NAVISTAR™ THERMOCOOL® Diagnostic/Ablation Catheter
INSTRUCTIONS FOR USE

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 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 radiofrequency generator and a dispersive pad (reference 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 radiofrequency current from the radiofrequency 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" – 3"). Four curve types designated "B", "C", "D", and "F" are available. 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 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, normal saline is passed through the 0.027" diameter lumen of the catheter and through the tip electrode, to irrigate and cool the ablation site. An irrigation pump may be used to control the saline irrigation.

A feature of this catheter consists of 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(tm) ThermoCool(r) 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 Type I atrial flutter in patients age 18 or older. The NaviStar(tm) ThermoCool(r) catheter provides location information when used with the Carto EP/XP Navigation System.

3. CONTRAINDICATIONS

Do not use this device:

- in patients with active systemic infection; and
- if the patient has intracardiac mural thrombus or has had a ventriculotomy or atriotomy within the preceding four weeks.

4. WARNINGS AND PRECAUTIONS

WARNINGS

Do not rely on the temperature reading detected by the temperature sensor located within the tip electrode of the catheter since the temperature 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 radiofrequency current, a decrease in electrode temperature confirms the onset of saline irrigation of the ablation electrode. Recording temperature from the electrode during the application of radiofrequency current ensures that the irrigation flow rate is being maintained.

It is important to carefully follow the power titration procedure as specified in the instructions for use. Too rapid increase in power during ablation may lead to perforation.

This catheter may damage the prosthetic tricuspid valve of a patient if the catheter is accidentally advanced through the valve.

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.

In accordance with your hospital's protocol, monitor the patient's fluid balance throughout the procedure to avoid fluid overload.

The device has not been shown to be safe at electrode temperatures above 50°C; therefore, the temperature limiter on the Stockert generator should be set for a maximum of 50°C.

Implantable pacemakers and implantable cardioverter/defibrillators (ICDs) may be adversely affected by radiofrequency 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.

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.

PRECAUTIONS

- Do not expose the catheter to organic solvents such as alcohol.
- Do not autoclave the catheter.
- Do not immerse proximal handle in fluids; electrical performance could be affected.
- Do not scrub or twist the distal tip electrode during cleaning.
- Inspect irrigation saline for air bubbles prior to its use in the procedure. Air bubbles in the irrigation saline may cause emboli.
- Electrophysiology catheters and systems are intended for use only in X-ray shielded rooms due to electromagnetic compatibility requirements.
- 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.
- 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.
- The long-term risks of protracted fluoroscopy and creation of RF induced lesions have not been established.
- 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.
- 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.

- Always pull the thumbknob back to straighten the catheter tip before insertion or withdrawal of the catheter.
- Always maintain a constant saline infusion to prevent coagulation within the lumen of the catheter.
- When radiofrequency 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. 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-use.
- Apparent low power output, high impedance reading, or failure of the equipment to function correctly at normal settings may indicate faulty application of the dispersive electrode(s) or failure of an electrical lead. Do not increase power before checking for obvious defects or misapplication.
- Read and follow the dispersive electrode manufacturer's instructions for use; the use of dispersive electrodes that meet or exceed ANSI/AAMI requirements (HF18) is recommended.
- The Biosense Webster NAVISTAR™ THERMOCOOL® Diagnostic/Ablation Deflectable Tip Catheter is indicated for use only with the Stockert 70 RF Generator, Biosense Webster cables, and other appropriate interface cables and connectors.
- The Biosense Webster NAVISTAR™ THERMOCOOL® Diagnostic/Ablation Deflectable Tip Catheter has been shown to create larger lesions than standard radiofrequency ablation catheters. Care should be taken when ablating near structures such as the sino-atrial and atrioventricular nodes.
- The sterile packaging and catheter should be inspected prior to use.
- 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.
- The Biosense Webster NAVISTAR™ THERMOCOOL® Diagnostic/Ablation Deflectable Tip Catheter is intended for single patient use only.
- Do not resterilize and reuse.
- Do not use near MRI equipment since movement or heating of the catheter may occur and the image on the display may become distorted.
- Use both fluoroscopy and electrogram data to monitor catheter advancement and reduce risk of tissue injury.
- 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 dispersive 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 ablation immediately and remove.
- 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.

- 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.
- 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 dispersive electrode. Protective impedance may reduce the risk of burns, and permit continuous monitoring of the electrocardiogram during energy delivery.
- The temperature sensor measures electrode tip 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 is still not displayed, there may be a malfunction in the temperature sensing system that must be corrected prior to applying radiofrequency power.
- The temperature measurement accuracy of the Biosense Webster NaviStar™ ThermoCool® Diagnostic/Ablation Deflectable Tip Catheter, as with temperature measurement electrophysiology catheters, is given 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.
- Before use, check irrigation ports are patent by infusion of saline through the catheter and tubing. This infusion will also purge any air from inside the catheter and tubing.
- Regularly inspect and test re-useable cables and accessories.
- Do not use the catheter if the small vent hole at the connector end of the handpiece is occluded as evidenced by difficulty in deflecting the catheter tip and the inability of the catheter to hold a curve.

5. ADVERSE EVENTS

Of the 190 subjects in the Safety Population, 33 major adverse events were reported in 30 subjects. See Section 6, "Clinical Studies", below for a complete description of the adverse events encountered during the study.

6. SUMMARY OF CLINICAL STUDIES

The clinical testing described below was performed with the NaviStar™ ThermoCool® catheter, and not with the Celsius™ ThermoCool® catheter. Since the ablation capabilities of both NaviStar™ and Celsius™ ThermoCool® catheters were shown with pre-clinical testing to be similar, clinical testing results from the NaviStar™ ThermoCool® study, as reported below, may be extrapolated to what would be expected when using the Celsius™ ThermoCool® catheter.

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

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

Table 9 - 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 non-investigational 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

* 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 10 – Subject Demographics
(All Subjects who Received Ablation Therapy - n=190)

Gender	N	%
Female	44	23.2
Male	146	76.8
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 10 and 11 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 11 - 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 12 – 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 13 describes the acute ablation outcomes.

Table 13 - Acute Ablation Outcomes (n=186)

	# Success / # Subjects Ablated	Percentage (one-sided 95% confidence bound)
Acute Study Results	159/186	85% (81%)
OPC		88% (80%)

C.3. – Composite Assessment of Atrial Flutter Ablation Success
As noted in the above section, 159 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 14 summarizes the composite results.

Table 14 – Composite Assessment of Atrial Flutter Success

	# Success / # Subjects Ablated	Percentage (one-sided 95% confidence bound)
Study Results	162/190	85.3% (80.2%)
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 15 - 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 16 summarizes the major adverse events.

Table 16 - 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 total = 8 subjects acute respiratory distress syndrome = 2 subjects aspiration pneumonia = 2 subjects pneumonia = 3 subjects asthma = 1 subject
Anesthesia related total = 2 subjects sedation induced apnea (intubation not required) sedation induced co2 retention with lethargy (intubation not required)
Vascular total = 2 subjects arteriovenous fistula/femoral artery-saphenous vein pseudoaneurysm/right femoral artery
Urologic total = 2 subjects urinary tract infection urinary retention
Cholecystitis 1 subject
Neurologic 2 subjects 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 patient population from which the OPCs were derived. See section C.1 for a list of concomitant ablation procedures.

C.6. - Statistical Analysis

Table 17 summarizes the safety and effectiveness of the device when compared to the control group OPC established for safety and acute success.

Table 17 - 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%	85.3% (162/190)	80.2% (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 (80.2% 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.

7. HOW SUPPLIED

- The NAVISTAR ™ THERMOCOOL® Diagnostic/Ablation Catheter is supplied STERILE.
- The catheter is supplied with a choice of four curve types: B, C, D, and F.
- The Stockert 70 RF Generator with appropriate interface cables is supplied separately.

- A grounding (dispersive) pad is supplied separately.
- The CARTO™ EP Navigation System is supplied separately.
- The REFSTAR™ with QWIKPATCH™ Reference Patch is provided separately.

7.1 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.

7.2 Storage

The NAVISTAR™ THERMOCOOL® Diagnostic/Ablation Catheter must be stored in a cool, dry place. Storage temperature should be between 5 and 25° C (41 and 77° F).

7.3 Shelf-Life

The NAVISTAR™ THERMOCOOL™ Diagnostic/Ablation Catheter has a shelf-life of one (1) year.

8. DIRECTIONS FOR USE

Please refer to both these instructions for Use and the CARTO™ System User Manual when using the NAVISTAR ™ THERMOCOOL® Diagnostic/Ablation Catheter in conjunction with the CARTO™ System.

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. May be used with an 8F introducer sheath.
4. Connect the catheter to the junction box via the appropriate Biosense Webster cable with 25-pin Hypertronics interlocking connectors on both ends. Connect the junction box to the Stockert 70 RF Generator via the Biosense Webster cable with 10-pin Redel connectors on both ends. Connect the junction box 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 a dispersive pad to the reference electrode input on the generator.
5. Turn the CATHETER SELECTION KNOB on the Stockert 70 RF Generator to the "Biosense Webster" option.
6. Purge catheter and tubing per standard technique.
7. Connect the irrigation input of the catheter to a 3-way stopcock through an extension tube set. Connect one of the remaining arms of the 3-way stopcock to an injector pump preset to the recommended flow rate and the other to a slower rate infusion pump preset to 2 ml/min. Open the 3-way stopcock to use the 2 ml/min. infusion to check the irrigation holes are patent.

8. Set the temperature cutoff limit to 50°C. Press MENU and select the TEMPERATURE menu, select 'cutoff' and adjust the cutoff temperature to 50°C using the SELECTOR KNOB.
9. Set the RF generator to *power control mode* by pressing the MANUAL button. Set the initial power level to 15-20 watts.
10. Start continuous irrigation with room temperature, heparinized saline (1 u heparin/ml) at a flow rate of 2 ml/min.
11. Increase the irrigation flow rate to 17 ml/min up to 5 seconds before the onset of RF energy delivery and maintain this higher flow rate until 5 seconds after termination of the energy application. If it is necessary to ablate with power levels 31-50 watts, irrigation flow rate should be increased to 30 ml/min starting 5 seconds before onset and ending 5 seconds after RF energy delivery.
12. The application of RF energy must not be initiated until the increase in irrigation flow rate is confirmed by a 3-5°C decrease in tip electrode temperature.
13. If the temperature increases to 50° C during RF application, power delivery will be interrupted by the temperature cutoff. The irrigation system must be rechecked prior to restarting RF.
14. Insert the catheter via the entrance site, using an introducer sheath.
15. Advance the catheter to the area under investigation. Use both fluoroscopy and electrograms to aid in proper positioning.
16. 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.
17. When the ablation site is identified, turn the 3-way stopcock to use the injector pump and stand by while the voltage and power application time of the radiofrequency generator are set.
18. Turn the injector pump on. Watch the electrode tip temperature decrease.
19. When it has been determined that the tip electrode is in stable contact with the intended ablation site, the catheter tip electrode connection must be switched from the recording equipment to the radiofrequency generator in preparation for delivery of radiofrequency current. Verify that the CATHETER SELECTION KNOB on the Stockert 70 RF Generator is on the "Biosense Webster" option. Circuit impedance should be approximately 100 ohms upon initiation of radiofrequency current.
20. Monitor the temperature throughout the procedure. The peak temperature should be maintained at 50°C during RF energy delivery. Note: The displayed temperature represents the temperature of the electrode only, not the temperature of the tissue.
21. 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 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 will not exceed 120 seconds. Dragging the catheter to the next site is permissible during the 120 second energy application.
22. After radiofrequency current is discontinued, turn stopcock back to 2 ml/min. infusion pump.

23. Radiofrequency current may be re-applied to the same or alternate sites using the same catheter. However, in the event of a generator cutoff (impedance or temperature), the catheter must be withdrawn and the tip electrode cleaned of coagulum before radiofrequency current is re-applied. 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.

    If irrigation hole occlusion occurs:
    a. Remove the catheter from the patient.
    b. Fill a 1 or 2 ml syringe with sterile saline and attach to the sidearm.
    c. Carefully inject the saline from the syringe into the catheter. A stream of fluid should be visible from all six (6) holes.
    d. Repeat steps b and c, if necessary.
    e. If the holes are cleared, the catheter can be reintroduced into the patient.

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

24. If the RF generator does not display temperature, verify that the appropriate cable is plugged into the generator. If the generator still does not display temperature, there may be a malfunction in the temperature sensing system. Correct this malfunction prior to reapplying RF energy.
25. If preset temperature or impedance levels are exceeded during operation, design safety features of the RF generator cause the RF energy to stop. A likely cause of this may be accumulated coagulum on the tip electrode. Withdraw the catheter and examine the tip electrode. If coagulum accumulation is present, clean the tip electrode by gently wiping with a sterile gauze pad dampened with sterile saline. Use caution to not twist the tip electrode relative to the catheter shaft during cleaning because this may damage the tip electrode bond and loosen the tip electrode.

DISCLAIMER OF WARRANTY AND LIMITATION OF LIABILITY

THERE IS NO EXPRESS OR IMPLIED WARRANTY, INCLUDING WITHOUT LIMITATION ANY IMPLIED WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE, ON THE PRODUCT(S) DESCRIBED HEREIN. UNDER NO CIRCUMSTANCES SHALL BIOSENSE WEBSTER, INC., OR ITS AFFILIATED COMPANIES, BE LIABLE FOR ANY SPECIAL, DIRECT, INCIDENTAL, CONSEQUENTIAL, OR OTHER DAMAGES OTHER THAN AS EXPRESSLY PROVIDED BY SPECIFIC LAW.

WITHOUT LIMITING THE FOREGOING, BIOSENSE WEBSTER, INC., OR ITS AFFILIATED COMPANIES, SHALL NOT BE LIABLE FOR ANY SPECIAL, DIRECT, INCIDENTAL, CONSEQUENTIAL, OR OTHER DAMAGES, ARISING OUT OF THE REUSE OF ANY OF ITS PRODUCT(S) LABELED FOR SINGLE USE OR WHERE REUSE IS PROHIBITED BY APPLICABLE LAW.

Biosense Webster, Inc.
3333 Diamond Canyon Road
Diamond Bar, CA 91765, USA

Customer Service: 909-839-8500
Telephone: 800-729-9010 (US only)
Fax: 909-468-2905
The NAVISTAR ™ THERMOCOOL™ Diagnostic/Ablation Catheter and accessories are protected under one or more of the following U.S. Patent Nos.: 5, 827, 278; 5,6, 171, 277, and other patents pending in the U.S. and other countries.

NAVISTAR, CARTO, and CELSIUS are Trademarks of Biosense Webster, Inc.

Tyvek is a Registered Trademark of DuPont.

Celsius™ THERMOCOOL™ Ablation Catheter
INSTRUCTIONS FOR USE

Biosense Webster Celsius™ THERMOCOOL® Diagnostic/Ablation Deflectable Tip 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 Celsius™ THERMOCOOL® Diagnostic/Ablation Deflectable Tip Catheter is a 7 F multi-electrode luminal catheter with a deflectable tip designed to transmit radiofrequency current to the catheter tip electrode for ablation purposes. It is used in conjunction with a radiofrequency generator and a dispersive pad (reference electrode).

The catheter has a high-torque shaft with a 3.5 mm deflectable tip, and incorporates either a thermocouple or thermistor temperature sensor that is embedded in the tip electrode. This catheter does not have a magnetic location sensor embedded in the tip electrode, and, therefore, cannot be used with the CARTO™ EP Navigation System. It is, however, otherwise similar to the NaviStar ThermoCool Catheter.

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" – 3"). Three curve types designated "B", "D", and "F" are available. 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 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, normal saline is passed through the 0.027" diameter lumen of the catheter and through the tip electrode, to irrigate and cool the ablation site. An irrigation pump may be used to control the saline irrigation.

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 Stockert 70 RF Generator, refer to the operating instructions for these instruments.

2. INDICATIONS AND USAGE

The Biosense Webster Celsius(tm) ThermoCool(r) 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 Type I atrial flutter in patients age 18 or older.

3. CONTRAINDICATIONS

Do not use this device:

- in patients with active systemic infection; and
- if the patient has intracardiac mural thrombus or has had a ventriculotomy or atriotomy within the preceding four weeks.

4. WARNINGS AND PRECAUTIONS

WARNINGS

Do not rely on the temperature reading detected by the temperature sensor located within the tip electrode of the catheter since the temperature 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 radiofrequency current, a decrease in electrode temperature confirms the onset of saline irrigation of the ablation electrode. Recording temperature from the electrode during the application of radiofrequency current ensures that the irrigation flow rate is being maintained.

It is important to carefully follow the power titration procedure as specified in the instructions for use. Too rapid increase in power during ablation may lead to perforation.

This catheter may damage the prosthetic tricuspid valve of a patient if the catheter is accidentally advanced through the valve.

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.

In accordance with your hospital's protocol, monitor the patient's fluid balance throughout the procedure to avoid fluid overload.

The device has not been shown to be safe at electrode temperatures above 50°C; therefore, the temperature limiter on the Stockert generator should be set for a maximum of 50°C.

Implantable pacemakers and implantable cardioverter/defibrillators (ICDs) may be adversely affected by radiofrequency 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.

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.

PRECAUTIONS

- Do not expose the catheter to organic solvents such as alcohol.
- Do not autoclave the catheter.
- Do not immerse proximal handle in fluids; electrical performance could be affected.
- Do not scrub or twist the distal tip electrode during cleaning.
- Inspect irrigation saline for air bubbles prior to its use in the procedure. Air bubbles in the irrigation saline may cause emboli.
- Electrophysiology catheters and systems are intended for use only in X-ray shielded rooms due to electromagnetic compatibility requirements.
- Do not attempt to operate the Biosense Webster Celsius™ THERMOCOOL® Diagnostic/Ablation Deflectable Tip Catheter or the Stockert 70 RF generator prior to completely reading and understanding the applicable instructions for use.
- 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.
- The long-term risks of protracted fluoroscopy and creation of RF induced lesions have not been established.
- 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.
- When using the Biosense Webster Celsius™ 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.
- Always pull the thumbknob back to straighten the catheter tip before insertion or withdrawal of the catheter.
- Always maintain a constant saline infusion to prevent coagulation within the lumen of the catheter.

- When radiofrequency 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. 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-use.
- Apparent low power output, high impedance reading, or failure of the equipment to function correctly at normal settings may indicate faulty application of the dispersive electrode(s) or failure of an electrical lead. Do not increase power before checking for obvious defects or misapplication.
- Read and follow the dispersive electrode manufacturer's instructions for use; the use of dispersive electrodes that meet or exceed ANSI/AAMI requirements (HF18) is recommended.
- The Biosense Webster Celsius™ THERMOCOOL® Diagnostic/Ablation Deflectable Tip Catheter is indicated for use only with the Stockert 70 RF Generator, Biosense Webster cables, and other appropriate interface cables and connectors.
- The Biosense Webster Celsius™ THERMOCOOL® Diagnostic/Ablation Deflectable Tip Catheter has been shown to create larger lesions than standard radiofrequency ablation catheters. Care should be taken when ablating near structures such as the sino-atrial and atrioventricular nodes.
- The sterile packaging and catheter should be inspected prior to use.
- 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.
- The Biosense Webster CELSIUS™ THERMOCOOL® Diagnostic/Ablation Deflectable Tip Catheter is intended for single patient use only.
- Do not resterilize and reuse.
- Do not use near MRI equipment since movement or heating of the catheter may occur and the image on the display may become distorted.
- Use both fluoroscopy and electrogram data to monitor catheter advancement and reduce risk of tissue injury.
- The Biosense Webster Celsius™ 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 dispersive 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 ablation immediately and remove.
- 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.
- Electromagnetic interference (EMI) produced by the Biosense Webster Celsius ™ 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.
- 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 dispersive electrode. Protective impedance may reduce the risk of burns, and permit continuous monitoring of the electrocardiogram during energy delivery.

- The temperature sensor measures electrode tip 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 is still not displayed, there may be a malfunction in the temperature sensing system that must be corrected prior to applying radiofrequency power.
- The temperature measurement accuracy of the Biosense Webster Celsius™ ThermoCool® Diagnostic/Ablation Deflectable Tip Catheter, as with temperature measurement electrophysiology catheters, is given 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.
- Before use, check irrigation ports are patent by infusion of saline through the catheter and tubing. This infusion will also purge any air from inside the catheter and tubing.
- Regularly inspect and test re-useable cables and accessories.
- Do not use the catheter if the small vent hole at the connector end of the handpiece is occluded as evidenced by difficulty in deflecting the catheter tip and the inability of the catheter to hold a curve.

5. ADVERSE EVENTS

Note that data on adverse events are from the clinical study on the NAVISTAR™ THERMOCOOL Diagnostic/Ablation Catheter. See justification for the equivalency of the CELSIUS™ and NAVISTAR™ Diagnostic/Ablation Catheters in section one of these Instructions for Use.

Of the 190 subjects in the Analysis Cohort, 33 major adverse events were reported in 30 subjects. See Section 6, "Clinical Studies", below for a complete description of the adverse events encountered during the study.

6. SUMMARY OF CLINICAL STUDIES

The clinical testing described below was performed with the NaviStar™ ThermoCool® catheter, and not with the Celsius™ ThermoCool® catheter. Since the ablation capabilities of both NaviStar™ and Celsius™ ThermoCool® catheters were shown with pre-clinical testing to be similar, clinical testing results from the NaviStar™ ThermoCool® study, as reported below, may be extrapolated to what would be expected when using the Celsius™ ThermoCool® catheter.

The clinical testing described below was performed with the NaviStar™ ThermoCool® catheter, and not with the Celsius™ ThermoCool® catheter. Since the ablation capabilities of both NaviStar™ and Celsius™ ThermoCool®

catheters were shown with pre-clinical testing to be similar, clinical testing results from the NaviStar™ ThermoCool® study, as reported below, may be extrapolated to what would be expected when using the Celsius™ ThermoCool® catheter.

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

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

Table 9 - 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 non-investigational 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

* 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 10 – Subject Demographics
(All Subjects who Received Ablation Therapy - n=190)

Gender	N	%
Female	44	23.2
Male	146	76.8
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 10 and 11 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 11 - 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 12 – 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 13 describes the acute ablation outcomes.

Table 13 - Acute Ablation Outcomes (n=186)

	# Success / # Subjects Ablated	Percentage (one-sided 95% confidence bound)
Acute Study	159/186	85% (81%)

Results		
OPC		88% (80%)

C.3. – Composite Assessment of Atrial Flutter Ablation Success
As noted in the above section, 159 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 14 summarizes the composite results.

Table 14 – Composite Assessment of Atrial Flutter Success

	# Success / # Subjects Ablated	Percentage (one-sided 95% confidence bound)
Study Results	162/190	85.3% (80.2%)
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 15 - 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 16 summarizes the major adverse events.

Table 16 - 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 total = 8 subjects acute respiratory distress syndrome = 2 subjects aspiration pneumonia = 2 subjects pneumonia = 3 subjects asthma = 1 subject
Anesthesia related total = 2 subjects sedation induced apnea (intubation not required) sedation induced co2 retention with lethargy (intubation not required)
Vascular total = 2 subjects arteriovenous fistula/femoral artery-saphenous vein pseudoaneurysm/right femoral artery
Urologic total = 2 subjects urinary tract infection urinary retention
Cholecystitis 1 subject
Neurologic 2 subjects 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 patient population from which the OPCs were derived. See section C.1 for a list of concomitant ablation procedures.

C.6. - Statistical Analysis

Table 17 summarizes the safety and effectiveness of the device when compared to the control group OPC established for safety and acute success.

Table 17 - 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%	85.3% (162/190)	80.2% (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 (80.2% 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.

7. HOW SUPPLIED

- The CELSIUS™ THERMOCOOL® Ablation Catheter is supplied STERILE (EO).
- The catheter is supplied with a choice of three curve types: B, D, and F.
- The Stockert 70 RF Generator with appropriate interface cables is supplied separately.

- A grounding (dispersive) pad is supplied separately.

7.1 Packaging

The CELSIUS™ THERMOCOOL® 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.

7.2 Storage

The CELSIUS™ THERMOCOOL® Ablation Catheter must be stored in a cool, dry place. Storage temperature should be between 5 and 25° C (41 and 77° F).

7.3 Shelf-Life

The CELSIUS™ THERMOCOOL® Ablation Catheter has a shelf-life of one (1) year.

8. DIRECTIONS FOR USE

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. May be used with an 8F introducer sheath.
4. Connect the catheter to the recording equipment and/or the Stockert 70 RF Generator using the appropriate interface cables.
5. Turn the CATHETER SELECTION KNOB on the Stockert 70 RF Generator to the "Biosense Webster" option.
6. Purge catheter and tubing per standard technique.
7. Connect the irrigation input of the catheter to a 3-way stopcock through an extension tube set. Connect one of the remaining arms of the 3-way stopcock to an injector pump preset to the recommended flow rate and the other to a slower rate infusion pump preset to 2 ml/min. Open the 3-way stopcock to use the 2 ml/min. infusion to check the irrigation holes are patent.
8. Set the temperature cutoff limit to 50°C. Press MENU and select the TEMPERATURE menu, select 'cutoff' and adjust the cutoff temperature to 50°C using the SELECTOR KNOB.
9. Set the RF generator to *power control mode* by pressing the MANUAL button. Set the initial power level to 15-20 watts.
10. Start continuous irrigation with room temperature, heparinized saline (1 u heparin/ml) at a flow rate of 2 ml/min.
11. Increase the irrigation flow rate to 17 ml/min up to 5 seconds before the onset of RF energy delivery and maintain this higher flow rate until 5 seconds after termination of the energy application. If it is necessary to ablate with power levels 31-50 watts irrigation flow rate should be increased to 30 ml/min starting 5 seconds before onset and ending 5 seconds after RF energy delivery.
12. The application of RF energy must not be initiated until the increase in irrigation flow rate is confirmed by a 3-5°C decrease in tip electrode temperature.

13. If the temperature increases to 50° C during RF application, power delivery will be interrupted by the temperature cutoff. The irrigation system must be rechecked prior to restarting RF.
14. Insert the catheter via the entrance site, using an introducer sheath.
15. Advance the catheter to the area under investigation. Use both fluoroscopy and electrograms to aid in proper positioning.
16. 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.
17. When the ablation site is identified, turn the 3-way stopcock to use the injector pump and stand by while the voltage and power application time of the radiofrequency generator are set.
18. Turn the injector pump on. Watch the electrode tip temperature decrease.
19. When it has been determined that the tip electrode is in stable contact with the intended ablation site, the catheter tip electrode connection must be switched from the recording equipment to the radiofrequency generator in preparation for delivery of radiofrequency current. Verify that the CATHETER SELECTION KNOB on the Stockert 70 RF Generator is on the "Biosense Webster" option. Circuit impedance should be approximately 100 ohms upon initiation of radiofrequency current.
20. Monitor the temperature throughout the procedure. The peak temperature should be maintained at 50°C during RF energy delivery. Note: The displayed temperature represents the temperature of the electrode only, not the temperature of the tissue.
21. 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 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 will not exceed 120 seconds. Dragging the catheter to the next site is permissible during the 120 second energy application.
22. After radiofrequency current is discontinued, turn stopcock back to 2 ml/min. infusion pump.
23. Radiofrequency current may be re-applied to the same or alternate sites using the same catheter. However, in the event of a generator cutoff (impedance or temperature), the catheter must be withdrawn and the tip electrode cleaned of coagulum before radiofrequency current is re-applied. 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.

    If irrigation hole occlusion occurs:
    a. Remove the catheter from the patient.
    b. Fill a 1 or 2 ml syringe with sterile saline and attach to the sidearm.
    c. Carefully inject the saline from the syringe into the catheter. A stream of fluid should be visible from all six (6) holes.
    d. Repeat steps b and c, if necessary.
    e. If the holes are cleared, the catheter can be reintroduced into the patient.

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

24. If the RF generator does not display temperature, verify that the appropriate cable is plugged into the generator. If the generator still does not display temperature, there may be a malfunction in the temperature sensing system. Correct this malfunction prior to reapplying RF energy.
25. If preset temperature or impedance levels are exceeded during operation, design safety features of the RF generator cause the RF energy to stop. A likely cause of this may be accumulated coagulum on the tip electrode. Withdraw the catheter and examine the tip electrode. If coagulum accumulation is present, clean the tip electrode by gently wiping with a sterile gauze pad dampened with sterile saline. Use caution to not twist the tip electrode relative to the catheter shaft during cleaning because this may damage the tip electrode bond and loosen the tip electrode.

DISCLAIMER OF WARRANTY AND LIMITATION OF LIABILITY

THERE IS NO EXPRESS OR IMPLIED WARRANTY, INCLUDING WITHOUT LIMITATION ANY IMPLIED WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE, ON THE PRODUCT(S) DESCRIBED HEREIN. UNDER NO CIRCUMSTANCES SHALL BIOSENSE WEBSTER, INC., OR ITS AFFILIATED COMPANIES, BE LIABLE FOR ANY SPECIAL, DIRECT, INCIDENTAL, CONSEQUENTIAL, OR OTHER DAMAGES OTHER THAN AS EXPRESSLY PROVIDED BY SPECIFIC LAW.

WITHOUT LIMITING THE FOREGOING, BIOSENSE WEBSTER, INC., OR ITS AFFILIATED COMPANIES, SHALL NOT BE LIABLE FOR ANY SPECIAL, DIRECT, INCIDENTAL, CONSEQUENTIAL, OR OTHER DAMAGES, ARISING OUT OF THE REUSE OF ANY OF ITS PRODUCT(S) LABELED FOR SINGLE USE OR WHERE REUSE IS PROHIBITED BY APPLICABLE LAW.

Biosense Webster, Inc.
3333 Diamond Canyon Road
Diamond Bar, CA 91765, USA
Customer Service: 909-839-8500
Telephone: 800-729-9010 (US only)
Fax: 909-468-2905

The NAVISTAR™ THERMOCOOL™ Diagnostic/Ablation Catheter and accessories are protected under one or more of the following U.S. Patent Nos.: 5, 827, 278; 5,6, 171, 277, and other patents pending in the U.S. and other countries.

NAVISTAR, CARTO, and CELSIUS are Trademarks of Biosense Webster, Inc.

Tyvek is a Registered Trademark of DuPont.