SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Names:

Contact Force Irrigated RF Ablation Catheter

Contact Force Visualization Equipment and Accessories

Device Trade Names:

TactiCath™ Quartz Contact Force Ablation Catheter

TactiSys™ Quartz Equipment Composed of:

- TactiSys™ Quartz Unit
- TactiSoft™ Software
- TactiSys™ Quartz RF Cable
- TactiSys™ Quartz Ethernet Cable
- Equipotential Cable
- Mains Cord and Adapter

Optional Accessories:

- TactiSys™ Quartz Mount
- TactiSys™ Analog Output Cable
- TactiSys™ Quartz Integration Module

Device Product Code:

OAE

Applicant's Name and Address:

St. Jude Medical
One St. Jude Medical Drive
St. Paul, MN 55117

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P130026

Date of FDA Notice of Approval: 10/24/2014

Priority Review: Not Applicable

II. INDICATIONS FOR USE

The TactiCath™ Quartz Contact Force Ablation Catheter is indicated for use in cardiac electrophysiological mapping and for the treatment of drug refractory recurrent

symptomatic paroxysmal atrial fibrillation, when used in conjunction with a compatible radiofrequency generator and three-dimensional mapping system.

TactiSys™ Quartz Equipment and accessories are indicated for use in conjunction with a TactiCath™ Quartz Contact Force Ablation Catheter. TactiSys™ Quartz Equipment allows the visualization of the force information coming from the catheter tip.

III. CONTRAINDICATIONS

The TactiCath™ Quartz Contact Force Ablation Catheter is contraindicated for:

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

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the TactiCath™ Quartz Contact Force Ablation Catheter Instructions for Use (IFU), and the TactiSys™ Quartz Equipment User Manual.

V. DEVICE DESCRIPTION

The TactiCath™ Quartz Set is comprised of the following components:

- **TactiCath™ Quartz Contact Force Ablation Catheter:** A sterile, 7F steerable, open irrigated radiofrequency (RF) ablation multi-electrode catheter with a deflectable tip incorporating a force sensor and a thermocouple temperature sensor. The catheter is designed to facilitate electrophysiology mapping of the heart chambers and to transmit RF current to the catheter tip electrode for intracardial ablation. The deflectable distal section of the catheter shaft includes four platinum-iridium electrodes (three ring electrodes and one tip electrode) and is available in 65 mm or 75 mm length, with a total useable length of 115 cm. At the proximal end of the catheter, a saline port is used to deliver isotonic saline solution to irrigate and cool the tip electrode and ablation site,

through the 0.7 mm diameter catheter lumen and the six small holes on the distal electrode tip. The catheter features a tri-axial optical force sensor embedded in the tip section which transmits contact force information to the TactiSys™ Quartz Equipment.

- **TactiSys™ Quartz Equipment:** The contact force visualization equipment is composed of the TactiSys™ Quartz unit (hardware and associated cables) and TactiSoft™ (stand-alone software). The TactiSys™ Quartz unit is a non-sterile active signal and data processing unit that interconnects the TactiCath™ Quartz catheter to an external RF generator, and collects data from the catheter to compute contact force and related information transmitted from the catheter. The optical measurement system, which is compatible with the force sensing technology incorporated in the TactiCath™ Quartz catheter, is composed of three optical sensor analyzer modules. The TactiSoft™ software displays the contact force information transmitted from the catheter through an Ethernet connection on a dedicated, properly configured computer.

The following devices are required in addition to the TactiCath™ Quartz Set to perform catheter ablation procedures:

- RF generator and related disposable grounding pad (dispersive pad)
- Irrigation pump
- Electrophysiology recording system
- Dedicated Personal Computer with display screen provided by Endosense to run TactiSoft™ software.

Optional accessories include: choice of RF cable, Ethernet cables available in different lengths, an analog output cable, a mount and an integration module (Ethernet - switch) that will allow the integration of contact force information with third party equipment (e.g. integration in the screen of 3D mapping system for enhanced electrophysiology laboratory set-up).

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Alternative therapy for symptomatic paroxysmal atrial fibrillation includes the following:

- Commercially available PMA-approved devices
- Pharmacological therapy for rate and/or rhythm control
- Electrical or pharmacologic cardioversion
- Surgical intervention to create atrial lesions
- Implantable devices to control heart rate

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

VII. MARKETING HISTORY

The TactiCath™ Quartz Set is currently marketed outside the United States in Europe, Australia, and New Zealand.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

The following adverse events have been documented for catheter ablation procedures:

- Air embolism
- Anesthesia reaction
- Aorto-right atrial fistula
- Arrhythmias; bradycardia and tachycardia
- Atrio-Ventricular fistula
- Cardiac perforation/tamponade
- Cardiac thromboembolism
- Cerebrovascular incident or Attack / Stroke
- Chest pain/discomfort
- Coronary artery dissection
- Coronary artery spasm
- Coronary artery thrombosis / occlusion
- Death
- Diaphragmatic paralysis
- Dislodgement of implantable cardioverter defibrillator or permanent pacing leads
- Endocarditis
- Gastroparesis
- Heart failure / pump failure
- Hemothorax
- Hospitalization (initial and prolonged)
- Increased creatinine phosphokinase (CPK) level
- Infections
- Laceration
- Leakage of air or blood into the lungs or other organs due to perforation
- Left atrial esophageal fistula
- Major bleeding, requiring surgery or transfusion
- Myocardial infarction
- Obstruction or perforation or damage to the vascular system
- Pericarditis
- Pericardial effusion
- Phrenic nerve damage including diaphragmatic paralysis
- Pleural effusion
- Pneumonia
- Pneumothorax
- Pseudoaneurysm
- Pulmonary edema
- Pulmonary embolism
- Pulmonary vein dissection
- Pulmonary vein thrombus
- Pulmonary hypertension
- Respiratory depression
- Skin burns
- Severe pulmonary vein (PV) stenosis (>70%), or complete occlusion of a PV, even in the absence of symptoms
- Tamponade, potentially requiring surgery
- Temperature elevation or fever
- Transient Ischemic Attack (TIA)
- Thromboembolism
- Thrombosis
- Unintended complete or incomplete Atrioventricular (AV), Sinus node, or other heart block or damage
- Valvular damage
- Vascular bleeding / local hematomas / ecchymosis
- Vasovagal reactions
- Ventricular tachyarrhythmia
- Volume overload

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

IX. SUMMARY OF PRECLINICAL STUDIES

Pre-clinical testing of the TactiCath™ Quartz Contact Force Ablation Catheter and TactiSys™ Quartz Equipment included verification and validation testing (catheter testing and hardware/software testing), biocompatibility, shelf life testing, and animal studies. Performance testing was conducted to demonstrate design integrity. All tests performed which were identified in standards or guidance documents were based on the product specification requirements. In the tests described below, the catheters were manufactured by trained manufacturing operators. "Pass" as used below denotes that the devices and system met established product specifications and/or performance criteria, or were in conformance with the requirements of the standards identified. Testing results confirmed that the catheters meet product specifications.

A. Laboratory Studies

In Vitro Bench Studies – TactiCath™ Quartz Catheter

In-vitro bench testing was conducted to ensure the TactiCath™ Quartz catheter met product requirements and applicable standards. **Table 1** summarizes the bench testing for the catheters including mechanical and electrical integrity, and performance test results.

Table 1: TactiCath™ Quartz Catheter Bench Testing Results Summary

	Test Description	Acceptance Criteria	Result
Mechanical Performance	Steering, planarity, handle, pullwire force	Length of bend within specification Maximal / minimal angles of bend within specifications Radius of curvature at maximum bending within specification Steering section maintaining its position when the pull force is released Steered tip planarity when the catheter is fully steered Steering force over 150 cycles within specification	Pass
	Kink, stiffness, tip side force, hook force	No kink, no fracture, no visible peeling of catheter shaft Distal tip side force within specification Hook force within specification Stiffness on non-steering section of catheter within specification	Pass
	External cable torsion resistance	No kinks or breaks of external cables. Catheter fully functional after several full rotations of cables	Pass
	External cable tension resistance	Catheter fully functional under tensile force	Pass
	Shaft torsion and buckling	No kinks or breaks after 360° rotation of distal part of catheter Buckling force within specification	Pass

	Test Description	Acceptance Criteria	Result
	Force sensor mechanical integrity after high forces	No catheter part separation when extreme axial or lateral force applied	Pass
	Introducer extraction tests and force at break	Pullwire force resistance within specification No loose part when extracting steered or unsteered catheter through introducer Forces at break ≥ 15N for each catheter section (per ISO 10555-1 standard)	Pass
	Corrosion resistance	No corrosion after 48h of soaking, per ISO-10555-1 standard, Annex A	Pass
	Catheter removal from blister	No loose parts or detectable damage to catheter or force sensor when catheter removed from blister	Pass
Force Sensor Performance	Humidity drift	Force sensing drift due to humidity within specification	Pass
	Force sensor repeatability	Standard deviations of Delta force within specifications	Pass
	Force sensor accuracy	Delta force between measured Total force and reference force within specifications Delta angle α between measured and reference angle within specifications Delta angle θ between measured and reference angle within specifications	Pass
	Scale measurement of force	Return to zero of Total force after application of high forces within specifications	Pass
	Force reading sensitivity	Force reading standard deviation within specification	Pass
	Sensitivity to steering mechanism	Average value of delta Total force within specification	Pass
	Sensitivity to cable manipulation	Total force variations during cable manipulation within specification	Pass
	Distal tip thermocouple accuracy	Difference between measurement and reference within specification	Pass
	Force sensor temperature reading	Difference between reference temperature and force sensor thermocouple within specification	Pass
	Plug cold junction temperature reading	Difference between reference temperature and thermistor temperature within specification	Pass
	Drift during ablation	Means of the absolute value of the “Force total” drift during ablation within specifications	Pass
	Fatigue and high forces test	Force sensor fully functional after 200 cycles of axial and lateral force applied Return to zero of Total force within specifications	Pass

	Test Description	Acceptance Criteria	Result
	Trackability - Tortuous path	Catheter fully functional, including force sensor, after navigation in tortuous path Electrical insulation/resistance measurements within specifications	Pass
	Operating temperature range and temperature compensated range	Force total drift of the force sensor in the limit conditions	Pass
	Transversal force effect	Accuracy of the force sensor and plot of the transversal force effect	Pass
	Heart beating simulation	Test the force sensor with a variable force applied on the tip in the axial direction and lateral direction	Pass
	Repeatability and reproducibility	Test the repeatability and the reproducibility of the calibration method and the inspection method with 3 catheters and 3 operators	Pass
Functional Performance	Sheath introduction test	Catheter fully functional, including force sensor, after passing 10 times back and forth through St Jude SL1 8.5F introducer	Pass
	Irrigation test	Catheter and Luer free from leakage Tight and firm Luer connection Pressure drop for different flow rates within specifications	Pass
	Kink Simulation	No kink of irrigation tube in hard conditions Pressure drop for different flow rates within specifications	Pass
	Joint Seal Leakage	Catheter shall be free from leakage per ISO 10555-1 standard	Pass
Electrical Performance	Electrical test	Measurements of electrical insulation between all electrodes, thermocouples and memory in wet condition within specifications Measurements of electrical resistance of all electrodes within specifications	Pass
Compatibility with external devices	Electrical Connector Separation Force	Axial force necessary to disconnect the electrical connector from the TactiSys Quartz within specifications	Pass
	RF Generator Compatibility	Power deviation for different ablation powers and load resistances within specifications	Pass

In Vitro Bench Testing – TactiSys™ Quartz Equipment (Hardware & Software)

The TactiCath™ Quartz Set was evaluated in accordance with internationally recognized standards for electrical safety and electromagnetic compatibility. External third party agency testing was completed to ensure all applicable IEC 60601-1 and applicable collateral and particular standards requirements were

met. Passing results were concluded for testing conducted to IEC 60601-1, IEC 60601-1-2, IEC 60601-2-2, and IEC 62366.

Biocompatibility Testing

The TactiCath™ Quartz catheter biocompatibility testing was conducted in accordance with ISO 10993-1 for external communicating devices in contact with circulating bloods for less than 24 hours. Biocompatibility testing was performed in accordance with applicable parts of ISO 10993-1 and establishes biocompatibility and material safety of the proposed device. The biocompatibility results are summarized in **Table 2**.

Table 2: Biocompatibility Testing Summary

Biological Test/Method	Result
Cytotoxicity – MEM Elution Assay (ISO 10993-5)	Pass
Sensitization – Guinea Pig Maximization (ISO 10993-10)	Pass
Intracutaneous Reactivity – Rabbit (ISO 10993-10)	Pass
Acute Systemic Toxicity – Mouse Systemic Injection (ISO 10993-11)	Pass
Pyrogenicity – Material Mediated Rabbit Pyrogen (ISO 10993-11)	Pass
Haemocompatibility – Blood Compatibility Test for Hemolysis (ISO 10993-4)	Pass
Haemocompatibility – Complement Activation (ISO 10993-4)	Pass
Thrombogenicity – Porcine (ISO 10993-4)	Pass

Patient contacting materials of the TactiCath™ Quartz catheter are provided in **Table 3**.

Table 3. List of Patient Contact Materials and Components

Description	Material	Patient Contact
Tip and ring Electrodes	Platinum-iridium	Direct contact
Outer shaft	Polyether block amide Polyurethane elastomer	Direct contact
Strain relief	Silicone elastomer	Direct contact
Adhesives	Cyanoacrylate ester	Direct contact
	Acrylate urethane	Direct and indirect contact
	Loctite epoxy	Indirect contact
Irrigation tubing	Inox 316L Polyimide	Indirect contact
Female luer lock	Methyl Methacrylate Acrylonitrile Butadiene Styrene (MABS)	Indirect contact
Single lumen	Polyether block amide	Indirect contact
Tip o-ring	Clear silicone	Indirect contact

B. Animal Studies

Acute *in vivo* animal testing was conducted using the TactiCath™ Set to demonstrate safety and acute effectiveness in a setting that simulated a clinical ablation procedure. The animal study was conducted on a total of 8 animals (4 Yorkshire pigs and 4 Mongrel dogs). Applied contact force and tip temperatures at pre- and post-ablations, RF power, time and heart sites were recorded. Testing demonstrated that the catheters successfully delivered RF energy to target endocardial locations. The overall device performance from a gross pathological perspective was characteristic of cardiac ablation. No safety issues related to the device were recorded. All animals survived the procedures without any significant adverse events such as cardiac tamponade, respiratory distress, or uncontrollable bleeding. One animal experienced a pericardial effusion, which was interpreted as related to the procedure and not related to the investigational device.

Out of 183 ablations, 9 (4.9%) steam pops (4 audible pops and 3 impedance pops during procedure, and 2 through histology) were observed during and after ablation procedure. Eight (8) pops occurred with energy set at 50W while and one (1) pop occurred with energy set at 30W. During ablation, the median contact force was 20 grams, ranging between 4 and 74 grams.

C. Other Studies

Sterilization

The TactiCath™ Quartz catheter is supplied sterile. The catheters are sterilized using ethylene oxide (EO) gas to a sterility assurance level (SAL) of 10^{-6}. The sterilization process was validated according to ISO 11135-1. Catheters meet the ISO allowable limits for EO/ECH gas residuals as set forth in ISO 10993-7. Catheters are routinely tested for pyrogens of non-material mediated origin and meet the USP criteria for devices in contact with blood. The catheters are single use only.

Packaging, and Shelf Life

The TactiCath™ Quartz catheter is packaged in a coiled configuration, within a blister tray sealed with a Tyvek Lid. The sealed tray is packaged in a heat sealed pouch, which is then packaged in a rectangular cardboard box. The catheter has been validated for a two year shelf life. The catheters are labeled with the appropriate shelf life. **Table 4** provides a summary of testing conducted to support the shelf life and packaging.

Table 4. TactiCath™ Quartz Catheter Shelf Life and Packaging Testing

Test	Method	Acceptance Criteria	Result
Packaging Stability Testing	ISO 11607-1: 2006 ISO 11607-2: 2006	• Packaging integrity after: o Dye penetration test o Burst test on blister o Seal strength test on blister o Seal strength test on pouch • Sterility: The sterile barrier system shall maintain sterile • Labels: remains legible, no smearing ink, adherence to the support, no deterioration • Manual peel-off force (lid and pouch): o Packaging easy to open o Peel-off – Adhesive o No material torn	Pass
Device Stability Testing	ASTM F1980-07	• Functionality and sterility of packaged catheter after sterilization and aging: o No catheter degradation o No interaction with packaging which could adversely affect the device o No degradation of catheter integrity: assembly tip and deformable body	Pass
Pre-shipment transport testing	ISTA 2A	Functionality and sterility of packaged catheter after simulated shipping testing	Pass

X. SUMMARY OF PRIMARY CLINICAL STUDY

A clinical study named TOCCASTAR was performed to establish a reasonable assurance of safety and effectiveness of the TactiCath™ Set to treat drug refractory recurrent symptomatic paroxysmal atrial fibrillation when compared with an approved control device in the US and outside of the US under IDE G100230. The clinical study was conducted on the TactiCath™ Set. The TactiCath Quartz Set is a product evolution relative to the original TactiCath Set, with minor changes to the irrigated RF ablation catheter and enhancements to the graphical user interface designed to enhance reliability and manufacturability. The indications for use and functionalities remain unchanged, as does the catheter basic design. The TactiCath™ Quartz Set, was evaluated through bench testing and a supplemental clinical study. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is provided below.

A. Study Design

The TOCCASTAR clinical study was a prospective, randomized, multicenter, interventional clinical investigation conducted at 17 investigational sites (10 in the US and 7 outside of the US). The study was conducted on patients 18 or older.

Subjects were enrolled between January 11, 2011 and June 4, 2012. A total of 317 patients were enrolled in the study. Twelve month follow-up was completed on the last randomized patient June 25, 2013.

B. Clinical Endpoints

Primary Effectiveness
The primary effectiveness endpoint was a noninferiority comparison of treatment success between the TactiCath™ Set and the control device.

Acute success was defined as electrical isolation of all 4 PVs, or in the event of a common PV, the clinical equivalent of all PVs by the end of the index procedure.

Chronic success was defined as acute procedural success and freedom from recurrence of symptomatic paroxysmal atrial fibrillation (PAF), arial flutter (AFL), and atrial tachycardia (AT) lasting longer than 30 seconds through 9 months of follow-up after a 3 month blanking period. Reablation for AF occurring 80 or more days after the index procedure or the use of class I or class III AADs after the 3-month follow-up constitutes treatment failure.

Secondary Effectiveness
The secondary effectiveness endpoints were related to the use of the contact force sensor and assess the procedural effectiveness superiority of the

TactiCath™ Set over the control device by use of a hierarchical closed test procedure.

Primary Safety

The primary safety endpoint was a noninferiority comparison of device-related early-onset primary serious adverse events (SAEs) between the TactiCath™ Set and the control device occurring within 7 days of the index procedure or hospital discharge, whichever was later, and diagnosed at any time during the follow-up period.

Primary SAEs that met the severity criteria described in **Table 5** contributed to the primary safety endpoint only in subjects in whom a study device (TactiCath or control) was introduced. Hospitalizations solely for arrhythmia recurrence (without coexisting conditions such as thromboembolism, worsening heart failure, etc.) were not considered primary SAEs.

Table 5. Primary Serious Adverse Events and Severity Criteria

Primary SAE	**Severity criteria**
Atrial perforation	Visible (either with radiographic and/or ultrasonagraphic imaging and/or direct visualization) movement of ablation catheter, needle or sheath through the atrial wall as evidenced by bleeding and the need for pericardial drainage or surgical intervention
AV block	New, persistent 2nd or 3rd degree atrioventricular (AV) block not attributable to a vasovagal reaction or medication effect and requiring permanent pacing
Death	Adverse event resulting in subject death
Diaphragmatic paralysis	Change in baseline diaphragmatic function as evidenced by elevation of a hemidiaphragm above its normal position or loss of normal respiratory excursion but not due to a pulmonary process such as atelectasis and persisting longer than the end of the procedure
Gastroparesis	Gastroparesis as a result of ablation requiring intervention or hospitalization
Hospitalization (initial or prolonged)	Adverse event leading to new hospital admission or extension of initial hospital stay beyond expected timeframe due to ablation procedure-related cause. Excludes hospitalization solely for arrhythmia recurrence.
Left atrial esophageal fistula	Creation of a direct communication (fistula) between the left atrium and esophagus necessitating surgical intervention or resulting in permanent impairment (eg, due to hemorrhage or septic emboli)
Myocardial infarction	Requires 2 of the following 3 criteria: • Elevation of biochemical markers of myocardial necrosis (preferably troponin levels) • Ischemic symptoms • Development of pathologic Q waves on the electrocardiography (ECG) or persistent ECG changes indicative of ischemia (ST segment elevation or depression)
Pericarditis	Pleuritic chest discomfort associated with either pericardial rub and/or ECG changes that requires or prolongs hospitalization

Primary SAE	Severity criteria
Pneumothorax	Identification of air in the pleural space which either prolongs hospital stay (for observation) or requires surgical intervention or chest tube placement
Pulmonary edema	Pulmonary alveolar fluid accumulation accompanied by typical symptoms (dyspnea), physical findings (rales, hypoxemia), radiologic findings, and response to diuretic therapy and requiring hospitalization
PV stenosis	Severe (≥70%), or complete occlusion of a PV, even in the absence of symptoms
Stroke	Brain disorder involving loss of brain functions (that persists for >24 hours) that occurs when the blood supply to any part of the brain is interrupted as determined by the consulting neurologist
Tamponade	Pericardial effusion of sufficient size to cause hemodynamic compromise and requiring drainage based on hypotension, echocardiographic findings, or other clinical factors
Thromboembolism	Deep vein thrombosis or pulmonary embolism
Transient ischemic attack	Acute episode of temporary (<24 hrs.) and focal loss of cerebral function of vascular (occlusive) origin as determined by the consulting neurologist
Vascular access complications	Vascular access complication requiring surgical repair, blood transfusion (eg, groin hematoma, AV fistula) or significant intervention such as thrombin injection (eg, pseudoaneurysm)

Secondary Safety

The secondary safety endpoint was to evaluate the incidence of all SAEs during the 12-month follow-up period.

C. Statistical Analysis

Analysis Populations

The following populations were analyzed for this study:

- Full analysis (FA): The FA population includes all randomized subjects.
- Safety (SAF): The SAF population includes all randomized subjects in whom a study device was introduced.
- Modified intent-to-treat (mITT): The mITT population includes all randomized subjects in whom a study device was introduced and PVI was attempted.
- Per-protocol (PP): The PP population includes all subjects in the mITT population who did not have major protocol deviations that would have compromised the effectiveness or safety evaluation of the study device.
- Roll-in population: Subjects recruited into the roll-in subject population – these subjects were not randomized but were followed for safety. Their data were summarized separately and were also included in the listings.
- Supplemental clinical study: Subjects treated with the TactiCath Quartz Set were not randomized and are reported separately.
- Extended follow-up data: Subject data provided after the end of the required 12-month follow-up period.

Sample Size Calculation

The treatment success rate and the incidence of primary SAEs within 7 days of the index procedure for the TOCCASTAR study was based on data from previous pivotal and feasibility studies in similar populations to estimate event rates.

Sample size was calculated based on the estimated treatment success rate and the incidence of primary SAEs. Let Pt denote the percent of treatment success or the incidence of primary SAEs in the TactiCath arm and Pc denote the corresponding rate in the control arm. Under these assumptions, a total of 274 subjects (137 subjects per treatment arm) would provide 80% power to reject the null hypothesis that (Pt - Pc <-0.15) with a one-sided 0.05 significance level for the primary effectiveness endpoint. A total of 274 subjects (137 subjects per treatment arm) would provide 83% power to reject the null hypothesis that (Pt - Pc >0.09) with a one-sided 0.05 significance level for the primary safety endpoint. We further assumed that approximately 10% of the randomized subjects would be excluded from the denominator due to early terminations unrelated to a study device or excluded from the PP population due to major protocol violations. Therefore, the study was designed to include approximately 300 randomized subjects.

In order to prevent bias in the results due to different performance of a single site, no more than 15% of subjects were enrolled at any individual site.

Endpoint Performance Goals

Study success was achieved when the protocol-defined primary effectiveness endpoint and primary safety endpoint were met, demonstrating noninferiority of the TactiCath Set to the control.

Based on these estimates, a noninferiority margin of 15% for effectiveness (treatment success rate at the end of the 9-month effectiveness assessment follow-up period post blanking) and 9% for safety (incidence of primary SAEs with onset within 7 days of the index procedure or prior to hospital discharge and diagnosed throughout the study) were utilized in the TOCCASTAR study analyses.

Effectiveness Analyses

Primary effectiveness endpoint analysis

The one-sided 95% lower confidence limit (LCL) was calculated for the difference between the 2 treatment groups (Pt - Pc) based on the PP population. If the 95% LCL was ≥-15%, noninferiority was demonstrated in terms of effectiveness.

Secondary effectiveness endpoint analysis
For the 3 secondary effectiveness endpoints related to the use of the contact force sensor a superiority test was performed comparing the TactiCath Set to the control device using a hierarchical closed test procedure. It was hypothesized that the use of the contact force sensor information would result in added procedural effectiveness through a reduction in (1) the number of electrically reconnected PVs, (2) the time to achieve total pulmonary vein isolation (PVI), and (3) the total time of RF application. These endpoints were tested sequentially, in the order they appear above, using a one sided, $\alpha = 0.025$ test based on the PP population. Secondary endpoint (1) was tested using the Wilcoxon rank sum test; secondary endpoints (2) and (3) were tested using a log-rank test, stratified by site.

Safety Analyses

Primary safety endpoint analysis
For the primary safety endpoint analysis, the one-sided 95% upper confidence limit (UCL) was calculated using the normal approximation method for the difference between the 2 treatment arms (Pt - Pc) based on the SAF population. If the 95% UCL was ≤9%, noninferiority was demonstrated in terms of safety.

Secondary safety endpoint analysis
The secondary safety endpoint was the incidence of all SAEs during the 12-month follow-up period. All non-primary SAEs were assessed by the CEC for relationship to study device and relationship to study procedure. SAEs related to arrhythmia recurrence and those adjudicated as effectiveness endpoints were described separately.

D. External Evaluation Groups

Two independent governance committees were utilized for the study to ensure overall integrity of the study conduct and evaluation of study results.

Clinical Events Committee (CEC)
An independent, standing CEC consisting of members not otherwise associated with the study, reviewed all serious adverse events (SAEs) and the effectiveness endpoints and adjudicated causality relative to the primary safety endpoints. The CEC was blinded to subject treatment assignments. The CEC is comprised of physicians with experience in clinical study event adjudication, including at least 1 physician with expertise in electrophysiology.

Data Safety Monitoring Board (DSMB)
An independent DSMB comprised of members not otherwise associated with the study was convened to review the proposed research protocol and plans for data and safety monitoring and oversight prior to the start of the study. Thereafter, the DSMB met biannually to provide assessment of the overall study safety and

advise the sponsor on the continuation of the study. The DSMB members include 3 experts in clinical electrophysiology and ablation as voting members as well as a qualified statistician and medical monitor as nonvoting members.

Core Laboratories
Three core labs were utilized during the study to evaluate and assess the transtelophonic event monitor (TTM) tracings, 24-hour Holter, and selected computed tomography (CT)/magnetic resonance imaging (MRI) scans.

E. Study Design Discussion

Subjects undergoing elective catheter radio frequency (RF) ablation for symptomatic PAF who were refractory or intolerant to at least 1 anti-arrhythmic drug (AAD; class I-IV) were screened for enrollment. Subjects who met the study entry criteria and signed the informed consent form (ICF) were enrolled and treated in accordance with the 2007 HRS/EHRA/ECAS Expert Consensus Statement on Catheter and Surgical Ablation for Atrial Fibrillation.

Eligible subjects were randomly assigned 1:1 to receive ablation treatment with either the TactiCath Set or the control device. Use of 3-dimensional (3D) mapping equipment was required for both treatment arms. Subjects were blinded to treatment assignment.

After the index procedure, subjects were followed for a total of 12 months for chronic effectiveness assessment, beginning with a 3-month blanking period and ending with a 9-month effectiveness assessment period. During the blanking period, subjects were permitted to be prescribed an AAD and undergo up to 2 reablation procedures (no later than 10 days before the end of the blanking period) using the same device specified by the initial randomization. Subjects were evaluated before discharge; at 7 days; and at 3, 6, and 12 months after the index procedure for the primary study endpoint. After completion of the 12-month visit, subjects continue to be evaluated every 6 months under the current investigational device exemption (IDE) protocol until FDA approval of the Premarket Approval (PMA) application.

Clinical Inclusion and Exclusion Criteria
Enrollment in the TOCCASTAR study was limited to patients who met the following inclusion criteria:

- A catheter ablation procedure was planned due to symptomatic paroxysmal atrial fibrillation (PAF) that was refractory or intolerant to at least 1 class I-IV AAD
- Minimum of 1 episode of PAF greater than 30 seconds in duration within 12 months prior to enrollment documented by 12-lead ECG, Holter monitor, TTM, telemetry strip, or implanted device
- Minimum of 3 episodes of PAF within the preceding 12 months documented by subject history
- Age 18 years or older

- Willing and capable of complying unassisted with the study protocol requirements, including all specified follow-up visits
- Provided written informed consent prior to enrollment in the study

Subjects were not permitted enrollment in the TOCCASTAR study if they met any of the following exclusion criteria:

- Persistent or long-standing persistent atrial fibrillation (AF)
- Four or more cardioversions in the last 12 months
- Active systemic infection
- Presence of implantable cardiac defibrillator (ICD)
- Arrhythmia due to reversible causes including thyroid disorders, acute alcohol intoxication, and other major surgical procedures in the preceding 3 months
- Myocardial infarction (MI), acute coronary syndrome, percutaneous coronary intervention (PCI), or valve or coronary bypass grafting surgery within the preceding 3 months
- Left atrial diameter >5.0 cm
- Left ventricular ejection fraction <35%
- New York Heart Association (NYHA) class III or IV (Appendix G of the protocol)
- Previous left atrial ablation procedure, either surgical or catheter ablation
- Previous left atrial surgical procedure or incision with resulting scar
- Previous tricuspid or mitral valve replacement or repair
- Heart disease in which corrective surgery was anticipated within 12 months
- Bleeding diathesis or suspected procoagulant state
- Contraindication to long-term antithromboembolic therapy
- Presence of condition that precluded appropriate vascular access
- Renal failure requiring dialysis
- Known sensitivity to contrast media (if needed during the procedure) not controlled with premedication
- Contraindication to CT and MRI procedures
- Severe pulmonary disease (eg, restrictive pulmonary disease, constrictive or chronic obstructive pulmonary disease) or any other disease or malfunction of the lungs or respiratory system that produces severe chronic symptoms
- Positive pregnancy test results for female subject of childbearing potential
- Other anatomic or comorbid conditions that, in the investigator's opinion, limited the subject's ability to participate in the study or to comply with follow-up requirements, or impacted the scientific soundness of the study results
- Currently participating in another clinical study or had participated in a clinical study within 30 days prior to screening that could have interfered with this study
- Unlikely to survive the protocol follow-up period of 12 months

Treatment Procedure and Follow-up Schedule

Table 6 lists the protocol-required baseline, procedural, and follow-up assessments for all subjects.

Table 6. Schedule of Required Assessments

Assessment	Baseline	Procedure	Predischarge	7 days ±2 days Telephone	3 months ±2 weeks	6 months ±3 weeks	12 months ±3 weeks	Extended every 6 mos ±4 weeks
Informed consent	X							
Inclusion/exclusion criteria review	X							
Documentation of PAF episodes	X							
Medical history	X							
Thyroid and renal function (standard practice)	X							
PT/PTT or INR	X		X					
Physical examination, vital signs, height, weight[1]	X		X		X	X	X	
Pregnancy test (women of childbearing potential)	X							
12-lead ECG	X		X		X	X	X	
Cardiac medications	X		X	X	X	X	X	
NYHA functional class	X				X	X	X	
Quality of life survey	X						X	X
Randomization	X							
Activated clotting time		X						
Ablation procedure data		X						
Force sensing data (TactiCath arm only)		X						
Arrhythmia events	X		X	X	X	X	X	
Adverse events		X	X	X	X	X	X	X[6]
Protocol deviation	X	X	X	X	X	X	X	
TEE (ICE)[2]	X	(X)						
TTE (recommended)[3]	X		(X)					
CT or MRI scan[4]	X				X			
Transtelephonic monitoring[5]					X	X	X	
Holter monitoring							X	
Arrhythmia history								X

Abbreviations: CT, computed tomography; ECG, electrocardiogram; ICE, intracardiac echocardiography; INR, international normalized ratio; MRI, magnetic resonance imaging; NYHA, New York Heart Association; PAF, paroxysmal atrial fibrillation; PT, prothrombin time; PTT, partial thromboplastin time; TEE, transesophageal echocardiography; TTE, transthoracic echocardiography; TTM, transtelephonic monitoring.

[1] Weight and height were assessed at baseline only.

[2] TEE within 24 hours or ICE at time of procedure to exclude atrial thrombus.

[3] TTE within 6 months to measure left atrial dimension. Recommended within 24 hours post procedure to exclude pericardial effusion.

[4] Not required for supplemental study subjects. If evidence of stenosis was seen at 3 months, the investigator may have prescribed additional serial scans.

[5] TTMs were required weekly for months 4 and 5, monthly for months 6-12, and as needed to document symptomatic episodes.

[6] Survival and hospitalizations only.

F. Accountability of PMA Cohort

The study was initiated on 11 January 2011 at 10 United States (US) and 7 international sites with a total of 317 subjects enrolled, of which 300 were randomized. Subjects were followed for 12 months after the index ablation procedure. The last subject's 12-month visit was completed on 25 June 2013. The database lock date for this report was 02 August 2013. **Table 7** provides a summary of the subject disposition for the study.

Table 7. Subject Accountability and Disposition

Subject Accountability	TactiCath	Control	Total
Subjects enrolled in study	172	145	317
Subjects in Roll-in population	17	NA	17
Full Analysis Population-all subjects randomized (FA)	155	145	300
Subjects who had no study device introduced	3	2	5
Safety Analysis Population (SAF)	152	143	295
Subjects who did not have PVI attempted	3	2	5
Modified Intent-to-treat Population (mITT)	149	141	290
Subjects excluded from analysis due to major protocol deviation	3	7	10
Per Protocol Population (PP)	146	134	280

G. Study Population Demographics and Baseline Parameters

Tables 8 and 9 below summarize the demographic information. Subjects were randomized 1:1 upon signing the informed consent.

Table 8. Subject Demographics (SAF Population)

Demographic		**TactiCath N=152**	**Control N=143**	**Total N=295**
Age, years		59.6 (9.32) 61.0 [53.0, 66.0] 31, 78	61.0 (10.84) 62.0 [53.0, 68.0] 28, 82	60.3 (10.09) 61.0 [53.0, 67.0] 28, 82
Sex, male		100 (65.8%)	91 (63.6%)	191 (64.7%)
Race	American Indian or Alaska Native	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Asian	1 (0.7%)	0 (0.0%)	1 (0.3%)
	Black	1 (0.7%)	0 (0.0%)	1 (0.3%)
	Native Hawaiian or Pacific Islander	0 (0.0%)	0 (0.0%)	0 (0.0%)

Demographic		TactiCath N=152	Control N=143	Total N=295
	White	148 (97.4%)	141 (98.6%)	289 (98.0%)
	Other	2 (1.3%)	2 (1.4%)	4 (1.4%)
Ethnicity	Hispanic or Latino	3 (2.0%)	5 (3.5%)	8 (2.7%)
	Not Hispanic or Latino	149 (98.0%)	138 (96.5%)	287 (97.3%)
Height (cm)[a]		174.6 (10.55) 175.0 [167.0, 182.0] 152, 205	174.5 (9.87) 175.0 [167.0, 180.0] 137, 203	174.5 (10.21) 175.0 [167.0, 182.0] 137, 205
Weight (kg) [a]		86.70 (17.290) 86.70 [75.00, 98.00] 37.8, 133.8	85.35 (17.246) 84.00 [72.00, 96.00] 54.0, 148.8	86.04 (17.252) 85.15 [74.00, 97.50] 37.8, 148.8

Continuous variables are presented as mean (SD), median [IQR], min, max; categorical variables are presented as n (%).
[a] Height and weight were not reported for 1 TactiCath subject.

Table 9. Medical History (SAF Population)

Medical history	TactiCath N=152		Control N=143		Total N=295	
	All history	Currently active	All history	Currently active	All history	Currently active
Cardiovascular system	43 (28.3%)	31 (20.4%)	57 (39.9%)	44 (30.8%)	100 (33.9%)	75 (25.4%)
Head, eyes, ears, nose, throat	8 (5.3%)	4 (2.6%)	10 (7.0%)	5 (3.5%)	18 (6.1%)	9 (3.1%)
Respiratory system	31 (20.4%)	26 (17.1%)	16 (11.2%)	15 (10.5%)	47 (15.9%)	41 (13.9%)
Musculoskeletal system	29 (19.1%)	10 (6.6%)	27 (18.9%)	14 (9.8%)	56 (19.0%)	24 (8.1%)
Integumentary system	4 (2.6%)	2 (1.3%)	3 (2.1%)	1 (0.7%)	7 (2.4%)	3 (1.0%)
Gastrointestinal system	35 (23.0%)	16 (10.5%)	29 (20.3%)	17 (11.9%)	64 (21.7%)	33 (11.2%)
Genitourinary system	23 (15.1%)	7 (4.6%)	16 (11.2%)	4 (2.8%)	39 (13.2%)	11 (3.7%)
Nervous/ neurological system	7 (4.6%)	5 (3.3%)	3 (2.1%)	2 (1.4%)	10 (3.4%)	7 (2.4%)
Endocrine system	13 (8.6%)	9 (5.9%)	21 (14.7%)	13 (9.1%)	34 (11.5%)	22 (7.5%)
Lymphatic system	1 (0.7%)	0 (0.0%)	3 (2.1%)	1 (0.7%)	4 (1.4%)	1 (0.3%)
Immunological system	3 (2.0%)	2 (1.3%)	3 (2.1%)	2 (1.4%)	6 (2.0%)	4 (1.4%)
Psychiatric	6 (3.9%)	6 (3.9%)	3 (2.1%)	3 (2.1%)	9 (3.1%)	9 (3.1%)
Allergic conditions	2 (1.3%)	2 (1.3%)	2 (1.4%)	2 (1.4%)	4 (1.4%)	4 (1.4%)

Pediatric Patient Population

Atrial fibrillation (AF) is rare in pediatric populations. When observed, the pediatric patient usually has a genetic abnormality and/or disease state that causes enlargement of the heart. Due to the infrequency of AF in pediatric populations, targeting directly to AF is rarely indicated or necessary. Therefore, the TactiCath Quartz Contact Force Ablation Catheter was not studied in patients less than 18 years of age.

Lone AF is defined as occurring in patients with AF who are less than 60 years of age and do not suffer from other forms of cardiovascular disease or hypertension. Lone AF in younger patients is rare and constitutes less than 5% of all types of AF [1].

H. Procedural Data

Tables 10 and 11 below summarize the index procedural data and the TactiCath contact force results:

Table 10. Index Procedural Data (PP Population)

Index Procedure data	TactiCath N=146	Control N=134
Total fluoroscopy time (minutes)	30.5 (17.6) 4.0, 131.8	27.3 (17.4) 3.8, 105.0
Number of RF applications	59.7 (32.6) 13.0, 204.0	64.7 (42.9) 10.0, 241.0
Total RF time (seconds)	3103 (1699) 709, 8728	3435 (1493) 1036, 10135
Duration of ablation (seconds)	56 (29) 24, 190	74 (62) 14, 464
Power (Watts)[a]	28.8 (4.4) 19.3, 41.1	28.5 (4.6) 19.0, 41.0

Results are presented as mean (SD), min, max. Includes data from all lesions delivered.
[a] sample size for Power, : TactiCath (n=148), Control (n=133).

I. Safety and Effectiveness Results

Primary Effectiveness Results

The primary effectiveness endpoint success criterion was met, to demonstrate noninferiority of the TactiCath™ device compared to the control.

Table 11. Summary of Treatment Success: Primary Effectiveness Analysis (PP Population)

Endpoint	TactiCath N=146	Control N=134
Acute procedural success	146 (100%)	134 (100%)
Acute procedural failure	0 (0.0%)	0 (0.0%)
Chronic success	99 (67.8%)	93 (69.4%)
Chronic failure	47 (32.2%)	41 (30.6%)

Figure 1 below presents the plot for time-to-treatment failure for protocol-defined effectiveness for the PP population.

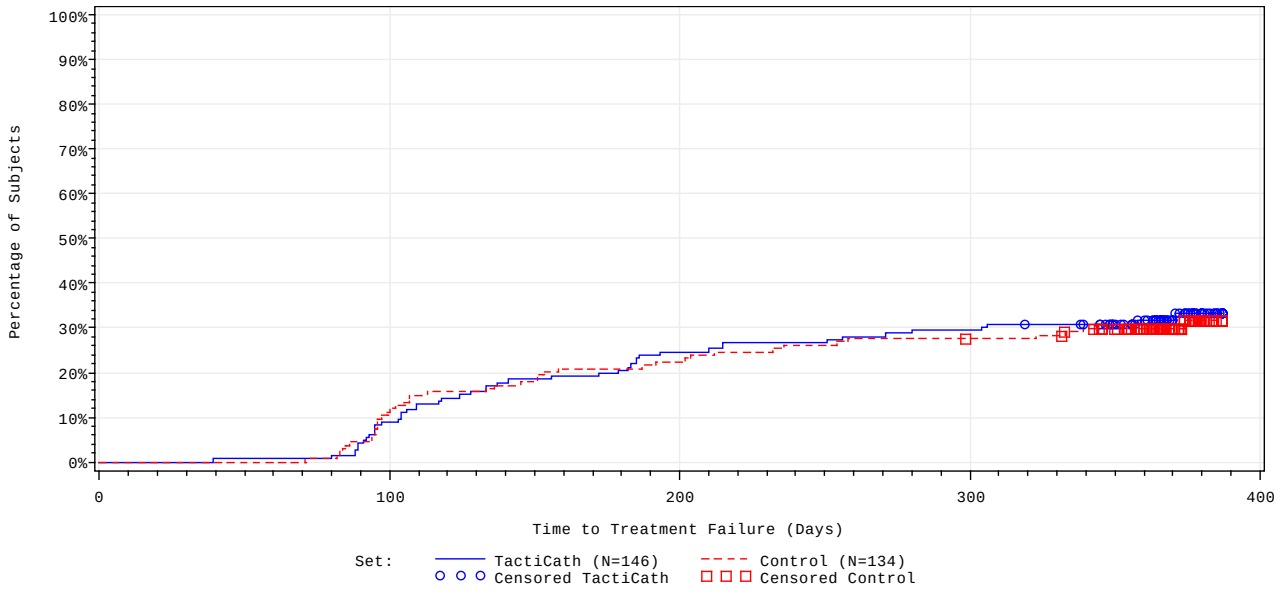

Figure 1. Kaplan-Meier Plot for Time-to-Treatment Failure (PP Population)

Figure 2 below presents the Kaplan-Meier plot for time-to-treatment failure due to the reablation procedure in the PP population. As shown, over time, more subjects in the control arm experienced reablation than in the TactiCath™ arm.

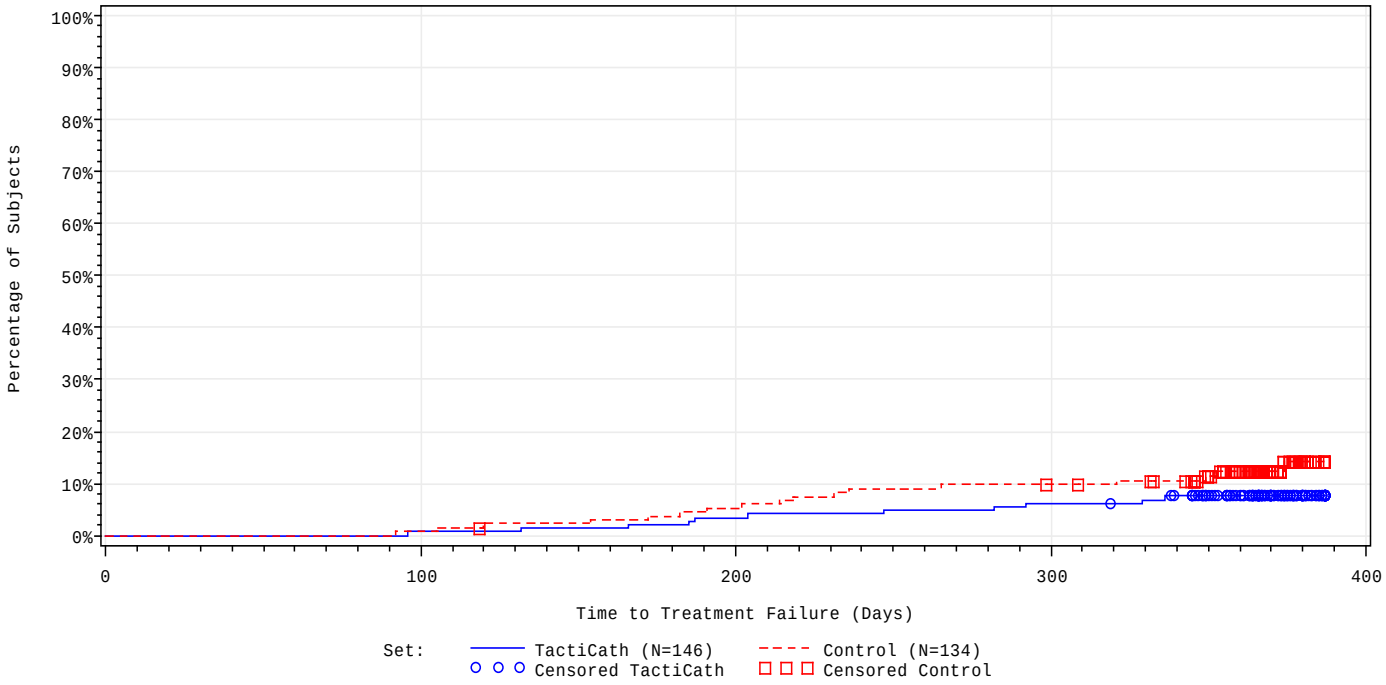

Figure 2. Kaplan-Meier Plot – Time-to-Treatment Failure Due to Re-Ablation Procedures (PP Population)

Secondary Effectiveness Results

Table 12 provides a summary of the procedural efficiency. The descriptive effectiveness endpoints in the study were related to the use of the contact force sensor and demonstrated a significant reduction in mean total RF application time with the TactiCath Set versus the control (51.7 vs 58.3 min, P=0.002).

Table 12. Summary of Procedural Efficiency (PP Population)

Secondary effectiveness endpoint	TactiCath N=146	Control N=134	*P* value (1-sided)
Percentage of lesion sets with electrically reconnected PVs following a 30-minute waiting period assessed by entrance block (%) at index procedure	n=145 11.09 (22.738) 0.00 [0.00, 0.00] 0.0, 100.0	n=134 14.61 (27.751) 0.00 [0.00, 25.00] 0.0, 100.0	0.209
Time to achieve initial PV isolation at index procedure (minutes)	n=146 90.4 (43.71) 87.0 [55.0, 117.0] 16, 261	n=134 86.4 (38.67) 85.5 [58.0, 108.0] 18, 224	0.941
Total time of RF application at index procedure (minutes)	n=146 51.72 (27.671) 46.40 [28.30, 65.30] 13.0, 139.3	n=133 58.31 (27.333) 53.50 [40.80, 72.80] 17.1, 196.0	0.002

Results are presented as mean (SD), median [IQR], min, max.

Primary Safety Results

The primary safety endpoint of noninferiority when compared to the control device was met. The predefined analysis for the primary safety endpoint is based on the SAF cohort of 295 subjects (**Tables 13 and 14).**

Table 13. Primary Safety Endpoint (SAF Population)

Primary safety endpoint	TactiCath N=152	Control N=143	Difference in primary SAE rates (TactiCath minus control)	
			Point estimate	One-sided 95% UCL[a]
Subjects experienced primary SAEs	3 (2.0%)	2 (1.4%)	0.6%	3.0%

[a] Noninferiority of TactiCath to the control device is demonstrated if the 95% UCL for the difference in rates (TactiCath minus control) is less than 9

Table 14. Summary of Primary SAEs by Term (SAF Population)

Event	TactiCath N=152		Control N=143		Total N=295	
	Subjects (%)	Events	Subjects (%)	Events	Subjects (%)	Events
Atrial perforation	0 (0.0%)	0	1 (0.7%)	1	1 (0.3%)	1
Cardiac perforation/cardiac tamponade	1 (0.7%)	1	0 (0.0%)	0	1 (0.3%)	1
Pericarditis	2 (1.3%)	2	0 (0.0%)	0	2 (0.7%)	2
PV stenosis	0 (0.0%)	0	1 (0.7%)	2	1 (0.3%)	2
Total subjects with at least 1 primary SAE	**3 (2.0%)**	**3**	**2 (1.4%)**	**3**	**5 (1.7%)**	**6**

Secondary Safety Results

The secondary safety endpoint consists of an evaluation of all SAEs during the 12-month follow-up period. A total of 32 (10.8%) subjects experienced 39 safety-related SAEs in the study. Six (6) of these SAEs were primary safety events, the other 33 SAEs were non-primary events and are summarized in the**Tables 15 and 16** below.

Table 15. Procedure-Related, Non-Primary SAEs (SAF Population)

	TactiCath N=152		**Control N=143**		**Total N=295**	
Serious adverse event	**Subjects n (%)**	**Events**	**Subjects n (%)**	**Events**	**Subjects n (%)**	**Events**
Total number (%) subjects with at least 1 non-primary SAE[a]	10 (6.6)	11	11 (7.7)	11	21 (7.1)	22
Atrial perforation[b]	0	0	1 (0.7)	1	1 (0.3)	1
Cardiac perforation/cardiac tamponade[b]	1 (0.7)	1	0	0	1 (0.3)	1
Pulmonary edema	2 (1.3%)	2	2 (1.4)	2	4 (1.4)	4
Vascular access complications	3 (2.0)	3	3 (2.1)	3	6 (2.0)	6
Hospitalizations (initial or prolonged)	4 (2.6)	4	5 (3.5)	5	9 (3.1)	9
GI bleeding	1 (0.7)	1	0	0	1 (0.3)	1
Anemia	0	0	1 (0.7)	1	1 (0.3)	1
Hematuria	0	0	1 (0.7)	1	1 (0.3)	1
Rule out esophageal injury	0	0	1 (0.7)	1	1 (0.3)	1
Secondary to groin hematoma	1 (0.7)	1	0	0	1 (0.3)	1
Secondary to pneumonia	0	0	1 (0.7)	1	1 (0.3)	1
Secondary to small bowel obstruction	1 (0.7)	1	0	0	1 (0.3)	1
Secondary to urinary retention	0	0	1 (0.7)	1	1 (0.3)	1
Vascular access complication	1 (0.7)	1	0	0	1 (0.3)	1
Non-primary SAE (other)	1 (0.7)	1	0	0	1 (0.3)	1
Secondary to cardiac arrest	1 (0.7)	1	0	0	1 (0.3)	1

[a] Subjects reporting more than one SAE in each level are only counted once. Only SAEs adjudicated as non-primary SAE are included

[b] Was not related to the use of a study device

Table 16. Not Procedure Related, Non-Primary SAEs (SAF Population)

	TactiCath N=152		Control N=143		Total N=295	
Serious adverse event	**Subjects n (%)**	**Events**	**Subjects n (%)**	**Events**	**Subjects n (%)**	**Events**
Total number (%) subjects with at least 1 non-primary SAE[a]	6 (3.9)	7	5 (3.5)	5	11 (3.7)	12
Hospitalizations(initial or prolonged)	3 (2.0)	4	2 (1.4)	2	5 (1.7)	6
Pericardial effusion at redo (not with study device)	1 (0.7)	1	0	0	1 (0.3)	1
Coronary artery disease	1(0.7)	1	1 (0.7)	1	2 (0.7)	2
Mitral valve incompetence	1 (0.7)	1	0	0	1 (0.3)	1
Pneumonia	0	0	1 (0.7)	1	1 (0.3)	1
Pulmonary hypertension	1 (0.7)	1	0	0	1 (0.3)	1
Non-primary SAE (other)	3 (2.0)	3	3 (2.1)	3	6 (2.0)	6
Pacemaker implant	0	0	1 (0.7)	1	1 (0.3)	1
Redo during blanking	3 (2.0)	3	2 (0.7)	2	5 (1.7)	5

[a]Subjects reporting more than one SAE in each level are only counted once. Only SAEs adjudicated as non-primary SAE are included

TactiCath™ Set Contact Force Results

The TactiCath™ Set generates a summary of contact force parameters applied during the ablation procedure. A statistical summary of the distribution of contact force averaged over all subjects in the TactiCath™ arm is presented in **Table 17**.

Table 17. Distribution of Contact Force in the TactiCath Arm (PP Population)

Contact Force Distribution	**TactiCath N=146[a]**
Number of ablations	n=145 61.1 (32.97) 55.0 [37.0, 76.0] 17, 204
Average contact force (g)	n=144 22.2 (7.47) 22.0 [17.0, 27.0] 7, 44
Standard deviation of contact force (per procedure) (g)	n=144 12.3 (9.88) 11.0 [8.0, 14.5] 3, 113
Minimum contact force (g)	n=144 4.2 (3.46) 4.0 [2.0, 6.0] 0, 16
5^{th} Percentile average contact force (g)	n=144 7.8 (4.38) 7.0 [5.0, 10.0] 0, 30

Contact Force Distribution	TactiCath N=146[a]
95th Percentile average contact force (g)	n=144 42.6 (14.99) 42.0 [33.0, 53.0] 2, 80
Maximum average contact force (g)	n=144 66.5 (95.35) 53.0 [39.5, 69.5] 17, 1111

Results are presented as mean (SD), median [IQR], min, max.
[a]For those subjects with evaluable data

Previous studies have suggested that optimizing contact force during lesion delivery yields better acute and chronic outcomes. Recent analysis of study subjects experiencing reablation procedures demonstrated a strong correlation between contact force parameters and site of reconnection. A significant determinant of durable PV isolation was the number of low contact force lesions.

A post hoc analysis of treatment success for all TactiCath™ subjects in the PP population who were treated with greater than 10 g of contact force (CF) in at least 90% of all lesions (n=83) is presented in **Table 18**.

Table 18. Success Rates for TactiCath™ Subjects with a High and Low Percentage of Lesions Above 10g (PP Population)

Contact force	Subjects (n)	Success (%)	*P* value
Optimal (≥90% of lesions with CF >10 g)	83	75.9%	0.018
Suboptimal (<90% of lesions with CF >10 g)	62	58.1%	

Using protocol-defined criteria for success, TactiCath subjects who were treated with "optimal" contact force (≥90% of lesions with CF >10 g) were significantly more successful (75.9% vs 58.1%, P=0.018) than those treated with suboptimal contact force.

Subjects treated with optimal contact force who failed after 12 months (n=20) tended to fail for TTM and/or AAD use, and less for reablation procedures as shown in **Table 19**.

Table 19. Failure mode for TactiCath subjects treated with optimal contact force

Reason for failure	Subjects with failure mode (n)
Acute failure	0
Reablation only	1
AAD only	4
TTM/ECG only	8
Reablation + AAD	0
Reablation + TTM/ECG	1
Reablation + AAD + TTM/ECG	2
AAD + TTM/ECG	4
Total	20

Control subjects had a higher failure rate due to reablation procedures after the blanking period compared to TactiCath subjects (12.7% vs 7.5%, respectively). Only 4 of the 83 (4.8%) subjects treated with optimal contact force required treatment with repeat ablation during the effectiveness assessment period compared to 17 of 134 (12.7%) subjects in the control arm (*P*=0.044).

Quality of Life Results

Quality of Life was measured at baseline and at 12 month follow-up, using the 'Atrial Fibrillation Effect on QualiTy-of-life' (AFEQT) questionnaire. From the 280 patients in the Per-Protocol (PP) Population, 254 patients answered to both questionnaires at baseline and 12 months. The results are represented **Figure 3** below .

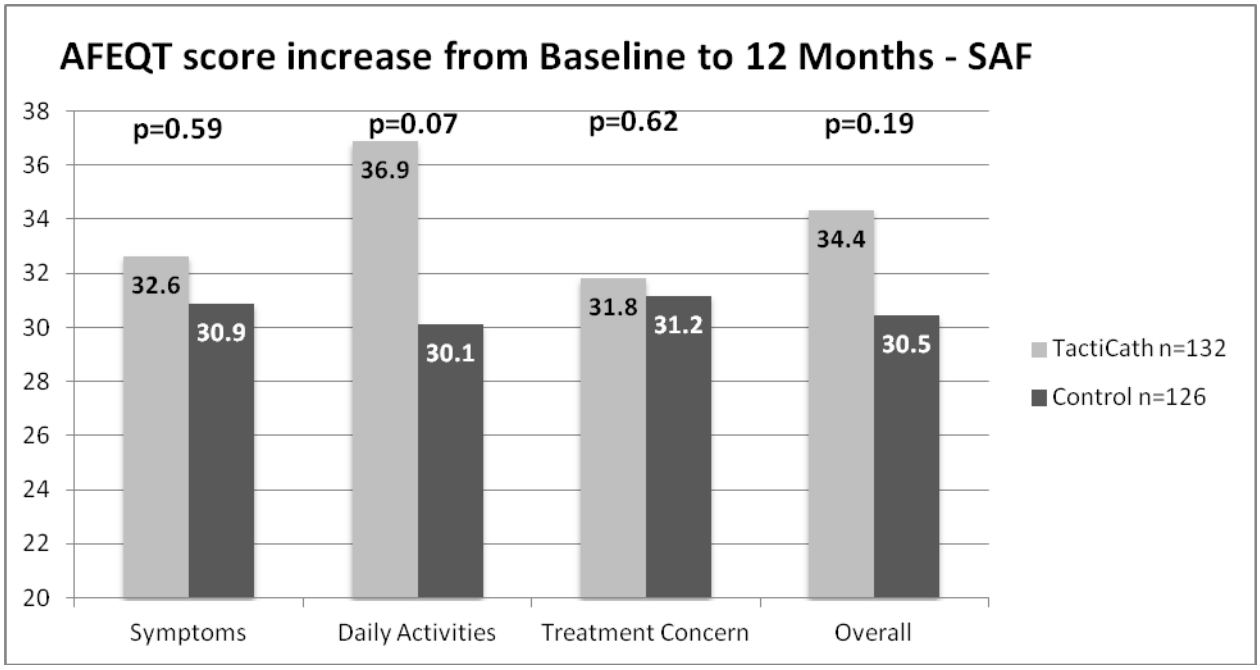

Figure 3. Atrial Fibrillation Effect of QualiTy-of-life Score from Baseline to 12 months (SAF Population)

Gender Subgroup Analysis

A summary of treatment success by gender is provided in **Table 20** below.

Table 20. Treatment Success (Protocol-Defined Effectiveness) by Gender (PP Population)

	Male		Female		Difference in success rates (TactiCath minus control)	
Endpoint	**TactiCath N=97**	**Control N=86**	**TactiCath N=49**	**Control N=48**	**Male point estimate % [95% LCL]**	**Female point estimate % [95% LCL]**
Acute procedural success	97 (100%)	86 (100%)	49 (100%)	48 (100%)	0 [NA]	0 [NA]
Acute procedural failure	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		

Chronic success	66 (68.0%)	56 (65.1%)	33 (67.3%)	37 (77.1%)	2.9 [-8.6]	-9.7 [-24.6]
Chronic failure	31 (32.0%)	30 (34.9%)	16 (32.7%)	11 (22.9%)		

Endpoint success/failures are reported as n (%), point estimate is reported as % [95% LCL].

J. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR Part 54), requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation.

The clinical investigation included 104 investigators, of which none were full-time or part-time employees of the sponsor. Four investigators had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: no investigators.
- Significant equity interest held by investigator in sponsor of covered study: two investigators.
- Proprietary interest in the product tested held by the investigator: one investigator.
- Significant payment of other sorts: two investigators.

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

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

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory System Devices Advisory Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Safety Conclusions

The adverse events of the device are based on data collected in the clinical study conducted to support PMA approval of the TactiCath™ Quartz Set as described

above. The TOCCASTAR pivotal study demonstrated that the TactiCath™ Set had met the safety goal for its intended use as defined in the protocol.

B. Effectiveness Conclusions

The TOCCASTAR pivotal study demonstrated that the TactiCath™ Set had met the efficacy performance goal for its intended use as defined in the protocol.

C. Benefit-Risk Conclusion

The pre-clinical and clinical information presented support that the probable benefits outweigh the probable risks when the device is used for the treatment of drug refractory recurrent symptomatic paroxysmal atrial fibrillation when used in accordance with the product labeling.

D. Overall Conclusions

The data in this application supports the reasonable assurance of safety and effectiveness of the TactiCath™ Quartz Set when used according to the product labeling.

XIII. CDRH DECISION

CDRH issued an approval order on 10/24/2014. The final conditions of approval cited in the approval order are described below.

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

XIV. APPROVAL SPECIFICATIONS

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

XV. REFERENCES

1. "Lone Atrial Fibrillation in the Pediatric Population," by Lindsay C. Mills, MD, Robert M. Gow, MBBS, Kim Myers, MD, Michal J. Kantoch, MD, Gil J. Gross, MD, Anne Fournier, MD, and Shubhayan Sanatani, MD, Canadian Journal of Cardiology, Volume 29/Issue 10 (October 2013), DOI: http://dx.doi.org/10.1016/j.cjca.2013.06.014, published by Elsevier