Clinical Evaluation of the StablePoint Catheter and Force-Sensing System for Paroxysmal Atrial Fibrillation

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To demonstrate the safety and effectiveness of the IntellaNav StablePoint Catheter and Force Sensing System with DIRECTSENSE for treatment of drug refractory, recurrent, symptomatic Paroxysmal Atrial Fibrillation (PAF).

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Cardiac arrhythmias
Study type	Observational invasive

Summary

ID

NL-OMON50243

Source
ToetsingOnline

Brief title
NEWTON AF

Condition

- Cardiac arrhythmias

Synonym
Atrial Fibrillation - Abnormal heart rhythm

Research involving
Human

Sponsors and support

Primary sponsor: Boston Scientific
Source(s) of monetary or material Support: Boston Scientific Corporation

Intervention

Keyword: Cardiac Catheter Ablation, Paroxysmal Atrial Fibrillation, PVI (Pulmonar Vein Isolation)

Outcome measures

Primary outcome

Primary Safety Endpoint at 30 Days

The primary safety endpoint at 30 days is defined as the safety event-free rate at 30 days post-procedure.

Primary safety events at 30 days will consist of a composite of the following serious procedure-related and/or device-related adverse events. Events will be counted through 7 days post index procedure or hospital discharge, whichever is later, unless denoted as events counting through 30 days post index procedure.

* Death
* Myocardial infarction (MI)
* Vagal Nerve Injury/Gastroparesis
* Transient ischemic attack (TIA)
* Stroke/Cerebrovascular accident (CVA)
* Thromboembolism
* Pericarditis
* Cardiac tamponade/perforation
* Pneumothorax
* Major vascular access complications
* Pulmonary edema/heart failure

* AV block

* Atrial esophageal fistula

* Severe pulmonary vein stenosis (*70% reduction in the diameter of the PV or PV branch from baseline)

Primary Safety Endpoint at 12 Months

The primary safety endpoint at 12 months is defined as the safety event-free rate at 12 months post-procedure.

Primary safety events at 12 months will consist of a composite of the following serious procedure-related and/or device-related adverse events.

The following events will be counted through 7 days post index procedure or hospital discharge, whichever is later:

* Death

* Myocardial infarction (MI)

* Vagal Nerve Injury/Gastroparesis

* Transient ischemic attack (TIA)

* Stroke/Cerebrovascular accident (CVA)

* Thromboembolism

* Pericarditis

* Pneumothorax

* Major vascular access complications

* Pulmonary edema/heart failure

* AV block

The following events will be counted through 30 days post index procedure:

* Cardiac tamponade/perforation

And the following events will be counted through 12 months post index procedure:

* Atrial esophageal fistula

* Severe pulmonary vein stenosis (*70% reduction in the diameter of the PV or PV branch from baseline)

* Persistent phrenic nerve palsy

Primary Effectiveness Endpoint * Acute Procedural Success

The primary effectiveness endpoint of acute procedural success is defined as the achievement of electrical isolation of all PVs using the IntellaNav StablePoint Catheter only. Electrical isolation of a PV is demonstrated by entrance block after a 20-minute waiting period. If exit block testing is performed, the PV will only be considered isolated if both entrance and exit block testing was successful.

Primary Effectiveness Endpoint at 6 Months

This primary effectiveness endpoint at 6 months is defined as the primary effectiveness event-free rate at 6 months post-procedure.

Primary effectiveness events determining a failure are defined as:

* Acute procedural failure

* Use of amiodarone post index procedure

* Use of non-study ablation catheter in the index procedure or in a repeat procedure during the blanking period

* More than one repeat procedure during the blanking period (90 days post index procedure)

* Surgical ablation of Atrial Fibrillation (AF)/Atrial Tachycardia (AT)/Atrial Flutter (AFL) post index procedure

* Documented atrial fibrillation, or new onset of atrial flutter or atrial tachycardia between 91 days and 183 days post index procedure captured by one of the following methods:

o * 30 seconds in duration recording from the study specific event monitor or Holter Monitor

o * 10 seconds 12-lead Electrocardiography (ECG)

* Any of the following interventions for atrial fibrillation, or new onset of atrial flutter or atrial tachycardia between 91 days and 183 days post index procedure:

o Repeat procedure

o Electrical and/or pharmacological cardioversion

o Prescribed any AAD

Primary Effectiveness Endpoint at 12 Months

This primary effectiveness endpoint at 12 months is defined as the primary

effectiveness event-free rate at 12 months post-procedure.

Secondary outcome

Secondary Endpoints include the following:

* Secondary Safety Endpoint * SAE and AE Rates

* Secondary Effectiveness Endpoint 1 * New or Increased Dose of AAD

* Secondary Effectiveness Endpoint 2 * Single Procedure Success defined as freedom from primary effectiveness failure without a repeat procedure

* Secondary Effectiveness Endpoint 3 * Symptomatic Recurrence: freedom from documented symptomatic AF/AT/AFL recurrence

Other additional endpoints and analysis include, but are not limited to:

* Changes in the quality of life measures (AFEQT and EQ-5D-5L) between baseline and 12 months follow up

* Total RF time for the index procedure (defined as the summation of all RF application durations)

* Total number of RF applications

* Total fluoroscopy time for the index procedure

* Total index procedure time

* Freedom from recurrence of individual types of atrial arrhythmias between 91 and 365 days from index procedure: 1) AF 2) AT 3) AFL

* Freedom from cardiovascular hospitalization at 12 months

* Quantification of parameters used during RF Application including RF power,

RF duration, contact force and Local Impedance via DIRECTSENSE* technology

* Descriptive summaries of primary safety and effectiveness endpoints at 12

months using the data available at the time of the 6-month analysis

* The predicted probability of success for the primary effectiveness endpoint

at 12 months based off the data available at the time of the 6-month analysis.

Study description

Background summary

Atrial fibrillation (AF) is the most commonly encountered sustained cardiac arrhythmia in clinical practice. It currently affects approximately 2.3 million people in North America and 4.5 million people in Europe. In addition, the prevalence and incidence of AF are increasing over time due to the aging of the population and a substantial increase in the age-specific occurrence of AF.
AF causes symptoms that impair quality of life, increases the risk of stroke fivefold and also increases mortality. There are multiple therapies in current use for the treatment of AF; however, it is recognized that many of these therapies are suboptimal for most patients. Treatment options include medical management, pacing, cardioversion, implantable devices, surgery, and ablation therapy to eliminate the arrhythmia. It has been increasingly recognized that focal pulmonary vein triggers of AF can account for 80 to 95 percent of paroxysmal cases that are drug resistant. As outlined in the 2017 Heart Rhythm Society (HRS) consensus document, *electrical isolation of the PVs is now recognized as the cornerstone of AF ablation. At most centers where AF ablation is performed, a strategy of creating a series of point-by-point radiofrequency lesions that encircle the PVs is used.*
In the current clinical state of the art, power, time, and tissue contact are monitored to balance the formation of effective transmural lesions with the risk of adverse effects (cardiac perforation, steam pops, and thrombus formation). When using conventional ablation catheters, like the predecessor catheters, tissue contact is determined by surrogate parameters like tactile feel, generator impedance, intracardiac electrogram amplitude, catheter position on a visualization system relative to the anatomy or using ancillary products like intracardiac echo. Catheter to tissue contact has been shown to be a determinant of individual lesion dimensions and adverse events (i.e. steam pop, thrombus or char) via ex vivo tissue preparations and in vivo pre-clinical studies were incorporated into the distal tip of cardiac ablation catheters.
With the introduction of force sensing catheters, physicians gained access to additional feedback on the mechanical coupling between the catheter tip and

tissue which provides additional feedback for consistent RF application. The use of contact force is now a mature, state of the art technology for open irrigated ablation with several years of clinical experience, holding great potential for improving the safety and success rates of AF ablation procedures by reducing suboptimal and excessive CF during ablation.
Boston Scientific (BSC) has developed the IntellaNav* StablePoint Catheter, an 8.5F compatible, steerable, open irrigated, radiofrequency ablation catheter with multiple diagnostic electrodes that leverages the existing BSC OI platform and incrementally provides the ability to measure a force applied to the distal tip. The catheter is designed to incorporate force-sensing elements while preserving the core therapeutic functionality of the prior Blazer* OI family of catheters (including both Blazer* Open-Irrigated and IntellaNav* Open-Irrigated [BOI-NOI]) relative to RF delivery, cooling performance, and maneuverability within the cardiac environment.
In addition to the contact force sensing capability, the IntellaNav* StablePoint Catheter is also enabled to measure Local Impedance via DIRECTSENSE* technology. Local Impedance is a measure of the impedance properties closest to the catheter distal electrode that allows for a diagnostic metric that can be used in conjunction with other clinical measures to inform the physician on catheter proximity relative to cardiac tissue and resistive heating directly under the ablation electrode of the catheter. Local impedance measured at the ablation catheter tip has been shown to provide a superior method of assessing catheter-tissue coupling compared to generator impedance in both preclinical and clinical settings. Additionally, a strong correlation has been demonstrated between local impedance drop and lesion formation preclinically (in vitro and in vivo), and in the clinical setting via pace capture. Tissue temperature changes due to local heating with application of radiofrequency (RF) energy during catheter ablation results in decreasing local electrical resistivity surrounding the RF electrode and a characteristic decrease in local impedance. Monitoring electrode impedance changes via the ablation generator can provide real-time feedback on the tissue response to RF ablation.
Both contact force sensing and local impedance capabilities implemented in the StablePoint Catheter may concur to improve ablation procedures as their complementary use can provide an advantage over the use of one metric alone. When studying the complementary nature of the two features with discrete lesions in vitro and in vivo, it resulted that the confirmation of stable mechanical contact and viewing of real-time local impedance drops enabled a significant reduction in RF time while creating a continuous linear lesion.
The IntellaNav StablePoint Catheter System includes the IntellaNav StablePoint Catheter and Cable, the Maestro Force Sensing Connection Box and the Force Computation Software Module. When used with the Rhythmia HDx* Mapping System with Software 4.0.1 or greater and the BSC Cardiac Ablation System, the Force Sensing System can be used for treatment of drug refractory, recurrent, symptomatic Paroxysmal Atrial Fibrillation. The catheter system is based on BSC*s Blazer* Open-Irrigated and IntellaNav* Open Irrigated ablation catheter platform. This platform has been investigated in the BLOCk-CTI and ZERO AF

clinical trials and have demonstrated safe and effective use.
The IntellaNav StablePoint Catheter System received CE mark on June 5, 2020 and will be commercially available in geographies that accept CE mark.

Study objective

To demonstrate the safety and effectiveness of the IntellaNav StablePoint Catheter and Force Sensing System with DIRECTSENSE for treatment of drug refractory, recurrent, symptomatic Paroxysmal Atrial Fibrillation (PAF).

Study design

The NEwTON AF study is a multi-center, global, prospective, single arm study to establish the safety and effectiveness of the IntellaNav StablePoint Catheter and Force-Sensing System in subjects with symptomatic, drug refractory, recurrent paroxysmal atrial fibrillation. The study will be conducted in North America, Europe and Asia Pacific. A 6-month endpoint analysis is planned and will be conducted after all 299 TREATMENT subjects have completed 30 days of follow up and 183 TREATMENT subjects have completed their 6-month follow-up. If effectiveness is not demonstrated at the 6-month endpoint analysis, then it may be re-evaluated at the 12-month endpoint analysis. All subjects undergoing the index procedure with the study devices will be followed up to 12 months.

Study burden and risks

Risks associated with an ablation procedure. Risks associated with the RF ablation procedure do not differ from the standard ablation procedure.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

* History of recurrent symptomatic Paroxysmal Atrial Fibrillation (PAF), defined as atrial fibrillation (AF) that terminates spontaneously or with intervention (either procedure or drug therapy) within seven days of onset. Minimum documentation includes the following:
o a physician*s note indicating recurrent self-terminating atrial fibrillation (AF) which includes at least two symptomatic AF episodes in the patient*s history within the last 6 months prior to enrollment, and
o any electrocardiographically documented AF episode within 12 months prior to enrollment.
* Subjects who are eligible for an ablation procedure for PAF according to 2017 HRS expert consensus statement on catheter ablation of atrial fibrillation;
* Subjects refractory or intolerant to at least one class I or class III antiarrhythmic medication or contraindicated to any class I or III medications;
* Subjects who are willing and capable of providing informed consent;
* Subjects who are willing and capable of participating in all testing associated with this clinical investigation at an approved clinical investigational center;
* Subjects whose age is 18 years or above, or who are of legal age to give informed consent specific to state and national law.

Exclusion criteria

* Subjects with New York Heart Association (NYHA) Class III or IV heart failure < 180 days prior to enrollment
* Left atrial diameter > 5.0 cm or left atrial volume >50 ml/m² indexed based on the most recent echocardiography
* Left ventricular ejection fraction < 35% based on the most recent

echocardiogram
* Continuous AF lasting longer than seven (7) days
* Subjects who have undergone any previous left atrial cardiac ablation (RF, Cryo, surgical)
* Atrial fibrillation secondary to electrolyte imbalance, thyroid disease, or reversible or non-cardiac cause
* Subjects who have undergone any cardiac ablation or any surgery within 30 days prior to enrollment
* Currently implanted with a pacemaker, ICD, CRT device, or an implanted arrhythmia loop recorder
* Active systemic infection
* Unstable angina or ongoing myocardial ischemia
* Myocardial Infarction (MI) within 90 days prior to enrollment
* Evidence of myxoma, left atrial thrombus or intracardiac mural thrombus
* Previous cardiac surgery (i.e. ventriculotomy, atriotomy, CABG, PTCA, PCI, coronary stenting procedures) * 90 days prior to enrollment.
* Severe valvular disease, including mechanical prosthetic mitral or tricuspid heart valves (patients with successful mitral valve repair allowed * annular ring constitutes repair);
* Any prior history of documented cerebral infarct, TIA or systemic embolism [excluding a post-operative deep vein thrombosis (DVT)] <180 days prior to enrollment
* Moderate or severe mitral stenosis (severity assessed on the most recent TTE *180 days prior to enrollment. Defined as pulmonary artery systolic pressure >30 mmHg)
* Presence of left atrial appendage closure device
* Interatrial baffle, closure device, patch, or patent foramen ovale (PFO) occluder
* Subjects who, in the judgment of the investigator, have a life expectancy of less than two (2) years
* Women of childbearing potential who are, or plan to become, pregnant during the time of the study (method of assessment upon investigator*s discretion)
* Amiodarone use within 60 days prior to enrollment
* Any carotid stenting or endarterectomy
* Stage 3B renal disease or higher (estimated glomerular filtration rate, eGFR <45 mL/min)
* Known coagulopathy disorder (e.g. von Willebrand*s disease, hemophilia)
* Any known contraindication to an AF ablation
* Any known contraindication for anticoagulation (e.g. patients unable to receive heparin or an acceptable alternative to achieve adequate anticoagulation)
* Vena cava embolic protection filter devices and/or known femoral thrombus that prevents catheter insertion from the femoral approach
* Known sensitivity to contrast media (if needed during the procedure) that cannot be controlled with pre-medication
* Rheumatic Heart Disease
* Presence of intramural thrombus, tumor or other abnormality that precludes

vascular access, or manipulation of the catheter
* Subjects unable or unwilling to complete follow-up visits and examinations for the duration of the clinical study
* Subjects who are currently enrolled in another investigational study or registry that would directly interfere with the current study, except when the subject is participating in a mandatory governmental registry, or a purely observational registry with no associated treatments; each instance must be brought to the attention of the sponsor to determine eligibility.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-03-2022
Enrollment:	20
Type:	Actual

Medical products/devices used

Generic name:	IntellaNav StablePoint Catheter System
Registration:	Yes - CE intended use

Ethics review

Approved WMO

Date:	17-11-2021
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
ClinicalTrials.gov	NCT04580914
CCMO	NL79342.100.21