

NAVISTAR® THERMOCOOL® Diagnostic/Ablation Catheter
INSTRUCTIONS FOR USE

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Refer to accompanying Instructions for Use.

STERILE	EO
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Sterilized with ethylene oxide gas.

REF

Catalog No.



Use by.

LOT

Lot No.



For one use only.

NAVISTAR® THERMOCOOL® Diagnostic/Ablation Catheter

INSTRUCTIONS FOR USE

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

SINGLE USE ONLY. DO NOT RESTERILIZE.

1. DEVICE DESCRIPTION

The Biosense Webster NAVISTAR® THERMOCOOL® Diagnostic/Ablation Deflectable Tip Catheter is a luminal catheter with a deflectable tip designed to facilitate electrophysiological mapping of the heart and to transmit radiofrequency (RF) current to the catheter tip electrode for ablation purposes. The catheter shaft measures 7.5 F with 8.0 F ring electrodes. For ablation, the catheter is used in conjunction with a RF generator and a dispersive pad (indifferent electrode).

The catheter has a high-torque shaft with a deflectable tip section containing an array of platinum electrodes. All of the electrodes may be used for recording and stimulation purposes. The tip electrode serves to deliver RF current from the RF generator to the desired ablation site. The tip electrode and ring electrodes are made from platinum-iridium.

The catheter incorporates either a thermocouple or thermistor temperature sensor that is embedded in the 3.5mm tip electrode. Tip deflection is controlled at the proximal end by a handpiece in which a piston slides; a thumbknob on the piston controls piston travel. When the thumbknob is pushed forward, the tip is deflected (curved). When the thumbknob is pulled back, the tip straightens. The shape of the curve depends on the deflectable tip length (2" – 4.3" or 51 mm – 109 mm). Five curve types designated "B", "C", "D", "E", and "J" are available. The "J" curve type is only available with the thermocouple and not with the thermistor temperature sensor. 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 0.027" (0.69 mm) diameter lumen of the catheter and through the tip electrode, to irrigate and cool the ablation site as well as the electrode tip. The COOLFLOW® Irrigation pump is approved for use to control the saline irrigation. This catheter features a magnetic location sensor embedded in the tip electrode that transmits location information to the CARTO® EP Navigation System.

The catheter interfaces with standard recording equipment and the Stockert 70 RF Generator via accessory extension cables with the appropriate connectors.

For further description of the operation of the CARTO® EP Navigation System and Stockert 70 RF Generator, refer to the operating instructions for these instruments.

2. INDICATIONS AND USAGE

The Biosense Webster NAVISTAR® THERMOCOOL® Diagnostic/Ablation Deflectable Tip Catheters and related accessory devices are indicated for catheter-based cardiac electrophysiological mapping (stimulating and recording), and when used with the Stockert 70 generator, for the treatment of

- a) Type I atrial flutter in patients age 18 or older.
- b) Recurrent drug/device refractory sustained monomorphic ventricular tachycardia (VT) due to prior myocardial infarction (MI) in adults.
- c) Drug refractory recurrent symptomatic paroxysmal atrial fibrillation, when used with compatible three-dimensional electroanatomic mapping systems.

The NAVISTAR® THERMOCOOL® Catheter provides location information when used with the CARTO® EP Navigation System.

3. CONTRAINDICATIONS

Do not use this device:

- If the patient has had a ventriculotomy or atriotomy within the preceding eight weeks because the recent surgery may increase the risk of perforation
- In patients with prosthetic valves as the catheter may damage the prosthesis
- In the coronary vasculature due to risk of damage to the coronary arteries
- In patients with an active systemic infection because this may increase the risk of cardiac infection
- In the patient with a myxoma or an intracardiac thrombus as the catheter could precipitate an embolus
- Via the transseptal approach in a patient with an interatrial baffle or patch because the opening could persist and produce an iatrogenic atrial shunt
- Via the retrograde trans-aortic approach in patients who have had aortic valve replacement

4. WARNINGS AND PRECAUTIONS

1. Do not use the temperature sensor to monitor tissue temperature. The temperature sensor located within the tip electrode 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 RF 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 current, 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 current ensures that the irrigation flow rate is being maintained.
2. It is important to carefully follow the power titration procedure as specified in the instructions for use. Too rapid an increase in power during ablation may lead to perforation caused by steam pop.
3. This catheter may damage the prosthetic tricuspid valve of a patient if the catheter is accidentally advanced through the valve.
4. The patient who has had a prior atrial flutter ablation procedure may be at greater risk for perforation and/or pericardial effusion with the use of this catheter system.

5. 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 ACC/AHA/ESC 2006 Guidelines for the Management of Patients in Atrial Fibrillation (Fuster V, Ryden LE, Cannom DS et al. ACC/AHA/ESC 2006 Guidelines for the management of the patients with atrial fibrillation Circulation 2006: 114:257-354).
6. The safety and effectiveness of radiofrequency ablation for the treatment of atrial fibrillation in patients with significant left ventricular dysfunction, advanced heart failure, substantial left atrial enlargement, and structural heart disease have not been established.
7. 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 procedure, always identify the patient's risk of volume overload.
8. The device has not been shown to be safe at electrode temperatures above 50° C; verify that the CATHETER SELECTION KNOB on the Stockert 70 RF Generator is on the "ThermoCool" option to ensure that the maximum temperature is set at 50° C. If the Stockert 70 generator does not have a "Thermocool" option, contact Biosense Webster Technical Support immediately.
9. Implantable pacemakers and implantable cardioverter/defibrillators (ICDs) may be adversely affected by RF current. It is important to have temporary external sources of pacing and defibrillation available during ablation, and to temporarily reprogram the pacing system to minimum output or OFF mode to minimize the risk of inappropriate pacing. Exercise extreme caution during ablation when in close proximity to atrial or ventricular permanent leads; program the ICD to the OFF mode during the ablation procedure; and, perform complete implantable device analysis on all patients after ablation.
10. Patients undergoing septal accessory pathway ablation are at risk for complete AV block which requires the implantation of a permanent pacemaker. Patients who experience inadvertent complete AV block as a result of RF ablation may also require permanent pacing.
11. During the trans-aortic approach, adequate fluoroscopic visualization is necessary to avoid placement of the catheter in the coronary vasculature. Intracoronary placement of the ablation catheter, RF energy application, or both have been associated with myocardial infarction.
12. If phrenic nerve location is a concern, precautionary measures are recommended to evaluate the proximity of the nerve to the ablation electrode, such as pacing maneuvers.
13. To minimize risk of atrio-esophageal fistula, precautionary measures should be taken when ablating on posterior wall of the left atrium in proximity to the esophagus
14. Minimize X-ray exposure during the procedure. Catheter ablation procedures 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 the fluoroscopic imaging. Catheter ablation should only be performed after adequate attention has been given to the potential radiation exposure associated with the procedure, and steps have been taken to minimize this exposure. Careful consideration must therefore be given to the use of the device in pregnant women.
15. Do not expose the catheter to organic solvents such as alcohol.
16. Do not autoclave the catheter.
17. Do not immerse proximal handle or cable connector in fluids; electrical performance could be affected.
18. Do not scrub or twist the distal tip electrode during cleaning.
19. Inspect irrigation saline for air bubbles prior to its use in the procedure. Air bubbles in the irrigation saline may cause emboli.
20. Purge catheter and irrigation tubing with heparinized normal saline.
21. Electrophysiology catheters and systems are intended for use only in X-ray shielded rooms due to electromagnetic compatibility requirements and other hospital safety guidelines.
22. Do not attempt to operate the Biosense Webster NAVISTAR® THERMOCOOL® Diagnostic/Ablation Deflectable Tip Catheter or the Stockert 70 RF generator prior to completely reading and understanding the applicable instructions for use.
23. Cardiac ablation procedures should be performed by appropriately trained personnel in a fully-equipped electrophysiology laboratory. Appropriate clinical instruction in use of the THERMOCOOL® Irrigated Catheters should also be completed.
24. The long-term risks of protracted fluoroscopy and creation of RF induced lesions have not been established. Furthermore the risk/benefit in asymptomatic patients has not been studied.
25. To avoid thromboemboli, intravenous heparin should be used when entering the heart during ablation, and many physicians prescribe aspirin, less often warfarin, for about 3 months afterward. No consensus yet exists about the need for short-term anticoagulation after ablation.
26. When using the Biosense Webster NAVISTAR® THERMOCOOL® Diagnostic/Ablation Deflectable Tip Catheter with conventional systems (using fluoroscopy to determine catheter tip location), or with the CARTO® EP Navigation System, careful catheter manipulation must be performed in order to avoid cardiac damage, perforation, or tamponade. Catheter advancement should be done under fluoroscopic 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.
27. Always pull the thumbknob back to straighten the catheter tip before insertion or withdrawal of the catheter.
28. Always maintain a constant heparinized normal saline infusion to prevent coagulation within the lumen of the catheter.
29. When RF current 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, as twisting may damage the tip electrode bond and loosen the tip electrode. Make sure the irrigation holes are not plugged prior to re-insertion.
30. 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 electrode(s) or failure of an electrical lead. Do not increase power before checking for obvious defects or misapplication of the indifferent electrode or other electrical leads.
31. Read and follow the indifferent electrode manufacturer's instructions for use; the use of indifferent electrodes that meet or exceed ANSI/AAMI requirements (HF18) is recommended, eg, the 3M Model 1149F or Valley Lab Model 7505.
32. The Biosense Webster NAVISTAR® THERMOCOOL® Diagnostic/Ablation Deflectable Tip Catheter is indicated for use only with the Stockert 70 RF Generator, CARTO EP Navigation System, Biosense Webster cables, and other appropriate interface cables and connectors. Use of the COOLFLOW® Pump is recommended to assure proper irrigation flow rate. In addition, the Stockert-COOLFLOW® interface automates the switching of the COOLFLOW® Pump between its high and low flow rate settings to assure accurate pump control.
33. The Biosense Webster NAVISTAR® THERMOCOOL® Diagnostic/Ablation Deflectable Tip 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.
34. The sterile packaging and catheter should be inspected prior to use. Do not use if the packaging or catheter appears damaged.

35. The catheters are sterilized with ethylene oxide gas and should be used by the "Use By" date on the device package. Do not use the device if past the "Use By" date.
36. The Biosense Webster NAVISTAR® THERMOCOOL® Diagnostic/Ablation Deflectable Tip Catheter is intended for single patient use only.
37. Do not resterilize and reuse.
38. Do not use near MRI equipment since movement or heating of the catheter may occur and the image on the display may become distorted.
39. Use both fluoroscopy and electrogram data to monitor catheter advancement and reduce risk of tissue injury.
40. The Biosense Webster NAVISTAR® THERMOCOOL® Diagnostic/Ablation Deflectable Tip Catheter used in conjunction with the Stockert 70 Generator is capable of delivering significant electrical power. Patient or operator injury can result from improper handling of the catheter and indifferent electrode, particularly when operating the device. During energy delivery, the patient should not be allowed to come in contact with grounded metal surfaces. If during ablation, temperature does not rise, discontinue delivery of energy and check set-up.
41. 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.
42. Electromagnetic interference (EMI) produced by the Biosense Webster NAVISTAR® THERMOCOOL® Diagnostic/Ablation Deflectable Tip Catheter, when used in conjunction with the Stockert 70 RF during normal operation, may adversely affect the performance of other equipment.
43. 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 electrode. Protective impedance may reduce the risk of burns and permit continuous monitoring of the electrocardiogram during energy delivery.
44. The temperature sensor measures electrode tip temperature, not tissue temperature. The temperature displayed on the RF generator is for the cooled electrode only and does not represent tissue temperature. If the RF generator does not display temperature, verify that the appropriate cable is plugged into the RF generator. If temperature is still not displayed, there may be a malfunction in the temperature sensing system that must be corrected prior to applying RF power.
45. The temperature measurement accuracy of the Biosense Webster NAVISTAR® THERMOCOOL® Diagnostic/Ablation Deflectable Tip Catheter, as with any temperature measurement electrophysiology catheters, is largely determined by the temperature accuracy specification of the Stockert RF generator used. Please consult the user manual of the RF generator to be used for the temperature accuracy specification. If no temperature accuracy specification is provided in the Stockert RF generator user manual, assume an accuracy of +/- 5° C for this catheter.
46. Before use, check irrigation ports are patent by infusion of heparinized normal saline through the catheter and tubing.
47. Regularly inspect and test reuseable cables and accessories.

5. ADVERSE EVENTS

Clinical trial 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 Postmarket Study, 4 cardiovascular specific adverse events were reported in 4 of the 291 enrolled subjects. See Section 6, "Summary of Clinical Studies Conducted for Atrial Flutter Indication", below for a complete description of the adverse events encountered during the studies.

Clinical trial for ventricular tachycardia indication

Of the 233 subjects in the Safety Analysis Cohort, 53 major adverse events (AEs) were reported in 42 subjects. See Section 7, "Summary of Clinical Studies Conducted for Ventricular Tachycardia Indication", below for a complete description of the AEs encountered during the study.

Clinical trial 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 Section 8, "Summary of Clinical Studies Conducted for Atrial Fibrillation Indication", below for a complete description of the AEs encountered during the study.

6. 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 CARTO® EP/XP Navigation System, Stockert 70 RF Generator 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 1 - 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*	19
Subjects ablated only with NAVISTAR® THERMOCOOL® Catheter	171
Subjects in whom BDB was not assessable	4

The table above documents the accountability and disposition of enrolled subjects.

- * 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 2 – 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

Tables 3 and 4 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.

Table 3 - 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 (Watts)/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 (Ohms)/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 4 – 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).

Table 5 describes the acute ablation outcomes.

Table 5 - Acute Ablation Outcomes (n=186)

	# Success / # Subjects Ablated	Percentage (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 6 summarizes the composite results.

Table 6 – Composite Assessment of Atrial Flutter Success

	# Success / # Subjects Ablated	Percentage (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 the table below.

**Table 7 - Freedom from Type I atrial flutter at 6 months
(Results based on 147 subjects)**

Description	N	Percent
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.

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 8 summarizes the major adverse events.

Table 8 - Major Adverse Events observed within 7 days post-ablation

Total Number Subjects with a Major AE n=30
Cardiovascular total = 15 subjects Arrhythmia complications = 5 subjects complete atrioventricular 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 acute respiratory distress syndrome = 2 subjects aspiration pneumonia = 2 subjects pneumonia = 3 subjects asthma = 1 subject	total = 8 subjects
Anesthesia related sedation induced apnea (intubation not required) sedation induced CO ₂ retention with lethargy (intubation not required)	total = 2 subjects
Vascular arteriovenous fistula/femoral artery-saphenous vein pseudoaneurysm/right femoral artery	total = 2 subjects
Urologic urinary tract infection urinary retention	total = 2 subjects
Cholecystitis	1 subject
Neurologic parkinson's disease transient extremity numbness/possible tia	2 subjects

* 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 patient population from which the OPCs were derived. See section C.1 for a list of concomitant ablation procedures.

C.6. - Statistical Analysis

Table 9 summarizes the safety and effectiveness of the device when compared to the control group OPC established for safety and acute success.

Table 9 - 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.

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).

41

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 10 below documents the accountability and disposition of enrolled subjects.

Table 10. Subject Disposition (N=291)

Category	N	Percentage
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%

¹Bidirectional 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 subeustachian (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 were a total of 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

The table below summarizes the demographic information of all study subjects enrolled in the study

Table 11 – 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. - Intra-procedural Data

Tables 12 and 13 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 12 describes the efficacy success.

Table 12 - Efficacy Success (n=253)

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

C.3. - Adverse Events

A cardiac-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%. Table 13 summarizes the CSAEs observed.

Table 13 –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 14 summarizes the safety and effectiveness of the device compared to the OPC established for safety and efficacy.

Table 14 – Endpoints comparison between NAVISTAR® THERMOCOOL® 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.

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7. SUMMARY OF CLINICAL STUDIES CONDUCTED FOR VENTRICULAR TACHYCARDIA INDICATION

A. Objective

The objective of the study was to evaluate the safety and effectiveness of the NAVISTAR THERMOCOOL catheter used in conjunction with CARTO EP/XP Navigation System and the STOCKERT 70 RF Generator and related accessories for ablation of recurrent drug/device refractory sustained monomorphic VT due to prior MI in adults.

B. Study Design

The study was a single-arm, prospective, non-randomized, unblinded, multi-center study conducted at 18 investigational sites located in the United States.

B.1 - Study Endpoints

The endpoints for the study were as follows:

Acute procedural success for VT was defined as the termination and non-inducibility of all clinically relevant VTs upon hospital discharge. A clinically relevant VT was defined as any spontaneous VT or any induced VT, with cycle lengths equal to (\pm 20 msec) or greater than that of the spontaneous clinical VT.

Acute procedural success in subjects with incessant VT was defined as termination of the incessant VT and no recurrence prior to hospital discharge. Incessant VT was defined as those VTs which continue despite attempted electrical or pharmacological cardioversion such that the VT is present more than 50% of the time for a period of > 12 hours. Subjects with incessant VT were considered acute failures if incessant VT recurred prior to hospital discharge.

Chronic success for VT was defined at 6 months following the RF ablation procedure as no recurrence of clinically relevant monomorphic VT(s) that were targeted at ablation. In order to qualify for chronic success, a patient must have already met the acute procedural success endpoint. Chronic success was the primary effectiveness endpoint for the study. VT recurrences were to be documented by ICD telemetry for subjects who had an implanted defibrillator, or by transtelephonic monitoring (TTM), ECG recordings from paramedics or emergency room visits in the event of recurrence of sustained VT in subjects who did not have an ICD implant. Chronic success for incessant VTs was also defined as no recurrence of incessant VTs during the 6-month follow-up period.

Note: Acute procedural success and chronic success were determined from the last study ablation procedure prior to hospital discharge. Subjects who underwent an ablation procedure during the 6-month follow-up period (after hospital discharge) were deemed chronic failures.

Procedural safety was determined by the number of subjects who experienced acute or sub-chronic major complications associated with the use of the investigational device within seven days of the ablation procedure.

B.2 - Protocol Endpoints

The protocol endpoints were prospectively established. The protocol endpoint for the safety endpoint was based on selected medical literature. The success criteria are defined below:

- **Safety:** major adverse events (AEs) within 7 days of the procedure occur at a rate of **22%** or less with a **30%** one-sided 95% upper confidence bound;
- **Acute procedural success:** **75%** with a **65%** one-sided 95% lower confidence bound.
- **Chronic success:** **50%** with a **40%** one-sided 95% lower confidence bound.

The trial design and endpoints of this study were based on historical controls. Limitations of the historical controls used for this study included the following:

- Available literature included incomplete recording of safety results.
- Literature patient populations were not necessarily comparable to current study population in disease severity, treatment of ischemic heart disease, duration of follow up, type of ablation treatment, ablation treatment not standardized, percent of patients with implanted defibrillators, and percent of patients treated with amiodarone.
- Available literature included some non-randomized descriptions of patient care.

B.3 - Subject Accountability

Table 15 documents the accountability and disposition of enrolled subjects.

Table 15. Subject Enrollment and Accountability

Subject Disposition	
Total Number of Subjects Enrolled	240
Subjects Excluded (prior to ablation)	7
Safety Analysis Cohort	233
Discontinued Subjects (prior to ablation)	7
Effectiveness Analysis Cohort	226
Subjects who underwent ablation with only NAVISTAR THERMOCOOL catheter	205
Subjects who underwent ablation with NAVISTAR THERMOCOOL catheter and non-investigational catheter*	21

* This category involved enrolled subjects that were treated with the investigational catheter at the beginning of the procedure and the investigator then switched to a non-protocol catheter to complete the treatment of VT. Furthermore, subjects who could not be treated due to investigational device failure are included in this category. These subjects were considered acute procedural and chronic failures.

The following definitions were used to classify subjects:

Enrolled Subjects (n = 240) are subjects who signed informed consent.

Excluded Subjects (n = 7) are subjects that were enrolled but never underwent insertion of the investigational catheter.

Discontinued Subjects (n = 7) are subjects that had the investigational catheter inserted but did not undergo an ablation procedure with the investigational device, (ie, no RF energy was applied).

Effectiveness Analysis Cohort (n = 226) included the 226 subjects that underwent an ablation procedure with the investigational device.

Safety Analysis Cohort (n = 233) included the 226 subjects in the Effectiveness Analysis Cohort plus the 7 discontinued subjects.

The Safety Analysis Cohort (n = 233) and Effectiveness Analysis Cohort (n = 226) include 205 subjects who underwent ablation with the investigational device and 21 subjects who underwent ablation with the investigational device and a non-investigational device due to investigator preference, procedural complications, suspected catheter malfunction, perceived lack of effectiveness, subject anatomy, fluid management, or non-investigational device malfunction (and were deemed an effectiveness failure under the protocol). The results of this study were evaluated as point estimates and qualitatively compared to existing literature and the current state of clinical practice for this patient group and indication.

B.4 – Subject Demographics

Table 16 summarizes the demographic information of all enrolled subjects in the study.

Table 16. Summary Demographics (Enrolled Subjects with Data, n = 240)

Description	Enrolled	
	n	%
Gender		
Female	25	10.4
Male	215	89.6
Total	240	100.0
Age (years)		
Mean	65.1	
Standard Deviation	10.8	
Minimum	31	
Maximum	87	

Of the 240 enrolled subjects, 232 (96.7%) had a preexisting history of myocardial infarction (MI). Additionally, 225 (93.8%) subjects were confirmed to have an ICD implanted prior to study enrollment. Spontaneous monomorphic VT characteristics were reported in 199 of the 240 subjects with data enrolled in the study. Three hundred and ten (310) spontaneous VTs were reported in 199 subjects. The predominant VT QRS morphology of those reported was right bundle branch block superior axis (24.2%, 75/310), followed by left bundle branch block superior axis (9.4%, 29/310) and right bundle branch block inferior axis (8.1%, 25/310). The average cycle length of the VTs was 397.4 ms, with a median at 400 ms.

A total of 889 VTs were induced in 224 subjects, an average of approximately 3.97 VTs per subject. (VTs were not induced in two subjects who underwent ablation with the investigational device). The majority of the subjects (171/226; 75.7%) had induction of at least one unmappable VT during the procedure. Thirty point five percent of subjects (30.5%; 69/226) exhibited only unmappable induced VTs.

C. Results

C.1 - Intraprocedural Data

Tables 17 and 18 present the procedural data.

Table 17. Summary of RF Applications, Saline Infused, Power, Temperature and Impedance Data (Effectiveness Analysis Cohort, n = 226¹)

Description	Mean ± Standard Deviation
Number of RF Applications (n = 256 procedures)	26.4 ± 16.5
Total Saline Infused (ml) by NAVISTAR THERMOCOOL Catheter (n = 233 procedures)	1483.8 ± 838.4
Maximum Power (W)/application (n = 6509 RF applications)	42.5 ± 13.1
Maximum Temperature (°C)/application (n = 6506 RF applications)	39.3 ± 7.8
Maximum Impedance (ohms)/application (n = 6531 RF applications)	103.0 ± 58.2

¹ Complete procedural data were not reported for all subjects.

Note: Above table includes all ablation procedures including repeat procedures.

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Table 18. Summary of Overall Fluoroscopy and Procedure Time (Effectiveness Analysis Cohort, n = 226)

Description	Mean ± Standard Deviation
Total fluoroscopy time (hrs)/procedure (n = 244 procedures)	1.0 ± 1.8
Total procedure time (hrs)/procedure ¹ (n = 258 procedures)	5.6 ± 2.2

¹ Time from first cannula placed into vein/artery of subject to time when all catheters were removed from subject.

Note: Above table includes all ablation procedures including repeat procedures.

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

C.2 - Acute Procedural Success

Acute procedural success results are presented in Table 19.

Table 19. Summary of Acute Procedural Success (Effectiveness Analysis Cohort, n = 226)

Subset Description	n	Acute Success	Percent (%)	95% C.I. ¹
Effectiveness Analysis Cohort ^{2,3}	226	171	75.7	71
Protocol Endpoint			75	65

¹ Exact binomial confidence bound.

² Data includes non-protocol catheter procedures considered *a priori* acute failures.

³ Data includes subjects with incessant VT.

The results from the acute outcome analysis based on termination of all clinical relevant VT upon hospital discharge demonstrate that the percentage of subjects achieving acute success (75.7%; 95% lower confidence bound of 71%) met the protocol endpoint for acute procedural success.

C.3 - Chronic Success - Freedom from VT Recurrence at Six-Month Follow-Up

Chronic success results are described in Table 20.

Table 20. Summary of Chronic Success (Effectiveness Analysis Cohort, n = 226)

Subset Description	n	Chronic Success	Percent (%)	95% C.I. ¹
Effectiveness Analysis Cohort ^{2,3}	226	107	47.3	41.7
Protocol Endpoint			50	40

¹ Exact binomial confidence bound.

² Data includes non-protocol catheter procedures considered *a priori* acute failures.

³ Data includes subjects with incessant VT.

The results demonstrate that the percentage of subjects achieving chronic success (47.3%, 95% lower confidence bound of 41.7%) met the protocol endpoint for chronic success. This is due to the fact that although the point estimate for chronic success was lower than the protocol endpoint, the 95% lower confidence bound of the estimate was higher than the protocol endpoint.

Kaplan-Meier Analysis

A Kaplan-Meier analysis was performed to estimate the time to VT recurrence. Standard errors were computed by the Peto method. The one hundred and seventy-one (171) subjects who achieved acute success were included in this analysis. Table 21 provides the number of subjects at risk (number of subjects entering the follow-up interval with acute success), number of subjects censored (number of subjects for whom the last follow-up exhibited freedom from recurrence of VT, at the time-point), number of events (subjects who experienced recurrence of VT), and the point and one-sided 95% C.I. estimation of VT recurrence-free probability. These numbers are defined at the exact time-point indicated, and do not necessarily correspond to the number of subjects followed with the follow-up windows. Figure 1 provides the freedom from VT recurrence curve.

Freedom from VT recurrence following acute success was 67.5% at 6 months.

Table 21. Kaplan-Meier Data Including the Nominal Interval, Number of Subjects at Risk, Number of Subjects Censored, and Number of Events, Point and One-sided 95% Confidence Interval Estimation of Recurrence-Free Probability Using Peto Method (Acute Success Subjects, n = 171)

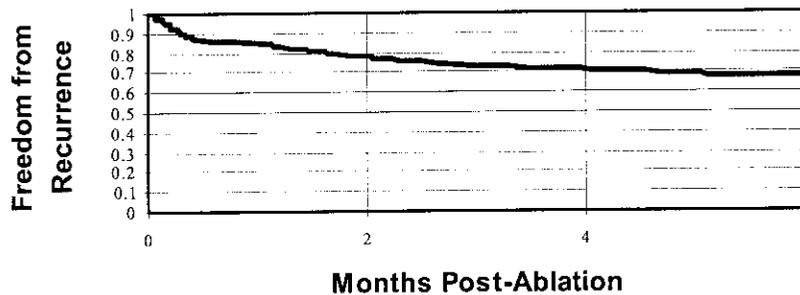
Nominal Interval	No. of Subjects at Risk ¹	Cumulative		Recurrence-Free Probability		
		No. of Subjects Censored	No. of Subjects with Events	Point Estimate	Peto Standard Error	One-sided 95% Lower Confidence Limit (Peto)
Day 0	171	0	0	1.0000	0.0000	1.0000
Discharge ²	164	0	8	0.9529	0.0162	0.9262
3-weeks ³	145	2	24	0.8586	0.0268	0.8145
1-month	143	3	25	0.8526	0.0274	0.8076
2-months	132	3	36	0.7870	0.0316	0.7350
3-months	124	3	45	0.7332	0.0343	0.6768
4-months	115	8	48	0.7148	0.0356	0.6563
5-months	107	14	52	0.6890	0.0379	0.6267
6-months	54	64	54	0.6754	0.0534	0.5876

¹ The number of subjects at risk is the number who did not have events or censoring before the time-point. If there are no events at a time-point, the total number of subjects in the analysis (171) equals the number at risk + the cumulative number censored + the cumulative number of events. This equation holds except at discharge, 3-months, 5-months, and 6-months. There are an event exactly at discharge, an event at 3-months, an event and a censoring at 5-months, and a censoring at 6-months.

² Subjects were discharged within 5 days from ablation. For the purpose of computation, discharge was defined as 5 days.

³ For purposes of this table, 3 weeks = 21 days, 1 month = 30 days, 2 months = 61 days, 3 months = 91 days, 4 months = 122 days, 5 months = 152 days, and 6 months = 183 days.

Figure 1 Freedom from VT Recurrence (Acute Procedural Success Subjects, n = 171)



Post hoc analysis of the treatment of Unmappable VT

Acute procedural success in subjects with only mappable induced VTs and in subjects with only unmappable induced VTs was 73.6% and 75.4%, respectively. Acute outcome for subjects with both mappable and unmappable VTs induced during the ablation procedure was 77.5%. Additionally, 67.3% of the 205 subjects who underwent an electrical stimulation protocol at the end of the procedure had no inducible VTs.

In addition, chronic success rates did not significantly differ among subjects with only mappable, only unmappable, or both mappable and unmappable VTs. Chronic success in subjects with only induced mappable VTs was 52.8% while in subjects with induced unmappable VT only, the success rate was 52.2%. Chronic success outcome for subjects with both mappable and unmappable VTs induced during the ablation procedure was 41.2%. Although the success rate was slightly lower for the combined mappable and unmappable group, this is not unexpected considering that multiple different VTs in a single subject have previously been associated with lower success outcomes.

Reduction in Post-ablation ICD therapies analyzed in selected subset of the study population

Data were available to calculate the reduction in ICD therapies after the ablation procedure for 130 subjects in the effectiveness analysis cohort. While not an endpoint for the study, a reduction in the number of VT therapies is also considered clinically relevant and has been used in literature to define "clinical success". The significant proportion of subjects with ICDs allowed for a comparison of the frequency of VT episodes before and after ablation (utilizing subjects as their own control). Of the effectiveness analysis cohort, 130 subjects were available for analysis through 6 months follow-up. There were a total of 79.2% (103/130) subjects with evidence of reduction in the rate of VT episodes post-ablation, while in 20.8% (27/130), there was an increase in the rate of VT episodes post-ablation. In this study, all sustained VTs detected by ICD were considered, not just VTs that met the predefined endpoint as significant, thus representing a conservative evaluation of the endpoint. The absolute magnitude of the reduction in rate of ICD therapies was substantial for more than two thirds of this group. Approximately 70% (70.0%; 91/130) of the subjects had a documented reduction of more than 75% in ICD therapies during the follow-up period. For chronic failure subjects with available data, 55.4% (31/56) demonstrated a reduction in ICD therapies during the follow-up period.

C.4 - Adverse Events (AE)

The protocol defined a major AE as any clinical event within seven days of the procedure that resulted in death, a life-threatening complication, or a persistent or significant disability/incapacity that requires inpatient hospitalization or prolongs hospitalization or requires intervention to prevent a permanent impairment of a body function or damage to a body structure. A minor AE was defined as any AE

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resulting in minimal transient impairment of a body function or damage to a body structure, or which does not require any intervention other than monitoring or events occurring more than 7 days after the procedure.

The study was not designed nor statistically powered to measure the long-term impact of ablation with the NaviStar ThermoCool catheter on cardiac function and mortality.

Major Adverse Events

Of the 233 subjects in the safety analysis cohort, 53 major AEs were reported for 42 subjects. The overall percentage of subjects who experienced a major AE was 18%. Table 22 summarizes the major AEs.

Table 22. Major AEs observed within 7 Days Post-Ablation (Safety Analysis Cohort, n = 233)

Description	No. of Subjects	
Cardiovascular	21	9.01%
Incessant VT – Death	4	1.72%
Hypotension	2	< 1%
VT Storm – Death	2	< 1%
Recurrent VT	1	< 1%
Acute MI – Death	1	< 1%
Congestive Heart Failure	1	< 1%
Cardiogenic Shock - Death	1	< 1%
Atrial ICD Lead Malfunction	1	< 1%
VF Refractory to Monophasic Defibrillation	1	< 1%
Mitral Valve Regurgitation	1	< 1%
Mild Pericarditis	1	< 1%
Recurrent Atrial Flutter	1	< 1%
Mild Congestive Heart Failure	1	< 1%
Cardiac Ischemia	1	< 1%
Incessant VT	1	< 1%
Multiple VT	1	< 1%
Recurrent ICD Shocks	1	< 1%
Pulmonary	8	3.43%
Pulmonary Edema	4	1.72%
Transient Respiratory Insufficiency (no intubation required)	1	< 1%
Hypoxia - Volume Overload	1	< 1%
Respiratory Distress (required intubation)	1	< 1%
Pleural Effusion	1	< 1%
Peripheral Vascular	13	5.58%
Hematoma	4	1.72%
Pseudoaneurysm	3	1.29%
Groin Bleeding	2	< 1%
Hematoma/Hypotension	1	< 1%
Hematoma and Pseudoaneurysm	1	< 1%
Hematoma Post-cardiac Catheterization	1	< 1%

Bilateral Cephalic Vein Thrombosis	1	< 1%
Genitourinary	3	1.29%
Bleeding - Traumatic Foley Insertion	1	< 1%
Hematuria, Urinary Retention	1	< 1%
Hypergastric Pain Related to Urinary Retention	1	< 1%
Hematologic	3	1.29%
Anemia	1	< 1%
Heparin-Induced Thrombocytopenia and Disseminated Intravascular Coagulation	1	< 1%
Epistaxis secondary to over anticoagulation	1	< 1%
Systemic Infection	1	< 1%
Methicillin Resistant <i>S. aureus</i> Infection	1	< 1%
Neurovascular	1	< 1%
CVA	1	< 1%
Gastrointestinal	1	< 1%
Diverticulosis	1	< 1%
Musculoskeletal	1	< 1%
Atypical chest pain	1	< 1%

Note: 1. Fifty-three major AEs were reported for 42 subjects. 2. Some subjects are listed more than once in above table.

Preexisting Conditions as a Predictor of Major AEs

So that one may determine if a sub-population of subjects is at differential risk, preexisting cardiac function (LVEF) data were analyzed as a potential predictor of major AEs. Table 23 lists the LVEF measurements stratified by the presence or absence of major AEs. Survival status stratified by LVEF (%) is presented in Table 24.

Data showed that the subjects who had LVEF measurements ≤ 30% had a significantly higher major AE rate than the subjects with LVEF measurements > 30% (22.6% vs 10.0%, p = 0.0258, Fisher's Exact test). Of note, 62.7% (146/233) of the Safety Analysis Cohort had LVEF ≤ 30% and would therefore be considered at higher risk of morbidity than study subjects who had higher LVEF. A cut off of 30% LVEF was used to dichotomize the analysis.

Table 23. Major AEs by LVEF (%) (Safety Analysis Cohort, n = 233)

LVEF (%)	Total Number of Subjects	With Major AE*	Without Major AE
		n (%)	n (%)
≤ 30	146	33 (22.6)	113 (77.4)
> 30	70	7 (10.0)	63 (90.0)
Not Reported	17	2 (11.8)	15 (88.2)

* p = 0.0258

The subjects who had LVEF measurements ≤ 30% had a significantly higher death rate than the subjects with LVEF measurements > 30% (24.7% vs 8.6%, p = 0.0055 Fisher's Exact test). This reflects a study population at high risk of mortality at study entrance secondary to their baseline cardiovascular condition. In the Safety Analysis Cohort, a total of 45 (45/233, 19.3%) deaths occurred.

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Table 24. Survival Status by LVEF (%) (Safety Analysis Cohort, n = 233)

LVEF (%)	Total Number of Subjects	Deceased Subjects*		Subjects Alive	
		n	(%)	n	(%)
≤ 30	146	36	(24.7)	110	(75.3)
> 30	70	6	(8.6)	64	(91.4)
Not Reported	17	3	(17.6)	14	(82.4)

* p = 0.0055

The overall percentage of subjects who experienced a major AE was 18% (42/233) (one-sided upper confidence bound (UCB) of 23%). The safety protocol endpoints specified in the protocol was 22% (UCB of 30%). Therefore, this study population met the protocol safety endpoint for this clinical trial (see Table 25).

Table 25. Comparison of Safety Endpoint between NAVISTAR THERMOCOOL Study and Protocol Endpoint (Safety Analysis Cohort, n = 233)

Endpoint	Protocol Established Endpoints ¹		NAVISTAR THERMOCOOL Study	
	%	One-sided 95% Confidence Bound ²	% (n)	One-sided 95% Confidence Bound ²
Major Complications	22	30	18.0 (42/233)	23 (Upper Bound)

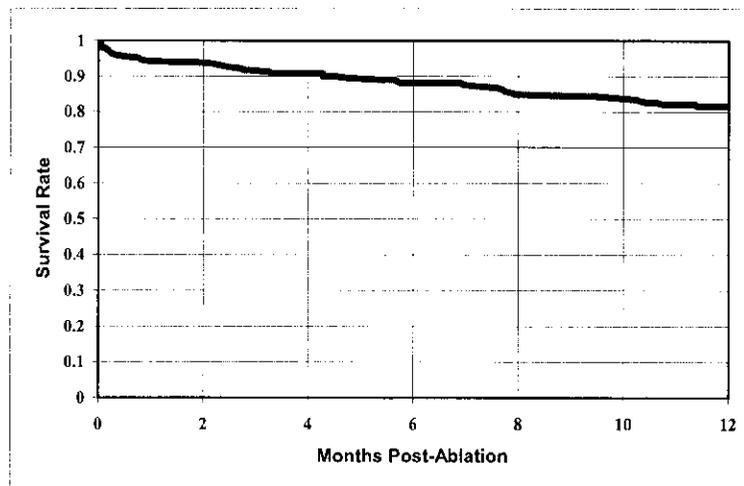
¹ Safety endpoint based on literature search.

² Exact binomial using a commercially-available software package.

A total of 45 deaths (45/233, 19.3%) occurred during the study. Eight subjects (8/233; 3.4%) expired within seven days of the ablation procedure, while an additional 37 (37/233; 15.9%) subjects expired more than 7 days post-procedure.

A Kaplan-Meier Analysis was performed to estimate survival rate after first ablation procedure. Standard errors were computed by the Peto method. Two hundred and thirty-three subjects were included in this analysis. The survival rate was 82 % at 12-months. Figure 2 provides the survival curve over 12-months after first ablation procedure.

Figure 2. Survival Rate by Time Post-Ablation (Safety Analysis Cohort, n=233)



C.5 - Analysis of study results compared to protocol endpoints

Table 26 summarizes the results of the open label single arm observational trial when compared to the protocol established for safety and effectiveness endpoints.

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Table 26. Comparison of Endpoints Between NAVISTAR THERMOCOOL Study and Protocol Endpoint

Endpoint	Protocol Established Endpoints ¹		NAVISTAR THERMOCOOL Study	
	%	One-sided 95% Confidence Bound ²	% (n)	One-sided 95% Confidence Bound ²
Acute Procedural Success	75	65	75.7	71(Lower bound)
Chronic Success	50	40	47.3	41.7(Lower bound)
Procedural Safety	22	30	18.0 (42/233)	23 (Upper bound)

¹ Effectiveness endpoints established in the protocol are based on protocol endpoint; Safety endpoint based on literature search

² Exact binomial using a commercially-available software package.

In conclusion, the results demonstrate that the NAVISTAR THERMOCOOL catheter met all the protocol endpoints for safety and effectiveness.

8. SUMMARY OF CLINICAL STUDIES CONDUCTED FOR ATRIAL FIBRILLATION INDICATION

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, multicenter pivotal clinical investigation conducted at 19 investigational sites (15 in the US and 4 outside of the US).

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 AAD regimen during comparable evaluation periods for the THERMOCOOL 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 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

B.2. – Subject Accountability:

Table 27 – Subject Accountability and Disposition

Subject Disposition	
Total Number of Subjects Enrolled	167
Subjects randomized to THERMOCOOL	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
AAID (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:

The table below summarizes the demographic information. Subjects were randomized 2:1 upon signing informed consent.

Table 28 – Subject Demographics

	THERMOCOOL n/N (%)	AAID (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	
LA Dimension (mm)**				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	
LV Ejection Fraction (%)***				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	

** Data are not available for 15 subjects (6 in ThermoCool group and 9 in AAD group).

*** Data are not available for 14 subjects (7 in ThermoCool group and 7 in AAD group).

The age in the above table 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 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 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

Tables 29 and 30 present the procedural data.

Table 29: Summary of RF Applications, Saline Infused, Power, Temperature and Impedance Data (THERMOCOOL 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 (ohms)/procedure (n = 125 RF procedures)	135.4 ± 25.4

¹ Complete procedural data were not reported for all subjects.

Table 30: Summary of Ablation Procedure Parameters – All Ablation Procedures (THERMOCOOL Effectiveness Cohort, n = 103*)

Procedure Parameters	THERMOCOOL 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)

*Data parameters not available for all ablation procedures.

Note: Tables 29 and 30 include all ablation procedures for subjects randomized to the THERMOCOOL 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) procedure time and all other procedures performed during the subject’s stay in the 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 31 summarizes the lesion sets applied to THERMOCOOL group subjects during the index ablation procedures.

Table 31: Outcomes by Ablation Targets per Subject – 1st Ablation Procedure (THERMOCOOL Group Subjects, n=103)*

Ablation Targets	THERMOCOOL Group (n =103)		
	Success n (%)	Fail n (%)	Total n (100%)
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)

* 14 Subjects were still within the effectiveness evaluation period and therefore not included in this analysis.

C.2 - Acute Procedural Success

Acute procedural success results are presented in Table 32.

Table 32: Acute Effectiveness Outcome for THERMOCOOL Group (n=103)*

	THERMOCOOL n
Underwent RF Study procedure	103
Entrance Block Confirmed	102**
Ablation Procedure >80 days	2
Non-study Catheter Utilized for AF Targets	0
>2 Repeat Ablation Procedures	0
Acute Effectiveness Success	100

* Includes all THERMOCOOL group subjects undergoing ablation with the study catheter.

**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 group. The posterior probability that the THERMOCOOL 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 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 33.

Table 33: Summary of Data Available* - 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	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

* 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 3 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 group (64%) compared to AAD group (16%) for the primary effectiveness endpoint.

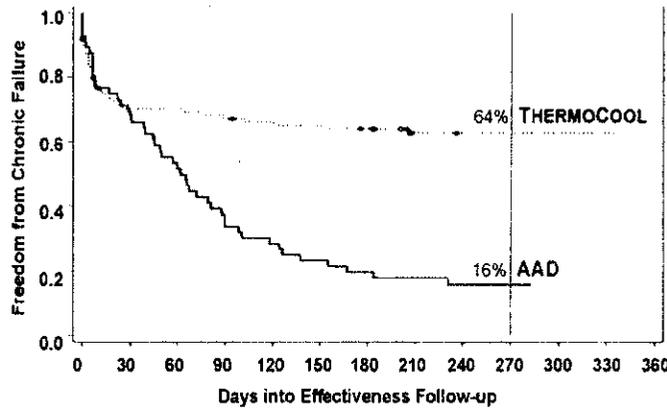


FIGURE 3 Kaplan-Meier Analysis – Probability of Freedom from Chronic Effectiveness Failure For Each Treatment Group*

The June 2008 dataset status of each of the 159 subjects is reported in Table 34. 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 34: Summary of the Status for Each of the Enrolled Subjects

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

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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 4 shows that the 9-month failure-free rate in the THERMOCOOL 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.

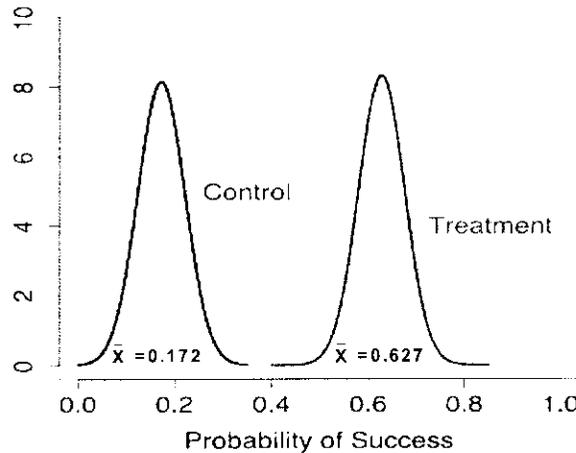


FIGURE 4: The Posterior Distributions of the Probabilities of 9-month Failure-Free Treatment Success for Each Treatment Group

Figure 5 demonstrates that the ThermoCool 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.

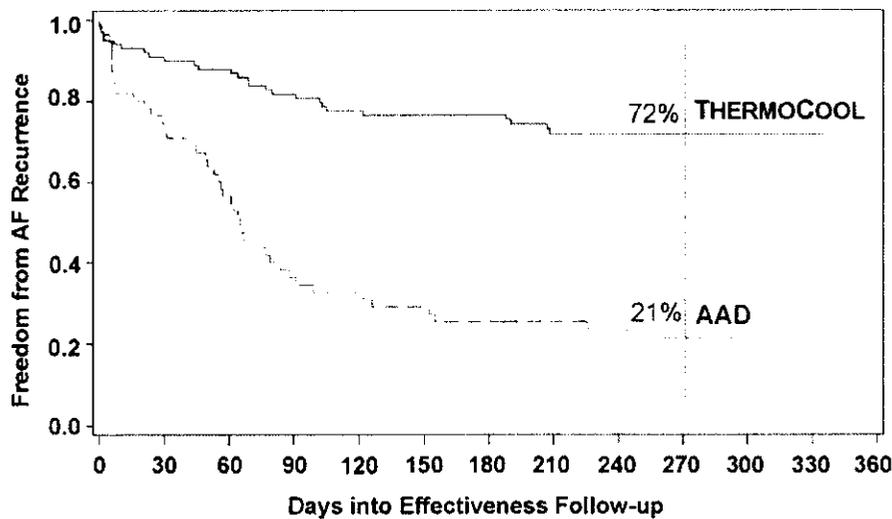


FIGURE 5 Kaplan-Meier Analysis – Probability of Freedom from Any Observed AF Recurrence For Each Treatment Group (n=159)

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 group subjects (n=103) and AAD (Control) group subjects undergoing an ablation procedure (n=36).

Primary Safety Endpoint – Primary Adverse Events

Table 35 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 35: 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*	16.0	16.1

* Exact binomial using a commercially available software package.

Table 36 summarizes the major primary AEs.

Table 36: 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 37 compares the incidence of early onset serious adverse events between the two treatment groups occurring within the first 90 days of initial therapy.

TABLE 37 Percentage of Early Onset SAE by Randomization Group (Overall Safety Cohort, n=160)

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

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

One subject in the THERMOCOOL 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 ablation catheter for the treatment of drug refractory recurrent symptomatic paroxysmal atrial fibrillation, when used with advanced three-dimensional electroanatomic mapping systems.

9. HOW SUPPLIED

- The NAVISTAR® THERMOCOOL® Diagnostic/Ablation Catheter is supplied STERILE.
- The catheter is supplied with a choice of five curve types: B, C, D, F, and J.
- The Stockert 70 RF Generator with appropriate interface cables is supplied separately.
- A grounding pad (indifferent electrode) is supplied separately.
- The CARTO® EP Navigation System is supplied separately.
- The appropriate Reference Patch is provided separately.

9.1 Packaging

The NAVISTAR® THERMOCOOL® Diagnostic/Ablation Catheter is provided in sterile packaging. The catheter is secured to a mounting card placed in a sealed film/Tyvek pouch and packaged inside a cardboard box. Both the pouch and the shipping container are labeled sterile.

9.2 Storage

The NAVISTAR® THERMOCOOL® Diagnostic/Ablation Catheter must be stored in a cool, dry place. Storage temperature should be

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between 5 and 25° C (41 and 77° F).

9.3 Shelf-Life

The NAVISTAR® THERMOCOOL® Diagnostic/Ablation Catheter has a shelf life of three (3) years.

9.4 Compatible EP Navigation Systems

The NAVISTAR® THERMOCOOL® Diagnostic/Ablation Catheter provides location information when used with the following compatible 3D electroanatomic mapping systems: CARTO®, CARTO® XP, and CARTO® 3. Compatibility with these systems has been demonstrated via bench testing to confirm that the device is capable of providing accurate location information when used in accordance with the instructions for use.

10. DIRECTIONS FOR USE

Please refer to the User Manuals for the CARTO® EP Navigation System, COOLFLOW® Pump, Stockert 70 RF Generator, and the Instructions for Use for the COOLFLOW® Irrigation Tubing Set for instructions on connecting and operating these systems in conjunction with the NAVISTAR® THERMOCOOL® Diagnostic/Ablation Catheter.

1. Remove catheter from package and place in a sterile work area.
2. Create a vascular access in a large central vessel using aseptic techniques.
3. To verify compatibility between sheath and catheter, advance catheter through sheath prior to insertion.
4. Connect the catheter to the Patient Interface Unit (PIU) via the appropriate Biosense Webster cable with 25-pin Hypertronics interlocking connectors on both ends. Connect the PIU to the Stockert 70 RF Generator via the Biosense Webster cable with 10-pin Redel connectors on both ends. Connect the PIU to appropriate recording and mapping systems, including the CARTO® EP Navigation System, with appropriate interface cables. Use only Biosense Webster interface cables. If electrogram recording equipment is used, the catheter tip electrode must be switched from the electrogram equipment (via the generator controls or an external switch) to the RF generator power output for ablation. To complete the electrical circuit, connect an indifferent electrode to the indifferent electrode input on the generator.
5. Connect the COOLFLOW® Irrigation Tubing Set to a room temperature, heparinized (1 u 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.
6. Load the COOLFLOW® Irrigation Tubing Set in the pump. Open the stopcock and press and hold the Flush button on the COOLFLOW® Pump until the air is expelled through the open end of the tubing.
7. Connect the stopcock on the end of the COOLFLOW® Irrigation Tubing Set to the luer fitting of the NAVISTAR® THERMOCOOL® Diagnostic/Ablation Catheter.
8. Flush the catheter and tubing to ensure purging of trapped air bubbles and to verify that the irrigation holes are patent.
9. Start continuous irrigation at a flow rate of 2 ml/min by pressing the Low Flow button on the COOLFLOW® pump.
10. Insert the NAVISTAR® THERMOCOOL® Diagnostic/Ablation Catheter via the entrance site, using an appropriately sized introducer sheath and advance the catheter to the area under investigation. Use both fluoroscopy and electrograms to aid in proper positioning.
11. The catheter tip can be deflected to facilitate positioning by using the thumbknob to vary tip curvature. Pushing the thumbknob forward causes the catheter tip to deflect; when the thumbknob is pulled back, the tip straightens.
12. Verify that the CATHETER SELECTION KNOB on the Stockert 70 RF Generator is on the "ThermoCool" option. When this option is chosen, the Stockert 70 RF generator defaults to the safety parameters established for the ThermoCool catheter.
13. Recommendation for irrigation: Increase the irrigation to high flow rate starting up to 5 seconds before the onset of RF energy delivery and maintaining this higher flow rate until 5 seconds after termination of the energy application. For power levels up to 30 watts, a high flow rate of 17ml/min should be used. For power levels between 31-50 watts, a high flow rate of 30ml/min should be used.
14. 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.
15. Monitor the catheter tip temperature throughout the procedure to ensure adequate irrigation. If the temperature increases to 50° C during RF application, power delivery will be interrupted by the temperature cutoff of the Stockert 70 RF Generator. The irrigation system must be rechecked prior to restarting RF application.
16. Recommendation for RF power delivered:
 - For treatment of atrial flutter: Start a procedure at 15 - 20 Watts. After 15 seconds, power may be increased by 5 - 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. It is recommended that power not exceed 50 W when the catheter is parallel to the tissue and 35 W if the catheter is perpendicular to the tissue. The duration of each RF application should not exceed 120 seconds. Dragging the catheter to the next site is permissible during the 120 second energy application. RF current may be reapplied to the same or alternate sites using the same catheter.
 - For treatment of ventricular tachycardia: Start a procedure at 31 Watts. If needed, increase power in 5 W increments (to maximum 50 W) until a transmural lesion is achieved. The duration of each RF application should not exceed 120 seconds. Dragging the catheter to the next site is permissible during the 120 second energy application.
 - For treatment of atrial fibrillation: It is recommended that power not exceed 50 W and 35 W if the catheter is perpendicular to the tissue. Refer to Summary of Clinical Studies above lesion recommendations.
17. In the event of a generator cutoff (impedance or temperature), the catheter must be withdrawn and the tip electrode cleaned of coagulum, if present before RF current is reapplied. 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. Prior to reinsertion, ensure that the irrigation holes are not plugged by increasing flow rate and verifying flow from each of the six irrigation holes.

If irrigation hole occlusion occurs:

- a. Fill a 1 or 2 ml syringe with sterile saline and attach to the stopcock on the end of the tubing set
- b. Carefully inject the saline from the syringe into the catheter. A stream of fluid should be visible from all six (6) holes.
- c. Repeat steps a and b, if necessary until the holes are cleared.
- d. Flush 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

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

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