonary vein stenosis evolving to occlusion (1). The non-PAEs included pulmonary vein stenosis (1) and anaphylactic shock (1). The details of SADEs by SOC and PT are presented in Table 43.

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Table 43 – Serious Adverse Device Effects by SOC and PT (Safety Population Analysis Set, N=140)

System Organ Class (SOC) Preferred Term (PT)	Number of Events	Number of Subjects with Event	Event Rate ¹ n/N (%)
Overall	5	5	5 / 140 (3.6%)
Cardiac disorders	2	2	2 / 140 (1.4%)
Cardiac tamponade	2	2	2 / 140 (1.4%)
Respiratory, thoracic and mediastinal disorders	2	2	2 / 140 (1.4%)
Pulmonary vein stenosis	2	2	2 / 140 (1.4%)
Immune system disorders	1	1	1 / 140 (0.7%)
Anaphylactic shock	1	1	1 / 140 (0.7%)

¹ Event rate is the percentage of subjects with the event.

C.4.2 – Incidence of unanticipated (serious) adverse device events (UADEs and USADEs)

No subjects had a UADE or USADE.

C.4.3 – Incidence of Serious Adverse Events (SAEs)

The study reported 26 SAEs in 23 (16.4%) subjects. By time of Onset, 10 SAEs occurred in 8 (5.7%) subjects during the initial 30 days post ablation (Table 44).

Table 44 – Serious Adverse Events by Timing of Onset (Safety Population analysis Set, N=140)

Timing ¹	Number of Events	Number of Subjects with Event	Event Rate n/N (%) ²
Total	26	23	
Prior to Procedure	0	0	0 / 140 (0.0%)
0 - 7 Days	7	6	6 / 140 (4.3%)
8 - 30 Days	3	2	2 / 140 (1.4%)
≥ 31 Days	16	15	15 / 139 (10.8%)

¹ Timing of AE based on onset in days post the procedure (index or repeat).

² N denotes the number of subjects with follow-up duration surpassing the left bound of the time interval.

Note: Subject 1472-017 withdrew from the study before Day 31

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Table 45 presents SAEs by SOC and PT. The common SAEs by SOC included Cardiac disorders (5.0%), infections and infestations (2.9%), and nervous system disorders (2.9%).

Table 45 – SAEs by SOC and PT (Safety Population Analysis Set, N=140)

System Organ Class (SOC) Preferred Term (PT)	Number of Events	Number of Subjects with Event	Event Rate ¹ n/N (%)
Overall	26	23	23 / 140 (16.4%)
Cardiac disorders	7	7	7 / 140 (5.0%)
Atrial flutter	2	2	2 / 140 (1.4%)
Atrial tachycardia	2	2	2 / 140 (1.4%)
Cardiac tamponade	2	2	2 / 140 (1.4%)
Supraventricular tachycardia	1	1	1 / 140 (0.7%)
Infections and infestations	4	4	4 / 140 (2.9%)
Diverticulitis	2	2	2 / 140 (1.4%)
Pneumonia	1	1	1 / 140 (0.7%)
Postoperative wound infection	1	1	1 / 140 (0.7%)
Nervous system disorders	4	4	4 / 140 (2.9%)
Carpal tunnel syndrome	1	1	1 / 140 (0.7%)
Hemianaesthesia	1	1	1 / 140 (0.7%)
Migraine with aura	1	1	1 / 140 (0.7%)
Radiculopathy	1	1	1 / 140 (0.7%)
Injury, poisoning and procedural complications	2	2	2 / 140 (1.4%)
Radius fracture	1	1	1 / 140 (0.7%)
Rib fracture	1	1	1 / 140 (0.7%)
Musculoskeletal and connective tissue disorders	2	2	2 / 140 (1.4%)
Arthralgia	1	1	1 / 140 (0.7%)
Cervical spinal stenosis	1	1	1 / 140 (0.7%)
Respiratory, thoracic and mediastinal disorders	2	2	2 / 140 (1.4%)
Pulmonary vein stenosis	2	2	2 / 140 (1.4%)
Gastrointestinal disorders	1	1	1 / 140 (0.7%)
Large intestine polyp	1	1	1 / 140 (0.7%)

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System Organ Class (SOC) Preferred Term (PT)	Number of Events	Number of Subjects with Event	Event Rate ¹ n/N (%)
General disorders and administration site conditions	1	1	1 / 140 (0.7%)
Chest pain	1	1	1 / 140 (0.7%)
Immune system disorders	1	1	1 / 140 (0.7%)
Anaphylactic shock	1	1	1 / 140 (0.7%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1	1	1 / 140 (0.7%)
Adenocarcinoma	1	1	1 / 140 (0.7%)
Vascular disorders	1	1	1 / 140 (0.7%)
Hypotension	1	1	1 / 140 (0.7%)

¹ Event rate is the percentage of subjects with the event.

Most of the SAEs were not related to Dual Energy THERMOCOOL SMARTTOUCH™ SF (DE STSF) Catheter, TRUPULSE™ Generator or study procedure (Table 46). Only one (1) subject with an SAE was possibly related to THERMOCOOL SMARTTOUCH™ SF (STSF) Catheter.

Table 46 – SAEs by Causality (Safety Population Analysis Set, N=140)

Relationship to the Device and Procedure	Number of Events	Number of Subjects with Event	Event Rate ¹
Overall	26	23	23 / 140 (16.4%)
THERMOCOOL SMARTTOUCH™ SF Catheter			
Causal Relationship to Device	0	0	0 / 140 (0.0%)
Probable Device Related	0	0	0 / 140 (0.0%)
Possible Device Related	1	1	1 / 140 (0.7%)
Not Device Related	25	22	22 / 140 (15.7%)
Multi-Channel TRUPULSE™ Generator			
Causal Relationship to Device	0	0	0 / 140 (0.0%)
Probable Device Related	0	0	0 / 140 (0.0%)
Possible Device Related	1	1	1 / 140 (0.7%)
Not Device Related	25	22	22 / 140 (15.7%)
Procedure			
Causal Relationship to Procedure	3	3	3 / 140 (2.1%)
Probable Procedure Related	1	1	1 / 140 (0.7%)
Possible Procedure Related	1	1	1 / 140 (0.7%)
Not Procedure Related	21	19	19 / 140 (13.6%)

¹ Event rate is the percentage of subjects with the event.

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C.4.4 – Incidence of Non-serious Adverse Events

The study reported a total of 227 NSAEs in 90 (64.3%) subjects (Table 47). By timing of onset, 39 (27.9%) subjects reported NSAE during the initial 7 days after the procedure, 71 (51.1%) reported NSAEs after one month of the procedure.

Table 47 – NSAEs by Time of Onset (Safety Population Analysis Set, N=140)

Timing ¹	Number of Events	Number of Subjects with Event	Event Rate n/N (%) ²
Total	227	90	
Prior to Procedure	4	4	4 / 140 (2.9%)
0 - 7 Days	54	39	39 / 140 (27.9%)
8 - 30 Days	9	9	9 / 140 (6.4%)
≥ 31 Days	160	71	71 / 139 (51.1%)

¹ Timing of AE based on onset in days post the procedure (index or repeat).

² N denotes the number of subjects with follow-up duration surpassing the left bound of the time interval.

Note: *Subject 1472-017 withdrew from the study before day 31.

The majority of the NSAEs were not related to Dual Energy THERMOCOOL SMARTTOUCH™ SF (DE STSF) Catheter, TRUPULSE™ Generator or study procedure (Table 48). Only three (3) subjects with NSAEs were possibly related to THERMOCOOL SMARTTOUCH™ SF (STSF) Catheter.

Table 48 – NSAEs by Causality (Safety Population Analysis Set, N=140)

Relationship to the Device and Procedure	Number of Events	Number of Subjects with Event	Event Rate ¹
Overall	227	90	90 / 140 (64.3%)
THERMOCOOL SMARTTOUCH™ SF Catheter			
Causal Relationship to Device	0	0	0 / 140 (0.0%)
Probable Device Related	0	0	0 / 140 (0.0%)
Possible Device Related	3	3	3 / 140 (2.1%)
Not Device Related	224	88	88 / 140 (62.9%)
Multi-Channel TRUPULSE™ Generator			
Causal Relationship to Device	0	0	0 / 140 (0.0%)
Probable Device Related	0	0	0 / 140 (0.0%)
Possible Device Related	3	3	3 / 140 (2.1%)
Not Device Related	224	88	88 / 140 (62.9%)
Procedure			
Causal Relationship to Procedure	20	15	15 / 140 (10.7%)
Probable Procedure Related	3	3	3 / 140 (2.1%)
Possible Procedure Related	18	17	17 / 140 (12.1%)
Not Procedure Related	186	78	78 / 140 (55.7%)

¹ Event rate is the percentage of subjects with the event.

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C.5 – Additional Effectiveness Endpoints

C.5.1 – Acute Reconnection

Acute reconnections were detected in 11.0% of subjects or 3.2% of targeted PVs (Table 49).

Table 49 – Acute PV Reconnection – Subject Level (PP Analysis Set, N=136)

Variable	Number of Subjects ¹	Number of Subjects with Reconnection ²	Rate of Reconnection
Acute Reconnection	136	15	15 / 136 (11.0%)

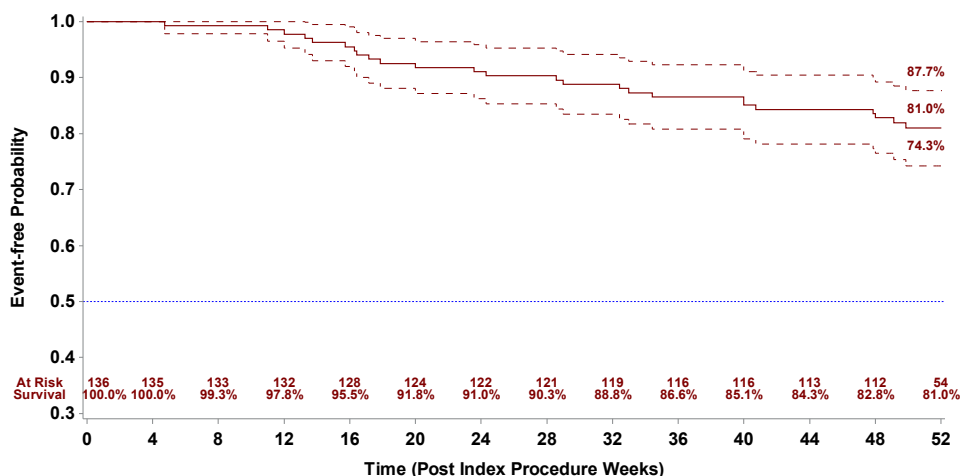
¹ Subjects undergone PV ablation procedure and adenosine/isoproterenol challenge.

² Subjects with at least one vein with reconnection identified after adenosine/isoproterenol challenge.

C.5.2 – Single Procedural Success

Kaplan-Meier (KM) estimates of the proportion of subjects who were free from symptomatic recurrences after single procedure at 12 months was 81.0%, with a two-sided 95% confidence interval of 74.3% to 87.7% in the PP analysis set (Figure 8).

Figure 8 – Kaplan-Meier Analysis of Single Procedure Success (PP Analysis Set, N=136)

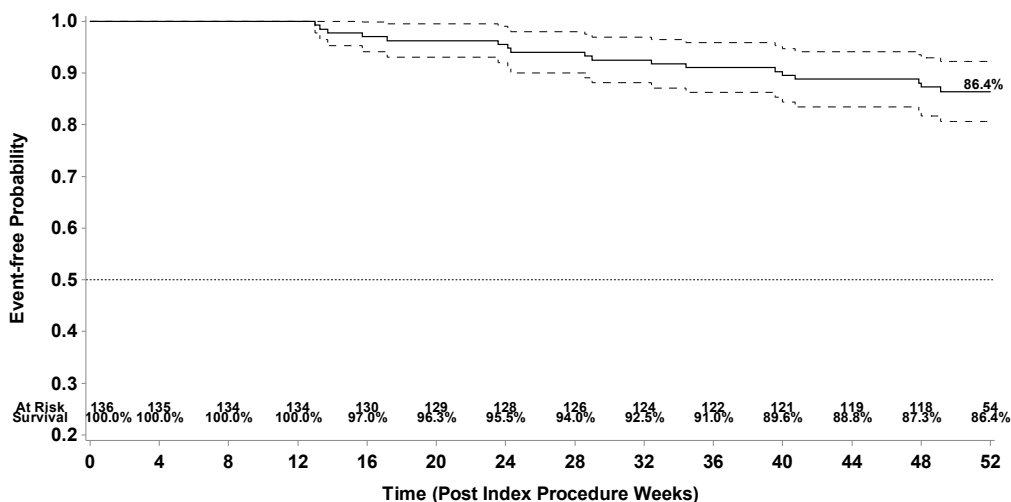


C.5.3 – Freedom from Documented symptomatic Atrial Arrhythmia

Kaplan-Meier estimates of the proportion of subjects who were free from documented symptomatic atrial arrhythmia episodes based on electrocardiographic data during the effectiveness evaluation period was 86.4%, with a two-sided 95% confidence interval of 70.6% to 92.3% in the PP analysis set (Figure 9).

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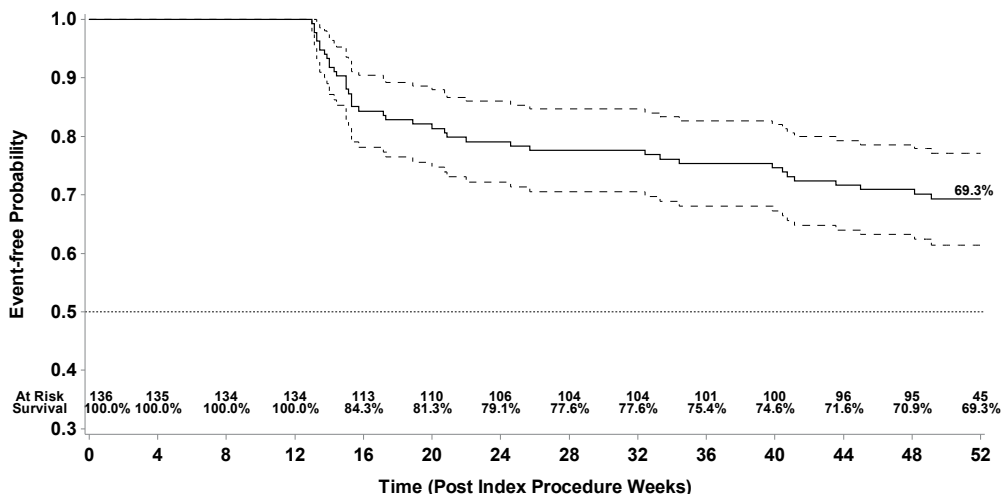
Figure 9 – Kaplan-Meier Analysis of time to Documented Symptomatic Recurrence (PP Analysis Set, N=136)



C.5.4 – Freedom from Documented Symptomatic and Asymptomatic Atrial Arrhythmia with Additional Failure Modes

Kaplan-Meier estimates of the proportion of subjects who were free from documented symptomatic and asymptomatic atrial arrhythmia during the effectiveness evaluation period and all additional failure modes was 69.3%, with a two-sided 95% confidence interval of 61.4% to 77.1% in the PP analysis set (Figure 10).

Figure 10 – Kaplan-Meier Analysis of Freedom from Documented Arrhythmia Recurrence with Additional Failure Modes (PP Analysis Set, N=136)

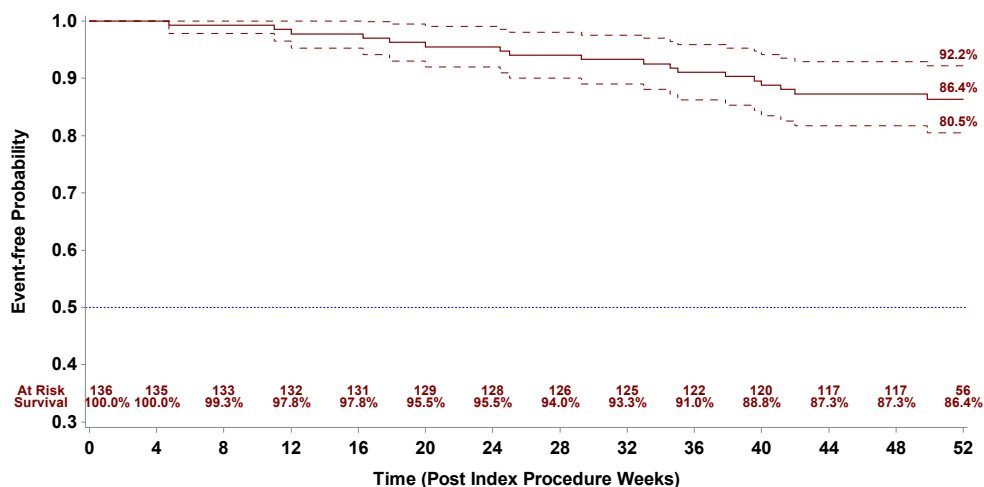


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C.5.5 – Freedom from Repeat Ablation

Kaplan-Meier estimates of the proportion of subjects who remained free from repeat ablation at 12 months was 86.4%, with two-sided 95% CI of 80.5% to 92.2% in the PP Population (Figure 11).

Figure 11 – Kaplan-Meier Analysis of Time to Repeat Ablation (PP Analysis Set, N=136)



C.5.6 – Quality of Life by AFEQT

In the PP analysis set, the overall AFEQT scores showed an average improvement of quality of life by 27.24 ± 21.463 at 12 months compared to baseline (Table 50). The average QOL improvements across the subscales were 23.82 ± 25.600 in AF-related symptoms, 29.36 ± 27.192 in daily activities, 26.66 ± 24.097 in treatment concerns, 29.89 ± 30.779 in satisfaction with current treatment control, and 29.20 ± 31.741 in satisfaction with relief of symptoms.

Table 50 – Quality of Life by AFEQT Questionnaire (PP Analysis Set, N=136)

Visit	Baseline	12 Month	Change from Baseline
Overall	59.3 ± 20.444	86.29 ± 16.176	27.24 ± 21.463
AF related symptoms	63.98 ± 23.151	87.58 ± 19.561	23.82 ± 25.600
Daily activities	55.07 ± 28.378	84.33 ± 20.691	29.36 ± 27.192
Treatment concerns	61.86 ± 22.587	88.02 ± 16.885	26.66 ± 24.097
Satisfaction Level –treatment controls	58.33 ± 26.977	87.58 ± 17.966	29.89 ± 30.779
Satisfaction Level –relief of symptoms	58.25 ± 26.795	86.76 ± 19.672	29.20 ± 31.741

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C.5.7 – Change in Cardiovascular Hospitalization Rate

Cardiovascular hospitalization rate changed from 20.1% during 12 months before ablation to 11.9% during 12 months after the ablation procedure (Table 51).

Table 51 – Change in Cardiovascular Hospitalization Rate (PP Analysis Set, N=136)

Time Interval	Number of Events	Number of Subjects with Events	CV Hospitalization Rate ² n/N (%)	Rate Change ³ %
Baseline ¹	46	27	27 / 134 (20.1%)	
> 0-12 months	22	16	16 / 134 (11.9%)	-8.2%

¹ Baseline is defined > 0 - 12 months pre-procedure.

² N represents the number of subjects with data available at both baseline and the entire duration of the follow-up interval. n represents the number of subjects with at least 1 CV hospitalization in the time interval.

³ Rate change is calculated as (follow-up rate - baseline rate).

Note: Subject 599-014 and 1472-017 withdrew consent prior to 12M and therefore not included in the denominator.

C.6 – Subset Analysis

C.6.1 – PVI Durability Rate

At a mean 79.3 ± 6.88 days post ablation, 60.0% of subjects showed that all PVs remained isolated (Table 52). The remaining 40% of subjects were found to have one or more non-isolated PVs.

Table 52 – Durability Assessment at Subject Level (PVI Durability Analysis Set, N=30)

Variable	Statistics
Subjects undergoing durability assessment	
Subjects with durable isolated veins	18/30 (60.0%)
Subjects with non-isolated veins	12/30 (40.0%)
Subjects with veins requiring re-isolation	12/30 (40.0%) *
Subjects with 1 non-isolated vein	10/30 (33.3%)
Subjects with 2 non-isolated veins	1/30 (3.3%)
Subjects with 3 non-isolated veins	1/30 (3.3%)
Days post index procedure	79.3 ± 6.88

* Additional ablation following the 3D Electro Anatomical mapping was performed in 13 subjects. Subject 1176-021 had durable isolated PVs however it was decided to ablate CTI line, no additional ablations were given in PV region.

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C.6.2 – Neurological Deficits

At discharge, two subjects had neurological events (Table 53). In the next 12 months of follow-up, one subject reported a neurological event.

Table 53 – Incidence of New or Worsening Neurologic Deficits (NA Analysis Set, N=30)

Visit	Number of Subjects ¹	Number of Neurological Events	Number of Subjects with Neurological Events
Screening/ Baseline	30	4	4
Discharge	30	2	2
1 Month Follow-Up	8	0	0
3 Month Follow-Up	2	0	0
6 Month Follow-Up	0	0	0
12 Month Follow-Up	0	0	0
Unscheduled	1	1	1

¹ Subjects with neurological assessment performed.

C.6.3 – PV narrowing

Three months after the procedure, 2 (6.7%) subjects had PV narrowing larger than 70% and 4 (13.3%) between > 50% and 70% (Table 54).

Table 54 – PV Narrowing Post Ablation Using Average Diameter, Subject Level (CT/MRA Analysis Set, N=30)

Pulmonary Vein	PV Narrowing ¹		
	Mild > 0-50%	Moderate > 50-70%	Severe > 70%
Subject-Level Summary, n/N (%)	24 / 30 (80.0%)	4 / 30 (13.3%)	2 / 30 (6.7%)

¹ Subject-Level Summary of PV Narrowing (%) = (number of subjects whose maximum percent of PV narrowing in a specific level of narrowing / number of subjects with available CT/MRA data).

C.6.4 – Esophageal Lesions

Based on esophageal endoscopy examination performed between 1 and 3 days post ablation, none of the subjects (0.0%) detected an esophageal lesion.

D. Study Conclusion

With the fulfillment of both the primary safety and effectiveness success criteria, the study is deemed successful. The Dual Energy THERMOCOOL SMARTTOUCH™ SF Catheter System has demonstrated both safety and effectiveness, meeting the study's success criteria. The outcomes affirm the conclusion that the investigational system has effectively showcased an acceptable safety and favorable effectiveness profile.

SUMMARY OF CLINICAL STUDIES CONDUCTED FOR THE THERMOCOOL SMARTTOUCH™ SF CATHETER

STUDY 1: PRECEPT Study

A. Objective

The purpose of this study was to demonstrate the safety and effectiveness of the THERMOCOOL SMARTTOUCH™ SF catheter in the treatment of drug refractory symptomatic persistent atrial fibrillation (PsAF) following standard electrophysiology mapping and RF ablation procedures.

B. Study Design

The study was a prospective, multicenter, non-randomized clinical evaluation compared to a predetermined performance goal. The study was conducted at investigational sites in the US and Canada.

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B.1 - Study Endpoints

The Endpoints for the study were as follows:

Primary effectiveness endpoint – freedom from documented atrial fibrillation, atrial flutter, and atrial tachycardia (AF/AFL/AT, atrial tachyarrhythmias) recurrence (episodes ≥ 30 sec on Holter recordings/TTM or continuously recorded on the standard 12-leads ECG) during the evaluation period (Day 181-450).

Acute success – confirmation of entrance block in all pulmonary veins.

Primary safety endpoint – incidence primary adverse events (PAE) occurring within 7 days of the initial and repeat AF ablation procedures using the study catheter per protocol. Primary adverse events included the following conditions:

- Death
- Atrio-esophageal fistula¹
- Cardiac tamponade/Perforation
- Myocardial Infarction (MI)
- Stroke/Cerebrovascular Accident (CVA)
- Thromboembolism
- Transient Ischemic Attack (TIA)
- Diaphragmatic paralysis
- Pneumothorax
- Heart block
- Pulmonary Vein (PV) stenosis¹
- Pulmonary edema (Respiratory insufficiency)
- Pericarditis
- Major vascular access complication/bleeding

¹ PV stenosis (PV) and atrio-esophageal fistula that occurs greater than one week (7 days) post-procedure shall be deemed Primary AEs.

Secondary safety endpoints included:

- Occurrence of early onset (within 7 days of initial ablation) Serious Adverse Event
- Occurrence of peri-procedural (> 7 to 30 days) Serious Adverse Event
- Occurrence of late onset (> 30 days) Serious Adverse Event

B.2 - Pre-determined Performance Goal

The performance goal was prospectively established.

- **Effectiveness** – Performance Goal = 40% lower bound of the of the 95% CI around the primary effectiveness success rate
- **Safety** – Performance Goal = 16.0% upper bound of the 95% CI around the primary AE rate

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B.3. - Subject Accountability

Table 55 – Subject Accountability and Disposition

Disposition	N
Enrolled Subjects	381
Excluded Subjects	33
Safety Population	348
Not Meeting Eligibility Criteria	14
mITT Population	334
Undergone RF Ablation	334
Subjects Treated with Non-Study Catheter	1
Per-Protocol Population	333

The following definitions were used to classify subjects:

Safety Population (n = 348) was comprised of all enrolled subjects who underwent insertion of the THERMOCOOL SMARTTOUCH™ SF Catheter.

Per-Protocol Population (n = 333) consisted of subjects who satisfied the following criteria:

- Were enrolled and met all eligibility criteria
- Had undergone RF ablation
- Were treated with the study catheters, and had been treated for the study-related arrhythmia

B.4 - Subject Demographics and Baseline Characteristics

Table 56 – Subject Demographics
(Enrolled Subjects, N = 381; Safety, N = 348; Per-Protocol, N = 333)

Demographics	Enrolled n/381 (%)	Safety n/348 (%)	Per-Protocol n/333 (%)
Gender (%)			
Male	271 (71.1)	246 (70.7)	237 (71.2)
Female	110 (28.9)	102 (29.3)	96 (28.8)
Ethnicity (%)			
Hispanic or Latino	7 (1.8)	7 (2.0)	6 (1.8)
Race (%)			
Asian	3 (0.8)	3 (0.9)	3 (0.9)
Black or African American	6 (1.6)	6 (1.7)	6 (1.8)
White	349 (91.6)	319 (91.7)	307 (92.2)
Not reported	23 (6.0)	20 (5.7)	17 (5.1)
Age (years)	65.6 ± 8.72	65.4 ± 8.71	65.4 ± 8.79
AF History (months)	15.2 ± 29.2	15.5 ± 30.2	15.9 ± 30.8
LA Dimension (mm)	42.6 ± 5.20	42.4 ± 5.14	42.6 ± 5.06
LVEF (%)	56.0 ± 7.43	56.2 ± 7.23	56.2 ± 7.24

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Table 57 – Baseline Characteristics
(Enrolled Subjects, N = 381; Safety, N = 348; Per-Protocol, N = 333)

Medical History	Enrolled n/381 (%)	Safety n/348 (%)	Per-Protocol n/333 (%)
Hypertension	260 (68.2)	238 (68.4)	227 (68.2)
Diabetes	69 (18.1)	62 (17.8)	61 (18.3)
Obstructive sleep apnea	145 (38.1)	134 (38.5)	132 (39.6)
AAD Failed			
Class I & III	1.3 ± 0.54	1.3 ± 0.55	1.3 ± 0.56
Heart Disease			
Coronary artery disease	86 (22.6)	77 (22.1)	74 (22.2)
Congestive heart failure	61 (16.0)	55 (15.8)	52 (15.6)
Prior myocardial infarction	23 (6.0)	19 (5.5)	19 (5.7)
Cardiomyopathy	43 (11.3)	42 (12.1)	39 (11.7)
Cardiac surgical procedures	41 (10.8)	36 (10.3)	34 (10.2)
Thromboembolic Event	27 (7.1)	25 (7.2)	24 (7.2)
Transient ischemic attack	10 (2.6)	10 (2.9)	9 (2.7)
Stroke	8 (2.1)	6 (1.7)	6 (1.8)
CHA2DS2-VASc score	2.3 ± 1.48	2.3 ± 1.48	2.3 ± 1.49
Other: Arrhythmia			
Atrial flutter	71 (18.6)	68 (19.5)	65 (19.5)
Atrial tachycardia	7 (1.8)	7 (2.0)	7 (2.1)

C. Results

C.1 - Procedural Data

Table 58 and Table 59 present the index procedural data. There were 348 procedures in 348 subjects. All subjects underwent one (1) study ablation procedure.

Table 58 – Summary of Power, Temperature, and Impedance Data per Procedure (Safety Population, n = 348)

Description	Mean ± SD (n)
Mean Power (W)	30.02 ± 7.83 (291)
Mean Temperature (°C)	24.25 ± 2.49 (291)
Mean Impedance (ohms)	117.72 ± 13.73 (277)

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**Table 59 – Summary of Ablation Procedure Parameters
(Safety Population, n = 348)**

Procedure Parameters	Mean ± SD (n)
Total Procedure Time (min)	178.0 ± 70.97 (348)
Ablation Procedure Time (min)	107.7 ± 48.64 (348)
Total Fluoroscopy Time (min)	15.29 ± 16.61 (348)
Fluid Input (ml)	2115.9 ± 1016.54 (343)
Fluid via Catheter (ml)	886.3 ± 391.19 (339)
Fluid via IV (ml)	1247.2 ± 857.14 (341)
Fluid Output (ml)	1044.2 ± 835.18 (189)
Balance (input - output) (ml)	1493.6 ± 914.34 (187)

All AF ablation procedures began with circumferential lesions targeting all pulmonary veins, with additional atrial ablation lines created as clinically required.

Table 60 summarizes the lesion sets applied to the subjects undergoing ablation during the index ablation procedures. Table 61 presents a summary of non-PV targets in the 186 procedures in the SP and 179 procedures in the PP that involved ablation beyond PVI.

**Table 60 – Outcomes by Ablation Targets per Procedure
(Safety Population, n = 348; Per-Protocol, n = 333)**

Ablation Targets	Safety n/348 (%)	Per-Protocol n/333 (%)
PVI only group	193 (55.5)	182 (54.7)
PVI+ CFAE group	60 (17.2)	59 (17.7)
PVI+ non-CFAE group	95 (27.3)	92 (27.6)

**Table 61 – Ablation Targets per Procedure
(Safety Population, n = 348; Per-Protocol, n = 333)**

Ablation Target	Safety n/186 (%)	Per-Protocol n/179 (%)
Left Inferior PV Mitral	14 (7.5)	14 (7.8)
Roof Line	90 (48.4)	87 (48.6)
Other: Linear Lesion	16 (8.6)	16 (8.9)
SVC	10 (5.4)	10 (5.6)
CFAE	60 (32.3)	59 (33.0)
Other: AF Foci	75 (40.3)	72 (40.2)
Cavo-Tricuspid Isthmus	67 (36.0)	63 (35.2)
RAGP	1 (0.5)	1 (0.6)

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C.2 - Acute Procedural Success

Acute success was defined as the confirmation of entrance block into all PVs. Any use of non-study catheters was considered acute procedural failures.

Acute procedural success results are presented in Table 62.

**Table 62 – Acute Effectiveness Summary
(Per-Protocol Population, n = 333)**

	Per Protocol
Number of Subjects with Success	330 / 333
Percentage of Subjects with Success	99.1%
One-Sided Exact 97.5% Lower Confidence Bound	97.4

C.3 - Contact Force Data

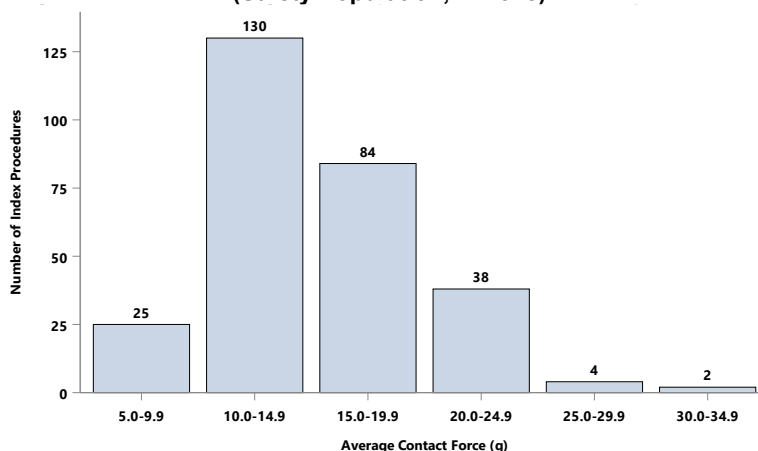
The graphical user interface (GUI) of the CARTO™ 3 workstation displays the pressure applied to the endocardial surface of the heart by the THERMOCOOL SMARTTOUCH™ SF in gram forces that the investigator can visualize during the procedure.

Table 63 presents the overall average contact force applied during the procedure for all subjects who underwent a study ablation procedure. As shown, the overall average CF applied during ablation procedures was 15.23 ± 4.41 grams. Figure 12 presents a distribution of average contact force in 5-gram increments. In the majority of procedures (239/283), the average contact force applied was less than 20 grams.

**Table 63 – Average Contact Force Measurements Overall
per Ablation Procedure (Safety Population, n = 348)**

	Average Contact Force (g)
n	298
Mean	15.23
Standard Deviation	4.41
Median	14.40
Q1 / Q3	12.10 / 18.13
Min / Max	6.6 / 33.7

**Figure 12 – Distribution of Average Contact Force per Ablation Procedure
(Safety Population, n = 348)**



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The real-time rolling graph display with the working ranges acts as a visual aid providing real-time feedback of the pressure being applied by the operator in relationship to their pre-selected CF values. In this study, the most frequently selected working range of contact force was 5 to 40 g (37.5%, 130/347), which accounted for 37.5% of the procedures (130/347).

The CARTO VISITAG™ Module of the CARTO™ 3 System provides a marker for stability during an RF application. The CARTO™ 3 System produces an auto tag on the screen at the site of RF application that is dependent on the user's pre-defined settings. The auto tag appears when the RF application reaches a pre-determined time of application and the catheter has remained stable within a pre-determined range (mm) for the time. In this study the majority of operators chose a time to auto tag from 3-5 seconds with a stability of 1.5-3.0 mm.

Figure 13 – Operator-Configured VISITAG™ Stability Time per VISITAG™ Point (Safety Population, N = 348)

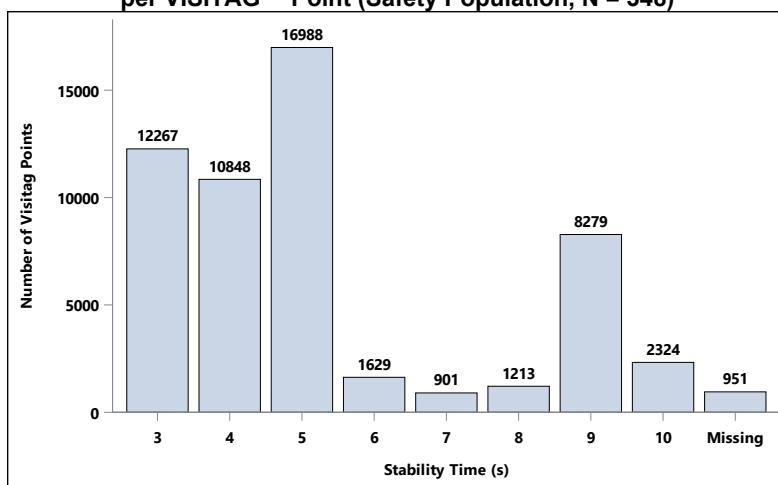
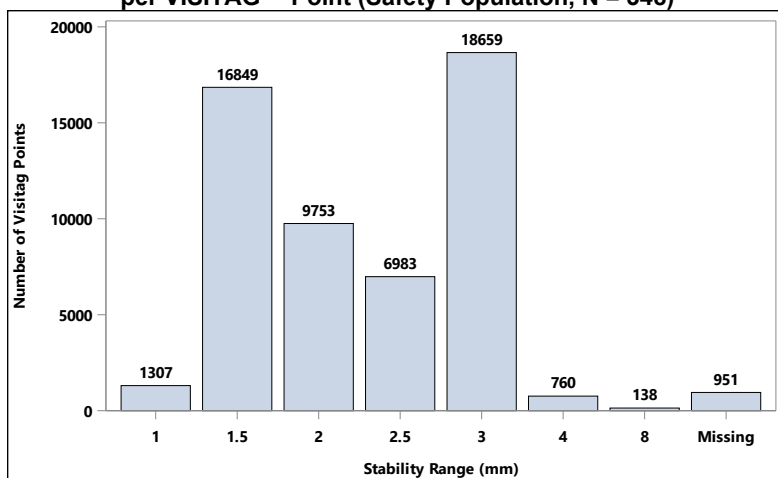


Figure 14 – Operator-Configured VISITAG™ Stability Range per VISITAG™ Point (Safety Population, N = 348)



Dual Energy THERMOCOOL SMARTTOUCH™ SF Uni-Directional Catheter

C.4 - Adverse Events (AE)

The primary safety endpoint for this study was defined as the incidence of early onset (within 7 days of ablation procedure) Primary AEs for subjects undergoing a study ablation procedure. The Safety Population (N = 348) was comprised of all enrolled subjects who had the study catheter inserted.

Primary Safety Endpoint – Primary Adverse Events

Table 64 presents the protocol-specified endpoint and safety results. There were 17 primary AEs reported in 16 subjects. Among 17 primary AEs, sixteen (16) were considered definitely procedure-related, and one (1) was considered possibly procedure-related. One (1) was considered definitely device-related, thirteen (13) were considered possibly device-related, and three (3) were considered not device-related. The overall percentage of subjects in the Safety Population who experienced a serious primary AE was 4.7% (16/344) with upper confidence at 7.4%, which is significantly less than the specified performance goal of 16.0%. Therefore, the results met the pre-specified performance goal for the safety endpoint.

**Table 64 – Primary Safety Endpoint Outcome – Primary Adverse Events
(Safety Population, n = 348)**

Variable	Number of Subjects with Event	Number of Events	Event Rate n/N (%)	One-Sided Exact 97.5% Upper Confidence Bound
Primary Adverse Event	16	17	16 / 344 (4.7)	7.4%
Death	0	0	0 / 344 (0.0)	
Atrio-esophageal Fistula	0	0	0 / 344 (0.0)	
Cardiac Tamponade	5	5	5 / 344 (1.5)	
Myocardial Infarction	0	0	0 / 344 (0.0)	
Cerebrovascular Accident (CVA)/Stroke	1	1	1 / 344 (0.3)	
Thromboembolism	0	0	0 / 344 (0.0)	
Transient Ischemic Attack	0	0	0 / 344 (0.0)	
Diaphragmatic Paralysis	1	1	1 / 344 (0.3)	
Pneumothorax	0	0	0 / 344 (0.0)	
Heart Block	0	0	0 / 344 (0.0)	
Pulmonary Vein Stenosis	0	0	0 / 344 (0.0)	
Pulmonary Edema (Respiratory Insufficiency)	5	5	5 / 344 (1.5)	
Pericarditis	2	2	2 / 344 (0.6)	
Major Vascular Access Complication/Bleeding	3	3	3 / 344 (0.9)	

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Table 65 summarizes the SAEs (by causality and body system) occurring within 30 days of a study ablation procedure that were not classified as Primary AEs by protocol definition.

Table 65 – Non Primary SAEs Occurring within 30 Days of the Ablation Procedure by Causality and Body System (Safety Population, n = 348)

Relationship to the Device/Procedure by Body System	Number of Subjects with Event	Number of Events
Occurring 0-7 Days Post Ablation Procedure		
Overall	20	20
Definitely device related	1	1
Esophageal ulcer	1	1
Possibly device related	1	1
Hypotension	1	1
Not device related	18	18
Atrial fibrillation	2	2
Hypotension	1	1
Complication associated with urinary catheter	3	3
Diplopia	1	1
Dyspnea	1	1
Fluid overload	2	2
Hypertensive crisis	1	1
Hypoxia	1	1
Pyrexia	1	1
Renal failure	1	1
Sepsis	1	1
Tachycardia	1	1
Torsade de pointes	1	1
Urinary tract infection	1	1
Definitely procedure related	9	9
Complication associated with urinary catheter	2	2
Hypotension	2	2
Fluid overload	2	2
Esophageal ulcer	1	1
Sepsis	1	1
Torsade de pointes	1	1

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Relationship to the Device/Procedure by Body System	Number of Subjects with Event	Number of Events
Occurring 0-7 Days Post Ablation Procedure		
Possibly procedure related	6	6
Complication associated with urinary catheter	1	1
Diplopia	1	1
Dyspnea	1	1
Hypoxia	1	1
Renal failure	1	1
Urinary tract infection	1	1
Not procedure related	5	5
Atrial fibrillation	2	2
Hypertensive crisis	1	1
Pyrexia	1	1
Tachycardia	1	1
Occurring 8-30 Days Post Ablation Procedure		
Overall	6	7
Not device related	6	7
Atrial flutter	1	1
Complication associated with device	1	1
Pleural effusion	1	1
Presyncope	1	1
Pulmonary embolism	1	1
Tachycardia	1	1
Tuberculosis	1	1
Definitely procedure related	1	1
Complication associated with urinary catheter	1	1
Possibly procedure related	2	2
Pleural effusion	1	1
Pulmonary embolism	1	1
Not procedure related	4	4
Atrial flutter	1	1
Presyncope	1	1
Tachycardia	1	1
Tuberculosis	1	1

Two subjects died during the study. Neither death was reported to be device or procedure-related. No deaths occurred within 3 months following the study procedure. An 80-year-old woman with known coronary artery disease, type II DM, and hypertension underwent an uncomplicated study procedure for the treatment of persistent AF. The subject developed dyspnea and was hospitalized and treated for pneumonia and congestive heart failure at 452 days following the study procedure. She was discharged

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with home oxygen and died shortly after on day 464 following the index ablation. The second death occurred in an 83-year-old man who was hospitalized on day 164 for management of non-ST-elevation myocardial infarction, atrial fibrillation, and COPD exacerbation. The hospital course was complicated by respiratory decompensation and multifactorial neurologic dysfunction requiring intubation and mechanical ventilation support. The family subsequently withdrew care, and the patient died on day 166 following the index ablation.

Table 66 summarizes the primary safety outcome for the safety population by sex. There were no statistically significant differences in the Primary AE rates between males and females ($p > 0.15$).

Table 66 – Primary Safety Endpoint by Sex (Safety Population, N = 348)

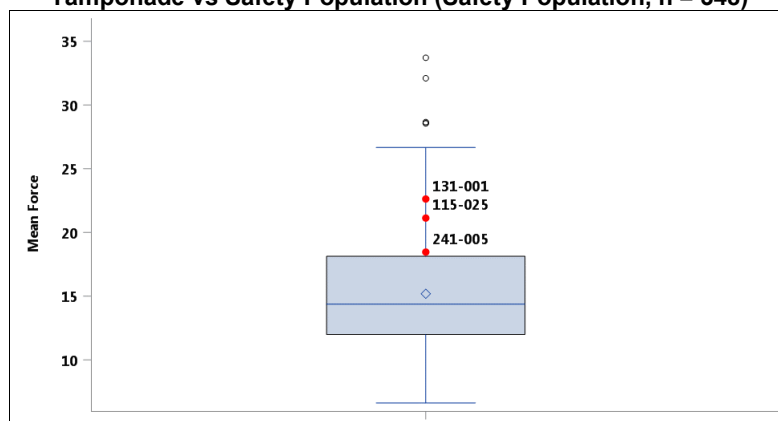
Primary Safety Endpoint	Male	Female	p-value ¹
Primary AE			1.000
n/N	12 / 244	4 / 100	
%	4.9%	4.0%	
One-Sided Exact 97.5% Upper Confidence Bound	8.4%	9.9%	

¹Fisher's exact test

C.4.1 - Average CF and Primary AEs

Figure 15 compares the average CF during procedures in subjects experiencing Primary AEs with those who did not. Average contact force was recorded for three (3) subjects with tamponade. These are marked with solid dots in the box plot of average contact force for all subjects in the safety population. Average contact force of these 3 subjects were above the Q3 (75th percentile) of overall average contact force.

Figure 15 – Comparison of Average Contact Force in Subjects with Tamponade vs Safety Population (Safety Population, n = 348)



C.5 - Primary Effectiveness Endpoint - Freedom from Atrial Tachyarrhythmias

Primary Effectiveness Analysis

The primary effectiveness endpoint was defined as freedom from documented symptomatic and asymptomatic AF/AFL/AT ("atrial tachyarrhythmias") based on electrocardiographic data and freedom from failure modes during the effectiveness evaluation period (day 181-450).

Approximately sixty percent (59.3%, 176/297) of the Per-Protocol population were free from documented atrial tachyarrhythmias and additional failure modes during their effectiveness evaluation period. The lower bound of the one-sided exact 97.5% lower confidence interval of the primary effectiveness rate was 53.4%, significantly higher than the pre-determined performance goal of 40%.

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Primary effectiveness results are described in Table 67.

Table 67 – Primary Effectiveness Endpoint through 15 Month Follow-Up Visit (Per-Protocol Population, n = 333)

Variable	Number of Subjects	Event Rate n/N (%) ¹	One-sided Exact 97.5% Lower Confidence Bound
Success	176	176/297 (59.3%)	53.4%
Failures ²	121	121/297 (40.7%)	
Missing ³	36		

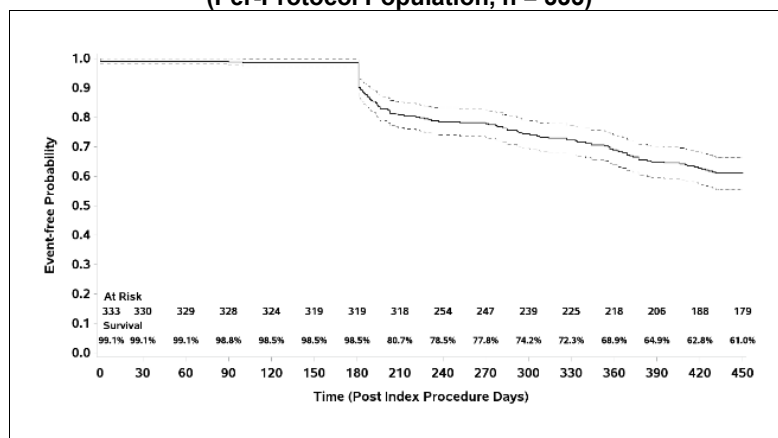
¹ N is the number of subjects with non-missing primary effectiveness endpoint.

² First failures: if a subject has more than one failure event, only the earliest failure event is considered.

³ Missing primary effectiveness endpoint: the endpoint is missing if a subject (1) did not experience any failure, (2) did not finish the 15-month follow-up, and (3) had no ECG, TTM, HM or Post Procedural Arrhythmia data beyond 422 days after index procedure.

Figure 16 shows the Kaplan-Meier survival curves for the per protocol population. The probability of freedom from primary effectiveness endpoint failure at 15 months post-blanking was 61.0%. The lower bound of the one-sided 97.5% CI for this KM graph (55.5%, as indicated by the lower dotted line) is greater than 40% of the pre-determined performance criterion. The primary effectiveness performance goal was met.

Figure 16 – Kaplan-Meier Analysis – Probability of Freedom from Chronic Effectiveness Failure through 15 Months Post-Procedure (Per-Protocol Population, n = 333)



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Comparison of Primary Effectiveness Endpoint by Sex

Table 68 presents the primary effectiveness outcome for the per-protocol population by sex. Males subjects had significantly higher success rates as compared to female subjects (64.3% vs 47.1%, nominal $p < 0.15$).

**Table 68 – Primary Effectiveness Endpoint by Sex
(Per-Protocol Population, N = 333)**

Variable	Male	Female	p-value ¹
Primary Effectiveness Endpoint			0.009
n/N	135 / 210	41 / 87	
%	64.3%	47.1%	
One-sided Exact 97.5% Lower Confidence Bound	57.4%	36.3%	

¹Fisher's exact test used to test whether primary effectiveness success rate differed by sex

C.6 - Study Design

In this study, a 6-month blanking period was employed to allow investigators additional time to adjust treatment following the index procedure. In the therapy consolidation period (months 4-6) interventions such as CV, AAD adjustment, and repeat ablation procedures were allowed without a negative impact on the primary effectiveness outcome. 77 subjects received interventions during the therapy consolidation period. Of these subjects, only 27.3% (21/77) went on to successfully complete the 15-month follow-up without recurrence of disease (AF/AFL/AT). While effectiveness success was lower for these subjects, they did contribute to the overall success of the effectiveness at 15 months.

**Table 69 – Primary Effectiveness Endpoint by
Heart Rhythm Management in Therapy Consolidation Period (Day 91-180)
(Per-Protocol Population, N = 333)**

Therapy Consolidation Period	Primary Effectiveness Success with Intervention, n/N (%)	Primary Effectiveness Success without Intervention, n/N (%)
CV	3 / 15 (20.0)	173 / 282 (61.3)
AAD Adjustment	12 / 50 (24.0)	164 / 247 (66.4)
Repeat Procedure	5 / 15 (33.3)	171 / 282 (60.6)
Recurrence	8 / 25 (32.0)	168 / 272 (61.8)
Any Intervention	21 / 77 (27.3)	155 / 220 (70.5)

C.7 - Study Conclusion

The results demonstrate that the THERMOCOOL SMARTTOUCH™ Catheter met the pre-specified performance goals for safety and effectiveness.

STUDY 2: Safety Study

A. Objective

The primary objective of this trial was to demonstrate the safety of the THERMOCOOL SMARTTOUCH™ SF Catheter with Contact Force Sensing Capability in the treatment of drug refractory symptomatic paroxysmal AF during standard electrophysiology mapping and ablation procedures.

B. Study Design

The study was a prospective, single-arm, unblinded, multi-center, pivotal, clinical investigation conducted at 19 investigational sites in the US.

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B.1 - Study Endpoints

The endpoints for the study were as follows:

Primary safety endpoint – incidence of any primary adverse event occurring within 7 days of any AF ablation procedure

Primary adverse events include the following conditions:

- Death
- Atrio-esophageal fistula¹
- Cardiac tamponade²/Atrial perforation
- Myocardial Infarction (MI)
- Stroke/Cerebrovascular Accident (CVA)
- Thromboembolism
- Transient Ischemic Attack (TIA)
- Diaphragmatic paralysis
- Pneumothorax
- Heart block
- Pulmonary Vein (PV) stenosis¹
- Pulmonary edema (Respiratory Insufficiency)
- Pericarditis
- Major vascular access complication/Bleeding

¹ Pulmonary Vein (PV) stenosis and atrio-esophageal fistula that occurred greater than one week (7 days) post-procedure were deemed primary AEs.

² Hemodynamic compromise or instability was defined as Systolic BP < 80 mm Hg.

Secondary Endpoints

Acute success – confirmation of entrance block in all pulmonary veins

Secondary safety endpoints included:

- Occurrence of early onset (within 7 days of initial ablation) serious adverse event
- Occurrence of peri-procedural (> 7 to 30 days) serious adverse event

B.2 - Pre-Specified Performance Goal

The performance goal was prospectively established.

- **Safety** – Performance Goal = 14.0% upper bound of the 95% CI around the primary AE rate

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B.3 - Subject Accountability

Table 70 – Subject Accountability and Disposition

Disposition	N	%
Enrolled Subjects	165	100.0
Excluded Subjects	6	3.6
Safety Population	159	96.4
Not Meeting Eligibility Criteria	4	2.4
mITT Population	155	93.9
Undergone RF Ablation	155	93.9
Per-Protocol Population	155	93.9
Subjects Treated with Non-Study Catheter	0	0
Subjects Treated for Non-Study Arrhythmia	0	0

The following definitions were used to classify subjects:

Safety Population (n = 159) was comprised of enrolled subjects undergoing insertion of the THERMOCOOL SMARTTOUCH™ SF Catheter.

Modified Intent-To-Treat (mITT) Population (n = 155) consisted of enrolled subjects who met the eligibility criteria and had the study catheter inserted.

B.4 - Subject Demographics and Baseline Characteristics

**Table 71 – Subject Demographics
(Enrolled Subjects, N = 165; mITT Population, N = 155)**

Demographics	Enrolled n/164	mITT n/155
Gender (%)		
Male	95 (57.9)	93 (60.0)
Female	69 (42.1)	62 (40.0)
Ethnicity – Hispanic or Latino (%)	2 (1.2)	1 (0.6)
Race (%)		
Asian	1 (0.6)	1 (0.6)
White	159 (97.0)	151 (97.4)
Pacific Islander	1 (0.6)	1 (0.6)
Black	2 (1.2)	2 (1.3)
Other	1 (0.6)	0
Age (Years)	62.7 ± 10.44	62.7 ± 10.13
AF History (months)	47.9 ± 67.45 (163)	46.0 ± 63.82 (155)
LA Dimension (mm)	38.8 ± 5.96 (154)	38.9 ± 5.87 (150)
LVEF (%)	60.1 ± 6.98 (155)	59.9 ± 6.74 (150)

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Table 72 – Baseline Characteristics
(Enrolled, N = 165; mITT Population, n = 155)

Medical History	Enrolled n/163 (%)	mITT n/155 (%)
Hypertension	93 (57.1%)	90 (58.1%)
Diabetes	23 (14.1%)	22 (14.2%)
AAD Failed		
Class I & III	116/161 (72.0)	110/155 (71.0)
Class II & IV Only	45/161 (28.0)	45/155 (29.0)
Heart Disease	44 (27.0%)	43 (27.7%)
Coronary artery disease	29 (17.8%)	28 (18.1%)
Congestive heart failure	6 (3.7%)	5 (3.2%)
Prior myocardial infarction	6 (3.7%)	6 (3.9%)
Cardiac surgical procedures	12 (7.4%)	12 (7.7%)
Thromboembolic Event	10 (6.1%)	10 (6.5%)
Transient ischemic attack	3 (1.8%)	3 (1.9%)
Stroke	4 (2.5%)	4 (2.6%)
Other Arrhythmia	68 (41.7%)	63 (40.6%)
Atrial flutter	51 (31.3%)	47 (30.3%)
Atrial tachycardia	8 (4.9%)	8 (5.2%)

C. Results

C.1 - Procedural Data

Table 73, Table 74, and Table 75 present the procedural data. There were 159 procedures in 159 subjects. All subjects underwent one (1) study ablation procedure.

Table 73 – Summary of Power, Temperature, and Impedance Data per Procedure (Safety Population, n = 159)

Description	Mean ± SD (n)
Mean Maximum Power (W)	31.3 ± 3.98 (151)
Mean Temperature (°C)	27.8 ± 3.30 (151)
Mean Impedance (Ω)	127.2 ± 15.13 (151)

On average, less power was used on the posterior wall during RF applications.

Table 74 – Mean Max Power by Pulmonary Vein Anatomical Location (Safety Population, n = 159)

Location	Mean ± SD	Median	Min / Max
Anterior	33.3 ± 4.24	35.0	12.0 / 45.8
Inferior	31.1 ± 5.30	30.9	15.3 / 45.4
Posterior	28.7 ± 5.84	30.0	10.0 / 45.5
Ridge	34.5 ± 4.64	35.5	15.4 / 45.9
Roof Line	32.2 ± 5.27	31.0	15.3 / 50.0

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**Table 75 – Summary of Ablation Procedure Parameters
(Safety Population, n = 159)**

Procedure Parameters	Mean ± SD (n)
Total Procedure Time (min)	181.1 ± 74.75 (159)
Ablation Procedure Time (min)	104.3 ± 51.48 (159)
Total Fluoroscopy Time (min)	18.5 ± 13.93 (159)
Fluid Input (ml)	2148.9 ± 1179.6 (158)
Fluid via Catheter (ml)	898.4 ± 586.33 (156)
Fluid via IV (ml)	1261.8 ± 901.76 (158)
Fluid Output (ml)	937.2 ± 962.98 (95)
Balance (input - output) (ml)	1443.0 ± 882.04 (95)

All AF ablation procedures began with circumferential lesions targeting all pulmonary veins, with additional atrial ablation lines created as clinically required.

Table 76 and Table 77 summarize the lesion sets applied to the subjects undergoing ablation during the index ablation procedures.

**Table 76 – Outcomes by Ablation Targets per Procedure
(Safety Population, n = 159)**

Ablation Targets	n/159 (%)
PV Only	60 (37.7)
PV + Atrial Linear Lesions	78 (49.1)
PV + Foci	5 (3.1)
PV + Atrial Linear Lesions + Foci	16 (10.1)
Total	159 (100.0)

**Table 77 – Atrial Linear Lesions per Procedure
(Safety Population, n = 159)**

Linear Lesions	n/159 (%)
Left Inferior PV to Mitral	3 (1.9)
SVC	3 (1.9)
Cavo-Tricuspid Isthmus	72 (45.3)
Roof line	29 (18.2)
Other	7 (4.4)

C.2 - Acute Procedural Success

Acute success was defined as the confirmation of entrance block into all PVs. Any use of non-study catheters and > 2 repeat ablations during the blanking period were considered acute procedural failures.

Acute procedural success results are presented in Table 78.

**Table 78 – Acute Effectiveness Summary
(Safety Population, n = 159)**

	Safety
Number of Subjects with Success	153 / 159
Percentage of Subjects with Success	96.2%
95% Exact Binomial Confidence Interval	(92.0%, 98.6%)

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C.3 - Contact Force Data

The THERMOCOOL SMARTTOUCH™ SF Catheter for measuring the contact force (CF) applied to the endocardial wall of the heart is comprised of the THERMOCOOL SMARTTOUCH™ SF Catheter and CARTO™ 3 EP navigation workstation with the CARTO SMARTTOUCH™ Module installed. The graphical user interface (GUI) of the CARTO™ 3 workstation displays the pressure applied to the endocardial surface of the heart as gram forces that the investigator can visualize during the procedure.

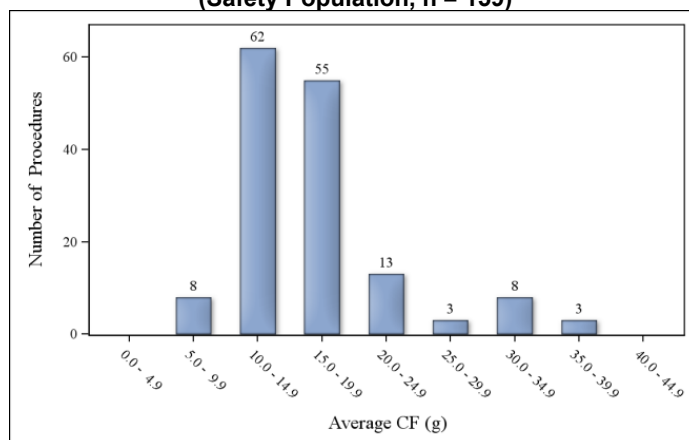
Table 79 presents the overall average contact force applied during the procedure for all subjects who underwent a study ablation procedure. As shown, the overall average CF applied during ablation procedures was 16.7 ± 6.14 grams. Figure 6 presents a distribution of average contact force in 5 gram increments. In the majority of procedures (125/152), the average contact force applied was less than 20 grams.

Table 79 – Average Contact Force Measurements Overall per Ablation Procedure (Safety Population, n = 159)

	Average Contact Force (g)
n ¹	152
Mean	16.7
Standard Deviation	6.14
Median	15.7
Q1 / Q3	12.9 / 18.7
Min / Max	7.4 / 38.3

¹ Contact force data available for 152 of 159 subjects.

Figure 17 – Distribution of Average Contact Force per Ablation Procedure (Safety Population, n = 159)



An integral part of the CARTO™ 3 graph display includes a real-time rolling graph of applied CF which includes a user configurable working range that is displayed on the graph as horizontal lines for a low and high range. The real-time rolling graph display with the working ranges acts as a visual aid providing real-time feedback of the pressure being applied by the operator in relationship to their pre-selected CF values.

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Table 80 presents the investigator-selected working ranges used during the study ablation procedures with the THERMOCOOL SMARTTOUCH™ SF Catheter.

**Table 80 – Working Ranges (g) Configured by Investigators
(Safety Population, n = 159¹)**

Lower	Upper	n / 159 (%)
0	38	1 (0.6%)
0	40	1 (0.6%)
2	23	1 (0.6%)
2	48	1 (0.6%)
3	50	5 (3.1%)
4	50	1 (0.6%)
5	20	6 (3.8%)
5	24	2 (1.3%)
5	25	8 (5.0%)
5	30	2 (1.3%)
5	35	16 (10.1%)
5	38	2 (1.3%)
5	40	70 (44.0%)
5	50	1 (0.6%)
5	60	1 (0.6%)
6	30	1 (0.6%)
6	40	1 (0.6%)
6	49	1 (0.6%)
7	46	1 (0.6%)
8	30	1 (0.6%)
9	58	1 (0.6%)
10	30	3 (1.9%)
10	40	28 (17.6%)
10	70	1 (0.6%)
15	20	1 (0.6%)
20	35	1 (0.6%)
20	40	1 (0.6%)

¹ Contact force data available for 152 of 159 subjects.

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C.3.1 - Average CF by Sex

Table 81 presents a comparison of average contact force by sex. There was no significant difference in the use of contact force between sexes.

Table 81 – Average Contact Force Measurements (g) by Sex per Ablation Procedure (Safety Population, n = 159¹)

	Male	Female	p-value
n	92	60	
Mean ± SD	16.6 ± 6.43	17.0 ± 5.73	0.3777
Median	15.5	15.8	
Min / Max	7.4 / 35.1	9.9 / 38.3	

¹ Contact force data available for 152 of 159 subjects.

C.4 - Adverse Events (AE)

The primary safety endpoint for this study was defined as the incidence of early-onset (within 7 days of ablation procedure) primary AEs for subjects undergoing a study ablation procedure. The Safety Population (n = 159) was comprised of all enrolled subjects who had the study catheter inserted.

Primary Safety Endpoint – Primary Adverse Events

Table 82 presents the protocol-specified endpoint and safety results. There were 4 primary AEs reported for 4 subjects. One primary AE was deemed related to the investigational catheter. Three (3) were deemed possibly device-related. The overall percentage of subjects in the Safety Population who experienced a serious primary AE was 2.5% (4/159) with upper confidence at 6.3%. The safety endpoint specified in the protocol was 7.0% (upper confidence bound of 14.0%). Therefore, the results met the pre-specified performance goal for the safety endpoint.

Table 82 – Primary Safety Endpoint Outcome – Primary Adverse Events (Safety Population, n = 159)

	Protocol Established Endpoint	n
Number of Subjects in Safety Cohort		159
Number of Subjects with Primary AEs		4
% Primary AEs	7.0	2.5
Upper Bound of 95% Exact CI	14.0	6.3

Table 83 summarizes the primary AEs. Of the two subjects who experienced cardiac tamponade/perforation, one underwent emergent open chest surgical repair and the other was managed medically. All primary AEs improved or resolved by the 30 day follow-up visit.

Table 83 – Primary Safety Endpoint – Early-Onset (within (≤) 7 Days) Primary Adverse Events (Safety Population, n = 159)

Description	Number of Safety with Primary AEs n/159 (%)
Total Primary AEs	4 (2.5)
Death	0
Atrio-Esophageal Fistula	0
Cardiac Tamponade/Perforation ¹	2 (1.3)
Myocardial Infarction	0
Stroke	0
Cerebrovascular Accident	0

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Description	Number of Safety with Primary AEs n/159 (%)
Thromboembolism (Ischemic Colitis)	1 (0.6)
Transient Ischemic Attack	1 (0.6)
Diaphragmatic Paralysis	0
Pneumothorax	0
Heart Block	0
Pulmonary Vein Stenosis	0
Pulmonary Edema (Respiratory Insufficiency)	0
Pericarditis	0
Major Vascular Access Complication/Bleeding	0

¹The Cardiac Tamponades/Perforation for subject 106-002 was adjudicated as both definitely device and definitely procedure related; the second for subject 265-003 was adjudicated as possible device related and definitely procedure related.

Table 84 summarizes the SAEs occurring within 30 days of a study ablation procedure that were not classified as primary AEs by protocol definition.

Table 84 – SAEs Occurring within 30 Days of the Ablation Procedure by Causality and Category (Safety Population, n = 159)

Description	Total Number of Subjects with SAEs	Total Number of SAEs
SAEs	6	6
Device-Related	0	0
Possibly Device-Related	0	0
Procedure-Related	2	2
Sepsis due to UTI	1	1
Aspiration Pneumonia	1	1
Possibly Procedure-Related	3	3
Hospitalization due to Transient Neurological Symptoms	1	1
Gastrointestinal Disorder	1	1
Septic Shock due to Pneumonia with Abscess	1	1
Not Related to Device or Procedure	1	1
AF Recurrence with Rapid Ventricular Response	1	1

There were no deaths during the study.

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C.4.1 - Average CF and Primary AEs

Table 85 compares the average CF during procedures in subjects experiencing primary AEs with those who did not. Procedural average contact force used in subjects who experienced primary AEs was similar to those that did not.

**Table 85 – Average Contact Force (g) by Primary Adverse Event
(Safety Population, n = 159¹)**

Subject ID	Primary AE	Mean ± SD	Median	Min / Max
106-001	Thromboembolism	19.4 ± 7.37	18.3	9.2 / 38.6
106-002	Cardiac Tamponade	15.7 ± 6.17	14.0	6.9 / 27.4
131-003	TIA	14.7 ± 4.79	15.0	8.2 / 25.4
Subjects who did not experience a primary AE (n = 155)		16.7 ± 6.14	15.7	7.4 / 38.3

¹ Necessary procedural data for subject 265-003 (adjudicated as cardiac tamponade/perforation due to the size of the pericardial effusion [1.3 cm]) was unavailable for analysis.

C.5 - Study Conclusion

The results demonstrate that the THERMOCOOL SMARTTOUCH™ SF Catheter met the pre-specified performance goal for safety.

SUMMARY OF CLINICAL STUDIES CONDUCTED FOR THE THERMOCOOL SMARTTOUCH™ CATHETER

STUDY 1: Pivotal Study

A. Objective

The primary objective of this trial was to demonstrate the safety and effectiveness of the THERMOCOOL SMARTTOUCH™ Catheter with Contact Force Sensing Capability for the radiofrequency ablation treatment of subjects with symptomatic Paroxysmal Atrial Fibrillation (PAF) who were refractory or intolerant to antiarrhythmic drug therapy.

B. Study Design

The study was a prospective, single-arm, unblinded, multi-center, pivotal clinical investigation conducted at 21 investigational sites in the US.

B.1 - Study Endpoints

The endpoints for the study were as follows:

Primary effectiveness endpoint – freedom from documented symptomatic atrial fibrillation (AF), atrial tachycardia (AT), or atrial flutter (AFL) episodes (hereinafter collectively referred to as “atrial tachyarrhythmias”) based on electrocardiographic data during the effectiveness evaluation period (Day 91-361) post a three-month blanking period

Acute success – confirmation of entrance block in all targeted pulmonary veins

Primary safety endpoint – incidence of early onset (within 7 days of an AF ablation procedure) primary adverse events. This included the following adverse events:

- Death
- Myocardial Infarction (MI)
- Pulmonary Vein (PV) stenosis¹
- Diaphragmatic paralysis
- Atrio-esophageal fistula¹
- Transient Ischemic Attack (TIA)

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- Stroke/Cerebrovascular Accident (CVA)
- Thromboembolism
- Pericarditis
- Cardiac tamponade
- Pericardial effusion
- Pneumothorax
- Atrial perforation
- Vascular access complications
- Pulmonary edema
- Hospitalization (initial and prolonged)
- Heart block

¹PV stenosis and atrio-esophageal fistula that occur greater than one week (7 days) post-procedure were also classified as primary AEs

Secondary safety endpoints included:

- Occurrence of peri-procedural serious adverse events > 7 but ≤ 30 days
- Occurrence of late onset (> 30 days) serious adverse events excluding PV stenosis and atrio-esophageal fistula
- Non-serious adverse events

B.2 - Objective Performance Criteria (OPC)

Objective performance goals were prospectively established.

- **Effectiveness** – Performance Goal = 50% lower bound of the 95% CI around the primary success rate
- **Safety** – Performance Goal = 16.6% upper bound of the 95% CI around the primary AE rate

B.3 - Subject Accountability

Table 86 – Subject Accountability and Disposition

Disposition	N	%
Enrolled Subjects	172	100.0
Subjects Not Meeting I/E Criteria	15	8.7
ITT Cohort	157	91.3
Enrolled Subjects	172	100.0
Excluded Subjects	11	6.4
Safety Cohort	161	93.6
Discontinued Subjects	1	0.6
Subjects Undergone RF Ablation	160	93.0
Roll-In Cases	38	22.1
Effectiveness Cohort	122	70.9
Subjects with Non-Study Arrhythmia	0	0
Subjects not meeting I/E Criteria	8	4.7
Primary Effectiveness Cohort	114	66.3

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The following definitions were used to classify subjects:

Enrolled Subjects (n = 172) Patients who signed the informed consent.

Excluded Subjects (n = 11) Subjects that were enrolled but never underwent insertion of the study catheter. Excluded subjects were not included in either the effectiveness or safety evaluation of the study catheter.

Discontinued Subjects (n = 1) Subjects that had the investigational catheter inserted but were not treated with the investigational device (i.e., no RF energy applied). Subjects were categorized as "discontinued" if ablation was not possible due to non-investigational equipment failure or if their arrhythmia was determined at the time of electrophysiologic study to be a non-study arrhythmia (e.g., atrial flutter). These discontinued subjects remained in follow-up for 7 days as part of the safety evaluation.

Intent-To-Treat (ITT) Cohort (n = 157) Enrolled subjects who met the inclusion/exclusion criteria.

Calibration Roll-In Subjects (n = 38) Enrolled subjects who underwent ablation with the study catheter during the calibration roll-in period were considered as part of the safety evaluation. Roll-in cases were prospectively identified prior to undergoing a study procedure.

Primary Effectiveness Cohort (n = 114) was comprised of subjects that received the treatment with the THERMOCOOL SMARTTOUCH™ Catheter and met the inclusion/exclusion criteria and did not meet the definitions of being excluded or discontinued. Roll-in cases were excluded from the primary effectiveness cohort.

Safety Cohort (n = 161) was comprised of enrolled subjects undergoing insertion of the THERMOCOOL SMARTTOUCH™ Catheter. The calibration roll-in subjects were included in this cohort.

B.4 - Subject Demographics

Table 87 – Subject Demographics (Enrolled Subjects, N = 172)

Table 07 – Subject Demographics (Enrolled Subjects, N = 172)				
	Total n/172 (%)	Male n/124 (%)	Female n/48 (%)	p-value
Gender				
	172 (100.0)	124 (72.1)	48 (27.9)	
Ethnicity				
Hispanic	4 (2.3)	4 (3.2)	0 (0.0)	0.5772
Race				
Asian	0 (0)	0 (0)	0 (0.0)	0.8141
Other	3 (1.7)	3 (2.4)	0 (0.0)	
Black	4 (2.3)	3 (2.4)	1 (2.10)	
White	165 (95.9)	118 (95.2)	47 (97.9)	
Age (years)				
Mean	58.8 ± 11.00	57.3 ± 10.86	62.5 ± 10.60	0.0026
Median	60.0	58.0	65.0	
Min / Max	23 / 79	23 / 79	27 / 78	

The age in the above table was when the subject signed the informed consent. The p-value listed compares the ethnicity, race and age by gender.

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C. Results

C.1 - Procedural Data

Table 88 and Table 89 present the procedural data. There were 175 procedures in 160 subjects. One hundred and forty-five (145) underwent one ablation procedure, 15 subjects (3 roll-in subjects and 12 in the effectiveness cohort) underwent a second ablation procedure. Of the 12 in the effectiveness cohort, 6 repeat ablations were during the blanking period and the remaining 6 were post-blanking due to effectiveness failure.

**Table 88 – Summary of Power, Temperature and Impedance Data
(Subjects Undergoing Ablation, n = 160¹)**

Description	Roll-In Subjects Mean ± SD (n)	Effectiveness Cohort Mean ± SD (n)	Total Mean ± SD (n)
Mean power (W)/procedure (n = 135 procedures)	31.2 ± 5.2 (29)	31.0 ± 3.7 (106)	31.1 ± 4.1 (135)
Mean temperature (°C)/procedure (n = 136 procedures)	36.3 ± 1.31 (29)	35.9 ± 1.9 (107)	36.0 ± 1.8 (136)
Mean impedance (Ω)/procedure (n = 136 procedures)	112.7 ± 11.6 (29)	120.4 ± 14.9 (107)	118.8 ± 14.5 (136)

¹ Complete procedural data were not reported for all subjects.

Note: Table 88 reflects available data from index procedures for roll-in subjects and effectiveness cohort subjects.

**Table 89 – Summary of Ablation Procedure Parameters – All Ablation Procedures
(Subjects Undergoing Ablation, n = 160¹)**

Procedure Parameters	Roll-In Subjects Mean ± SD (n)	Effectiveness Cohort Mean ± SD (n)	Total Mean ± SD (n)
Number of RF applications (n = 175 procedures)	59.0 ± 38.8 (41)	59.6 ± 44.2 (134)	59.5 ± 42.9 (175)
Mean saline infused (ml) by THERMOCOOL SMARTTOUCH™ Catheter (n = 173 procedures)	1725.7 ± 860.8 (39)	1803.6 ± 910.5 (134)	1786.0 ± 897.6 (173)
Total procedure time (min)	236.4 ± 89.1 (41)	211.6 ± 86.0 (134)	217.4 ± 87.1 (175)
Ablation procedure time (min)	116.3 ± 46.3 (39)	117.6 ± 62.6 (127)	117.3 ± 59.1 (166)
Total fluoroscopy duration (min)	47.2 ± 28.1 (39)	38.6 ± 24.6 (134)	40.5 ± 25.6 (173)
Total fluid input (ml)	3071.0 ± 1378.6 (40)	3541.6 ± 1606.6 (134)	3433.4 ± 1565.9 (174)
Total fluid output (ml)	986.8 ± 738.9 (37)	1079.3 ± 919.4 (116)	1056.9 ± 877.8 (153)
Balance (input-output) (ml)	2145.3 ± 1314.1 (36)	2689.6 ± 1511.6 (116)	2560.7 ± 1481.4 (152)

¹ Data parameters not available for all ablation procedures.

All AF ablation procedures began with circumferential lesions targeting all pulmonary veins, with additional atrial ablation lines created as clinically required.

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Table 90 summarizes the lesion sets applied to the subjects undergoing ablation during the index ablation procedures.

**Table 90 – Outcomes by Ablation Targets per Subject – 1st Ablation Procedure
(Subjects Undergoing Ablation, n = 160)**

Ablation Targets	Roll-In Subjects n ¹ /38 (%)	Effectiveness Cohort n ¹ /122 (%)	All n ¹ /160 (%)
PV Only	19 (50.0)	61 (50.0)	80 (50.0)
PV + Atrial Lines	14 (36.8)	52 (42.6)	66 (41.3)
PV + Foci	1 (2.6)	2 (1.6)	3 (1.9)
PV + Atrial Lines + Foci	4 (10.5)	7 (5.7)	11 (6.9)
Total	38 (100.0)	122 (100.0)	160 (100.0)

¹n represents number of subjects.

C.2 - Acute Procedural Success

Acute success was defined as the confirmation of entrance block into all targeted PVs. Any use of non-study catheters and > 2 repeat ablations during the blanking period were considered acute procedural failures.

Acute procedural success results are presented in Table 91.

**Table 91 – Acute Effectiveness Summary
(Primary Effectiveness Cohort, n = 114)**

	Number of Subjects n / n	Percentage of Subjects with Acute Success (%)	95% Exact Binomial Confidence Interval
Subjects Undergoing Ablation	158/160	98.8	(95.6, 99.8)
Roll-In	36/38	94.7	(82.3, 99.4)
Effectiveness Cohort	122/122	100.0	(97.0, 100.0)
Primary Effectiveness Cohort	114/114	100.0	(96.8, 100.0)

C.3 - Primary Effectiveness Endpoint - Freedom from Symptomatic Atrial Tachyarrhythmia

Primary Effectiveness Analysis

The primary effectiveness endpoint was defined as freedom from documented symptomatic AF/AT/AFL ("atrial tachyarrhythmias") based on electrocardiographic data and freedom from failure modes during the effectiveness evaluation period (Day 91-361). Any AF recurrence or repeat ablation procedure occurring greater than Day-361 post index procedure was deemed primary effectiveness successes at 12 months.

In the worst-case scenario analysis, over seventy-percent (70.2%, 80/114) of the primary effectiveness cohort were free from documented symptomatic atrial tachyarrhythmias during their effectiveness evaluation period. This includes 2 subjects who were protocol-adjudicated failures at 12 months follow-up who did not have documented symptomatic AF/AFL/AT recurrence. The lower bound of the 95% confidence interval of the primary effectiveness rate was 60.9%, significantly higher than the pre-determined performance goal of 50% ($p < 0.0001$).

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Primary effectiveness results are described in Table 92.

**Table 92 – Primary Effectiveness Endpoint through 12 Month Follow-Up Visit
(Primary Effectiveness Cohort, n = 114)**

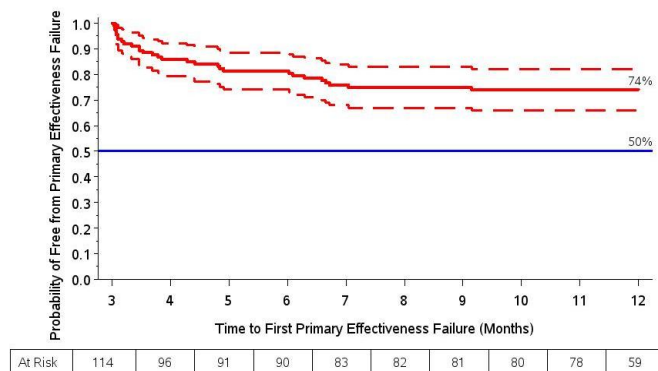
	Number of Subjects (n)	Percentage of Subjects (%)	95% Exact Binomial Confidence Interval	p-value
Freedom from Documented Symptomatic AF/AT/AFL	80	70.2	(60.9%, 78.4%)	< 0.0001
Primary Effectiveness Failures	29 ¹	25.4		
Missing Outcomes	5 ²	4.4		

¹ Two subjects were protocol adjudicated failures without documented symptomatic AF/AFL/AT recurrence.

² Five LTFU subjects were included in the denominator of the binomial exact analysis.

Figure 18 shows the Kaplan-Meier survival curves for the primary effectiveness cohort. The probability of freedom from primary effectiveness endpoint failure at 12 months post-blanking was 75.8% with a protocol-adjudicated success for this cohort of 74.0% (95% CI, 65.9%-82.2%). The lower bound of the 95% CI for this KM graph (as indicated by the lower dotted line) is greater than 50% pre-determined performance criterion. The primary effectiveness performance goal was met.

**Figure 18 – Kaplan-Meier Analysis – Probability of Freedom from Chronic Effectiveness Failure through 12 Months Post-Procedure
(Primary Effectiveness Cohort = 114)**



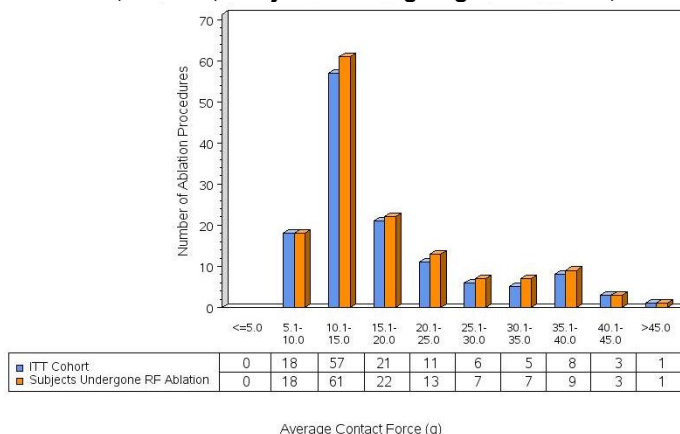
C.4 - Contact Force Data

The THERMOCOOL SMARTTOUCH™ system for measuring the contact force (CF) applied to the endocardial wall of the heart is comprised of the THERMOCOOL SMARTTOUCH™ Catheter and CARTO™ 3 EP navigation workstation with the CARTO SMARTTOUCH™ Module installed. The graphical user interface (GUI) of the CARTO™ 3 workstation displays the pressure applied to the endocardial surface of the heart as gram forces that the investigator can visualize during the procedure.

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Figure 19 presents the distribution of average contact force (CF) per ablation procedure. Overall, the average CF applied during the trial was 17.9 g $\pm$ 9.42 g.

**Figure 19 – Distribution of Average Contact Force per Ablation Procedure
(ITT Cohort, n = 157; Subjects Undergoing RF Ablation, n = 160)**



An integral part of the CARTO™ 3 System graph display includes a real-time rolling graph of applied CF which includes a user configurable working range that is displayed on the graph as horizontal lines for a low and high range. The real-time rolling graph display with the working ranges acts as a visual aid providing real-time feedback of the pressure being applied by the operator in relationship to their pre-selected CF values.

Table 93 presents the investigator-selected working ranges used during the study ablation procedures with the THERMOCOOL SMARTTOUCH™ Catheter.

**Table 93 – Working Ranges Configured by Investigators
(Subjects Undergoing an Ablation Procedure, n = 160)**

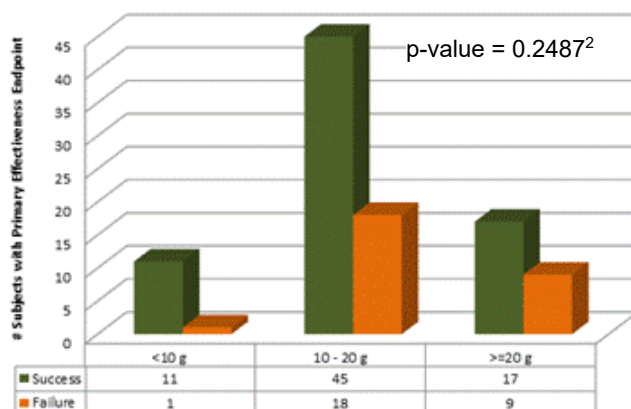
Investigator Range (g)		n / 141 (%)
Lower	Upper	
4	40	2 (1.4)
5	20	1 (0.7)
5	25	16 (11.3)
5	30	9 (6.4)
5	40	95 (67.4)
5	44	1 (0.7)
5	45	1 (0.7)
5	50	4 (2.8)
5	60	1 (0.7)
10	40	10 (7.1)
15	25	1 (0.7)

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C.4.1 - Correlation of Average CF and Primary Effectiveness

In this study the average CF during RF application for individual procedures did not correlate with the primary effectiveness endpoint. Figure 20 presents the analysis.

Figure 20 – Number of Subjects with Primary Effectiveness Endpoint by Average CF (Primary Effectiveness Cohort, n = 114¹)



¹ Subjects with censored primary effectiveness endpoint are not included in the analysis.

² Fisher's exact test

C.4.2 - Correlation of Average CF and Safety

Table 94 compares the average CF during procedures in subjects experiencing primary AEs with those who did not. Using CF as a continuous variable, there was no statistically significant difference in the average CF applied during procedures resulting in primary AEs and in those procedures that did not.

Table 94 – Average Contact Force by Primary Adverse Event (Primary Safety Cohort, n = 161)

Primary Adverse Event	Average Contact Force (g)			p-value
	Mean ± SD	Median	Min / Max	
Yes (n = 13)	18.2 ± 6.15	17.1	10.9 / 33.4	0.1995
No (n = 128)	17.8 ± 9.71	14.2	5.4 / 45.7	

C.4.3 - Correlation of CF and Tamponade

Table 95 presents the correlation of subjects experiencing cardiac tamponade AEs with the percentage of time with CF measurements were ≥ 40 grams and ≥ 50 grams. It was assumed that higher percentage of time with CF ≥ 40 grams and with CF ≥ 50 grams signified more excursions of CF applied during the procedure and that these excursions may possibly have resulted in more primary AEs and tamponades. On average 8.3% of the time was spent over 40 grams of CF with a median of 2.1% and on average only 4.8% of time was spent over 50 grams of CF, with a median of 0.8%. The data was skewed by one site where 23 cases had a mean of 35% of the time with CF ≥ 40 grams and 23% of the time with CF ≥ 50 grams. 2.1% of all cases were completed with average CF greater than or equal to 40 grams. In comparing procedures with CF ≥ 40 grams more than 2.1% of the time vs. those that were less than 2.1% of the time, there were no statistically significant differences exhibited in the comparisons presented in the table below. The four tamponade subjects all had percentage of time with CF ≥ 40 grams over 2.1%. Due to the sparse data of tamponade, the correlation was only borderline significant (p-value = 0.0581).

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**Table 95 – Correlation of Tamponade Cases with % of Time
CF Measurements $\geq$ 40 grams (Safety Cohort, n = 161¹)**

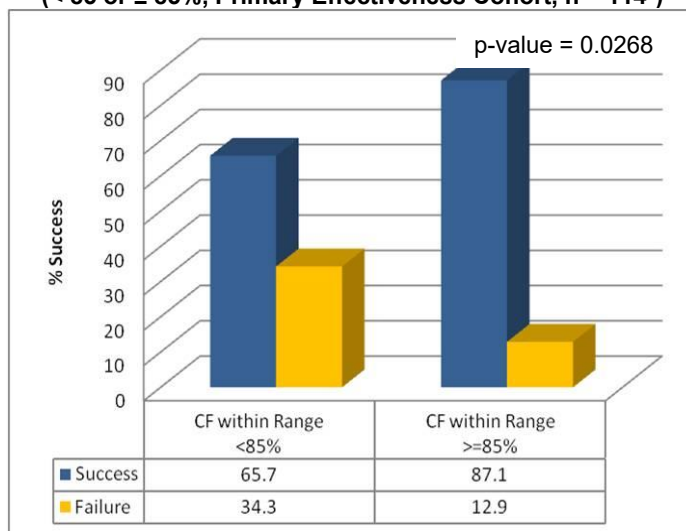
Tamponade Adverse Event	Percentage of Time with CF Measurements $\geq$ 40 Grams		p-value
	< 2.1% n / 71 (%)	$\geq$ 2.1% n / 70 (%)	
Yes	0	4 (5.7%)	0.0581
No	71 (100.0%)	66 (94.3%)	

¹ CF data were missing or not analyzable for 19 subjects.

C.4.4 - Percent of Time within Investigator-Selected Range and Primary Effectiveness and Safety

Sensitivity analysis showed that the percentage of time the investigator stayed within his selected working range (regardless of the range selected) correlated positively with primary effectiveness success. If the investigator maintained pressure on the heart endocardial surface within their selected working range 85% or more of the time during RF application, the success rate was greater than 87%. Figure 21 presents the results.

Figure 21 – Number of Subjects with Primary Effectiveness Endpoint by Percentage of Time with CF Measurements within Investigator-Selected Working Range (< 85 or $\geq$ 85%, Primary Effectiveness Cohort, n = 114¹)



¹ 101 subjects with non-missing data for primary effectiveness outcome and CF data were included in the analysis.

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Figure 22 – Time to Primary Effectiveness Failure through 12 Months Post-Procedure, by Percentage of Time in CF Working Range – Kaplan-Meier Curve (< 85% vs. ≥ 85%, Primary Effectiveness Cohort, n = 114)

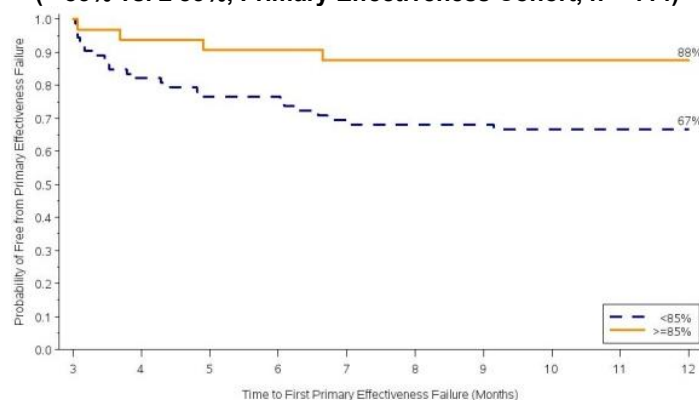


Table 96 – Primary AEs and Tamponade Adverse Event by Percentage of Time CF Measurements were within the Investigator-Selected Working Range (Primary Safety Cohort, n = 161)

Working Range (Primary Safety Cohort, n = 101)			
Percent Time within Working Range (n)	Yes n (%)	No n (%)	p-value
Primary AE			
< 85% (100)	8 (8.0)	92 (92.0)	0.5229
≥ 85% (41)	5 (12.2)	36 (87.8)	
Cardiac Tamponade Events			
< 85% (100)	2 (2.0)	98 (98.0)	0.5798
≥ 85% (41)	2 (4.9)	39 (95.1)	

C.5 - Adverse Events (AE)

The primary safety endpoint for this study was defined as the incidence of early-onset (within 7 days of ablation procedure) primary AEs for subjects undergoing a study ablation procedure. The Safety Cohort (n = 161) was comprised of all enrolled subjects who had the study catheter inserted.

Primary Safety Endpoint – Primary Adverse Events

Table 97 presents the protocol-established endpoint and safety results. There were 17 primary AEs reported for 16 subjects. One primary AE was deemed related to the investigational catheter. Two were deemed possibly device-related. The remainder were deemed unrelated to the investigational catheter. The overall percentage of subjects who experienced a serious primary AE was 9.9% (16/161) and the upper confidence bound based on the Primary Safety Cohort was 15.6%. The safety endpoint specified in the protocol was 8.6% (upper confidence bound of 16.6%). Therefore, the results met the protocol-established performance criteria for the safety endpoint.

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**Table 97 – Primary Safety Endpoint Outcome – Primary Adverse Events
(Primary Safety Cohort, n = 161)**

	Protocol Established Endpoint	n
Number of Subjects in Safety Cohort		161
Number of Subjects with Primary AEs		16
% Primary AEs	8.6	9.9
Upper Bound of the Two-Sided 95% Confidence Interval ¹	16.6	15.6

¹ Exact binomial using a commercially available software package.

Table 98 summarizes the major primary AEs.

**Table 98 – Primary Safety Endpoint – Early-Onset (within (≤) 7 Days)
Primary Adverse Events (Primary Safety Cohort, n = 161)**

Description	Number of Subjects with Primary AEs n/161 (%)
Total Serious Primary AEs	16¹ (9.9%)
Death	0
Atrio-Esophageal Fistula	0
Atrial Perforation	0
Cardiac Tamponade	4 (2.48)
Myocardial Infarction	0
Stroke	0
Cerebrovascular Accident	0
Thromboembolism	0
Transient Ischemic Attack	0
Diaphragmatic Paralysis	0
Pneumothorax	0
Heart Block	1 (0.62)
Pulmonary Vein Stenosis	0
Pulmonary Edema	0
Pericarditis	3 (1.86)
Hospitalization (initial and prolonged)	6 (3.72)
Pericardial Effusion	0
Vascular Access Complication	3 (1.86)

¹ One subject appears in two categories.

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Table 99 summarizes the SAEs occurring within 30 days of a study ablation procedure that were not classified as primary AEs by protocol definition.

**Table 99 – SAEs Occurring within 30 Days of the Ablation Procedure
by Causality and Category (Safety Cohort, n = 161)**

Description	Total Subjects with SAEs	Total Number of SAEs
Non-SAEs	8	8
Device-Related	0	0
Possibly Device-Related	0	0
Procedure-Related	1	1
Hospitalization: AF Recurrence	1	1
Possibly Procedure-Related	1	1
Loss of Consciousness	1	1
Not Related	6	6
Other: Dysphagia	1	1
Hospitalization:		
AF Recurrence	4	4
Rectal Bleed	1	1

There were no deaths during the study.

C.6 - Study Conclusion

The results demonstrate that the THERMOCOOL SMARTTOUCH™ Catheter met the objective criteria performance for safety and effectiveness.

STUDY 2: Continued Access Study

A. Objective

The purpose of this study was to allow continued access of the THERMOCOOL SMARTTOUCH™ Catheter for the ablation treatment of subjects with drug refractory symptomatic paroxysmal atrial fibrillation while the sponsor completed analysis of the pivotal study under the current IDE protocol and the FDA reviewed the pre-market application. This study provided additional corroborative safety and effectiveness data for the THERMOCOOL SMARTTOUCH™ Catheter system.

B. Study Design and Endpoints

The study design and endpoints were the same as those outlined above in the pivotal study.

B.1 - Subject Accountability

Table 100 – Subject Accountability (N = 148)

Subject Disposition	No. of Subjects
Enrolled Subjects	148
Excluded	3
ITT Cohort	145
Withdrawn	1
Data Not Available	1
Safety Analysis Cohort	143
Discontinued	2
Subjects Undergoing Ablation	141
Number of Subjects Currently in Follow-Up	141

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Enrolled Subjects (n = 148) Patients who sign the informed consent.

Excluded Subjects (n = 3) Subjects that are enrolled but never undergo insertion of the study catheter. Excluded subjects will not be included in either the effectiveness or safety evaluation of the study catheter.

Discontinued Subjects (n = 2) Subjects that have the investigational catheter inserted but are not treated with the investigational device (i.e., no RF energy applied). Subjects will be categorized as “discontinued” if ablation was not possible due to non-investigational equipment failure or if their arrhythmia was determined at the time of electrophysiologic study to be a non-study arrhythmia (e.g., atrial flutter). These discontinued subjects will remain in follow up for 7 days as part of the safety evaluation.

Intent To Treat (ITT) Cohort (n = 145) Enrolled subjects who meet the inclusion/exclusion criteria.

Subjects Undergoing Ablation/Effectiveness Cohort (n = 141) was comprised of subjects that received the treatment with the THERMOCOOL SMARTTOUCH™ Catheter and met the inclusion/exclusion criteria and did not meet the definitions of being excluded or discontinued. Roll in cases were excluded from the primary effectiveness cohort.

Safety Cohort (n = 143) was comprised of enrolled subjects undergoing insertion of the THERMOCOOL SMARTTOUCH™ Catheter. The calibration roll in subjects were included in this cohort.

B.2 - Subject Demographics

Table 101 – Subject Demographics (N = 148¹)

Characteristic	
Gender	n/147 (%)¹
Male	104 (70.7)
Female	43 (29.3)
Race	n/147 (%)¹
Caucasian	146 (99.3)
Black	1 (0.7)
Asian	0 (0.0)
Other	0 (0.0)
Ethnic Origin	n/147 (%)¹
Hispanic/Latino	2 (1.4)
Age (years)	
N	147 ¹
Mean	61
S.D.	10.44
Median	62
Min / Max	32 / 88

¹ At the time of publication, data was only available for 147 subjects.

C. Results

C.1 - Acute Procedural Success

Acute success was defined as the confirmation of entrance block into all targeted PVs. Any use of non-study catheters and > 2 repeat ablations were considered acute procedural failures.

At the time of publication, data analysis results for acute procedural success are not available for the Continued Access Study.

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C.2 - Primary Effectiveness Endpoint – Freedom from Symptomatic Atrial Tachyarrhythmia

Primary Effectiveness Analysis

The primary effectiveness endpoint was defined as freedom from documented symptomatic AF/AT/AFL (“atrial tachyarrhythmias”) based on electrocardiographic data and freedom from failure modes during the effectiveness evaluation period (Day 91-361). Any AF recurrence or repeat ablation procedure occurring greater than Day-361 post index procedure was deemed primary effectiveness successes at 12 months.

At the time of publication, the Continued Access Study data analysis is ongoing and 12 month follow-up data is not available.

C.3 - Primary Safety Endpoint

The primary safety endpoint for this study was defined as the incidence of early-onset (within 7 days of ablation procedure) primary AEs for subjects undergoing a study ablation procedure. The Safety Cohort (n = 143) was comprised of all enrolled subjects who had the study catheter inserted.

There were 27 primary AE in 25 subjects who had the investigational catheter inserted or underwent an ablation procedure. The percentage of subjects who experienced a primary AE in the safety cohort was 17.5% (25/143) and the upper bound of the two-sided 95% interval was 24.7%.

**Table 102 – Primary Safety Endpoint – Early-Onset (within (≤) 7 Days)
Primary Adverse Events (Primary Safety Cohort, n = 143)**

Description	# of Subjects with Primary AEs n/143 (%)
Total Serious Primary AEs	25¹ (17.5)
Death	0
Atrio-Esophageal Fistula	0
Atrial Perforation	0
Cardiac Tamponade	2 (1.40)
Myocardial Infarction	0
Stroke	0
Cerebrovascular Accident	1 (0.70)
Thromboembolism	0
Transient Ischemic Attack	0
Diaphragmatic Paralysis	0
Pneumothorax	0
Heart Block	2 (1.40)
Pulmonary Vein Stenosis	0
Pulmonary Edema	2 (1.40)
Pericarditis	1 (0.70)
Hospitalization (initial and prolonged)	10 (6.99)
Pericardial Effusion ²	1 (0.70)
Vascular Access Complication	8 (5.59)

¹ Two subjects had events in two categories.

² Treated with pericardiocentesis.

No deaths have occurred during the reporting period, and there have been no unanticipated adverse effects.

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SUMMARY OF CLINICAL STUDIES CONDUCTED FOR ATRIAL FLUTTER INDICATION

STUDY 1: Pivotal Study

A. Objective

The objective of the study was to determine if the NAVISTAR™ THERMOCOOL™ Catheter, when used in conjunction with the CARTO™ EP/XP Navigation System, RF generator (Stockert 70), and related accessories, is safe and effective for the treatment of Type I atrial flutter in patients age 18 or older.

B. Study Design

The study was a prospective, non-randomized, unblinded, multi-center study conducted at 22 investigational sites (21 sites in US; 1 in Canada).

B.1 - Study Endpoints

The endpoints for the study were as follows:

- **Procedural safety** – defined by the absence of serious complication associated with the use of the investigational device within seven days of the ablation procedure; and
- **Acute procedural success** – defined as complete bi-directional conduction block (BDB) across the isthmus, and the inability to induce Type I atrial flutter post-procedure.

Long-term freedom from atrial flutter recurrence was not specifically identified as a study endpoint. Instead, acute procedural success was used as a surrogate endpoint for this parameter. Long-term (defined as 6 months post-treatment) freedom from atrial flutter recurrence information was also collected, in order to enable FDA to assess whether the surrogate endpoint was reasonable.

B.2 - Objective Performance Criteria (OPC)

Objective performance criteria (OPC) were prospectively established. The OPC for the safety endpoint used for this study was derived from the FDA guidance document "Cardiac Ablation Catheters Generic Arrhythmia Indications for Use; Guidance for Industry, July 2002 1998 NASPE Registry." The OPC for the effectiveness endpoint was based on an extensive literature search involving acute success rates associated with radiofrequency ablation of atrial flutter. The OPCs are defined below:

- **Safety** – major adverse events within 7 days of the procedure occur at a rate of 2.7% or less with a 7% one-sided 95% upper confidence bound;
- **Acute success** – 88% with an 80% one-sided 95% lower confidence bound.

B.3 - Subject Accountability

The table below documents the accountability and disposition of enrolled subjects.

Table 103 – Subject Accountability and Disposition

Subjects enrolled in study	198
Subjects not ablated with the NAVISTAR™ THERMOCOOL™ Catheter	8
Excluded subjects - enrolled but in whom the investigational catheter was not inserted	3
Discontinued subjects - either (1) in whom the investigational catheter was inserted but did not receive RF energy because of <u>non-investigational</u> equipment failure, or (2) for whom the arrhythmia was determined to be non-study arrhythmia at the time of electrophysiologic study (e.g., atypical atrial flutter)	5
Subjects ablated with NAVISTAR™ THERMOCOOL™ Catheter	190
Subjects ablated with NAVISTAR™ THERMOCOOL™ Catheter and non-investigational catheter ¹	19
Subjects ablated only with NAVISTAR™ THERMOCOOL™ Catheter	171
Subjects in whom BDB was not assessable	4

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¹ This category includes enrolled subjects who received ablation therapy with the investigational catheter at the start of the procedure and for whom the investigator then switched to a non-protocol catheter to complete the procedure. Further subjects who could not receive ablation due to investigational device failure are included in this category. These subjects were considered acute effectiveness failures.

Effectiveness Analysis Population (n = 190) was defined as all subjects who received ablation therapy with the investigational catheter and for whom a valid assessment of BDB at the acute endpoint could be made OR if 6 month follow-up data were available.

Safety Analysis Population (n = 190) was defined as all enrolled subjects in whom the investigational catheter was inserted and received ablation therapy. Additionally, the rate of major adverse events is also reported for subjects in whom the investigational catheter was inserted and used for either mapping and/or ablation and for discontinued subjects. This additional category is referred to as the Inserted Patient Cohort (n = 195).

B.4 - Subject Demographics

The table below summarizes the demographic information of all study subjects who received ablation therapy.

**Table 104 – Subject Demographics
(All Subjects Who Received Ablation Therapy, n = 190)**

Gender	N	%
Female	43	22.6
Male	147	77.4
Age (years)		
Mean ± standard deviation	59.8 ± 12.6	
Range	18 - 90	

Additionally, for the Inserted Patient Cohort of 195 subjects, 72 subjects (36.9%) did not have a concomitant arrhythmia reported in addition to Type I atrial flutter. One hundred and sixty-five (165) concomitant arrhythmias were reported for 123 subjects. The most common concomitant arrhythmias were atrial fibrillation (n = 104) and atypical atrial flutter (n = 27).

C. Results

C.1 - Intraprocedural Data

Table 105 and Table 106 describe the procedural data.

Twenty-eight (28) subjects received ablation therapy for an arrhythmia other than Type I atrial flutter during the same index ablation procedure. The additional arrhythmias ablated were: 14 atrial fibrillation, 9 atrial tachycardia, 3 AVNRT, 1 intra-atrial tachycardia, 1 non-isthmus atrial flutter and 1 macro-reentry around the SVC eustachian ridge. One subject had more than one concomitant arrhythmia ablated.

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Table 105 – Power, Temperature, and Impedance Data

Description	Mean ± Standard Deviation	Range
# RF applications/procedure ¹ (n = 188 procedures)	19 ± 16	1 - 86
Total saline infused by THERMOCOOL™ Catheter (ml) ² (n = 169 procedures)	999.7 ± 605.5	60 - 3750
Maximum power (W)/application ³ (n = 3502 RF applications)	35.0 ± 9.5	2 - 59
Maximum temperature (°C)/application ³ (n = 3476 RF applications)	39.6 ± 5.1	14 - 87
Maximum impedance (Ω)/application ³ (n = 3431 RF applications)	112.1 ± 21.0	13 - 251

¹ One subject had missing RF information; one subject did not undergo ablation with the NAVISTAR™ THERMOCOOL™ Catheter.

² Some procedural data are missing.

³ Power, temperature, and impedance not documented for several RF applications.

Table 106 – Overall Fluoroscopy/Procedure Time (minutes)

Description	Mean ± Standard Deviation	Range
Total fluoroscopy time/procedure ¹ (n = 189 procedures)	50.2 ± 32.4	8 - 174
Total procedure time ¹ (n = 190 procedures)	341.6 ± 166.9 (5.7 ± 2.8 hours)	96 - 925
Total fluoroscopy time/procedure for subjects with additional rhythms ablated during index procedure (n = 28 procedures)	58.8 ± 24.7	18 - 115
Total fluoroscopy time/procedure for subjects without concomitant ablation (n = 161 procedures)	48.7 ± 33.4	8 - 174
Total procedure time for subjects with additional rhythms ablated during index procedure (n = 28 procedures)	503.8 ± 193.0 (8.4 ± 3.2 hours)	158 - 804
Total procedure time for subjects without concomitant ablation (n = 162 procedures)	313.5 ± 145.2 (5.1 ± 2.4 hours)	96 - 925

¹ Incomplete fluoroscopy time was reported for one (1) subject and incomplete procedure time was reported for one (1) subject.

C.2 - Acute Procedural Success

Acute success, defined as complete bi-directional conduction block across the isthmus at a minimum of 60 minutes following application of the last RF application, was analyzed. Acute success evaluation was based on the Efficacy Population, which was defined as all subjects who received ablation therapy with the investigational catheter and in whom a valid assessment of BDB could be made (n = 190 - 4 = 186).

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Table 107 describes the acute ablation outcomes.

Table 107 – Acute Ablation Outcomes (n = 186)

	# Success/ # Subjects Ablated	% (One-Sided 95% Confidence Bound)
Acute study results	158/186	85% (80%)
OPC		88% (80%)

C.3 - Composite Assessment of Atrial Flutter Ablation Success

As noted in the above section, 158 subjects had BDB confirmed acutely after the ablation procedure.

In addition, of the four subjects in whom BDB was not measured acutely after the ablation procedure, 3 subjects were free of recurrence of atrial flutter at 6 months follow-up and one could not be validated. For the composite assessment, the 3 subjects were considered a success and the 1 subject a failure.

Table 108 summarizes the composite results.

Table 108 – Composite Assessment of Atrial Flutter Success

	# Success/ # Subjects Ablated	% (One-Sided 95% Confidence Bound)
Study results	161/190	85% (80%)
OPC		88% (80%)

C.4 - Freedom from Type I Atrial Flutter Recurrence at Six-Month Follow-Up

As indicated in section B.1 above, long-term freedom from atrial flutter recurrence was not a study endpoint. The long-term results are presented here in order to assess the suitability of the surrogate endpoint BDB.

Freedom from Type I atrial flutter recurrence was evaluated in subjects in whom BDB was achieved (as measured acutely) and for whom 6-month post-ablation information was available. Based on these criteria, information was available on a total of 147 subjects.

Results are described in Table 109 below.

**Table 109 – Freedom from Type I Atrial Flutter at 6 Months
(Results Based on 147 Subjects)**

Description	N	%
Subjects in whom BDB was achieved acutely and for whom 6-month information was available	147	100%
Subjects free from recurrence	136	93%
Subjects free from recurrence and anti-arrhythmic drug change	118	80%
Subjects with recurrence of atrial flutter	11	
Subjects with AAD changes to treat atrial fibrillation	15	
Subjects with AAD changes to treat atrial or supraventricular tachycardias	3	

These results provide reasonable evidence that acute procedural success serves as an appropriate surrogate for long-term freedom from atrial flutter recurrence.

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C.5 - Adverse Events

A major adverse event was defined as any clinical event that occurred within seven days post-ablation and which resulted in (1) death, (2) a life-threatening complication, or (3) a persistent or significant disability/incapacity that required inpatient hospitalization or prolonged hospitalization or required intervention to prevent a permanent impairment of a body function or damage to a body structure. A minor adverse event was defined as any adverse event resulting in minimal transient impairment of a body function or damage to a body structure, or which did not require any intervention other than monitoring or events occurring more than 7 days post-ablation.

Major Adverse Events

Of the 190 subjects who received ablation therapy with the investigational catheter, 33 major adverse events were reported in 30 subjects. The overall percentage of subjects who experienced a major adverse event was 15.8%. The one-sided 95% confidence bound rate was 20.9%. For subjects who had the investigational catheter inserted and used for mapping and/or ablation (n = 195), the major adverse event rate was 15.4%, and the one-sided 95% confidence bound rate was 20.4%.

Table 110 summarizes the major adverse events.

Table 110 – Major Adverse Events Observed within 7 Days Post-Ablation

Total Number Subjects with a Major AE (n = 30)	
Cardiovascular subjects	Total = 15
Arrhythmia complications = 5 subjects	
Complete atrio-ventricular block during procedure	
Bradycardia requiring pacemaker implant	
Ventricular tachycardia	
Atrial fibrillation	
Atrial fibrillation & atypical atrial flutter	
Pericardial effusion/tamponade = 4 subjects	
Pericardial tamponade	
Pericardial tamponade after mapping only	
Pericarditis with effusion	
RA thrombus, LV thrombus and pericardial effusion	
Intracardiac thrombus = 2 subjects	
RAA thrombus	
RA thrombus, LV thrombus and pericardial effusion	
Myocardial infarction = 1 subject	
Congestive heart failure = 4 subjects	
Pedal edema	
Dyspnea, rales requiring furosemide	
Dyspnea treated with one dose furosemide	
Pulmonary edema by PE treated with one dose furosemide	
Pulmonary subjects	Total = 8
Acute respiratory distress syndrome = 2 subjects	
Aspiration pneumonia = 2 subjects	
Pneumonia = 3 subjects	
Asthma = 1 subject	
Anesthesia related subjects	Total = 2
Sedation induced apnea (intubation not required)	
Sedation induced CO ₂ retention with lethargy (intubation not required)	

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Total Number Subjects with a Major AE (n = 30)	
Vascular subjects	Total = 2
Arteriovenous fistula/femoral artery-saphenous vein	
Pseudoaneurysm/right femoral artery	
Urologic subjects	Total = 2
Urinary tract infection	
Urinary retention	
Cholecystitis	Total = 1 Subject
Neurologic Subjects	Total = 2
Parkinson's disease	
Transient extremity numbness/possible TIA	

Note: Some subjects are listed more than once in the above table.

Three subjects died during the course of the study. One subject died due to cardiac arrest caused by cardiomyopathy and chronic obstructive pulmonary disease (COPD) complications 11 days post-ablation, one subject died following pulmonary valve replacement surgery 2 months post-ablation, and the third death was due to lung cancer more than 2 years following the ablation procedure. All deaths were determined to be unrelated to the procedure and device.

An overall risk/benefit evaluation of these adverse events was performed and a detailed review of each adverse event was completed. The adverse event rate described above was assessed to be specifically correlated to (1) the concomitant ablation procedures performed during the index procedure and (2) the increased number of co-morbid conditions present in the subject population enrolled relative to the patient population from which the OPCs were derived. See section C.1 for a list of concomitant ablation procedures.

C.6 - Statistical Analysis

Table 111 summarizes the safety and effectiveness of the device when compared to the control group OPC established for safety and acute success.

Table 111 – Comparison of Endpoints between NAVISTAR™ THERMOCOOL™ Study and OPC

Endpoint	OPC		NAVISTAR™ THERMOCOOL™ Study	
	%	One-Sided 95% Confidence Bound	% (n)	One-Sided 95% Confidence Bound
Acute success	88%	80%	85% (161/190)	80% (lower bound)
Major complications	2.7%	7%	15.8% (30/190)	20.9% (upper bound)

With comparison of the lower bounds of the acute success endpoints (80% vs. 80%), the results demonstrate that the NAVISTAR™ THERMOCOOL™ Catheter met the OPC for acute success. As previously explained in section C.5, although the device exceeded the upper bound of major complications, review of the specific events showed that they were related to the concomitant ablation procedures performed in addition to atrial flutter ablation and the subject population co-morbid conditions. Accordingly, study results demonstrate a reasonable assurance of the safety profile of the device.

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STUDY 2: Post-Approval Study

A. Objective

The primary objective was to provide additional, corroborative safety and efficacy data for the NAVISTAR™ THERMOCOOL™ Catheter for the treatment of subjects with typical atrial flutter (AFL).

B. Study Design

This study was a prospective, non-randomized, single-arm, multi-center post-approval evaluation.

B.1 - Study Endpoints

The endpoints for the study were as follows:

- **Primary safety endpoint** – the percentage of subjects experiencing Cardiovascular Specific Adverse Events (CSAE) within seven (7) days of the ablation procedure; and
- **Primary efficacy endpoint** – defined as complete bi-directional conduction block (BDB) across the sub-eustachian (cavo-tricuspid) isthmus at a minimum of 30 minutes following the last RF application.

B.2 - Objective Performance Criteria (OPC)

Objective performance criteria (OPC) were prospectively established. The OPCs are defined below:

- **Safety** – A CSAE rate below 2.7%, corresponding to a one-sided 95% upper confidence bound of 7%, was required to successfully achieve the safety endpoint.
- **Efficacy** – An efficacy success rate of 88% with a one-sided lower confidence bound of 80% was required for effectiveness success.

B.3 - Subject Accountability

Table 112 documents the accountability and disposition of enrolled subjects.

Table 112 – Subject Disposition (N = 291)

Category	N	%
Total Subjects Enrolled	291	100%
Excluded group	24	8.2%
Safety Cohort	267	91.8%
Discontinued group (no RF energy delivered via study catheter)	5	1.7%
Subject with typical AFL – non-evaluable ¹	1	0.3%
Subjects found to not have typical AFL	8	2.7%
Efficacy Cohort (evaluable subjects)	253	86.9%
Subjects with only typical AFL	236	81.1%
Subjects with typical AFL and other concomitant arrhythmia requiring ablation	17	5.8%

¹ Bidirectional block was not assessable in one subject due to an altered CS anatomy.

Safety Analysis Cohort (n = 267) The primary safety endpoint is the rate of occurrence of Cardiovascular Specific Adverse Events (CSAE), which is defined as “an event which occurs within the first week (7 days) following use of the device and is one of the following Cardiovascular Specific Adverse Events: cardiac perforation, pericardial effusion, pulmonary embolus, complete heart block, stroke, acute myocardial infarction, and death.” The protocol predetermined rate of CSAE was 2.7% with corresponding one-sided 95% upper confidence bound of 7%. The CSAE rate observed in the Safety Cohort (N = 267) was 1.5% (4/267). The one-sided 95% upper confidence bound for the Safety Cohort was 3.4%, which was below the cutoff rate of 7% required to achieve the safety endpoint.

Efficacy Analysis Cohort (n = 253) The primary efficacy endpoint of this study was defined as confirmation of complete bidirectional conduction block across the sub-eustachian (cavo-tricuspid) isthmus at a minimum of 30 minutes following the last RF application. An acute success rate of 88% was anticipated and the one-sided 95% lower confidence bound was compared to 80%. There was a total of 253 subjects in the Efficacy Cohort. The overall acute efficacy success in the Efficacy Cohort was 93.3%

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(236/253), corresponding with a one-sided lower confidence bound of 90.1%. Acute efficacy success exceeded one-sided lower confidence bound of 80% as established in the protocol, thus the primary efficacy endpoint was met.

B.4 - Subject Demographics

Table 113 summarizes the demographic information of all study subjects enrolled in the study.

**Table 113 – Subject Demographics
(All Enrolled Subjects, n = 291)**

Gender	N	%
Female	48	16.5
Male	243	83.5
Age (years)		
Mean ± standard deviation	65.2 ± 12.1	
Range	19 - 92	

C. Results

C.1 - Intraprocedural Data

Table 114 and Table 115 describe the procedural data.

Seventeen (17) subjects received ablation therapy for an arrhythmia other than Type I atrial flutter during the same index ablation procedure. The additional arrhythmias ablated were: 10 right atrial tachycardia/non isthmus dependent flutter/scar flutter/ectopic, 4 left atrial tachycardia/flutter/scar flutter, 3 AVNRT, and 2 atrial fibrillation. One subject had multiple concomitant arrhythmias treated.

C.2 - Efficacy Success

Efficacy success, defined as complete bi-directional conduction block across the isthmus at a minimum of 30 minutes following application of the last RF application, was analyzed. If conduction across the isthmus was present at the end of the procedure or if another device (non-study catheter), in addition to the study catheter, was utilized for ablation, the procedure was considered to be an acute failure.

Table 114 describes the efficacy success.

Table 114 – Efficacy Success (n = 253)

	# Efficacy Success/ # Subjects Ablated	% (one-sided 95% confidence bound)
Efficacy success	236/253	93.3% (90.1%)
OPC		88% (80%)

C.3 - Adverse Events

A Cardiovascular Specific Adverse Event (CSAE) was defined as an event that occurred within the first week (7 days) following use of the device and was one of the following Cardiovascular Specific Adverse Events: cardiac perforation, pericardial effusion, pulmonary embolus, complete heart block, stroke, acute myocardial infarction, and death.

Of the 267 subjects who received ablation therapy with the study catheter, four (4) CSAEs were reported in four (4) subjects (1.5% of Safety Cohort). The one-sided 95% confidence bound rate was 3.4%.

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Table 115 summarizes the CSAEs observed.

**Table 115 – Cardiovascular Specific Adverse Events
Observed within 7 Days Post-Ablation**

Total Number Subjects Experiencing a CSAE (n = 4)
Pulmonary embolus = 1 subject, possibly procedure related
Complete heart block = 2 subjects, both unrelated to device or procedure
Myocardial infarction = 1 subject, unrelated to device or procedure

Three of the four CSAEs were determined by the investigators to be unrelated to the procedure or device and the remaining CSAE was deemed to be possibly procedure related.

There were three reported deaths during the course of the study, though no deaths occurred during the ablation procedure or during the study follow-up period. One subject died prior to the scheduled study procedure due to either pulmonary embolus or myocardial infarction. The other two subjects died after the completion of the study follow up period due to cancers (metastatic adenocarcinoma and lung cancer). All deaths were determined to be unrelated to the device or procedure.

An overall risk/benefit evaluation of these adverse events was performed and a detailed review of each adverse event was completed.

C.4 - Statistical Analysis

Table 116 summarizes the safety and effectiveness of the device compared to the OPC established for safety and efficacy.

**Table 116 – Endpoints Comparison between
NAVISTAR™ THERMOCOOL™ Catheter Post-Approval Study and OPC**

Primary Endpoints	OPC		NAVISTAR™ THERMOCOOL™ Study	
	%	One-Sided 95% Confidence Bound	% (N)	One-Sided 95% Confidence Bound
Safety (CSAEs)	2.7%	7%	1.5% (4/267)	3.4% (upper bound)
Efficacy	88%	80%	93.3% (236/253)	90.1% (lower bound)

The results demonstrate that the NAVISTAR™ THERMOCOOL™ Catheter met the OPC for safety and efficacy.

SUMMARY OF CLINICAL STUDIES CONDUCTED FOR ATRIAL FIBRILLATION INDICATION

The clinical testing described below was performed with the NAVISTAR™ THERMOCOOL™ Catheter.

A. Objective

The primary objective of this trial was to demonstrate the safety and efficacy of the NAVISTAR™ THERMOCOOL™ Catheter for the radiofrequency ablation treatment of subjects with symptomatic Paroxysmal Atrial Fibrillation (PAF) who were refractory or intolerant to antiarrhythmic drug therapy.

B. Study Design

The study was a prospective, randomized, unblinded, multi-center pivotal clinical investigation conducted at 19 investigational sites (15 in the US and 4 outside of the US).

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B.1 - Study Endpoints

The endpoints for the study were as follows:

The **primary effectiveness endpoint** was the chronic success rate of the NAVISTAR™ THERMOCOOL™ Catheter for the treatment of symptomatic PAF.

Acute success was defined as confirmation of entrance block in all targeted pulmonary veins.

Chronic success was defined as freedom of symptomatic AF based on electrocardiographic data and no changes in Anti-Arrhythmic Drug (AAD) regimen during comparable evaluation periods for the THERMOCOOL™ Catheter and AAD (Control) groups. AF status was evaluated by periodic transtelephonic monitoring and 24-hour Holter recordings.

Quality of life was evaluated using the AF frequency/severity checklist and SF-36 questionnaire.

The **primary safety endpoint** was the incidence of early onset (within 7 days of the ablation procedure) primary adverse events. This included the following adverse events:

- Death
- Myocardial Infarction (MI)
- Pulmonary Vein (PV) stenosis
- Diaphragmatic paralysis
- Atrio-esophageal fistula
- Transient Ischemic Attack (TIA)
- Stroke
- Cerebrovascular accident (CVA)
- Thromboembolism
- Pericarditis
- Cardiac tamponade
- Pericardial effusion
- Pneumothorax
- Atrial perforation
- Vascular access complications
- Pulmonary edema
- Hospitalization (initial and prolonged)
- Heart block

Secondary safety endpoints included comparisons between the THERMOCOOL™ Catheter and AAD (Control) groups on the following:

- Early onset (≤ 90 days post treatment) of serious adverse events
- Late onset (≥ 90 days post treatment) of serious adverse events

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B.2 - Subject Accountability

Table 117 – Subject Accountability and Disposition

Total Number of Subjects Enrolled	167
Subjects randomized to THERMOCOOL™ Catheter	106
Excluded subjects	3
Subjects who underwent ablation with the study catheter	103
Discontinued subjects	0
Subjects randomized to AAD (Control)	61
Excluded subjects	4
Subjects administered AAD therapy	57
Discontinued subjects	1
AAD (Control) subjects undergoing RF ablation	36

The following definitions were used to classify subjects:

Effectiveness Analysis Cohort (n = 159) was comprised of subjects that received the treatment that they were randomized to and also did not meet the definitions of being excluded or discontinued.

Primary Safety Analysis Cohort (n = 139) was comprised of subjects that underwent insertion of the THERMOCOOL™ Catheter, including subjects that were randomized to AAD (Control) group and became eligible for RF ablation with the THERMOCOOL™ Catheter.

Secondary Safety Analysis Cohort (n = 160) was comprised of subjects that received the treatment that they were randomized to, including subjects classified as discontinued.

B.3 - Subject Demographics

Table 118 summarizes the demographic information. Subjects were randomized 2:1 upon signing informed consent.

Table 118 – Subject Demographics

	THERMOCOOL™ Catheter n/N (%)	AAD (Control) n/N (%)	Total n/N (%)	p-value
	N = 106	N = 61	N = 167	
Gender				0.3997
Female	33/106 (31.1)	23/61 (37.7)	56/167 (33.5)	
Male	73/106 (68.9)	38/61 (62.3)	111/167 (66.5)	
Ethnicity				0.7031
Hispanic	1/106 (0.9)	0/61 (0.0)	1/167 (0.6)	
Other	2/106 (1.9)	0/61 (0.0)	2/167 (1.2)	
White	103/106 (97.2)	61/61 (100.0)	164/167 (98.2)	
Age (years)				0.3009
Mean	55.5 ± 9.34	56.1 ± 12.84	55.7 ± 10.72	
Median	56	58	57	
Min/Max	32/76	19/77	19/77	
Left atrial dimension (mm)¹				0.7118
Mean	40.0 ± 5.5	40.3 ± 5.3	40.1 ± 5.4	
Median	40	41	40	
Min/Max	27.0/50.0	26.5/49.0	26.5/50.0	

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	THERMOCOOL™ Catheter n/N (%)	AAD (Control) n/N (%)	Total n/N (%)	p-value
	N = 106	N = 61	N = 167	
Left ventricular ejection fraction (%)²				0.4670
Mean	62.3 ± 9.8	63.1 ± 7.4	62.6 ± 9.0	
Median	62	63	63	
Min/Max	30.0/86.0	44.0/80.0	30.0/86.0	

¹ Data are not available for 15 subjects (6 in THERMOCOOL™ Catheter group and 9 in AAD group).

² Data are not available for 14 subjects (7 in THERMOCOOL™ Catheter group and 7 in AAD group).

The age in the Table 118 was when the subject signed the informed consent. The p-value listed compares the randomized groups. There was one subject of Arab ethnicity and one subject that was Native American.

Subjects enrolled in the study reported a mean of 63.2 ± 92.4 atrial fibrillation episodes in the six months prior to baseline. Patients classified as New York Heart Association (NYHA) Class III and IV were excluded from the study. Approximately half of the enrolled subjects had a history of hypertension at baseline; 48.6% (51/105) in the THERMOCOOL™ Catheter group and 50.0% (30/60) in the AAD (Control) group. Less than a third of the enrolled subjects (27.7%; 44/159) had a history of atrial flutter at baseline. The overall mean number of AADs failed at baseline was 2.2 ± 1.2, with 27 of the 167 enrolled subjects having previously failed only a Class II/IV AAD.

C. Results

C.1 - Procedural Data

Table 119 and Table 120 present the procedural data.

Table 119 – Summary of RF Applications, Saline Infused, Power, Temperature, and Impedance Data (THERMOCOOL™ Catheter Effectiveness Cohort, n = 103¹)

Description	Mean ± Standard Deviation
Number of RF applications (n = 125 procedures)	53.2 ± 36.6
Mean saline infused (ml) by NAVISTAR™ THERMOCOOL™ Catheter (n = 123 procedures)	1591.0 ± 752.7
Maximum power (W)/procedure (n = 125 procedures)	41.5 ± 7.1
Maximum temperature (°C)/procedure (n = 126 RF procedures)	43.9 ± 4.1
Maximum impedance (Ω)/procedure (n = 125 RF procedures)	135.4 ± 25.4

¹ Complete procedural data were not reported for all subjects.

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**Table 120 – Summary of Ablation Procedure Parameters –
All Ablation Procedures
(THERMOCOOL™ Catheter Effectiveness Cohort, n = 103¹)**

Procedure Parameters	THERMOCOOL™ Catheter Group Mean ± SD (n)
Total procedure time (min)	211.3 ± 86.1 (126)
Ablation procedure time (min)	111.0 ± 62.6 (127)
Total fluoroscopy duration (min)	47.9 ± 40.2 (127)
Total fluid input (ml)	2877.5 ± 1914.0 (125)
Total fluid output (ml)	783.8 ± 884.4 (126)
Balance (input-output) (ml)	2193.0 ± 1348.2 (121)

¹ Data parameters not available for all ablation procedures.

Note: Table 119 and Table 120 include all ablation procedures for subjects randomized to the THERMOCOOL™ Catheter group, including 24 repeat ablation procedures (average of 1.2 ablation procedures per subject).

The overall fluoroscopy and procedure times reported include both the investigational (NAVISTAR™ THERMOCOOL™ Catheter) procedure time and all other procedures performed during the subject's stay in the electrophysiology (EP) lab. Therefore, the data do not solely reflect the actual use of the NAVISTAR™ THERMOCOOL™ Catheter.

All AF ablation procedures began with circumferential lesions targeting all pulmonary veins, with additional atrial ablation lines created as clinically required.

Table 121 summarizes the lesion sets applied to THERMOCOOL™ Catheter group subjects during the index ablation procedures.

**Table 121 – Outcomes by Ablation Targets per Subject – 1st Ablation Procedure
(THERMOCOOL™ Catheter Group Subjects, n = 103)¹**

Ablation Targets	THERMOCOOL™ Catheter Group (n = 103)		
	Success n (%)	Fail n (%)	Total n (100%)
Pulmonary veins (PV) only	18 (41.9)	25 (58.1)	43 (100.0)
≥ 4 PV	17	24	
< 4 PV	1	1	
PV + atrial lines	28 (84.8)	5 (15.2)	33 (100.0)
+ Right atrial lines	11	3	
+ Left atrial lines	2	2	
+ Combination left and right	15	0	
PV + foci	3 (42.9)	4 (57.1)	7 (100.0)
PV + atrial lines + foci	4 (66.6)	2 (33.4)	6 (100.0)
TOTAL	53 (59.6)	36 (40.4)	89 (100.0)

¹ 14 subjects are still within the effectiveness evaluation period and were not included in this analysis.

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C.2 - Acute Procedural Success

Acute procedural success results are presented in Table 122.

**Table 122 – Acute Effectiveness Outcome
(NAVISTAR™ THERMOCOOL™ Catheter Group, n = 103¹)**

	NAVISTAR™ THERMOCOOL™ Catheter Group n
Underwent RF study procedure	103
Entrance block confirmed	102 ²
Ablation procedure > 80 days	2
Non-study catheter utilized for AF targets	0
> 2 repeat ablation procedures	0
Acute effectiveness success	100

¹ Includes all THERMOCOOL™ Catheter group subjects undergoing ablation with the study catheter.

² End of procedure information for one subject was not available.

C.3 - Chronic Success – Freedom from Chronic Effectiveness Failure

Primary Effectiveness Analysis

A pre-specified interim analysis was performed per the clinical trial protocol, and the results demonstrated sufficient statistical evidence of the study meeting the effectiveness endpoint. As a result, enrollment was stopped and the trial was declared an early success.

The critical results of the Bayesian analysis are the predictive probability of success for 230 patients and the posterior probability of superiority for the THERMOCOOL™ Catheter group. The posterior probability that the THERMOCOOL™ Catheter group is superior to the AAD (Control) group is essentially 1 (> 0.9999). The model estimates the probability of success for a subject in the THERMOCOOL™ Catheter group is 0.627 with a standard deviation of 0.048. For a subject in the AAD (Control) group, the posterior mean probability of success is 0.172 with a posterior standard deviation of 0.049. The predictive probability of success for the original maximum sample size of 230 subjects is also essentially 1 (> 0.9999). That is, if the full sample size of 230 had been enrolled, it is a virtual certainty that the final posterior probability would have been larger than 0.98 (protocol specified level needed for success).

Chronic success results are described in Table 123.

Table 123 – Summary of Data Available¹ – June 2008 Dataset

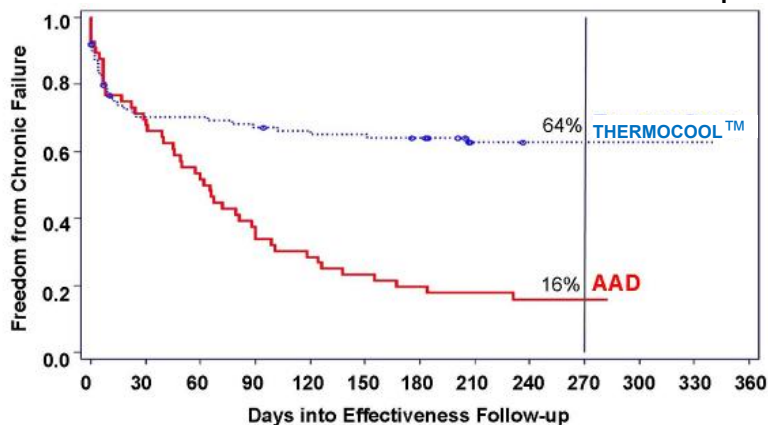
Group	0 < t ≤ 0.5			0.5 < t ≤ 2			2 < t ≤ 9		
	Expos	Fail	Rate	Expos	Fail	Rate	Expos	Fail	Rate
THERMOCOOL™ Catheter	40.21	26	0.647	104.17	3	0.029	413.09	7	0.017
AAD (Control)	23.27	13	0.559	54.21	14	0.258	90.46	20	0.221

¹ The exposure (Expos) time in months and number of failures (Fail) are reported for each of the three intervals in the time to event model.

Figure 23 shows the Kaplan-Meier curves for each of the treatment groups for freedom from chronic effectiveness failure (n = 159) and shows superiority of the THERMOCOOL™ Catheter group (64%) compared to AAD group (16%) for the primary effectiveness endpoint.

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Figure 23 – Kaplan-Meier Analysis – Probability of Freedom from Chronic Effectiveness Failure For Each Treatment Group



The June 2008 dataset status of each of the 159 subjects is reported in Table 124. At the time of this analysis, subjects were classified as “Success,” “Failure,” or “Censored” (i.e., those subjects that had not failed, but did not have complete 9-month follow-up).

Table 124 – Summary of the Status of Each of the Enrolled Subjects

Group	Success	Censored	Fail	n
THERMOCOOL™ Catheter	53	14	36	103
AAD (Control)	9	0	47	56

Site variation in primary effectiveness outcome was observed in this study. In particular, one investigational site located outside of the United States had a higher success rate than the remainder of the investigational sites. Various sensitivity analyses were performed which demonstrated that the study conclusions were robust to this site variation.

Figure 24 shows that the 9-month failure-free rate in the THERMOCOOL™ Catheter group is superior to that of the AAD (Control) group. The 95% credible interval for the difference between the treatment and control probability of success is (0.313, 0.584) with a median difference of 0.457.

Figure 24 – The Posterior Distributions of the Probabilities of 9-Month Failure-Free Treatment Success for Each Treatment Group

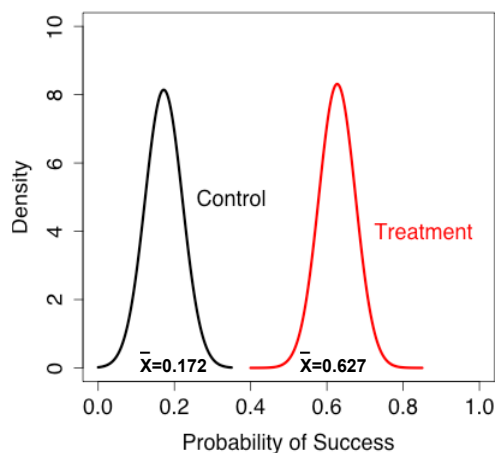
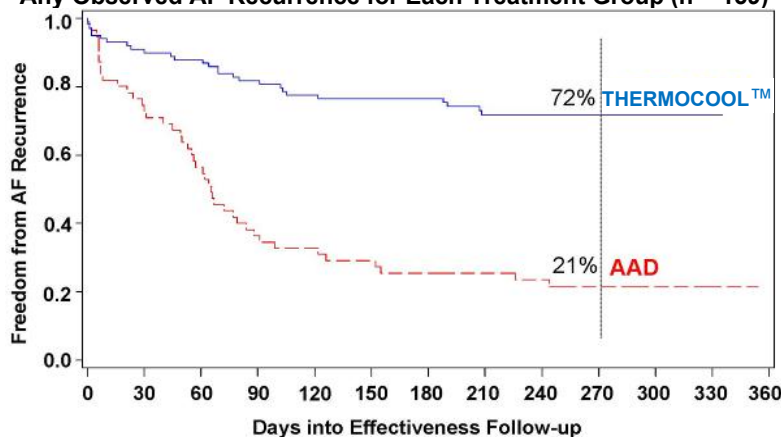


Figure 25 demonstrates that the THERMOCOOL™ Catheter group had a higher probability of freedom from any documented symptomatic or asymptomatic AF recurrence, subject to the monitoring provisions

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of the protocol, than the AAD (Control) subjects. The difference in likelihood of AF recurrence after 9 months of effectiveness evaluation was 51% (72% vs. 21%) in favor of the THERMOCOOL™ Catheter treatment group.

Figure 25 – Kaplan-Meier Analysis – Probability of Freedom from Any Observed AF Recurrence for Each Treatment Group (n = 159)



C.4 - Adverse Events (AE)

The primary safety endpoint for this study was defined as the incidence of early-onset (within 7 days of ablation procedure) primary AEs for subjects undergoing a study ablation procedure. The Primary Safety Cohort (n = 139) was comprised of THERMOCOOL™ Catheter group subjects (n = 103) and AAD (Control) group subjects undergoing an ablation procedure (n = 36).

Primary Safety Endpoint – Primary Adverse Events

Table 125 presents the protocol-established endpoint and safety results based on the June 2008 dataset. There were 16 primary AEs reported for 15 subjects. The overall percentage of subjects who experienced a serious primary AE was 10.8% (15/139) and the upper confidence bounds based on the Primary Safety Cohort was 16.1%. The safety endpoint specified in the protocol was 7.0% (upper confidence bound of 16.0%). While the primary safety results exceeded the protocol-established primary safety endpoint for this study, the nature and types of adverse events experienced in this trial nonetheless represent an acceptable risk profile.

Table 125 – Primary Safety Endpoint Outcome – Primary Adverse Events (Primary Safety Cohort, n = 139)

	Protocol Established Endpoint	n
Number of subjects in Safety Cohort		139
Number of subjects with primary AEs		15
% primary AEs	7.0	10.8
One-sided 95% confidence bound ¹	16.0	16.1

¹ Exact binomial using a commercially available software package.

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Table 126 summarizes the major primary AEs.

**Table 126 – Primary Safety Endpoint –
Early-Onset (within (≤) 7 Days) Primary Adverse Events
(Primary Safety Cohort, n = 139)**

Description	Number of Subjects with Primary AEs n/139 (%)
Total Serious Primary AEs	15 (10.8%)
Death	0
Atrio-esophageal fistula	0
Atrial perforation	0
Cardiac tamponade	0
Myocardial infarction	0
Stroke	0
Cerebrovascular accident	0
Thromboembolism	0
Transient ischemic attack	0
Diaphragmatic paralysis	0
Pneumothorax	0
Heart block	0
Pulmonary vein stenosis	0
Pulmonary edema	1 (0.7%)
Pericarditis	1 (0.7%)
Hospitalization (initial and prolonged)	7 (5.0%)
Pericardial effusion	1 (0.7%)
Vascular access complication	5 (3.6%)

Table 127 compares the incidence of early onset serious adverse events (SAE) between the two treatment groups occurring within the first 90 days of initial therapy.

**Table 127 – Percentage of Early Onset SAE by Randomization Group
(Overall Safety Cohort, n = 160)**

Randomization Group	Percent % of SAEs (n/N)	p-value
THERMOCOOL™ Catheter Group	18.4 (19/103)	0.022
AAD (Control) Group ¹	35.1 (20/57)	

¹ For AAD subjects undergoing an ablation procedure, only SAE prior to an ablation procedure were considered in this analysis.

One subject in the THERMOCOOL™ Catheter group expired during the effectiveness evaluation period. This event occurred 284 days after the ablation procedure and was considered to be unrelated to the investigational device and procedure.

C.5 - Study Conclusion

In conclusion, the results demonstrate that there is a reasonable assurance of safety and effectiveness to support the use of the NAVISTAR™ THERMOCOOL™ Catheter for the treatment of drug refractory recurrent symptomatic paroxysmal atrial fibrillation, when used with advanced three-dimensional electroanatomic mapping systems.

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SUMMARY OF CLINICAL STUDIES CONDUCTED FOR ALTERNATIVE IMAGING TO DETERMINE CATHETER TIP LOCATION

STUDY 1: Zero/Low Fluoroscopy: A nested sub-study of REAL AF Registry

A. Objective

The objective of the study was to evaluate the safety and acute effectiveness of radiofrequency catheter ablation of paroxysmal atrial fibrillation (PAF) using a zero/low fluoroscopy workflow during standard of care practice.

B. Study Design

The study was a multicenter, prospective/retrospective, non-randomized, observational clinical investigation to evaluate the safety and acute effectiveness of radiofrequency ablation of PAF using a zero/low fluoroscopy workflow.

Consecutive eligible first-time drug refractory PAF catheter ablation patients from the REAL AF Registry treated in a zero/low fluoroscopy workflow were included. The REAL AF Registry consists of centers of private and academic institutions with the primary purpose of obtaining real-world clinical experience of atrial fibrillation (AF) ablation using contemporary radiofrequency technologies (e.g., THERMOCOOL SMARTTOUCH™, THERMOCOOL SMARTTOUCH™ SF). Only data from 16 sites in the United States (US) were used in this sub-study. All operators in the 16 sites have a target fluoroscopy time of less than 3 minutes for an AF ablation procedure. If the primary safety endpoint for the REAL AF Registry was met the following were to be performed:

- Secondary acute effectiveness endpoint from the REAL AF Registry tested by comparing the observed acute effectiveness against the performance goal of 90%.
- Descriptive comparison of the secondary safety endpoint between the zero/low fluoroscopy workflow group and the conventional fluoroscopy workflow group within the Mercy electronic health record (EHR) system database. Mercy is a large US integrated delivery network with hospitals and clinics in several states across the US. The secondary descriptive analysis from the Mercy EHR system database included all PAF patients who met the eligibility criteria similar to those of the REAL AF Registry. Patients treated using either THERMOCOOL SMARTTOUCH™ SF or THERMOCOOL SMARTTOUCH™ catheters were included from the Mercy EHR system database. The data were analyzed using both covariate-unadjusted and covariate-balanced data with point estimates for the cumulative incidence and within each group and for the risk difference between the groups provided.

B.1 - Study Endpoints

The endpoints for the study were as follows:

The **primary safety endpoint** was the occurrence of procedure or device related primary adverse events (Table 128) within 7 days of the initial ablation procedures in the REAL AF Registry. Device or procedure related death, severe pulmonary vein stenosis, and atrio esophageal fistula up to 90 days and cardiac tamponade/perforation up to 30 days post-index procedure were also considered primary adverse events (Table 128).

Table 128 – REAL AF Zero/Low Fluoroscopy Sub-Study Primary Adverse Events

Primary Adverse Events (PAE)	
Atrio-Esophageal Fistula ¹	Phrenic Nerve Paralysis/injury
Cardiac Tamponade/Pericardial Effusion ¹	Severe Pulmonary Vein Stenosis (>70% reduction in the diameter of PV) ¹
Procedure or Device-Related Death ¹	Stroke/CVA
Major Vascular Access Complication/Bleeding including Hematoma, arteriovenous fistula, and pseudoaneurysm	Thromboembolism
Myocardial Infarction	Transient Ischemic Attack (TIA)
Pericarditis	Vagal nerve injury

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¹ Procedure or device related death, severe pulmonary vein stenosis, and atrio-esophageal fistula that occurred greater than 1 week (7 days) post-procedure up to 90 days and cardiac tamponade/pericardial effusion that occurred greater than 1 week (7 days) post-procedure up to 30 days were considered and analyzed as PAEs.

The **secondary acute effectiveness endpoint** was acute effectiveness success which was defined as confirmation of pulmonary vein isolation in all targeted pulmonary veins, evaluated in the REAL AF Registry.

The **descriptive comparison of the secondary safety endpoint** between the group with fluoroscopy time of ≤ 2 minutes and the group with fluoroscopy time of ≥ 3 minutes within the Mercy EHR database based on the covariate-balanced data with point estimates for the cumulative incidence within each group and for the risk difference between the groups.

B.2 - Objective Performance Criteria (OPC)

Objective performance goals were prospectively established.

- **Safety** – Performance Goal = 10% upper bound of the 95% confidence interval around the primary adverse event rate
- **Acute Effectiveness** – Performance Goal = 90% lower bound of the 95% confidence interval around the isolation of all targeted pulmonary vein rate (effectiveness success)

B.3 - Subject Accountability

Table 129 – REAL AF Zero/Low Fluoroscopy Sub-Study Analysis Sets

Analysis Set	n
Full Analysis Set ¹	208
Retrospective Enrollment	48
Prospective Enrollment	160

¹Full Analysis Set: Includes all consecutive sub-study protocol eligible subjects in the REAL AF Registry who underwent their first-time catheter ablation procedure for PAF using the THERMOCOOL SMARTTOUCH™ or THERMOCOOL SMARTTOUCH™ SF catheter.

Table 130 – REAL AF Zero/Low Fluoroscopy Sub-Study Subject Enrollment and Accountability

Subject Enrollment	n
Full Analysis Set ¹	208
Zero Fluoroscopy Subjects	104
Non-Zero Fluoroscopy Subjects	104
Lost to Follow-up Subjects ²	2
Death	1
Completed Subjects ³	10
Ongoing	195
Subjects with 3 Month Follow-up data	197

¹ Full Analysis Set: Includes all consecutive sub-study protocol eligible subjects in the REAL AF Registry who underwent their first-time catheter ablation procedure for PAF using the THERMOCOOL SMARTTOUCH™ or THERMOCOOL SMARTTOUCH™ SF catheter.

² Lost to Follow-up Subjects: Subjects with whom contact is lost after the index procedure or most recent follow-up visit.

³ Completed Subjects: Subjects who complete the 12-month follow-up visit.

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Table 131 – Mercy EHR Database Patient Population Attrition

Attrition Criteria	No. of Patients	No. of Patients Lost	% Patients Lost
Inclusion criteria			
Patients who underwent an intracardiac catheter ablation of AF since 2015	2,903	-	-
Patients with a primary or secondary diagnosis of PAF associated with the same intracardiac catheter ablation procedure encounter	1,392	1,511	52.05%
The first recorded intracardiac catheter ablation of AF with a primary or secondary diagnosis of PAF since 2015 was designated the index ablation procedure	1,392	0	0.00%
Index ablation procedure performed using either THERMOCOOL SMARTTOUCH™ SF or THERMOCOOL SMARTTOUCH™ catheters	1,107	285	20.47%
Had at least one class I or III antiarrhythmic drug prescription prior to the index ablation procedure	721	386	34.87%
18 years of age or older at the time of the index ablation procedure	721	0	0.00%
At least 6 months of encounter history prior to the index ablation procedure	629	92	12.76%
No recorded ablation prior to the index ablation procedure in the database	519	110	17.49%
Number of patients who met all inclusion criteria	519		
Exclusion criteria			
Did not have at least one class I or III antiarrhythmic drug prescription prior to the index ablation procedure	519	0	0.00%
Had a diagnosis of any primary safety events within 3 months prior to the index ablation procedure	503	16	3.08%
Missing fluoroscopy time of the index ablation procedure	349	154	30.62%
Number of patients who met at least one exclusion criterion		170	
Number of patients who met all eligibility criteria	349		
Fluoroscopy time: ≤ 2 minutes	129		
Fluoroscopy time: ≥ 3 minutes	170		
Fluoroscopy time: > 2 minutes and < 3 minutes	50		

Primary Safety Analysis Cohort (n = 197 from the 208 REAL AF Zero/Low Fluoroscopy Sub-study full analysis set [FAS] subjects) was comprised of subjects with available endpoint data.

Secondary Acute Effectiveness Cohort (n = 202 from the 208 REAL AF Zero/Low Fluoroscopy Sub-study FAS subjects) was comprised of subjects with available endpoint data.

Descriptive Comparison of the Secondary Safety Cohort was comprised of 299 subjects for the comparison of the group with fluoroscopy time of ≤ 2 minutes and the group with fluoroscopy time of ≥ 3 minutes and 349 subjects for the sensitivity analysis using an alternative cutoff (i.e., fluoroscopy ≤ 2 minutes vs > 2 minutes).

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B.4 - Subject Demographics and Baseline Characteristics

The tables below summarize the demographics and baseline characteristics information.

Table 132 – REAL AF Zero/Low Fluoroscopy Sub-Study Demographics

Analysis Variable	All (N=208)	Retrospective (N=48)	Prospective (N=160)
Age (year)¹			
N	208	48	160
Mean	65.1	62.5	65.8
Standard Deviation	10.63	11.84	10.15
Median	66.0	63.0	67.0
Q1/Q3	59.0/73.0	57.0/71.0	59.0/73.0
Min/Max	25/87	25/83	31/87
Sex, n/N (%)			
Male	106/208 (51.0%)	19/48 (39.6%)	87/160 (54.4%)
Female	102/208 (49.0%)	29/48 (60.4%)	73/160 (45.6%)
Ethnicity, n/N (%)			
Hispanic or Latino	3/208 (1.4%)	0	3/160 (1.9%)
Not Hispanic or Latino	196/208 (94.2%)	43/48 (89.6%)	153/160 (95.6%)
Declined/Unknown	6/208 (2.9%)	3/48 (6.3%)	3/160 (1.9%)
Race, n/N (%)			
American Indian or Alaska Native	0	0	0
Asian	3/208 (1.4%)	0	3/160 (1.9%)
Black or African American	14/208 (6.7%)	3/48 (6.3%)	11/160 (6.9%)
Native Hawaiian or Other Pacific Islander	0	0	0
White	184/208 (88.5%)	43/48 (89.6%)	141/160 (88.1%)
Other	3/208 (1.4%)	0	3/160 (1.9%)
Declined or Unable to Disclose	1/208 (0.5%)	0	1/160 (0.6%)
Baseline BMI (kg/m²)			
N	207	48	159
Mean	29.77	28.95	30.01
Standard Deviation	5.988	5.445	6.137
Median	29.32	29.08	29.41
Q1/Q3	25.90 / 33.38	25.86 / 31.66	25.99 / 34.53
Min/Max	15.4 / 47.7	19.2 / 42.2	15.4 / 47.7

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Analysis Variable	All (N=208)	Retrospective (N=48)	Prospective (N=160)
Current AAD, n/N (%)			
Class I	110/208 (52.9%)	24/48 (50.0%)	86/160 (53.8%)
Flecainide (Tambocar)	74/208 (35.6%)	20/48 (41.7%)	54/160 (33.8%)
Propafenone (Rythmol)	8/208 (3.8%)	1/48 (2.1%)	7/160 (4.4%)
Class III	53/208 (25.5%)	9/48 (18.8%)	44/160 (27.5%)
Amiodarone	36/208 (17.3%)	4/48 (8.3%)	32/160 (20.0%)
Dofetilide (Tikosyn)	1/208 (0.5%)	0	1/160 (0.6%)
Dronedaron (Multaq)	15/208 (7.2%)	4/48 (8.3%)	11/160 (6.9%)
Sotalol (Betapace)	29/208 (13.9%)	4/48 (8.3%)	25/160 (15.6%)
None	45/208 (21.6%)	15/48 (31.3%)	30/160 (18.8%)
Drug refractory (AAD Class I/III), n/N (%)	208/208 (100.0%)	48/48 (100.0%)	160/160 (100.0%)
Pre-ablation OAC, n/N (%)			
None	17/208 (8.2%)	6/48 (12.5%)	11/160 (6.9%)
Coumadin	13/208 (6.3%)	0	13/160 (8.1%)
Eliquis	146/208 (70.2%)	33/48 (68.8%)	113/160 (70.6%)
Pradaxa	1/208 (0.5%)	0	1/160 (0.6%)
Savayesa	0	0	0
Xarelto	31/208 (14.9%)	9/48 (18.8%)	22/160 (13.8%)
Taking Aspirin, n/N (%)	56/208 (26.9%)	12/48 (25.0%)	44/160 (27.5%)
Sleep apnea			
Yes	54/208 (26.0%)	13/48 (27.1%)	41/160 (25.6%)
No	132/208 (63.5%)	32/48 (66.7%)	100/160 (62.5%)
Suspected	22/208 (10.6%)	3/48 (6.3%)	19/160 (11.9%)

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Analysis Variable	All (N=208)	Retrospective (N=48)	Prospective (N=160)
HAS-BLED score²			
n	202	44	158
Mean	1.7	1.7	1.8
Standard Deviation	1.13	1.07	1.14
Median	2.0	1.5	2.0
Q1/Q3	1.0 / 3.0	1.0 / 2.5	1.0 / 3.0
Min/Max	0 / 5	0 / 4	0 / 5
CHA₂DS₂-VASc score³			
n	208	48	160
Mean	2.5	2.3	2.6
Standard Deviation	1.44	1.39	1.46
Median	2.0	2.0	2.0
Q1/Q3	2.0 / 3.0	1.0 / 3.0	2.0 / 3.0
Min/Max	0 / 8	0 / 6	0 / 8
Has an implantable device			
Implantable loop recorder	10/208 (4.8%)	2/48 (4.2%)	8/160 (5.0%)
Dual chamber or CRT Pacemaker	15/208 (7.2%)	2/48 (4.2%)	13/160 (8.1%)
Dual chamber or CRT ICD	15/208 (7.2%)	3/48 (6.3%)	12/160 (7.5%)
Left Ventricle Ejection Fraction (%)			
n	125	26	99
Mean	56.32	54.89	56.70
Standard Deviation	8.815	8.294	8.948
Median	57.00	55.00	60.00
Q1/Q3	55.00/60.00	55.00/60.00	55.00/60.00
Min/Max	23.0/75.0	30.0/65.0	23.0/75.0
LA Diameter (cm)			
n	86	22	64
Mean	4.557	3.500	4.920
Standard Deviation	6.0996	0.8802	7.0296
Median	4.000	3.600	4.100
Q1/Q3	3.600/4.400	2.900/4.000	3.700/4.400
Min/Max	2.04/60.00	2.04/5.10	2.05/60.00

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Analysis Variable	All (N=208)	Retrospective (N=48)	Prospective (N=160)
LA Volume (mL/m²)			
n	78	9	69
Mean	34.726	29.689	35.383
Standard Deviation	12.5605	7.4827	12.9717
Median	32.450	31.000	33.000
Q1/Q3	27.000/39.000	23.400/34.000	27.000/39.500
Min/Max	16.67/100.00	18.00/40.00	16.67/100.00

¹Age at time of procedure

²The score for each subject is calculated as a sum of points given for each of the following conditions: 1 for hypertension, 1 for renal disease, 1 for liver disease, 1 for stroke history, 1 for prior major bleeding or predisposition to bleeding, 1 for labile INR, 1 for age > 65 years, 1 for medication usage predisposing to bleeding (e.g. aspirin, clopidogrel, NSAIDs), and 1 for alcohol use (≥ 8 drinks/week).

³The score for each subject is calculated as a sum of points given for each of the following conditions: 1 for congestive heart failure (or left ventricular systolic dysfunction), 1 for hypertension, 2 for age ≥ 75 years, 1 for diabetes mellitus, 2 for prior stroke or TIA or thromboembolism, 1 for vascular disease (e.g. peripheral artery disease, myocardial infarction, aortic plaque), 1 for age 65-74 years, and 1 for sex category (i.e. female gender).

Abbreviations: AAD = antiarrhythmic drug; BMI = body mass index; CRT = cardiac resynchronization therapy; ICD = implantable cardioverter-defibrillator; LA = left atrial; OAC = oral anticoagulant.

Table 133 – Mercy EHR Database Demographics and Baseline Characteristics

Characteristic	Covariate-Unadjusted		ASD	Covariate-Balanced*		ASD
	Group with Fluoroscopy Time of ≤ 2 minutes	Group with Fluoroscopy Time of ≥ 3 minutes		Group with Fluoroscopy Time of ≤ 2 minutes	Group with Fluoroscopy Time of ≥ 3 minutes	
	n (%)	n (%)		n (%)	n (%)	
Number of patients	129 (100.0)	170 (100.0)		129 (100.0)	121 (100.0)	
Age (years)			0.086			0.039
< 65	62 (48.1)	79 (46.5)		62 (48.1)	56 (46.1)	
65-74	46 (35.7)	67 (39.4)		46 (35.7)	45 (37.0)	
≥ 75	21 (16.3)	24 (14.1)		21 (16.3)	20 (16.9)	
Sex			0.036			0.033
Female	60 (46.5)	76 (44.7)		60 (46.5)	58 (48.2)	
Male	69 (53.5)	94 (55.3)		69 (53.5)	63 (51.8)	
Index year			0.562			0.129
2015/2016	22 (17.1)	38 (22.4)		22 (17.1)	20 (16.7)	
2017/2018	61 (47.3)	37 (21.8)		61 (47.3)	50 (41.6)	
2019/2020/2021	46 (35.7)	95 (55.9)		46 (35.7)	50 (41.6)	
Race			0.057			0.019
Black/Other	6 (4.7)	6 (3.5)		6 (4.7)	5 (4.3)	
White	123 (95.3)	164 (96.5)		123 (95.3)	116 (95.7)	

Dual Energy THERMOCOOL SMARTTOUCH™ SF Uni-Directional Catheter

	Covariate-Unadjusted			Covariate-Balanced*		
Characteristic	Group with Fluoroscopy Time of ≤ 2 minutes	Group with Fluoroscopy Time of ≥ 3 minutes	ASD	Group with Fluoroscopy Time of ≤ 2 minutes	Group with Fluoroscopy Time of ≥ 3 minutes	ASD
Ablation Catheter Type			0.132			0.048
THERMOCOOL SMARTTOUCH™	53 (41.1)	59 (34.7)		53 (41.1)	47 (38.7)	
THERMOCOOL SMARTTOUCH™ SF	76 (58.9)	111 (65.3)		76 (58.9)	74 (61.3)	
Medical history						
Anemia	9 (7.0)	12 (7.1)	0.003	9 (7.0)	8 (6.7)	0.013
Coagulopathy	9 (7.0)	7 (4.1)	0.125	9 (7.0)	8 (6.3)	0.026
Coronary artery disease	51 (39.5)	53 (31.2)	0.176	51 (39.5)	46 (38.1)	0.030
Chronic kidney disease	21 (16.3)	32 (18.8)	0.067	21 (16.3)	24 (19.9)	0.093
Chronic obstructive pulmonary disease	28 (21.7)	36 (21.2)	0.013	28 (21.7)	27 (22.5)	0.020
Congestive heart failure	24 (18.6)	45 (26.5)	0.189	24 (18.6)	27 (22.1)	0.087
Hypertension	95 (73.6)	131 (77.1)	0.079	95 (73.6)	89 (74.0)	0.007
Diabetes mellitus	28 (21.7)	50 (29.4)	0.177	28 (21.7)	27 (22.0)	0.008
Stroke or transient ischemic attack or thromboembolism	8 (6.2)	9 (5.3)	0.039	8 (6.2)	8 (6.8)	0.026
Vascular disease (peripheral arterial disease, previous myocardial infarction, or aortic atheroma)	57 (44.2)	57 (33.5)	0.220	57 (44.2)	49 (40.8)	0.069
	Mean (SD)	Mean (SD)		Mean (SD)	Mean (SD)	
HAS-BLED score prior to the index procedure	2.9 (1.4)	2.9 (1.5)	0.039	2.9 (1.4)	3.0 (1.4)	0.066
Body mass index† (kg/m²)	31.0 (6.5)	31.9 (7.4)	0.141	31.0 (6.5)	31.0 (6.8)	0.008
Atrial fibrillation history						
Time from first AF diagnosis recorded in database to the index procedure	2.8 (2.1)	2.4 (2.3)	0.187	2.8 (2.1)	2.8 (2.5)	0.022

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	Covariate-Unadjusted			Covariate-Balanced*		
Characteristic	Group with Fluoroscopy Time of ≤ 2 minutes	Group with Fluoroscopy Time of ≥ 3 minutes	ASD	Group with Fluoroscopy Time of ≤ 2 minutes	Group with Fluoroscopy Time of ≥ 3 minutes	ASD
(years)						
Number of AAD [‡] prescriptions prior to the index procedure	7.4 (5.7)	7.2 (6.4)	0.023	7.4 (5.7)	7.7 (6.5)	0.051
Number of AF ablations performed by cardiac electrophysiologists (12 months prior to the index ablation)	111.7 (14.7)	105.4 (42.9)	0.196	111.7 (14.7)	114.9 (39.2)	0.107
	n (%)	n (%)		n (%)	n (%)	
Missing data for the number of AF ablations performed by cardiac electrophysiologists missing	3 (2.3)	9 (5.3)	0.156	3 (2.3)	4 (3.2)	0.053
Number of ASDs > 0.20			2			0
Average ASD			0.129			0.045

*Using the propensity score weighting method of the average treatment effect on the treated with weight trimming at the 99th percentile of the weight distribution in the comparator group

[†]Latest prior to the index procedure

[‡]Class I or III AAD

Abbreviations: AAD: antiarrhythmic drug; ASD: absolute standardized difference; EHR: electronic health records; PAF: paroxysmal atrial fibrillation; SD: standard deviation

Left atrial size and left ventricular ejection fraction were available only among a subset of patients. These variables were not included in the propensity score model but were reported descriptively within each treatment group being compared, and both were similarly distributed between the group with fluoroscopy time of ≤ 2 minutes and the group with fluoroscopy time of ≥ 3 minutes.

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Table 134 – Additional Baseline Characteristics of PAF Patients by Fluoroscopy Workflow Type in the Mercy EHR Database (Covariate-Unadjusted Data)

Characteristic	Group with Fluoroscopy Time of ≤ 2 minutes	Group with Fluoroscopy Time of ≥ 3 minutes	Absolute Standardized Difference
Number of patients	129	170	
Left atrial diameter (mm)			
N(%)	65 (50.39)	89 (52.35)	
Mean (SD)*	39.22 (6.11)	39.68 (6.83)	0.072
Missing, n (%)	64 (49.61)	81 (47.65)	0.039
Left Ventricular ejection fraction (%)			
≥ 50, n (%)*	90 (82.57)	102 (86.44)	0.107
< 50, n (%)*	19 (17.43)	16 (13.56)	
Missing, n (%)	20 (15.50)	52 (30.59)	0.364

*Based on non-missing data

Abbreviations: EHR: electronic health records; PAF: paroxysmal atrial fibrillation; SD: standard deviation

C. Results

The below tables summarize the results.

C.1 – REAL AF Zero/Low Fluoroscopy Sub-Study Procedure Counts and Device Utilization

Table 135 – REAL AF Zero/Low Fluoroscopy Sub-Study Procedure Type and Distribution of Device Utilization

Device	Frequency of Using, n/N (%) ¹
Index Procedure (N=208)	
THERMOCOOL SMARTTOUCH™ Catheter	1/208 (0.5%)
THERMOCOOL SMARTTOUCH™ SF Catheter	207/208 (99.5%)
PENTARAY™ Nav eco High-Density Mapping Catheter	205/208 (98.6%)
DECANAV™ Catheter	78/208 (37.5%)
WEBSTER™ CS Catheter	94/208 (45.2%)
CARTO™ System	208/208 (100%)
Ablation Catheter Sheath	208/208 (100%)
Short	8/208 (3.8%)
Long Fixed	18/208 (8.7%)
Steerable	182/208 (87.5%)
CARTO VIZIGO™ Guiding Sheath	150/182 (82.4%)
Agilis	29/182 (15.9%)
Other	2/182 (1.1%)

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Device	Frequency of Using, n/N (%) ¹
Repeat Procedure (N=10)	
THERMOCOOL SMARTTOUCH™ Catheter	0/10 (0.0%)
THERMOCOOL SMARTTOUCH™ SF Catheter	10/10 (100%)
PENTARAY™ Nav eco High-Density Mapping Catheter	8/10 (80.0%)
DECANAV™ Catheter	6/10 (60.0%)
WEBSTER™ CS Catheter	3/10 (30.0%)
CARTO™ System	10/10 (100%)
Ablation Catheter Sheath	10/10 (100%)
Short	0
Long Fixed	3/10 (30.0%)
Steerable	7/10 (70.0%)
CARTO VIZIGO™ Guiding Sheath	5/7 (71.4%)
Agilis	1/7 (14.3%)
Other	1/7 (14.3%)

¹n and N Denotes number of catheters used in the index or repeat procedure.

C.2 – REAL AF Zero/Low Fluoroscopy Sub-Study Fluoroscopy Time Used During Procedure

Table 136 – REAL AF Zero/Low Fluoroscopy Sub-Study Total Fluoroscopy Time

Variable	All (N=208)	Non-Zero (N=104) ¹
Total Fluoroscopy Time (min)		
n	208	104
Mean	0.95	1.90
Standard Deviation	1.997	2.488
Median	0.05	1.00
Q1/Q3	0/1.0	0.3/2.5
Min/Max	0/15.6	0.1/15.6

¹Subjects treated with any fluoroscopy.

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C.3 – REAL AF Zero/Low Fluoroscopy Sub-Study Total Procedure Time

Table 137 – REAL AF Zero/Low Fluoroscopy Sub-Study Procedure Time

Variable	Statistics
Total Procedure Time (min)	
n	208
Mean	97.3
Standard Deviation	44.42
Median	84.5
Q1/Q3	65.0/115.0
Min/Max	35/249

C.4 – REAL AF Zero/Low Fluoroscopy Sub-Study Anesthesia Agent

Table 138 – REAL AF Zero/Low Fluoroscopy Sub-Study Anesthesia Agent

Variable	Statistics
Anesthesia Agent, n/N (%)	
Inhaled Anesthetics	149/208 (71.6%)
Paralytics	148/208 (71.2%)
Propofol	171/208 (82.2%)
Other	5/208 (2.4%)

C.5 – REAL AF Zero/Low Fluoroscopy Sub-study Ventilation Mode

Table 139 – REAL AF Zero/Low Fluoroscopy Sub-Study Ventilation Mode

Variable	Statistics
Ventilation Mode, n/N (%)	
Standard	135/208 (64.9%)
HFLV	91/208 (43.8%)
JET	6/208 (2.9%)
Intermittent Apnea	11/208 (5.3%)
Conscious sedation	5/208 (2.4%)

Abbreviations: HFLV = high frequency low volume.

C.6 – REAL AF Zero/Low Fluoroscopy Sub-Study Ablation Lesion Set

Table 140 – REAL AF Zero/Low Fluoroscopy Sub-Study Ablation Lesion Set

Variable	Statistics
Radiofrequency, n/N (%)	
PV only	63/208 (30.3%)
PV+CTI	96/208 (46.2%)
PV+CTI+SM	26/208 (12.5%)
PV+SM	23/208 (11.1%)
CTI+SM	0
SM only	0
CTI only	0

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Variable	Statistics
Substrate Modification, n/N (%)	
N/A	158/208 (76.0%)
Post Wall	26/208 (12.5%)
Mitral Isthmus	12/208 (5.8%)
Other	29/208 (13.9%)
Other Areas Ablated, n/N (%)	
None	184/208 (88.5%)
SVC	3/208 (1.4%)
CS	4/208 (1.9%)
AVNRT Pathway	4/208 (1.9%)
Other	13/208 (6.3%)

Abbreviations: AVNRT = atrioventricular nodal reentrant tachycardia; CS = coronary sinus;
CTI = cavotricuspid isthmus; PV = pulmonary vein; SM = substrate modification;
SVC = superior vena cava.

C.7 – REAL AF Zero/Low Fluoroscopy Sub-study Esophageal Monitoring

Table 141 – REAL AF Zero/Low Fluoroscopy Sub-Study Max Esophageal Temperature

Variable	Statistics
Max Esophageal Temp (C)	
n	166
Mean	36.56
Standard Deviation	6.487
Median	37.55
Q1/Q3	36.80/38.20
Min/Max	4.0/44.1

C.8 – REAL AF Zero/Low Fluoroscopy Sub-study Same Day Discharge

Table 142 – REAL AF Zero/Low Fluoroscopy Sub-Study Same Day Discharge

Variable	Statistics
Plan to discharge same day, n/N (%)	173/208 (83.2%)
Patient discharged same day (confirmed), n/N (%)	153/208 (73.6%)

C.9 - REAL AF Zero/Low Fluoroscopy Sub-study Primary Safety Success

Complications were adjudicated by an independent clinical events committee. A total of 3 subjects reported 3 primary adverse events (1.5% rate). These primary adverse events included one of each: pseudoaneurysm (definitely procedure related), pulmonary vein stenosis (definitely related to study device and procedure), and hematoma (definitely procedure related). A total of 194 subjects did not have a primary adverse event.

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Table 143 – REAL AF Zero/Low Fluoroscopy Sub-study Primary Safety Endpoint

Variable	Number of Subjects with Event	Number of Events	PAE Rate ¹	One-sided 95% Upper Confidence Interval ²
Primary Adverse Event	3	3	3/197 (1.5%)	3.9%

¹PAE rate is the percentage of subjects with PAEs. Subjects who did not have any documented encounter past post-index were excluded from the primary safety analysis.

²Exact test for binomial proportion. If the upper one-sided 95% CI of the primary safety endpoint is less than 10%, the primary endpoint will be met.

Note: Eleven subjects did not complete the 3-month visit and were excluded from analysis.

Two primary adverse events were observed in the zero fluoroscopy subgroup - pseudoaneurysm and pulmonary vein stenosis. One primary adverse event was observed in the non-zero fluoroscopy subgroup – hematoma.

Table 144 – REAL AF Zero/Low Fluoroscopy Sub-Study Primary Safety Endpoint by Zero vs Non-Zero Fluoroscopy

Subgroup	Number of Subjects with Event	Number of Events	PAE Rate ¹
Zero	2	2	2/94 (2.1%)
Non-Zero	1	1	1/103 (1.0%)

¹The percentage of subjects with PAEs within each group. Subjects who do not have any documented encounter past post-index will be excluded from the primary safety analysis.

C.10 – REAL AF Zero/Low Fluoroscopy Sub-Study Secondary Acute Effectiveness Success

Table 145 – REAL AF Zero/Low Fluoroscopy Sub-Study Secondary Acute Effectiveness Endpoint

Variable	Number of Subjects	Number of Subjects Reaching PVI	Success Rate, n/N (%) ²	One-sided 95% Lower Confidence Interval ³
Acute Effectiveness ¹	202	202	202/202 (100%)	98.5%

¹Acute effectiveness success is defined as confirmation of pulmonary vein isolation in all targeted pulmonary veins.

²Success rate is the proportion of subjects with acute effectiveness.

³Exact test for binomial proportion. If the lower bound of the one-sided 95% CI is greater than 90%, the secondary endpoint will be met.

Abbreviations: PVI=pulmonary vein isolation.

C.11 – Mercy EHR Database Procedural Information

Table 146 – Mercy EHR Database Count of Intracardiac Echocardiography

	Group with fluoroscopy time of ≤ 2 minutes	Group with fluoroscopy time of ≥ 3 minutes
Use of intracardiac echocardiography, n (%)	129 (100.00)	170 (100.00)

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Table 147 – Mercy EHR Database Repeat Ablation Events by Fluoroscopy Workflow Type

	Group with fluoroscopy time of ≤ 2 minutes	Group with fluoroscopy time of ≥ 3 minutes
	129 (100.00)	170 (100.00)
Repeat Ablation Events	3 (2.33%)	6 (3.53%)
Within 12 months post index ablation procedure	3 (2.33%)	6 (3.53%)
Number of repeat ablations*	3 (2.33%)	6 (3.53%)
Number of patients who had a repeat ablation*	3 (2.33%)	6 (3.53%)
Number of repeat ablations a patient underwent		
1	3 (2.33%)	6 (3.53%)
2	0 (0.00%)	0 (0.00%)
≥ 3	0 (0.00%)	0 (0.00%)

*Percentages were based on patients meeting the eligibility criteria in the study group.

C.12 – Descriptive Comparison of the Secondary Safety Endpoint

One subject in the group with fluoroscopy time of ≤ 2 minutes had 1 event, pericarditis. Similarly in the group with fluoroscopy time of ≥ 3 minutes, one subject had 1 event, death. The cause of death was not available.

Table 148 – Cumulative Incidences of the Secondary Safety Endpoint by Fluoroscopy Workflow Type in the PAF Study Population in the Mercy EHR Database (Covariate-Unadjusted Data)

Study Group	No. of Patients	No. of Patients with Event	Cumulative Incidence (%)	Standard Error
Covariate-Unadjusted data				
Group with fluoroscopy time of ≤ 2 minutes	129	1	0.80%	0.008
Group with fluoroscopy time of ≥ 3 minutes	170	1	0.59%	0.006

Table 149 – Cumulative Incidences of the Secondary Safety Endpoint by Fluoroscopy Workflow Type in the PAF Study Population in the Mercy EHR Database (Covariate-Balanced Data Using the Propensity Score Weighting Method*)

Study Group	No. of Patients	No. of Patients with Event	Cumulative Incidence (%)	Bootstrap Standard Error
Covariate-balanced data*				
Group with fluoroscopy time of ≤ 2 minutes	129	1	0.80%	0.008
Group with fluoroscopy time of ≥ 3 minutes	170	1	0.31%	0.003

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*Using the propensity score weighting method of the average treatment effect on the treated with weight trimming at the 99th percentile of the weight distribution in the comparator group

D. Study Conclusion

The analysis of real-world data from the REAL AF Registry Sub-study supported the notion that the use of a zero/low fluoroscopy workflow in radiofrequency catheter ablation of paroxysmal atrial fibrillation is safe and does not compromise the acute effectiveness of pulmonary vein isolation.

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ELECTRONIC INSTRUCTIONS FOR USE

This document is available at www.e-ifu.com.

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Appendix 43_nGEN™ Pump IFU (EML-1397-02-IFU)

nGEN™ Pump

User Manual

**Caution: Federal (USA) law restricts
this device to sale by or on the
order of a licensed healthcare practitioner.**



EML-1397-02-IFUD

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1 Device Description

The nGEN™ Pump is a peristaltic pump designed for use by electrophysiology laboratory staff in cardiac electrophysiology procedures. The pump delivers irrigation solution from a connected irrigation solution bag via a compatible irrigation tubing set to a compatible irrigated catheter.

The pump has an intuitive user interface that allows easy manual control of the pump's functions. Alternatively, the pump may be connected to a compatible generator so that the pump's irrigation flow rates (high and low) can be controlled by the generator. When the pump is connected to a generator that is capable of fully controlling the pump, the generator automatically sets the irrigation flow rate based on the connected catheter type, changes the flow rate when the delivery of energy starts and stops, and monitors the flow rate.

Only compatible accessories and devices provided by or recommended by Biosense Webster may be used with the nGEN™ Pump.

2 Indications

The nGEN™ Pump is a peristaltic pump designed to work with a compatible irrigation tubing set, either independently or with a compatible generator, to deliver irrigation solution to compatible irrigated catheters.

3 Contraindications

Refer to the catheter's instructions for use for contraindications that are specific to the catheter.

4 Warnings

Before using the nGEN™ Pump, completely read and understand this user manual. Also read and understand the instructions for use for the accessories and other devices connected to the pump. The order of the warnings below does not give any indication of their relative importance.

1. To avoid harm to the patient, use the pump only when the use of irrigation solution is appropriate for the medical condition of the patient. If it is not known what impact the irrigation solution might have on the patient, consult with appropriate medical professionals before using the pump.
2. The pump may be operated in the immediate vicinity of a compatible generator. However, do not operate the pump in the immediate vicinity of devices that are not approved for electromagnetic compatibility (EMC) with the pump. If such operation is unavoidable, regularly monitor the pump and move the pump if it does not function properly.
3. Use only compatible accessories and devices provided by or recommended by Biosense Webster. If you use accessories or devices that are not compatible, the safety of the pump is not guaranteed. Do not use settings above the maximum rated voltage for the accessories.
4. Use only the AC adapter provided with the pump. If an incompatible AC adapter is used, the pump might not function properly.
5. Use only a compatible irrigation tubing set provided by or recommended by Biosense Webster. If an incompatible irrigation tubing set is used, the pump might not function properly or improper irrigation might result.

6. The irrigation tubing set is sterile and is intended for one-time patient use. To avoid biological contamination and to ensure proper functioning, do not reuse or resterilize the irrigation tubing set. The irrigation tubing set can be damaged if installed incorrectly. See 6.5, *Installing the Irrigation Tubing Set* for additional information.
7. The pump, the generator, and all accessories connected to the pump or generator, when located within the patient area, must comply with IEC/EN 60601-1 and its sub-standards.
8. Do not connect the pump to other infusion systems, including gravity intravenous (IV) infusion systems.
9. The hospital staff is responsible for ensuring that the pump is functioning properly and that the irrigation solution and irrigated catheters that are used are compatible with each other. The pump and the compatible irrigation tubing set are intended for use with a standard irrigation solution such as a normal isotonic saline solution. The accuracy of the flow rate stated in 8.1, *Specifications* may not be maintained if incompatible irrigation solutions and/or incompatible irrigated catheters are used.
10. Parts of the pump, such as the intravenous (IV) pole clamp, the rotating pump head, and the door that covers the pump head, are designed for safe operation and must be used with caution.
11. After turning on the pump, wait until the automatic self-test has been successfully completed before starting the first steps of the procedure on the patient. The self-test helps to detect problems with the pump before use.
12. The pump is intended for use with irrigated catheters. Monitor the irrigation flow rate to avoid hazards caused by insufficient irrigation flow. Monitoring the flow rate on the pump screen alone is not sufficient because the flow rate is calculated from the pump motor speed. If the pump fails to rotate at the speed set by the user, the pump issues an error. However, because it is possible for a situation to arise during which the pump rotor is rotating but there is no flow, it is important to repeatedly monitor the approximate flow rate by observing the drip speed in the drip chamber. The drip chamber should be half to three-quarters filled to ensure that no bubbles enter the irrigation tubing and to provide visibility of the drip speed. The hospital staff is responsible for determining and monitoring the flow rate to avoid insufficient flow of the irrigation solution. The hospital staff is responsible for monitoring the total amount of solution delivered to the patient to avoid an excessive loading of the irrigation solution in the patient. For recommended flow rates, refer to the catheter's instructions for use. For starting the irrigation flow, see 6.8, *Starting the Irrigation Flow*.
13. If the pump repeatedly displays errors, stop using the pump and contact Customer Support.
14. Do not put any labels or stickers on the front of the pump that will obscure the screen, buttons, or indicator lights.
15. There are no parts in the pump that may be serviced by the user. Repairs or any changes may be performed only by Biosense Webster, a service engineer authorized by Biosense Webster, or a service center authorized by Biosense Webster. The warranty is voided if improper modifications or repairs are performed or if the device is not maintained according to the instructions in this user manual.
16. To avoid damage to the pump and its accessories, use only appropriate cleaning agents. (See 7, *Caring for the Pump*.)
17. If fluid penetrates into the pump, stop using the pump and contact Customer Support.
18. To prevent explosions and fires, do not use the pump near explosive or flammable substances.

19. To prevent electric shock and fires, connect the pump to a grounded mains outlet that meets the specifications in *8.1, Specifications* and do not expose the pump to excessive humidity.
20. To eliminate air bubbles, you must flush the irrigation tubing set and catheter before the catheter is inserted into the patient. Failure to flush the irrigation tubing may result in air embolism in the patient. Do not flush the catheter when it is in the patient. See *6.6, Flushing to Remove Bubbles from the Tubing and Catheter* for additional information.
21. To prevent electric shock, fires and harm to user, do not use liquids of any kind near the AC adapter. Position the solution bag and drip chamber away from the AC adapter during setup and use of pump to prevent unintentional exposure of fluids.

5 Overview of the Pump

5.1 Definitions of Notes, Cautions, and Warnings

This document uses notes, cautions, and warnings as described below.

Note: A note provides important information, emphasizing or supplementing the main text. The information does not relate directly to issues that might cause injury to patients or users, or damage to the device.

Caution: A caution provides information relating to issues that might cause injury to patients or users, or damage to the device.

WARNING

A warning provides information relating to issues that might cause serious, life-threatening injury to patients or users, or serious, irreparable damage to the device.

5.2 Components and Accessories

WARNING

Use only compatible accessories provided by or recommended by Biosense Webster. If you use accessories that are not compatible, the safety of the pump is not guaranteed.

The components listed in Table 1 are provided as part of the initial purchase of the nGEN™ Pump.

Table 1 – Components of the Pump

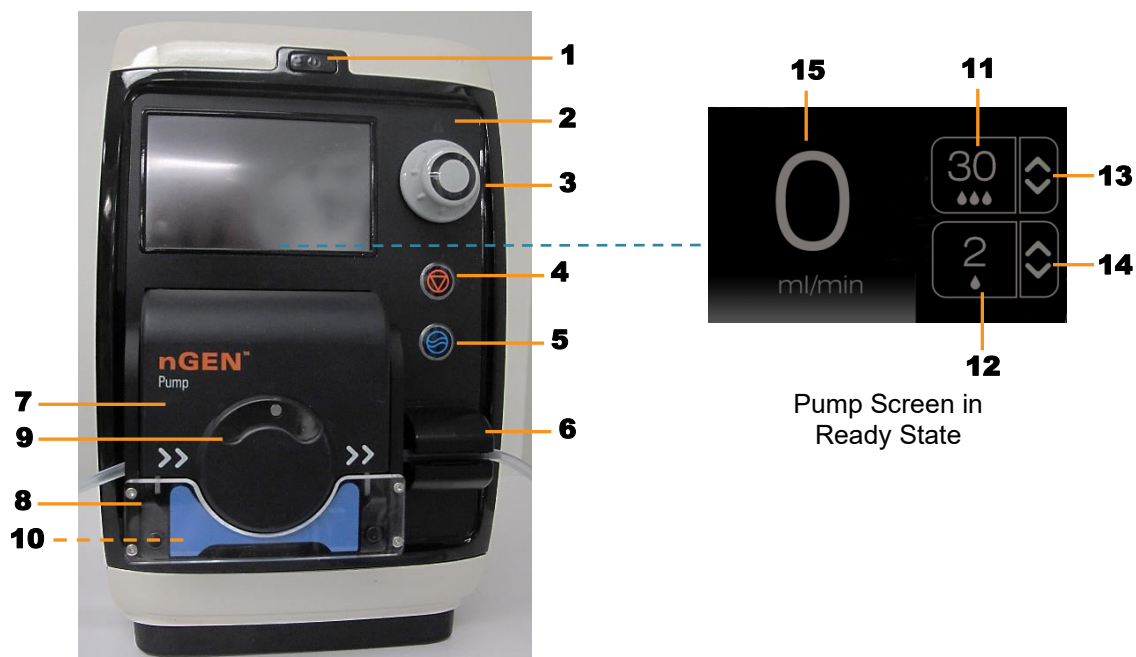
Component	Part #
nGEN™ Pump	
United States	D139702
AC adapter, 2.0 m (6.6 ft)	M529723
Mains cable, 3.05 m (10 ft)	M649001
IV pole clamp	M549104
nGEN™ Pump User Manual	EML-1397-02-IFU

The accessories in Table 2 are not provided with the nGEN™ Pump but are intended for use with the pump.

Table 2 – Accessories for the Pump

Item	Part #
Irrigation Tubing Set	SAT001
Stockert-COOLFLOW® interface cable, 6.0 m (19.7 ft)	M546371
nGEN™ Pump cable adapter, 25 mm (1 in)	M581505
Pump Test Kit	CFP006

5.3 Controls on the Front of the Pump



Note: The nGEN™ Pump may have an alternate appearance as mentioned in 12, *Appendix*.

Table 3 – Controls on the Front of the Pump

1	On/Off  button
2	Internal error indicator  (only visible when there is an internal error)
3	Flow Rate Adjustment  knob
4	Stop  button
5	Flush  button
6	Bubble sensor
7	Pump head
8	Pump door
9	Pump rotor
10	Pump bed
11	Activate High Flow  button
12	Activate Low Flow  button
13	Change High Flow Setting  button
14	Change Low Flow Setting  button
15	Active flow rate display

Note: See 6.2, *Explanation of Buttons and Indicators*.

5.4 Controls on the Back of the Pump

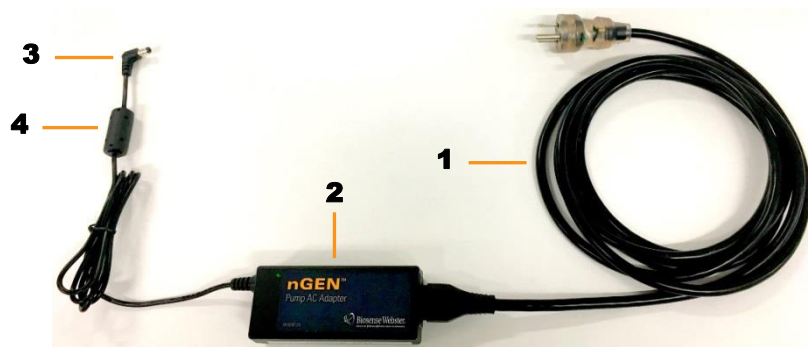


Table 4 – Controls on the Back of the Pump

1	Device label
2	COMM: socket for the generator connection cable
3	Service access door. Do not open.
4	Potential equalization pin
5	24VDC: socket for the AC adapter
6	Bracket
7	IV pole mounting pin

5.5 Setting up the Pump

Immediately upon receipt, remove the pump and its accessories from the shipping container and inspect for shipping damage or defects. Damage claims can only be filed if Biosense Webster or the shipping agent is notified immediately.



1	Mains cable	3	Plug
2	AC adapter	4	Ferrite

Quick Steps

1. Verify the AC adapter and Mains cable are dry and free of any fluids.
2. Connect the mains cable (**1**) to a grounded power outlet and to the AC adapter (**2**).
3. Insert the AC adapter plug (**3**) into the 24VDC socket on the back of the pump. Then put the AC adapter ferrite (**4**) behind the bracket on the back of the pump so that the ferrite is seated and the cable extends down from the left side of the back of the pump.
4. Optionally, connect the pump to a generator.
5. Secure the IV pole clamp to an IV pole or to a mounting railing near the patient.
6. Slide the IV pole mounting pin on the pump into the pole clamp.
7. Install the irrigation tubing set, and position the solution bag and drip chamber away from the AC adapter. (See 6.5, *Installing the Irrigation Tubing Set*.)

Notes

- See 5.4, *Controls on the Back of the Pump* and 5.6, *Connecting to a Generator*.
- To ensure stability, use an IV pole with 5 legs or an IV pole that is attached to a cart.

5.6 Connecting to a Generator

The pump can be controlled by a compatible generator that is connected to the pump. Connect one end of the generator connection cable to the COMM socket on the back of the pump. Connect the other end of the cable to the appropriate socket on the generator. Align the arrow on the connector at the end of the cable with the mark on the socket and push in without unnecessary force until a click indicates that the connector is locked in the socket. To remove the connector, gently pull back the sleeve on the connector and pull the connector out of the socket.

Note: When you are using the Stockert 70 RF generator or the EP-Shuttle RF generator, connect one end of the Stockert COOLFLOW® interface cable (M546371) to the Stockert generator and the other end to the nGEN™ Pump cable adapter (M581505). Connect the other end of the nGEN™

Pump cable adapter to the COMM socket on the back of the pump. Contact a Biosense Webster representative for further information.

When the pump identifies that the generator is successfully connected, the cable connection indicator  or the automatic control indicator  appears in the upper left corner of the screen. If communication is lost between the pump and the generator, the indicator disappears from the screen and the pump emits a short beep.

6 Operating the Pump

6.1 Operational Safety Inspection

To ensure the safety of the pump, perform the inspections below before each use. If any problems are discovered, contact Customer Support. (Also see 7.3, *Maintenance and Repairs*.)

- Verify that the pump and its accessories are properly connected.
- Verify that the pump and its accessories have no visual damage.
- Verify that the sockets are not damaged or loose.
- Verify that the mains cable is not damaged.
- Verify that the generator connection cable is not damaged.
- Verify that all cables and their connectors are free of foreign matter.
- Verify the AC adapter is not near any fluids and has not been exposed to any liquids and/or fluids prior and/or during use.
- Verify that the LEDs flash and that a long beep is emitted when the pump is turned on.
- Press the **Change Low Flow Setting**  button and turn the **Flow Rate Adjustment**  knob to verify that the low flow value changes as expected.
- Press the **Change High Flow Setting**  button and turn the **Flow Rate Adjustment**  knob to verify that the high flow value changes as expected.
- After installing an irrigation tubing set (see 6.5, *Installing the Irrigation Tubing Set*), press the **Flush**  button to verify that the pump starts flushing.
- Press the **Low Flow**  button to verify that the pump starts irrigation low flow.
- Press the **High Flow**  button to verify that the pump starts irrigation high flow.
- Press the **Stop**  button to verify that the pump stops the irrigation flow.

6.2 Explanation of Buttons and Indicators

Table 5 – Explanation of Buttons and Indicators

Button or Indicator	Image	Explanation
On/Off button		The pump is off.
		The pump is on.
Internal error indicator		This indicator (located at the top right corner of the front of the pump) illuminates when there is an internal error or malfunction. (See 10, <i>Errors and Troubleshooting</i> .) This indicator is not visible when the pump is functioning properly.
Stop button		When there is no active flow, this button is not lit.
		When high flow or low flow is active, this button is lit and orange. Pressing the button stops the flow.
		When the pump issues an alarm, this button flashes red. (See 6.10, <i>Alarms</i> .) Pressing the button stops the repeating alarm tone.
Flush button		When flushing is disabled, this button is not lit.
		When flushing is required, this button flashes. When flushing is enabled but not required, this button is lit but does not flash.
Activate High Flow button		This button displays the set high flow rate. When high flow is inactive, this button has gray text on a black background.
		When the high flow rate is being changed, this button has blue text. (See 6.7, <i>Setting the Low and High Flow Rates</i> .)
		When high flow is active, this button has a blue background. (See 6.8, <i>Starting the Irrigation Flow</i> .)
Activate Low Flow button		This button displays the set low flow rate. When low flow is inactive, this button has gray text on a black background.
		When the low flow rate is being changed, this button has green text. (See 6.7, <i>Setting the Low and High Flow Rates</i> .)
		When low flow is active, this button has a green background. (See 6.8, <i>Starting the Irrigation Flow</i> .)
Change High Flow Setting button		When high flow is inactive, this button has gray arrows on a black background. The background changes to blue when the button is pressed to change the high flow setting, (See 6.7, <i>Setting the Low and High Flow Rates</i> .)

Table 5 – Explanation of Buttons and Indicators

Button or Indicator	Image	Explanation
Change Low Flow Setting button		When low flow is inactive, this button has gray arrows on a black background. The background changes to green when the button is pressed to change the low flow setting (See 6.7, <i>Setting the Low and High Flow Rates.</i>)
Flow Rate Adjustment knob		This knob illuminates white and then turns off during the startup self-test procedure.
		This knob flashes blue when the Change High Flow Setting button is pressed.
		This knob flashes green when the Change Low Flow Setting button is pressed.
		This knob is unlit at all other times.
Cable connection indicator		This indicator appears at the top left of the screen when the pump is properly connected to a generator.
Automatic control indicator		This indicator appears at the top left of the screen when the pump establishes communication with a generator that supports automatic pump control.
Bubble indicators		This bubble alarm indicator appears when the pump detects bubbles in the irrigation tubing at the bubble sensor location during irrigation. (See 6.10, <i>Alarms.</i>)
		This bubble indicator appears when the pump detects bubbles in the irrigation tubing at the bubble sensor location and there is no irrigation flow (usually after a bubble alarm has been cleared). (See 6.6, <i>Flushing to Remove Bubbles from the Tubing and Catheter.</i>)
Flushing indicators		This indicator appears when the pump detects bubbles in the irrigation tubing at the bubble sensor location during flushing.
		This indicator appears when the pump does not detect any bubbles in the irrigation tubing at the bubble sensor location during flushing.
Open door indicator		This open door alarm indicator appears when the pump door is opened during irrigation. (See 6.10, <i>Alarms.</i>)
		This open door indicator appears when the pump door is opened when there is no irrigation flow. (See 6.3, <i>Turning On the Pump.</i>)

6.3 Turning On the Pump

Quick Steps

1. Press the **On/Off**  button.

Notes

- During startup, the pump conducts an automatic self-test of all critical functions, including the motor, bubble sensor, buttons, speaker (long beep), and LEDs. If it detects an internal error, the pump issues a repeating high priority alarm tone, the internal error indicator lights, and an error appears on the screen. (See 10, *Errors and Troubleshooting*.)
- If the pump detects bubbles after you turn it on, the screen displays a bubble indicator  and the **Flush**  button flashes. (See 6.6, *Flushing to Remove Bubbles from the Tubing and Catheter*.)
- If you open the pump door when the pump is on and there is no irrigation flow, the screen displays the open door indicator .
- After successful startup, the ready screen appears (see the figure in 5.3, *Controls on the Front of the Pump*) and displays the last flow settings that were used before the pump was turned off.

6.4 Turning Off the Pump

Quick Steps

1. Press and hold the **On/Off**  button for approximately 3 seconds.

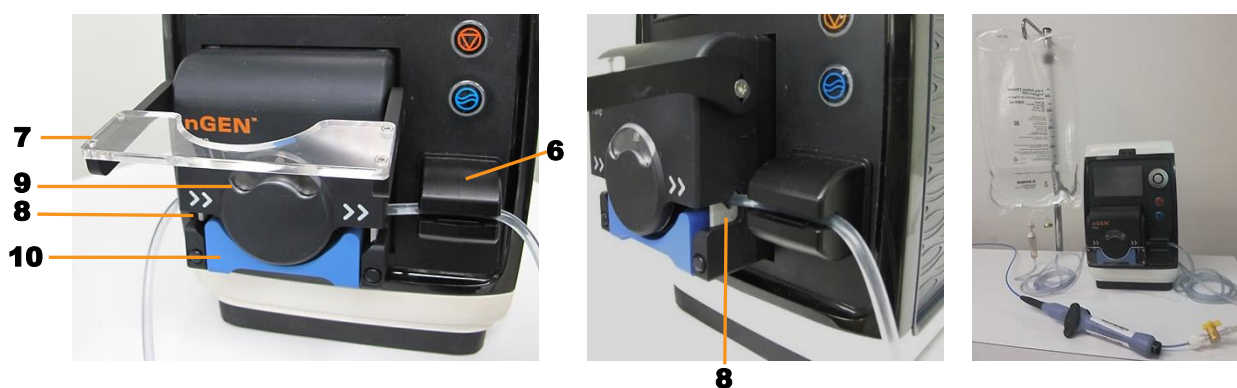
Notes

- After the pump has been turned off, power continues to be supplied to the pump through the AC adapter. To completely cut off power to the pump, disconnect the AC adapter.

6.5 Installing the Irrigation Tubing Set

WARNINGS

- The irrigation tubing set is sterile and is intended for one-time patient use. To avoid biological contamination and to ensure proper functioning, do not reuse or resterilize the irrigation tubing set.
- The irrigation tubing set can be damaged if installed incorrectly.
- The irrigation solution must flow toward the patient. The arrows on the irrigation tubing set must face in the same direction as the arrows on the pump head. The end of the tubing that extends from the left side of the pump must connect to the irrigation solution bag. The end of the tubing that extends from the right side of the pump must connect to the catheter.
- Before powering the unit, ensure the solution bag and drip chamber are not positioned near the AC adapter to prevent unintentional exposure of fluids.



Quick Steps

1. Open the pump door (7).
2. Insert the irrigation tubing between the pump rotor (9) and the pump bed (10). Ensure that the arrows on the tubing face in the same direction as the arrows on the pump head.
3. Ensure that the irrigation tubing is above or on the metal hooks on each side of the pump head (8).
4. Close the pump door.
5. Gently stretch the irrigation tubing that extends from the right side of the pump head and insert it into the slot in the bubble sensor (6) until the irrigation tubing snaps in place. Ensure that the tubing touches the back of the slot in the bubble sensor.
6. Flush the irrigation tubing. (See 6.6, *Flushing to Remove Bubbles from the Tubing and Catheter.*)

Notes

- The numbers in the images above correspond to the numbers in 5.3, *Controls on the Front of the Pump.*
- When you close the pump door, the irrigation tubing is compressed to prevent the irrigation solution from flowing freely through the tubing. Be careful not to pinch your fingers.

6.6 Flushing to Remove Bubbles from the Tubing and Catheter

WARNINGS

- To eliminate air bubbles, you must flush the irrigation tubing set and catheter before the catheter is inserted into the patient. Failure to flush the irrigation tubing may result in air embolism in the patient.
- Do not flush the catheter when it is in the patient.
- When you are flushing the irrigation tubing that is connected to a catheter inside the patient, turn the stopcock on the irrigation tubing set so that the flushed irrigation solution is diverted away from the catheter. Failure to do so may result in air embolism in the patient.

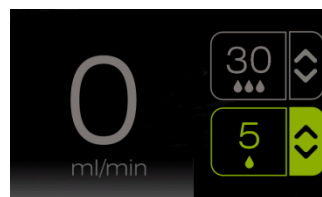
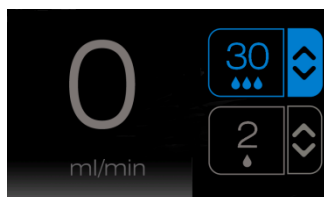
Quick Steps

1. Press and hold the **Flush**  button. The screen will display a bubble indicator containing bubbles .
2. Wait a few seconds after there are no bubbles in the flushing indicator  and then release the **Flush**  button.
3. Visually verify that there are no bubbles in the irrigation tubing.

Notes

- When flushing is required, the **Flush**  button flashes. When flushing is enabled but not required, the **Flush**  button is lit but does not flash.
- The pump detects bubbles in the irrigation tubing at the bubble sensor location. (See 5.3, *Controls on the Front of the Pump*.) It is important to continue flushing for a few seconds after there are no bubbles in the flushing indicator . This will ensure that the bubbles have been flushed from the irrigation tubing that extend past the bubble sensor.
- If the pump detects bubbles after you turn it on, the screen displays an image depicting bubbles  and the **Flush**  button flashes to indicate that you must flush before continuing.
- If the pump detects bubbles during active irrigation, the pump stops immediately and emits a repeating high priority alarm tone, and the screen displays a bubble alarm indicator . (See 6.10, *Alarms*.)

6.7 Setting the Low and High Flow Rates



Quick Steps

1. Press the **Change High Flow Setting** button (the button changes to blue ) or press the **Change Low Flow Setting** button (the button changes to green )
2. Turn the **Flow Rate Adjustment** knob until the desired setting is displayed on the **Activate High Flow**  button or the **Activate Low Flow**  button.

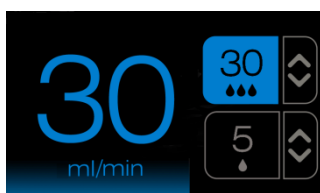
Notes

- When a button is pressed, the pump emits a short beep to confirm activation of the button.
- Refer to the instructions for use for the catheter to determine the appropriate flow rates for the catheter.
- The images above show changing the flow rates when the pump is in the ready state. The flow rates can also be changed during ablation.
- Low flow can be set between 1 and 5 ml/min. The range for high flow varies by geographic region (see 8.1, *Specifications*). Low flow cannot be set at or above the high flow setting.
- High flow can be set between 4 and 30ml/min. The range for high flow varies by geographic regions (see 8.1, *Specifications*). High flow cannot be set at or below the low flow setting.

6.8 Starting the Irrigation Flow

WARNINGS

- To prevent possible occlusion of the holes in the catheter's tip electrode, start low flow before inserting the catheter into the patient and verify that irrigation solution flows from the tip of the catheter.
- Be careful not to overload the patient with irrigation solution, especially at high flow rates.



Quick Steps

1. Ensure that there is sufficient solution in the irrigation solution bag.
2. Ensure that the irrigation tubing set is properly installed and that there are no bubbles in the tubing.
3. Press the **Activate High Flow**  button (the button changes to blue ) or press the **Activate Low Flow**  button (the button changes to green )
4. Verify that the pump rotor is rotating.

Notes

- If the pump is connected to a generator, it may be possible to start the irrigation flow from the generator's user interface or to configure the generator to automatically change the irrigation flow from low to high when ablation begins.

Caution: If the pump is not controlled by a generator, the irrigation flow must be controlled by the user. Start high flow before starting the delivery of energy to allow the desired flow rate to be reached at the tip of the catheter. Continue high flow for a few seconds after ending the delivery of energy to bring the electrode back to body temperature.

6.9 Stopping the Irrigation Flow



Quick Steps

1. Press the **Stop**  button to stop the irrigation flow.

Notes

- The irrigation flow will also stop if you press the **On/Off**  button or open the pump door.
- After the procedure, remove the irrigation tubing set from the pump.

6.10 Alarms

When an alarm condition occurs, the pump stops immediately and emits a repeating high priority alarm tone, and one of the images below appears on the screen.

For information about internal errors, see *10, Errors and Troubleshooting*.

Table 6 – Alarms

Image	Reason	What To Do
	The pump detected bubbles during irrigation. The pump stopped the irrigation flow.	1. Immediately turn the stopcock on the irrigation tubing set so that the irrigation solution is diverted away from the catheter. 2. Press the Stop  button to stop the repeating alarm tone. The alarm indicator triangle will disappear from the image. 3. The Flush  button will flash. 4. Verify that the irrigation tubing is properly installed. (See 6.5, <i>Installing the Irrigation Tubing Set</i>.) 5. Flush the irrigation tubing. (See 6.6, <i>Flushing to Remove Bubbles from the Tubing and Catheter</i>.) 6. Turn the stopcock to allow the irrigation solution to be routed to the catheter again.
	The door was opened during irrigation. The pump stopped the irrigation flow.	1. Press the Stop  button to stop the repeating alarm tone. The alarm indicator triangle will disappear from the image. 2. Verify that the irrigation tubing is installed correctly. (See 6.5, <i>Installing the Irrigation Tubing Set</i>.) 3. Close the pump door. The pump will return to the ready screen.

7 Caring for the Pump

7.1 Cleaning and Disinfecting the Pump

WARNINGS

- Turn off the pump and disconnect the AC adapter from the pump before cleaning and disinfecting the pump.
- Do not sterilize the pump, the AC adapter, or the generator connection cable with steam autoclave sterilization or ethylene oxide (EtO) sterilization.
- Do not immerse the pump in liquid or expose it to excessive moisture, especially when the pump is connected to the mains outlet.

Clean and disinfect the pump after each use.

Before cleaning the pump, inspect the pump and all connected accessories to ensure that there is no visual damage. Contact Customer Support or your Biosense Webster representative if you identify any problems.

To clean the screen, use a dry microfiber cloth. If damp cleaning is necessary, moisten a soft cotton or linen cloth with commercial grade glass cleaner that does not contain alcohol and wipe the screen. Do not spray the cleaner directly onto the screen.

To clean the pump's housing, wipe the housing with a soft, lint-free cloth dampened with distilled water, isopropyl alcohol, or an alcohol based cleaning product. Do not use ethyl alcohol or any acid based cleaner. Do not spray the cleaner directly onto the housing.

7.2 Cleaning the Cords and Connection Cables

The following instructions apply to the mains cable, the generator connection cable, and the AC adapter.

1. Before cleaning each cable, disconnect it from the equipment.
2. Lightly dampen a lint-free cloth with a mild soap solution. Fold the cloth and gently pull the cable through the fold. Ensure that none of the soap solution enters the connectors.
3. Gently wipe the AC adapter. Do not expose the AC adapter to any fluids and/or liquids during cleaning.
4. Use a dry lint-free cloth to dry each cable and the AC adapter.

7.3 Maintenance and Repairs

Before each use, perform the inspections described in 6.1, *Operational Safety Inspection*. Once a year, verify that the device label is present and readable (see 5.4, *Controls on the Back of the Pump*). To ensure that the pump is operating correctly, routinely check the flow accuracy using the Pump Test Kit (see 5.2, *Components and Accessories*). If any problems are discovered, contact Customer Support.

There are no parts in the pump that may be serviced by the user. Repairs of the pump and its accessories may be performed only by Biosense Webster, a service engineer authorized by Biosense Webster, or a service center authorized by Biosense Webster.

7.4 Protection Against Damage

In addition to being operated and maintained per the instructions in this user manual, the pump must also be protected against damage. This includes installing the pump in a safe location and protecting the pump against moisture, contamination, and contact with explosive or flammable substances.

Ensure that all cables to devices and accessories are arranged in a way that prevents tripping.

To transport the pump over long distances or to send the pump for service, use the original packaging. If the original packaging is not available, contact Customer Service or your Biosense Webster representative for a replacement.

7.5 Disposal

Inadequately treated electrical and electronic waste poses environmental and health risks. Follow local regulations for disposal of the pump and its electrical or electronic accessories. To ensure proper disposal, you may contact Customer Support or your Biosense Webster representative regarding return of the pump and its accessories.

8 Technical Data

8.1 Specifications

AC Adapter		
AC input	100 to 240 VAC	
Frequency	50 Hz / 60 Hz	
DC output	24 V, 3 A	
Flow Accuracy	1 to 5 ml/min	-10% to +20%
	6 to 39 ml/min	-5% to +15%
	40 to 60 ml/min	-10% to +20%
Bubble Detection	Designed to detect 0.4 µl or larger bubbles at the flow rates specified below (equivalent to minimum sensitivity of 2 µl bubbles at atmospheric pressure)	
Adjustment of the Flow Rates (in 1 ml/min steps)		
Low flow	1 ml/min to 5 ml/min	
High flow	4 ml/min to 30 ml/min	
Flush Flow Rate	100 ml/min	
Maximum Infusion Pressure	140 psi	
Sound Pressure Level for Alarm Tone	55 to 65 dBA (measured 1 m from pump, factory setting that cannot be changed by the user)	
Classification	Class I and defibrillation proof type CF (as defined in IEC/EN 60601-1)	
	Class III, FDA	
Weight	5.5 kg (14.7 lb)	
Dimensions	19 cm deep x 18 cm wide x 28 cm high (7.5 in x 7.1 in x 11.0 in)	
IP Rating	IP23	

8.2 Operating, Storage, and Shipping Specifications

	Minimum	Maximum
Operating Specifications		
Ambient temperature	10°C	40°C
Relative humidity	10%	90%, non-condensing
Atmospheric pressure	700 mbar	1060 mbar
Storage Specifications		
Ambient temperature	-30°C	65°C
Relative humidity	0%	90%, non-condensing
Atmospheric pressure	500 mbar	1060 mbar
Shipping Specifications		
Ambient temperature	-30°C	65°C
Relative humidity	0%	90%, non-condensing
Atmospheric pressure	500 mbar	1060 mbar

8.3 EMC Information and Technical Description

The use of accessories and cables other than those specified in this user manual or specified by Biosense Webster may result in increased emissions or decreased immunity of the pump.

The pump is intended for use in the electromagnetic environment specified in Table 7 through Table 9. The user of the pump should ensure that it is used in such an environment.

A false bubble alarm might occur if the pump is operated in an environment where the electromagnetic disturbances exceed those specified in the tables below. For information on alarms, see 6.10, *Alarms*.

Table 7 – Electromagnetic Emissions

Emissions Test	Compliance	Electromagnetic Environment – Guidance
RF emissions CISPR 11	Group 1	The pump uses RF energy only for its internal function. Therefore, its RF emissions are very low and are not likely to cause any interference in nearby electronic equipment.
RF emissions CISPR 11	Class A	The pump is suitable for use in establishments other than domestic and those directly connected to the public low-voltage power supply network.
Harmonic emissions IEC 61000-3-2	Class A	
Voltage fluctuations/flicker emissions IEC 61000-3-3	Complies	

Table 8 – Electromagnetic Immunity

Immunity Test	IEC 60601 Test Level	Compliance Level	Electromagnetic Environment – Guidance
Electrostatic discharge (ESD) IEC 61000-4-2	± 8 kV contact ± 2, ± 4, ± 8 & ± 15 kV air	± 8 kV contact ± 2, ± 4, ± 8 & ± 15 kV air	Floors should be wood, concrete, or ceramic tile. If floors are covered with synthetic material, the relative humidity should be at least 30%.
Electrical fast transient/burst IEC 61000-4-4	± 2 kV for power supply lines ±1 kV for input/output lines 5 kHz & 100 kHz repetition frequency	± 2 kV for power supply lines 5 kHz & 100 kHz repetition frequency	Mains power quality should be that of a typical commercial or hospital environment.
Surge IEC 61000-4-5	± 1 kV differential mode ± 2 kV common mode	± 1 kV differential mode ± 2 kV common mode	Mains power quality should be that of a typical commercial or hospital environment.
Voltage dips, short interruptions and voltage variations on power supply input lines IEC 61000-4-11	0% U_T for 0.5 cycle 0% U_T for 1 cycle 70% U_T for 25 cycles 0% U_T for 5 sec	0% U_T for 0.5 cycle 0% U_T for 1 cycle 70% U_T for 25 cycles 0% U_T for 5 sec	Mains power quality should be that of a typical commercial or hospital environment. If the user of the pump requires continued operation during power mains interruptions, it is recommended that the pump be powered from an uninterruptible power supply.
Power frequency (50/60 Hz) magnetic field IEC 61000-4-8	30 A/m	3 A/m	Power frequency magnetic fields should be at levels characteristic of a typical location in a typical commercial or hospital environment.
Note: U_T is the AC mains voltage prior to application of the test level. The pump was tested at 100 and 240 VAC.			

Table 9 – Electromagnetic Immunity

Immunity Test	IEC 60601 Test Level	Compliance Level	Electromagnetic Environment – Guidance
Conducted RF IEC 61000-4-6	3 V 0.15MHz to 80 MHz 6 V in ISM bands between 0.15 MHz and 80 MHz 80% AM at 1 kHz	3 V 0.15 MHz to 80 MHz 6 V in ISM bands between 0.15 MHz and 80 MHz 80% AM at 1 kHz	Portable and mobile RF communications equipment should be used no closer to any part of the pump, including cables, than the recommended separation distance calculated from the equation applicable to the frequency of the transmitter.
Radiated RF IEC 61000-4-3	3 V/m 80 MHz to 2.7 GHz 80% AM at 1 kHz Test frequency 385 MHz to 5.750 GHz with pulse modulation	3 V/m 80 MHz to 2.7 GHz 80% AM at 1 kHz Test frequency 385 MHz to 5.750 GHz with pulse modulation	Recommended separation distance: $d = 1.17 \sqrt{P}$ 150 kHz to 80 MHz $d = 1.17 \sqrt{P}$ 80 MHz to 800 MHz $d = 2.23 \sqrt{P}$ 800 MHz to 2.7 GHz where P is the maximum output power rating of the transmitter in watts (W) according to the transmitter manufacturer and d is the recommended separation distance in meters (m). Field strengths from fixed RF transmitters, as determined by an electromagnetic site survey^a, should be less than the compliance level in each frequency range^b. Interference may occur in the vicinity of equipment marked with the following symbol: 

Note 1: At 80 MHz and 800 MHz, the higher frequency range applies.

Note 2: These guidelines may not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from structures, objects, and people.

^a Field strengths from fixed transmitters, such as base stations for radio (cellular/cordless) telephones and land mobile radios, amateur radio, AM and FM radio broadcast, and TV broadcast cannot be predicted theoretically with accuracy. To assess the electromagnetic environment due to fixed RF transmitters, an electromagnetic site survey should be considered. If the measured field strength in the location in which the pump is used exceeds the applicable RF compliance level above, the pump should be observed to verify normal operation. If abnormal performance is observed, additional measures may be necessary, such as reorienting or relocating the pump.

^b Over the frequency range 150 kHz to 80 MHz, field strengths should be less than 3 V/m.

The pump is intended for use in an electromagnetic environment in which radiated RF disturbances are controlled. The user of the pump can help prevent electromagnetic interference by maintaining a minimum distance between portable and mobile RF communications equipment (transmitters) and

the pump as recommended in Table 10, according to the maximum output power of the communications equipment.

Table 10 – Recommended Separation Distances between Portable and Mobile RF Communications Equipment and the Pump

Rated Maximum Output Power of Transmitter (W)	Separation Distance According to Frequency of Transmitter (m)		
	150 kHz to 80 MHz $d = 1.17 \sqrt{P}$	80 MHz to 800 MHz $d = 1.17 \sqrt{P}$	800 MHz to 2.7 GHz $d = 2.33 \sqrt{P}$
0.01	0.12	0.12	0.23
0.1	0.38	0.38	0.73
1	1.2	1.2	2.3
10	3.8	3.8	7.3
100	12	12	23

For transmitters rated at a maximum output power not listed above, the recommended separation distance d in meters (m) can be estimated using the equation applicable to the frequency of the transmitter, where P is the maximum output power rating of the transmitter in watts (W) according to the transmitter manufacturer.

Note 1: At 80 MHz and 800 MHz, the separation distance for the higher frequency range applies.

Note 2: These guidelines may not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from structures, objects, and people.

9 Symbols

Table 11 – Symbols

Symbol	Description
	nGEN™ Pump
	Manufacturer
	Date of Manufacture
MANUFACTURED FOR:	Manufactured for:
	Contents: 1
	Consult Instructions for Use
	Refer to accompanying instructions for use
	Caution
	Temperature Limit (storage and shipping conditions)
	Humidity Limitation (storage and shipping conditions)
	Atmospheric Pressure Limitation (storage and shipping conditions)
	Keep Dry
	Keep Away from Sunlight
	Do not use if package is damaged.
	Catalog Number
	Serial Number
	Device is certified by TUV Rheinland to IEC 60601-1 and IEC 60601-1-2, 3 rd edition
	Separate collection for electrical and electronic equipment, in compliance with Waste Electrical and Electronic Equipment Directive (WEEE)
IP23	Protected against solid objects over 12 mm (for example, fingers). Protected against direct sprays of water up to 60 degrees from vertical.
	Caution: Federal (USA) law restricts this device to sale by or on the order of a physician.
	Flow direction

Table 11 – Symbols

Symbol	Description
COMM 	Communication connector (to generator, for example)
24VDC 1.5A 	Direct current 24V/1.5A. The center of the connector is positive (+) and the barrel of the plug is negative (-).
USB 	USB Port A (This symbol is located under the service access door and is not visible to the user.)
USB 	USB Port B (This symbol is located under the service access door and is not visible to the user.)
	Stacking limit by number

10 Errors and Troubleshooting

Table 12 – Errors and Troubleshooting

Problem	Explanation / What To Do
There is an internal error.  Error Code	When an internal error occurs, the pump stops immediately and emits a repeating high priority alarm tone, and the image at the left appears on the screen. Note: If the internal error stops the software from functioning, the internal error indicator  (located at the top right corner of the front of the pump) will turn on but the screen may turn off or may not respond. 1. Press and hold the On/Off  button for approximately 6 seconds until the pump turns off. 2. Press the On/Off  button to restart the pump. 3. If the error occurs again, note the error code at the bottom of the screen and contact Customer Support.
The pump will not turn on.	1. Disconnect the AC adapter from the pump. 2. Reconnect the AC adapter to the pump. 3. Verify that the AC adapter is properly connected to the mains cable. 4. Verify that the mains cable is properly connected to the mains outlet. 5. Press the On/Off  button. 6. If the pump does not turn on, contact Customer support.

Table 13 – External Error Codes

Error Code	Reason	What To Do
E4	Incorrect pump speed was detected	1. Press the STOP  button to clear the error. 2. Verify that the irrigation tubing is properly seated. 3. Start low flow and verify that the error is resolved. 4. If the problem persists, contact Customer Support.
E5	Pump rotor is not moving	1. Press the STOP  button to clear the error. 2. Verify that the irrigation tubing is properly seated. 3. Start low flow and verify that the error is resolved. 4. If the problem persists, contact Customer Support.

Table 14 – Internal Error Codes

Error Code	Reason
F1	Software error
F2	Motor movement detected when pump was inactive
F3	Error detected when saving configuration file
F4	CPU watchdog error detected
F5	Incorrect motor direction detected
F6	Incorrect motor direction detected at low speed
F7	Bubble sensor heartbeat failure detected
P1	Internal isolated voltage error detected during POST ¹
P2	Program CRC ² error detected during POST
P3	Calibration file CRC error detected during POST
P4	Settings file CRC error detected during POST
P5	24 V power supply error detected during POST
P6	Internal 10 V supply error detected during POST
P7	Internal 2.048 V voltage reference error detected during POST
P8	Internal 5 V supply error detected during POST
P9	CPU watchdog timer error detected during POST
P10	Motor watchdog timer error detected during POST
P11	Motor error detected during POST
P12	Bubble sensor error detected during POST
P13	Touch screen error detected during POST
P14	Stuck switch detected during POST

¹POST = Power On Self-Test²CRC = Cyclic Redundancy Code

11 Warranty

The warranty for the pump warrants that the pump will conform to its product specifications for a period of one year from the date of installation. The warranty does not cover normal wear and tear, damage due to improper handling, accessories, connection cables, and disposable parts. Repairs or any changes may be performed only by Biosense Webster, a service engineer authorized by Biosense Webster, or a service center authorized by Biosense Webster. The warranty is voided if improper modifications or repairs are performed or if the device is not maintained according to the instructions in this user manual. The warranty is not extended or renewed by services performed under warranty.

12 Appendix

The nGEN™ Pump may have the following appearance. All features and functions of the pump shown in *5.3 Controls on the Front of the Pump* remain the same as indicated throughout the user manual, except the irrigation tubing will not make an audible snap as indicated in *6.5, Installing the Irrigation Tubing Set*.





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Revised: 2025-06



EML139702IFUD

Appendix 42_ Sterile Interface Cable IFU (M-5276-1085)

Sterile Interface Cables

INSTRUCTIONS FOR USE

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Symbol Definitions

Following definitions are for reference only. Please refer to the product label for applicable usage.



Sterilized Using Ethylene Oxide



Caution



Consult Instructions for Use



Do not use if package is damaged.



Do not use if package is opened.



Keep Away from Sunlight



Keep Dry



Use-By Date



Batch Code



Catalog Number



Contents: 1



Manufacturer



Date of Manufacture



Pin Connector



Waste Electrical and Electronic Equipment Directive (WEEE)—Dispose of in a manner consistent with required EU Directives in your local jurisdiction.



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



Temperature Limit

Sterile Interface Cables

Caution: Federal (USA) law restricts this device to sale by or on the order of a licensed healthcare practitioner.

INDICATIONS FOR USE

These cables provide a means to connect a Biosense Webster electrophysiology catheter, external reference patch, sheath, or CARTO™ 3 System accessory to the appropriate equipment. The cables may be reused subject to the cleaning and sterilization restrictions in this document.

Table 1 – Cables

Note: Some of these cables might not be available in your country. Consult your Biosense Webster representative regarding the availability of a particular cable in your country.

Cable Name	Purpose	Catalog Numbers	Manufacturing Numbers
Interface Cable	Connects a REFSTAR™ with QWIKPATCH™ External Reference Patch to a CARTO™ XP System or a NOGA™ XP System.	C5MHREFMHS	C5MHREFMHS
	Connects a diagnostic catheter to a CARTO™ XP System.	C5MHDTCMHS	D-1195-07-S
CARTO™ 3 System Interface Cable	Connects a diagnostic catheter to a CARTO™ 3 System.	CB3410CT CG2025CT CY1210CT D128624 D128709	D-1286-15-S D-1297-03-S D-1287-01-S D-1286-24-S D-1287-09-S
	Connects a therapeutic catheter to a CARTO™ 3 System.	CR3425CT CR3434CT	D-1286-04-S D-1286-03-S
	Connects a diagnostic catheter to a recording system.	D128622	D-1286-22-S
	Connects a diagnostic catheter or an electrophysiology sheath to a CARTO™ 3 System.	CB3412CT	D-1286-16-S
	Connects a diagnostic catheter or an electrophysiology sheath to a CARTO™ 3 System.	CY1212CT	D-1287-05-S
	Connects a diagnostic catheter or a CARTO™ 3 System accessory to a CARTO™ 3 System.	CB3434CT	D-1286-01-S
CARTO™ 3 System eco Interface Cable	Connects a diagnostic “eco” catheter to a CARTO™ 3 System.	D134401	D-1344-01-S

CONTRAINDICATIONS

There are no known contraindications for these cables.

PATIENT TARGET GROUP

These cables are targeted at patients who have been diagnosed with cardiac arrhythmias and are undergoing an electrophysiology procedure.

INTENDED USERS

The intended users of these cables are appropriately trained personnel in a fully equipped electrophysiology laboratory.

CLINICAL BENEFIT

These cables provide a means to connect a Biosense Webster electrophysiology catheter, external reference patch, sheath, or CARTO™ 3 System accessory to the appropriate equipment.

DIRECTIONS FOR USE

1. Do not use the cable after the use-by date on the product label.
2. Before using or reusing the cable, visually inspect it for damage such as crushed or elongated sections, cuts, kinks, or nicks. If the cable is damaged, do not use the cable and dispose of it per the "DISPOSAL" section below.
3. Connect each cable to the proper equipment by referring to the connector designations at each end of the cable.
4. Follow the instructions in the "CLEANING AND STERILIZATION," "STORAGE," and "DISPOSAL" sections below.

CLEANING AND STERILIZATION

These cables are provided sterile. They may be resterilized as described below. These cables meet the requirements of the ANSI/AAMI EC53-2013.

Table 2 – Cleaning and Sterilization

Warnings and Precautions	1. Ensure proper cable connection by referring to the connector designations at each end of the cable. 2. Do not use the cable after the use-by date on the product label. 3. Do not immerse the cable connectors in liquid. Do not wipe the cable connectors with liquid. The presence of liquid inside the connectors may result in adverse effects, including improper functioning (such as noisy signals or signal degradation) or arcing of electricity between the connector pins, which can lead to patient injury. 4. Do not expose the cable to organic solvents because they may damage the cable. 5. Patient or operator injury may result from improper handling, improper connection, or improper use of the cable. 6. To prevent damage, store the cable in a clean and secure area. 7. If a break occurs in the cable wire or if the cable becomes otherwise electrically discontinuous, arcing may occur in the patient-return or active circuit and may burn the patient or create a fire. 8. Failure to properly clean the cable could lead to inadequate resterilization. 9. Do not use radiation sterilization because it will damage the cable. 10. When sterilizing the cables, do not exceed 140°C because temperatures higher than 140°C may damage the cable. 11. Automated cleaning of the cable is not recommended because fluid may enter the connectors and leave moisture or residue in or on the connectors. Resulting adverse effects may include improper functioning (such as noisy signals or signal degradation) or arcing of electricity between the connector pins, which can lead to patient injury.
Limitations on Cleaning and Sterilization	Clean and sterilize the cable after each use. The maximum number of sterilization cycles is specified in Table 3. Exceeding the specified number of sterilization cycles may impair the proper functioning of the cable.
Initial Treatment at Point of Use	There are no requirements for initial treatment at point of use.

Containment and Transportation	Place the cable in a clean biohazard bag after use for subsequent cleaning, disinfection, and sterilization. Clean, disinfect, and sterilize the cable as soon as it is reasonably practical after use.						
Preparation before Cleaning	Visually inspect the cable for any damage such as crushed or elongated sections, cuts, kinks, or nicks. If damage is observed, do not use the cable and dispose of it per the "Disposal" section below.						
Cleaning: Automated	Automated cleaning of the cable is not recommended because fluid may enter the connectors and leave moisture or residue in or on the connectors. Resulting adverse effects may include improper functioning (such as noisy signals or signal degradation) or arcing of electricity between the connector pins, which can lead to patient injury.						
Cleaning: Manual	1. Wear sterile gloves while handling the cable. 2. Using a wipe*, use a twisting motion to wipe the entire surface of the cable, but not the cable connectors, to remove soil. Pay particular attention to complex cable features (such as non-smooth areas, joints, and crevices). 3. Using another wipe*, use a twisting motion to thoroughly wipe the entire surface of the cable to remove soil. 4. Visually inspect the cable to ensure there is no visible soil. Additional wipes may be used to remove any visible soil. 5. Leave the cable in ambient conditions until it is visibly dry. 6. When the cable is dry, visually inspect the entire surface of the cable in adequate lighting to ensure complete removal of visible soil. *Recommended Wipes: A. CaviWipes™ or any other wipes with the chemical composition indicated in the table below may be used. <table border="1"> <thead> <tr> <th>Chemical Composition</th><th>% of Chemical</th></tr> </thead> <tbody> <tr> <td>Isopropanol</td><td>17.2%</td></tr> <tr> <td>Diisobutylphenoxyethoxyethyl dimethylbenzyl ammonium chloride</td><td>0.28%</td></tr> </tbody> </table> B. Clorox Healthcare® Bleach Germicidal Wipes or 70% isopropyl alcohol (IPA) wipes.	Chemical Composition	% of Chemical	Isopropanol	17.2%	Diisobutylphenoxyethoxyethyl dimethylbenzyl ammonium chloride	0.28%
Chemical Composition	% of Chemical						
Isopropanol	17.2%						
Diisobutylphenoxyethoxyethyl dimethylbenzyl ammonium chloride	0.28%						

Disinfection	Acceptable methods: A. CaviWipes™: 1. Wear sterile gloves while handling the cable. 2. Ensure manual cleaning (see the “Cleaning: Manual” instructions in this table) is performed before disinfection. 3. Using a wipe*, use a twisting motion to thoroughly wipe the entire surface of the cable. Pay particular attention to complex cable features (such as non-smooth areas, joints, and crevices). 4. Allow the surface of the cable to remain visibly wet for 3 minutes at room temperature (approximately 68°F/20°C). 5. Additional wipes may be used to ensure that the cable remains visibly wet for 3 minutes. 6. Leave the cable in ambient conditions until it is visibly dry. 7. Visually inspect the entire surface of the cable in adequate lighting to ensure the cable is visibly clean. *Recommended Wipes: CaviWipes™ or any other wipes with the chemical composition indicated in the table below may be used. <table> <tr> <th>Chemical Composition</th><th>% of Chemical</th></tr> <tr> <td>Isopropanol</td><td>17.2%</td></tr> <tr> <td>Diisobutylphenoxyethoxyethylmethylbenzyl ammonium chloride</td><td>0.28%</td></tr> </table> B. Clorox Healthcare® Bleach Germicidal Wipes or 70% isopropyl alcohol (IPA) wipes: 1. Wear sterile gloves while handling the cable. 2. Ensure manual cleaning (see the “Cleaning: Manual” instructions in this table) is performed before disinfection. 3. Using two (2) wipes**, use a twisting motion to thoroughly wipe the entire surface of the cable. Pay particular attention to complex cable features (such as non-smooth areas, joints, and crevices). 4. Using a wipe**, use a twisting motion to wipe the cable and allow the surface to remain visibly wet for the corresponding contact time***. 5. Additional wipes may be used to maintain the contact time. 6. Leave the cable in ambient conditions until it is visibly dry. 7. Visually inspect the entire surface of the cable in adequate lighting to ensure the cable is visibly clean. **Recommended Wipes: <table> <tr> <th>Wipes</th><th>***Contact Time</th></tr> <tr> <td>Clorox Healthcare® Bleach Germicidal Wipes</td><td>3 min</td></tr> <tr> <td>70% isopropyl alcohol (IPA) wipes</td><td>6 min</td></tr> </table>	Chemical Composition	% of Chemical	Isopropanol	17.2%	Diisobutylphenoxyethoxyethylmethylbenzyl ammonium chloride	0.28%	Wipes	***Contact Time	Clorox Healthcare® Bleach Germicidal Wipes	3 min	70% isopropyl alcohol (IPA) wipes	6 min
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Isopropanol	17.2%												
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Wipes	***Contact Time												
Clorox Healthcare® Bleach Germicidal Wipes	3 min												
70% isopropyl alcohol (IPA) wipes	6 min												
Drying	Drying is performed as part of the disinfection process (see the “Disinfection” instructions in this table).												
Maintenance, Inspection, and Testing	Before packaging, visually inspect the cable. If visible soil is present, repeat the “Cleaning: Manual” and “Disinfection” instructions in this table. If there is evidence of damage, do not use the cable and dispose of it per the “Disposal” section below.												

Packaging	If the cable is stored after cleaning and disinfection, place it in a breathable pouch that is approved by the FDA and/or by local authorities. Coil the cable into a loop when placing it into the pouch. Do not fold the cable because doing so may break the cable. Use a pouch large enough to prevent stress to the pouch seams and to prevent excessive bending of the cable. A pouch size of 19 cm x 33 cm (7.5" x 13") or larger is recommended. For storage conditions, refer to the "Storage" section below.
Resterilization	See Table 3 and Table 4 for resterilization methods, parameters, and the maximum number of sterilization cycles. Resterilize the cable after each use.

The instructions provided above have been validated by the medical device manufacturer as being capable of preparing a medical device for reuse. It remains the responsibility of the processor to ensure that the processing as performed (using equipment, materials, and personnel in the processing facility) achieves the desired result. This requires validation and routine monitoring of the process. Likewise, any deviation by the processor from the instructions provided should be properly evaluated for effectiveness and potential adverse consequences.

Table 3 – Validated Resterilization Methods for Each Cable

Maximum Number of EtO Resterilization Cycles	Maximum Number of Steam Resterilization Cycles	Cable Name	Cable Catalog Numbers
10X	---	Interface Cable	C5MHREFMHS C5MHDTCMHS
20X	20X	CARTO™ 3 System Interface Cable	CB3434CT CB3410CT CB3412CT D128624 CY1210CT CY1212CT CG2025CT CR3434CT CR3425CT D128622 D128709
		CARTO™ 3 System eco Interface Cable	D134401

Table 4 – Resterilization Parameters for Cables

	Exposure Temperature	Exposure Time	Minimum Drying Times	Gas Concentration	Humidity (RH)	Accommodation/Aeration Time at 55°C
Gravity Steam Resterilization	121°C (250°F)	30 min	15 - 30 min	---	---	---
	132°C (270°F)	15 min	15 - 30 min	---	---	---
	135°C (275°F)	10 min	30 min	---	---	---
Dynamic Air Removal (Pre-Vac) Resterilization	134°C (274°F)	3 min	16 min	---	---	---
	135°C (275°F)	3 min	16 min	---	---	---
100% EtO Gas Resterilization	55°C (131°F)	1 hr	---	725 mg/L	30% - 80%	12 hr

STORAGE

Refer to the product label for recommended storage conditions.

DISPOSAL

Recycle components or dispose of the product and its residual elements or waste items in accordance with local laws and regulations.

REPORTING INCIDENTS

Per regulation 2017/745/EU on medical devices, if this device is used in the European Union (or in a country with an identical regime) and a serious incident occurs during the use of this device or as a result of use of this device, report the incident to the manufacturer and/or its authorized representative and to your national authority.

ADVERSE REACTIONS

A number of adverse reactions have been documented for electrophysiology procedures including:

heart block, pulmonary vein stenosis, esophageal fistula and/or injury, stroke (cerebrovascular accident), other arrhythmias (outside diagnosis), life threatening arrhythmias, myocardial infarction, cardiac perforation, pericardial effusion, cardiac tamponade, thrombosis, embolism, pulmonary embolism, air embolism, valvular damage, phrenic nerve injury, vagal nerve injury, pericarditis, coronary artery stenosis, vessel perforation (peripheral and/or central), soft tissue injury, persistent atrial communication, device related infection, embolization of components, device entrapment, surgical intervention (additional), skin burns, and localized skin reaction.

The following complications associated with cardiac catheterization have also been reported in the literature:

major bleed, hematoma, reaction to medications, allergic reaction, vascular access complication, damage to vasculature, implanted device interactions, renal artery stenosis, pneumothorax, ST segment changes, fluid overload, urinary catheter complications, hypotension, sepsis, wound infection, respiratory failure, heart injury, renal injury, heart failure, cardiac arrest and death.

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ELECTRONIC INSTRUCTIONS FOR USE

This document is available at www.e-ifu.com.

NOTES



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