SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Ablation Catheter, Generator, and Accessories

Device Trade Name: PulseSelect™ Pulsed Field Ablation (PFA) system, PulseSelect™ Pulsed Field Ablation (PFA) loop catheter, PulseSelect™ Pulsed Field Ablation (PFA) generator, PulseSelect™ Pulsed Field Ablation (PFA) remote control, PulseSelect™ Pulsed Field Ablation (PFA) foot switch, power cord, PulseSelect™ Pulsed Field Ablation (PFA) catheter interface cable, and PulseSelect™ Pulsed Field Ablation (PFA) EGM cable

Device Procode: Class III / QZI: Percutaneous Cardiac Ablation Catheter For Treatment Of Atrial Fibrillation With Irreversible Electroporation

Applicant's Name and Address: Medtronic, Inc., 8200 Coral Sea Street NE, Mounds View, MN 55112

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P230017

Date of FDA Notice of Approval: December 13, 2023

Breakthrough Device: The Medtronic PulseSelect™ PFA system was granted designation as a Breakthrough Device on September 27, 2018, meeting several criteria (1, 2A, 2C and 2D) of the Breakthrough Devices Program.

II. INDICATIONS FOR USE

The PulseSelect™ PFA loop catheter is indicated for use in cardiac electrophysiological mapping (stimulation and recording) and for treatment of drug refractory, recurrent, symptomatic paroxysmal atrial fibrillation or persistent atrial fibrillation (episode duration less than 1 year) when used in conjunction with the PulseSelect™ PFA system.

III. CONTRAINDICATIONS

The PulseSelect™ PFA loop catheter is contraindicated for use in patients with the following conditions:

- Active systemic infections
- A known sensitivity to Heparin
- Blood clotting abnormalities
- Permanently implanted metallic objects in the left atrium

The catheter is also contraindicated in conditions where the manipulation of the catheter within the heart would be unsafe, such as intracardiac mural thrombus.

The catheter is not recommended for use in patients who cannot undergo standard anticoagulation protocol for a left-sided cardiac procedure, or who have had a recent coagulopathy or embolic event.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the PulseSelect™ PFA system labeling.

V. DEVICE DESCRIPTION

PulseSelect™ PFA Loop Catheter

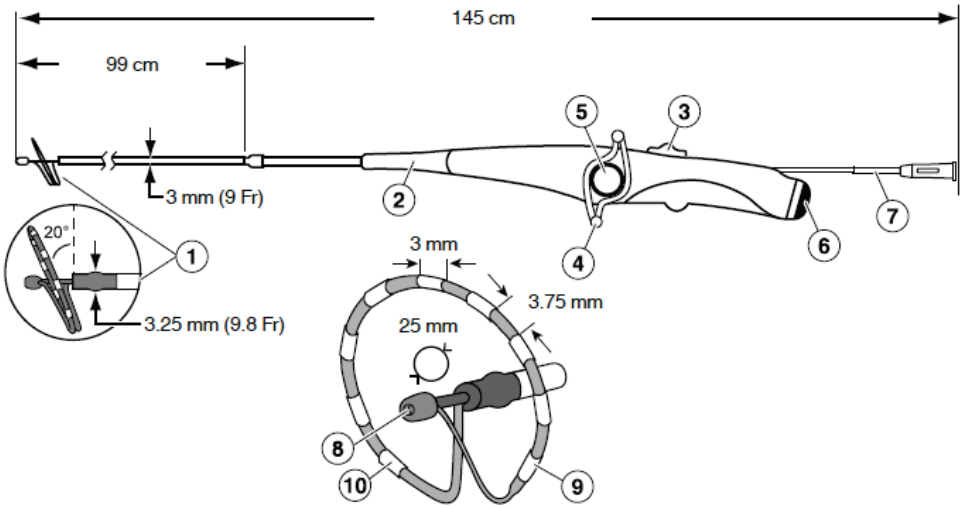
The PulseSelect™ PFA loop catheter (Figure 1) is a sterile, single use, anatomically designed, multi-electrode catheter used to detect electrical signals, pace, and ablate the pulmonary veins. The catheter is provided sterile via electron beam (e-beam) sterilization. The catheter is used to perform cardiac tissue ablation through the mechanism of irreversible electroporation. The catheter is compatible with the Medtronic PulseSelect™ PFA system. The catheter is designed to be used together with an introducer sheath with a minimum inside diameter of 3.33 mm (10 Fr) and a 0.81 mm (0.032 in) J-tip guide wire.

The catheter has the following 2 control features:

- A steering lever that controls bidirectional deflection of the distal shaft.
- A slide control to extend or retract the guide wire lumen and distal tip (8) and change the catheter geometry from circular to spiral to a longitudinal shape.

The slide control also allows for extension of the distal portions of the catheter to allow capture of the distal array into the capture device that is used to deliver the catheter into the sheath. The catheter is inserted into the patient's vasculature, typically through an introducer sheath via the femoral vein, then advanced into the left atrium. Once in the sheath, the catheter and guide wire are advanced through the sheath with the guide wire being guided into one of the pulmonary veins. After the catheter array exits the sheath, it is deployed into a circular shape pulling the slide control back. The catheter array is then placed in multiple sites for cardiac tissue ablation.

Figure 1: PulseSelect™ PFA Loop Catheter Drawing



1 Spiral array	6 Connector
2 Capture device	7 Luer
3 Slide control	8 Distal tip
4 Steering lever	9 Electrode 1
5 Steering lever tension control knob	10 Electrode 9

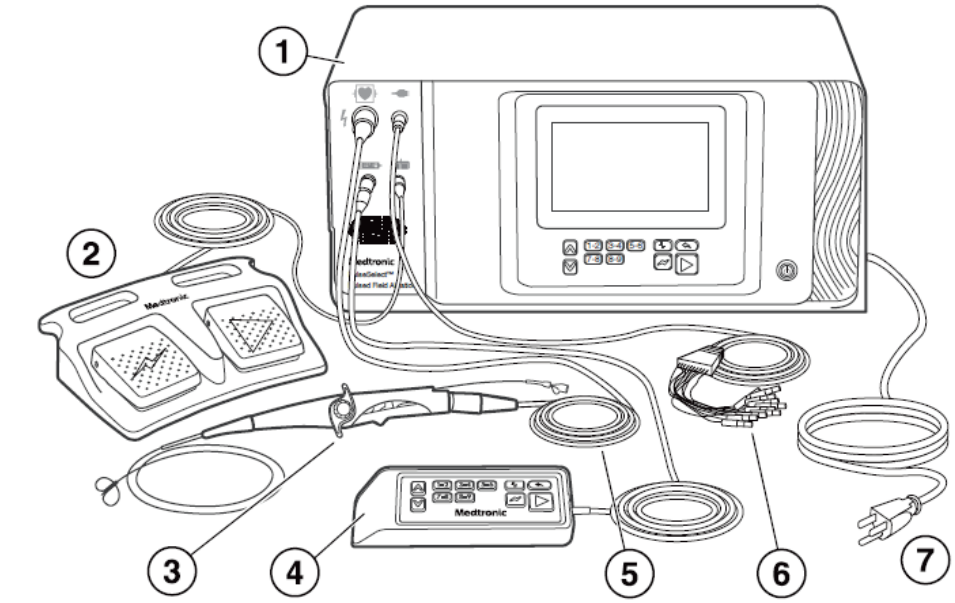
PulseSelect™ PFA Generator

The Medtronic PulseSelect™ Pulsed Field Ablation (PFA) generator (Figure 2) delivers bipolar, biphasic pulsed electric fields through a compatible Medtronic catheter to perform cardiac tissue ablation through the mechanism of irreversible electroporation. The generator accepts trigger pulses from an external cardiac trigger monitor to synchronize the PFA delivery to an R wave. The generator allows the user to:

- Charge the system in preparation for PFA delivery.
- Deliver a test pulse to identify phrenic nerve stimulation response to a low-voltage delivery.
- Initiate ablation.
- View system status and any notifications.

Ablation parameters such as PFA delivery status and faults are displayed on the generator's touchscreen display. The 1500 V displayed on the therapy setup screen represents the amplitude from baseline to peak of the pulsed field ablation waveform.

Figure 2: PulseSelect™ PFA System Drawing



1 Generator
2 Foot switch
3 Catheter
4 Remote control
5 Catheter interface cable
6 Electrogram (EGM) cable
7 Power cord

PulseSelect™ PFA Generator Accessories

The following nonsterile and sterile accessories (Figure 2) are compatible with the PulseSelect™ PFA system:

Remote control: The model PSRC100 series PulseSelect™ PFA remote control is an optional, nonsterile accessory that allows the operator to charge the system and deliver energy to perform ablation. The remote control connects to the PFA generator via a cable and allows the user to charge the system in preparation for PFA delivery, deliver a test pulse to identify phrenic nerve stimulation response to a low-voltage delivery, and to initiate PFA delivery. The remote control can be placed within the user's reach, either outside of the sterile field or inside once it has been draped in accordance with appropriate sterile techniques.

Foot switch: The model PSFS100 PulseSelect™ PFA foot switch is an optional, nonsterile accessory that allows the operator to charge the system and deliver energy to perform ablation. The foot switch is connected to the PulseSelect™ PFA generator.

Power cord: The power cord model PWC101 supplies electricity to the PFA generator via hospital mains during clinical use. The power cord connects to the specified inlet on the back of the generator and a source of line power. Different power cords will be used per local compatibility requirements.

Catheter interface cable: The model PSCIC101 PulseSelect™ PFA catheter interface cable (CIC) is a sterile, single use cable that provides a means for connecting the catheter to generator using a custom locking connector. This cable is provided sterile via electron beam (e-beam) sterilization.

Electrogram (EGM) cable: The model PSEGM100 PulseSelect™ PFA electrogram (EGM) cable is a nonsterile, reusable cable that connects the PFA generator to an external EP recording system and/or pacing equipment.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the treatment of drug refractory, recurrent, symptomatic paroxysmal atrial fibrillation or persistent atrial fibrillation (episode duration less than 1 year), including the following:

- Pharmacological therapy for rate and/or rhythm control
- Electrical or pharmacologic cardioversion
- Implantable devices to control heart rates
- Surgical intervention
- Endocardial catheter ablation

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 PulseSelect™ PFA system has not been marketed in the United States or any foreign country.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Potential adverse events associated with cardiac catheter ablation procedures include, but are not limited to, the following conditions:

- Access site complications (such as, bruising, ecchymosis, arteriovenous fistula, hematoma, pseudoaneurysm)
- Anemia
- Arrhythmias, proarrhythmia (such as, atrial flutter, bradycardia, heart block, tachycardia)
- Bleeding, possibly requiring transfusion
- Bruising
- Cardiopulmonary arrest
- Perforation of the heart or other organs during transseptal puncture or other procedures
- Cardiac tamponade
- Catheter entrapment in cardiac structures requiring intervention
- Cerebrovascular accident [such as stroke, transient ischemic attack (TIA)]
- Chest discomfort, pain, or pressure
- Collateral damage to the conduction system or coronary vasculature
- Cough
- Death
- Embolism

- Esophageal damage (including atrial esophageal fistula)
- Hemoptysis
- Hypotension
- Hypertension
- Infections (such as, sepsis)
- Myocardial infarction or ischemia
- Nerve injury or nerve damage (for example phrenic nerve injury)
- Pericarditis or endocarditis
- Pericardial effusion
- Pneumothorax
- Pulmonary edema
- Pulmonary vein dissection
- Pulmonary vein stenosis
- Radiation injury or damage and late malignancy
- Skin laceration or puncture
- Sore throat
- Unintended complete or incomplete atrioventricular node (AV-Node) or sinus node block or damage
- Valvular insufficiency or damage

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

IX. SUMMARY OF NONCLINICAL STUDIES

Nonclinical testing was performed to demonstrate the final design meets the defined design inputs. Testing was conducted to recognized standards and demonstrated acceptable results in accordance with the design inputs. Nonclinical testing included design verification (device level, system level, and software), design validation testing, biocompatibility of patient-contacting materials, sterilization, packaging, and shelf life testing.

A. Laboratory Studies

PulseSelect™ PFA Loop Catheter Design Verification

Non-clinical testing was performed and included the following areas:

- Functional performance: catheter deflection, bend diameter, reach, shaft flexibility and torsional rigidity, bend force, planarity, wire resistance, and luer leakage
- Physical: electrode spacing, working length, and array diameter
- Security: confirmation of single use
- Safety: dielectric withstand, bond strengths, basic safety in accordance with IEC 60601-1, and freedom from surface defect
- Reliability: cyclic performance, shelf life, and stability
- Compatibility with environment of intended use: confirmation over specified

temperature ranges and corrosion resistance
- Biocompatibility: in accordance with ISO-10993
- Sterility: electron beam (E-beam) sterilization to 10^{-6} SAL
- Endotoxin: not more than 20 EU/device
- Packaging and labeling: product labeling, sterile barrier performance, and ASTM D4169 evaluation for shipping and storage conditions

Testing at both real time and aged product confirmed acceptable results to all performance requirements, across all temperature ranges and conditions.

PulseSelect™ PFA Catheter Interface Cable Design Verification

Nonclinical testing was performed and included the following areas:

- Functional performance: connector retention strength, engage/disengage force, flexure, wire resistance, and confirmation of cable wiring
- Physical: cable length
- Safety: dielectric strength, high voltage integrity in accordance with IEC 60601-1, and cable integrity following sterilization exposure
- Compatibility with environment of intended use: confirmation of performance across specified temperature ranges and protection against fluid ingress
- Biocompatibility: in accordance with ISO-10993
- Sterility: E-beam sterilization to 10^{-6} SAL
- Endotoxin: not more than 20 EU/device
- Packaging and labeling: product labeling, sterile barrier performance, ASTM D4169 evaluation for shipping and storage conditions

Testing at both real time and aged product confirmed acceptable results to all performance requirements, across all temperature ranges and conditions.

PulseSelect™ PFA Generator, PulseSelect™ PFA Remote Control and Power Cord Design Verification

The PFA capital subsystem consists of the PFA generator, remote control, and power cable. Nonclinical testing was performed and included the following areas:

PulseSelect™ PFA Generator

- Functional performance: electrical performance for resistivity and noise levels and R wave input for cardiac gating of delivery
- Physical: generator dimensions, weight, front panel LEDs and control, ingress protection and tamper resistance, receptacles for peripheral connections, line power, HDMI, and serial data
- Safety: basic safety in accordance with IEC 60601-1, including leakage, dielectric withstand, and defibrillation protection and confirmation of fault thresholds
- Compatibility with environment of intended use: confirmed electrical performance across all specified geography input voltages and temperature ranges, protection against fluid ingress, wipe down, and service life

- Packaging and labeling: product labeling and ASTM D4169 for shipping and storage conditions

Note: additional testing was performed for basic safety/EMC as described below.

PulseSelect™ PFA Remote Control

- Functional performance: confirmation of communication and basic operation
- Physical: remote control dimensions, physical features, button controls and LEDs, and interfaces
- Safety: leakage and dielectric withstand in accordance with per IEC 60601-1
- Compatibility with environment of intended use: confirmation of performance across specified temperature ranges, protection against fluid ingress, wipe down, and service life
- Packaging and labeling: product labeling and ASTM D4169 for shipping and storage conditions

Power Cord

- Functional performance: confirmation of cord retention and current
- Physical: connectivity for hospital grade mains across multiple geographies
- Safety: cord impedance and review of technical specifications in accordance with IEC 60601-1
- Compatibility with environment of intended use: confirmed electrical performance across all specified geography input voltages and temperature ranges and protection against fluid ingress
- Packaging: product labeling and ASTM D4169 for shipping and storage conditions

Testing confirmed acceptable results to all performance requirements, across all temperature ranges and conditions.

PulseSelect™ PFA EGM Cable Design Verification

Non-clinical testing was performed and included the following areas:

- Functional performance: confirmation of generator connectivity, connector retention force, lead wire tensile strength, pin retention force, wire resistance, compatibility with EP recording system
- Physical: conduction specifications, cable length, and pin specifications
- Safety: dielectric strength in accordance with IEC 60601-1
- Compatibility with environment of intended use: confirmation of performance across specified temperature ranges and repeated use
- Packaging and labeling: product labeling, ASTM D4169 for shipping and storage conditions

Testing confirmed acceptable results to all performance requirements, across all temperature ranges and conditions.

PulseSelect™ PFA Foot Switch Design Verification

Nonclinical testing was performed and included the following areas:

- Functional performance: actuation and retention force; on/off activation levels
- Physical: multiple pedals, physical length, pinouts/mating with generator
- Safety: activation force and fluid protection in accordance with IEC 60601-1
- Compatibility with environment of intended use: confirmation of performance across specified temperature ranges and repeated use
- Packaging and labeling: product labeling and ASTM D4169 for shipping and storage conditions

Testing confirmed acceptable results to all performance requirements, across all temperature ranges and conditions.

Software Design Verification

The PulseSelect™ PFA generator is a software-controlled system. Software is comprised of two modules: the Computing Module and the Embedded Module. The Computing Module supports user operation and display. The Embedded Module serves as the main interface between the hardware controller and the Computing Module. Nonclinical testing was performed on all aspects of software/firmware. Included in the software are security layers which ensure privacy/cybersecurity protection. Nonclinical test areas included:

- Computing Module, which included test/assessment in the following areas:
  - Clinical application:
    - Graphical User Interface (GUI)
    - Therapy setup/delivery
    - Translations
  - Platform service/Medtronic Pathway Connect (MPC)
  - Platform application:
    - Ethernet communication
    - Communication between processes
    - Field upgrade / software updates
    - Windows Operating System security configuration
- Embedded Module, which included test/assessment in the following areas:
  - Embedded application:
    - Interfacing with Field Programmable Gate Arrays (FPGAs) for control of therapy
    - Catheter authentication
    - Peripheral management (foot switch, remote, and generator front panel)
  - Embedded bootloader:
    - Secure boot
    - Firmware upgrade
- Security Penetration testing was performed on the system, covering relevant elements of the Computing and Embedded software module designs.

Testing confirmed acceptable results to all software requirements.

Basic Safety and EMC Design Verification

The PulseSelect™ PFA system was tested in accordance with the following standards for basic safety and EMC:

- IEC 60601-1 Edition 3.2 2020-08: Medical Electrical Equipment - Part 1: General Requirements for Basic Safety and Essential Performance
- IEC 60601-1-2 Edition 4.1 2020-09: Medical Electrical Equipment – Part 1-2: General Requirements for Basic Safety and Essential Performance - Collateral Standard: Electromagnetic disturbances – Requirements and tests
- IEC 60601-2-2 Edition 6 2017-03: Medical electrical equipment - Part 2-2: Particular requirements for the basic safety and essential performance of high frequency surgical equipment and high frequency surgical accessories
- EN ISO 14971: 2019 Third Edition 2019-12: Medical devices – Application of risk management to medical devices

System Design Validation and Human factor Summative

Design validation and human factors validation (i.e., summative evaluation) were conducted together. The design validation process ensured that the PulseSelect™ PFA system (including all finished devices and software) met the defined user needs and intended uses, as defined by the design inputs. Human factors validation ensured that the PulseSelect™ system can be used safely and effectively and complied with the requirements described in IEC 62366-1: 2015+AMD1:2020.

This testing was completed both via direct user testing both in animal and non-animal models and via validation by review. The tasks identified to be tested via direct user testing were completed by fifteen (15) electrophysiologists and fifteen (15) allied health professionals/support staff users from the United States. All tasks defined in the study protocol were completed successfully, included the following:

- System use: catheter navigation, catheter features (ablate, sense, pace, and assessment of treatment effect), and system transportability.
- Effectiveness of design related risk controls.
- Effectiveness of information-for-safety risk controls.

All validation and summative evaluation acceptance criteria were met for the PulseSelect™ PFA system and the system was found to be safe for use by health care practitioners qualified to complete ablation procedures.

Additional details related to validation testing completed using an animal model can be found in Section B.

B. Animal Studies

A series of acute and chronic in vivo animal studies provide an in-depth characterization of the safety profile of the PulseSelect™ PFA system. A total of six (6) animal studies were conducted in simulated clinical environments. Some of the studies allowed for the collection of user feedback from trained electrophysiologists. The in vivo animal

information supplements the data generated from the PULSED AF study where the PulseSelect™ PFA system was used to treat subjects with atrial fibrillation successfully and safely. The tables below include the animal model, number of animals, objective, description of study, results, and study timepoint. Summaries of these six animal studies are found below in Table 1.

Table 1: Summary of Animal Studies[1]

Test	Purpose	Results
Evaluation of Acute and Chronic Effects of PFA and irrigated radiofrequency ablation (IRF) in Pigs	The purpose of this Good Laboratory Practice (GLP) study was to observe the acute and chronic (4 week) effects of creating cardiac lesions using PFA therapy in pigs (n=6) and compare to IRF energy application (n=2). The 4-week survival pig model allowed sufficient time post-ablation for evaluation of extra-cardiac injury to key collateral structures, as well as lesion evaluation.	The study demonstrated a superior safety profile of PFA versus IRF in terms of collateral damage. No signs of detrimental effects were noted in pathology in any of the ablation sites in spite of extensive overlap of catheter positions. Medtronic verified the safety of bipolar deliveries of PFA delivered using twice the standard number of ablation sites around the right pulmonary vein ostium and the RAA, with extensive overlap of catheter positions.
Chronic Injury Characterization of PFA in Canines	Canine subjects (n=8) were treated with either IRF or PFA energy at both a distal and proximal location within the pulmonary veins, with the intent of comparing PFA to IRF for the risk of causing PV stenosis or PV narrowing in this chronic non-GLP study. PFA was applied to the pulmonary veins with the same therapy profile used in the PULSED AF clinical trial (1500 V) delivered onto substantially the same area of tissue. IRF was applied at 25-30W with 25-30mL/min irrigation. Cardiac CT scans were performed pre-ablation and at 2, 4, 8, and 12 weeks post-ablation to measure changes in pulmonary vein cross-sectional areas due to the ablations.	RF energy caused significant reductions in PV diameters at the 2 and 4-week time points as compared to PFA. Maximum damage occurred around the 2 to 4-week time point following RF delivery. PFA-treated targets showed significantly fewer vessel restrictions compared with IRF. Histopathology indicated that PFA showed no extracardiac damage, while IRF treatments caused phrenic nerve damage, and bronchial damage and remodeling. Substantial vagal nerve damage was common adjacent to the IRF delivery sites while PFA deliveries had no such effect. In summary, IRF applications resulted in severe PV narrowing 2-4 weeks following ablation in comparison to PFA applications. IRF applications also caused downstream bronchial damage and

[1] Note that these studies do not include acceptance criteria, and hence this particular column has not been included in this table.

Test	Purpose	Results
		remodeling in the form of large lesions within the lungs, while PFA applications did not cause additional extracardiac injury. These results contribute to the potential safety profile of this energy source for cardiac ablation.
Extracorporeal Microemboli Evaluation during PFA	This acute non-GLP porcine study (n=3) focused on microbubble measurements during PFA and evaluated particulate formation using end-organ analysis and post-ablation filter analysis. The purpose of this exploratory study was to gain a thorough understanding of microemboli generation, to identify the relationship a set of pulse parameters have on microemboli generation, to evaluate whether the proposed clinical profiles are well within reasonable bounds of microemboli generation, and also whether PFA induces hemolysis.	All of the clinical profiles tested up to 1500 volts produced less than the acceptable 1µl volume of bubbles (per pulse train). Moreover, no thermal coagulum and no clinically relevant hemolysis was observed. The clinical profiles planned for PULSED AF use did not generate thermal coagulum nor exceed the suggested acceptable microbubble volume threshold.

Test	Purpose	Results
PulseSelect PFA System Verification Study	The purpose of this acute non-GLP porcine study (n=1) was to perform system level design verification using a live, clinically representative animal model to test the system against defined system level input requirements.	This study demonstrated the system is capable of creating lesions in cardiac tissue and that cardiac electrograms can be passed to an EP recording system within a clinical environment. A pathological examination was performed to document the gross findings. The system met all acceptance criteria as defined in the protocol: • Therapeutic energy was successfully delivered. • System notifications and alerts were demonstrated • Visibility of the catheter was demonstrated using fluoroscopy • Cardiac electrograms were passed and visualized on an EP recording system • Lesions were created and visualized post procedure through gross pathological evaluation • No failures were observed during the protocol execution.
Evaluation of Microbubble and Particulate Generation during PFA	This acute porcine GLP extracorporeal loop porcine study (n=6) was designed to evaluate microbubble and particulate generation with the PulseSelect PFA system. The study's first objective was to evaluate thermal coagulum observed on filters in the extracorporeal loop after 8 overlapping applications of PFA (clinical profile) in three different locations of the porcine's left atrium: right pulmonary	Acceptable levels of microbubbles and no thermal particulates were observed.

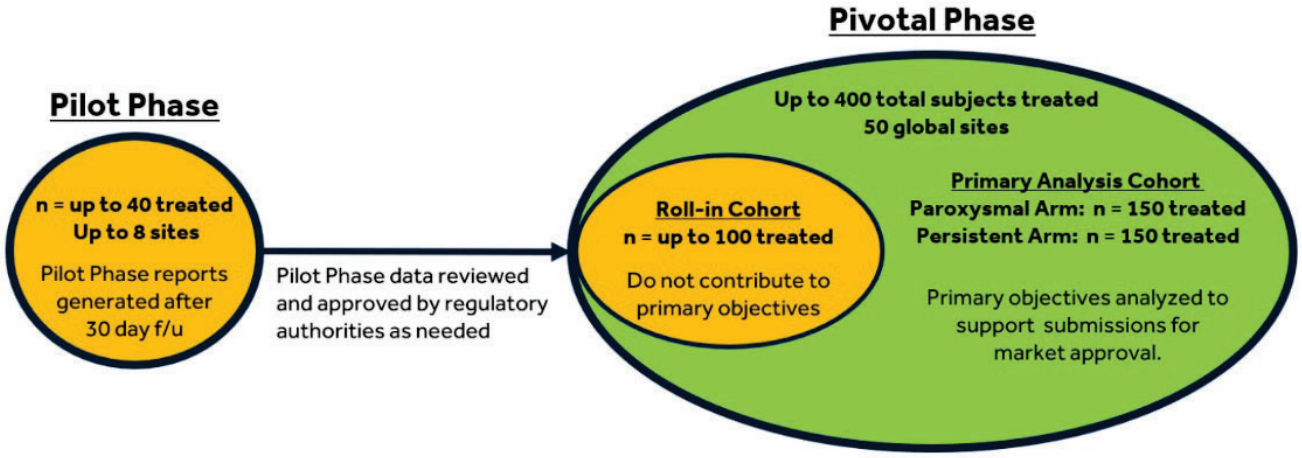
Test	Purpose	Results
	vein (RPV), and two locations in the left atrial appendage (LAA). The second objective was to evaluate microbubble generation.	
Contour Sheath[2] *and PFA Design Validation and Human Factors Validation*	This acute non-GLP porcine study (n=5) was designed to validate that the PulseSelect PFA system design meets the intended use and user needs for the system as they are defined in PulseSelect PFA System Design Input Sources document and to assess the effectiveness of the safety-related safety-by-design, protective measure, and information for safety risk control measures at preventing safety-related use error.	15 Electrophysiologist participants were able to successfully sense EGMs, pace, ablate, and assess treatment effect using the PulseSelect PFA system. The PulseSelect PFA system design meets the system user needs and intended purpose and is considered safe and effective.

[2] *Medtronic product under development at the time of this evaluation. Premarket clearance for FlexCath Contour is planned to be obtained via a future 510k submission.*

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study (PULSED AF) to establish a reasonable assurance of safety and effectiveness of ablation with the PulseSelect™ Pulsed Field Ablation (PFA) system for atrial fibrillation in the US, Australia, Canada, Europe, and Japan under IDE #G190272. As depicted in Figure 3, the study was designed to collect data and generate evidence in two phases, with data analyses planned at pre-specified timepoints. Data from the pivotal phase of this clinical study were the basis for the PMA approval decision. The pivotal phase included a roll-in cohort that did not contribute to primary objectives. The primary analysis cohort consisted of two treatment arms: paroxysmal and persistent atrial fibrillation. A summary of the clinical study is presented below. The summary below will refer to treated subjects enrolled in the primary analysis cohort of the pivotal phase unless otherwise indicated.

Figure 3: PULSED AF Phased Study Design



A. Study Design

The study was a prospective, multi-center, non-randomized, unblinded worldwide pre-market clinical study with 12 months of post-ablation follow-up. Adult subjects with a history of drug refractory recurrent symptomatic atrial fibrillation (AF) underwent ablation of pulmonary veins and confirmation of entrance block and, where assessable, exit block with the PulseSelect™ PFA system. Following the index ablation procedure and hospital discharge, study subjects from all participating geographies were followed at 7 days, 30 days, 3 months, 6 months, and 12 months, and exited from the study at the conclusion of the 12-month follow-up visit and associated 24-hour Holter.

Patients were treated in the pivotal phase between March 3, 2021 and November 27, 2021. The database for this PMA reflected data collected through the end of the study, December 15, 2022, and included 300 primary analysis cohort patients (150 paroxysmal AF and 150 persistent AF). There were 36 investigational sites that treated primary analysis cohort patients, 5 sites that treated only roll-in cohort subjects, and 1 site that enrolled but did not treat any subjects.

An active control group was not utilized in this study. Objective performance criteria for safety and efficacy were determined based on an international consensus statement and published peer-

reviewed literature of multi-centered ablation studies utilizing catheter ablation for a PVI-only approach for paroxysmal or persistent AF.

An independent imaging core laboratory reviewed pre-procedural and post-procedural visit cerebral MRI scans for silent cerebral lesions and silent cerebral events, and reviewed baseline and 3-month cardiac CT or MRI scans to characterize any potential occurrences of PV stenosis. And independent rhythm monitoring core laboratory distributed equipment for rhythm monitoring and adjudicated arrhythmias.

Oversight for this study was provided by an independent Data Monitoring Committee (DMC) comprised of one statistician with experience in the evaluation of clinical trials and five physicians who were not participating investigators for the study. The DMC was responsible for assessing the accumulating data on safety of the therapy during the study. The DMC was responsible for safeguarding the interests of study subjects, assessing the safety of the PulseSelect™ PFA System during the study, and for monitoring the overall conduct of the clinical study.

An independent Clinical Events Committee (CEC) reviewed and adjudicated, at a minimum, all procedure- and system-related adverse events, as well as all adverse events resulting in death. The CEC included five physicians (one neurologist and four electrophysiologists), who were neither participating Investigators for the study nor employees of Medtronic, including a CEC chairperson. Medtronic personnel facilitated CEC meetings but were non-voting members.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the PULSED AF study was limited to patients who met the following inclusion criteria:

1. Failure of at least one AAD (class I or III) for AF as evidenced by recurrent symptomatic AF, or intolerable side effects due to AAD.
2. A diagnosis of recurrent symptomatic paroxysmal or persistent AF:
   a. Symptomatic paroxysmal AF, which is defined as AF that terminates spontaneously or with intervention within 7 days of onset, documented by the following:
      i. Physician's note indicating at least 2 symptomatic paroxysmal AF episodes occurring within 6 months prior to enrollment; and
      ii. At least 1 ECG documented AF episode from any form of rhythm monitoring within 12 months prior to enrollment

   OR

   b. Symptomatic persistent AF, which is defined as continuous AF sustained beyond 7 days and less than 1 year, documented by the following:
      i. Physician's note indicating at least 1 symptomatic persistent AF episode occurring within 6 months prior to enrollment; and
      ii. Any 24-hour continuous ECG recording documenting continuous AF within 6 months prior to enrollment;

      OR

      2 ECGs from any form of rhythm monitoring taken at least 7 days apart, both showing continuous AF within 6 months prior to enrollment;
3. Age 18 through 80 years old (or older than 18 if required by local law)

Patients were not permitted to enroll in the PULSED AF study if they met any of the following exclusion criteria:

1. Long-standing persistent AF (continuous AF that is sustained >12 months)
2. Left atrial diameter > 5.0 cm (anteroposterior)
3. Prior left atrial ablation or surgical procedure (including left atrial appendage closures)
4. Planned LAA closure procedure or implant of a permanent pacemaker, biventricular pacemaker, loop recorder/insertable cardiac monitor (ICM), or any type of implantable cardiac defibrillator (with or without biventricular pacing function) for any time during the follow-up period
5. Patient who is not on oral anticoagulation therapy for at least 3 weeks prior to the ablation procedure
6. Presence of a permanent pacemaker, biventricular pacemaker, loop recorder/insertable cardiac monitor (ICM), or any type of implantable cardiac defibrillator (with or without biventricular pacing function)
7. Presence of any pulmonary vein stents
8. Presence of any pre-existing pulmonary vein stenosis
9. Pre-existing hemidiaphragmatic paralysis
10. Presence of any cardiac valve prosthesis
11. Moderate to severe mitral valve stenosis
12. More than moderate mitral regurgitation (i.e., 3+ or 4+ MR)
13. Any cardiac surgery, myocardial infarction, PCI / PTCA or coronary artery stenting which occurred during the 3-month interval preceding the consent date
14. Unstable angina
15. NYHA Class III or IV congestive heart failure or documented left ventricular ejection fraction (LVEF) less than or equal to 35% measure by acceptable cardiac testing (e.g. TTE)
16. Primary pulmonary hypertension
17. Rheumatic heart disease
18. Thrombocytosis, thrombocytopenia
19. Any condition contraindicating chronic anticoagulation
20. Active systemic infection
21. Hypertrophic cardiomyopathy
22. Known reversible causes of AF, including but not limited to uncontrolled hyperthyroidism, severe untreated obstructive sleep apnea, and acute alcohol toxicity
23. Any cerebral ischemic event (strokes or TIAs) which occurred during the 6-month interval preceding the consent date
24. History of thromboembolic event within the past 6 months or evidence of intracardiac thrombus at the time of the procedure
25. Any woman known to be pregnant or breastfeeding, or any woman of childbearing potential who is not on a reliable form of birth regulation method or abstinence
26. Patient with life expectancy that makes it unlikely 12 months of follow-up will be completed
27. Current or anticipated participation in any other clinical trial of a drug, device or biologic during the duration of the study not pre-approved by Medtronic
28. Known allergies or hypersensitivities to adhesives
29. Unwilling or unable to comply fully with study procedures and follow-up

30. Unable to provide own informed consent

2. Follow-up Schedule

Patients were evaluated prior to hospital discharge and at 7 days, 30 days, 3 months, 6 months, and 12 months post-ablation. Table 2 below provides the schedule of events for the study. Adverse events and complications were recorded at all visits.

Table 2: Schedule of Study Events

	Baseline	Procedure	Discharge	7 Day [1]	30 Day	3 Month [1]	6 Month [1]	12 Month	Unscheduled	Repeat Ablation [9]
Informed Consent	X									
Inclusion/Exclusion Criteria	X									
Medical History	X									
Physical Exam	X		X		X					
Pregnancy Screen [2]	X									
AAD & Anticoagulation Medication Review	X		X	X	X	X	X	X	X	
Arrhythmia Symptom Review	X				X	X	X	X	X	
12 Lead ECG	X		X		X	X	X	X	X	
NIHSS Assessment	X		X		X					
Cardiac CT Scan or MRI [3]	X					X	X	X		
AFEQT & EQ-5D-5L	X						X	X		
Transthoracic Echocardiogram (TTE) [4]	X									
Transesophageal Echocardiogram (TEE) [5]	X									
Intracardiac Echocardiography (ICE) [5]	X									
INR Assessment [6]	X									
Ablation Procedure Data		X								
Cerebral MRI [7]	X		X							
Mini-Mental State Examination (MMSE) [7]	X				X					
24h Continuous Monitoring with Holter							X	X		
Patient Activated Ambulatory ECG Monitor [8]			Weekly and symptomatic episodes							
Adverse Events	As they occur									
Device Deficiencies	As they occur									
Study Deviations	As they occur									

[1] Multiple modes of data collections were employed to support the collection of required visit data at the 7-day and 3- and 6-month visits such as: In office patient clinic visit, direct to patient contact (i.e. telephone, email, mail contact, etc.), and remote technology transmissions/uploads.

[2] Female subjects of childbearing potential only.

[3] Baseline and 3-month cardiac CT/MRI required for all subjects in the Pilot Phase, and for Pivotal Phase subjects consenting to the PV stenosis assessment. For the remaining Pivotal Phase subjects, cardiac CT/MRI was required only for subjects with suspected PV stenosis at 3-, 6- or 12-month visits and who had not undergone cardiac CT/MRI at a previous visit.

[4] Only required if data not available from within 6 months prior to consent date.

[5] Imaging to rule out left atrial thrombus must have been performed in all subjects within one day (on the day of or within the day prior to) the planned ablation procedure. TEE was the preferred method, but ICE may have been used in the event TEE was not preferred or possible for the subject or site.

[6] Subjects taking a vitamin K antagonist (VKA) were required to have a therapeutic INR (2-3.5) on the day of the planned ablation procedure. INR assessment was not required for subjects on other types of anticoagulants.

[7] Required only for subjects consenting to the Cerebral MRI assessment.
[8] Subjects submitted ECG transmissions weekly and whenever symptoms occurred from discharge through 12-months.
[9] The pre-ablation and discharge NIHSS assessments and the discharge physical examination were not required if the physician did not use the PFA system for any portion of the repeat ablation.

The key timepoints are shown below in the tables summarizing safety and effectiveness.

3. Clinical Endpoints

Primary Safety Endpoint

With regards to safety, for both persistent and paroxysmal treatment arms, the following were considered primary safety endpoints:

Within 6 months post-ablation:

- Pulmonary vein stenosis (≥70% diameter reduction)
- Phrenic nerve injury/diaphragmatic paralysis (ongoing at 6 months)
- Atrioesophageal fistula

Within 30 days of ablation procedure:

- Cardiac tamponade/perforation
- Cerebrovascular accident
- Major bleeding requiring transfusion
- Myocardial infarction
- Pericarditis requiring intervention
- Transient ischemic attack
- Vagal nerve injury resulting in esophageal dysmotility or gastroparesis
- Vascular access complications requiring intervention
- Systemic/pulmonary embolism requiring intervention
- Pulmonary edema
- Death
- Any PulseSelect™ PFA system-related or PFA procedure-related cardiovascular and/or pulmonary adverse event that prolongs or requires hospitalization for more than 48 hours (excluding recurrent AF/AFL/AT)

Safety events related to a repeat ablation procedure with the PulseSelect™ PFA system were not counted as safety events against the primary safety objective. However, all repeat PVI ablations using the PulseSelect™ PFA system and the safety events associated with them were reported separately.

Primary Efficacy Endpoint

With regards to efficacy, treatment failure was defined as any of the following components:

- Acute procedural failure, defined as the occurrence of any of the following:
  - Inability to isolate all accessible targeted pulmonary veins (minimally assessed

for entrance block and, where assessable, exit block) during the index procedure
    - Ablation using a non-study device in the left atrium
- Documented AF/AT/AFL on Holter/patient activated ambulatory/12-lead ECG after the 90-day post-ablation blanking period
    - Minimum of 30 seconds on Holter/patient activated ambulatory or 10 seconds on 12-lead ECG recording, excluding occurrence and treatment of typical right-sided cavotricuspid isthmus dependent atrial flutter if confirmed by entrainment maneuvers during EP testing.
- Any subsequent AF surgery or ablation in the left atrium, except for one repeat PVI ablation using PFA within the 90-day blanking period.
- Direct current cardioversion for atrial tachyarrhythmia recurrences after the 90-day blanking period.
- Class I or III antiarrhythmic drug (AAD) dose increase from the historic maximum ineffective dose (prior to the ablation procedure) or initiation of a new Class I or III AAD after the 90-day blanking period.
    - Note: remaining on the same pre-ablation dose or decreased dose of a previously failed or not tolerated Class I or III AAD after the 90-day blanking period is not considered a failure. Re-initiation, at any point after the blanking period, of a Class I or III antiarrhythmic medication that was failed or was not tolerated prior to the ablation procedure at any dose will be considered a primary endpoint failure.
    - Note: use of amiodarone at a dose greater than the historic maximum ineffective dose during the blanking period will result in a subject being classified as a primary efficacy failure.

Blanking period was defined as the first 90 days after the index ablation procedure. Recurrences of atrial arrhythmias during the blanking period were not counted in the determination of the first clinical failure for the primary endpoint. Within the blanking period, recurrent arrhythmias could have been managed with antiarrhythmic drugs or cardioversions. Titration or re-initiation of Class I and III antiarrhythmic medications were allowed during the blanking period.

Acute procedural failure was defined as the occurrence of any of the following:

- Inability to isolate all accessible targeted pulmonary veins (minimally assessed for entrance block and, where assessable, exit block) during the index procedure
- Ablation using a non-study device in the left atrium

With regard to success/failure criteria, individual patient success was defined as absence of a primary safety endpoint and freedom from treatment failure.

Secondary Endpoint

The secondary endpoint assessed changes in quality of life from baseline through 12 months after the index ablation procedure, based on two separate questionnaires as described below.

- The Atrial Fibrillation Effect on QualiTy of life (AFEQT) questionnaire is an atrial fibrillation-specific health-related quality of life questionnaire to assess the impact

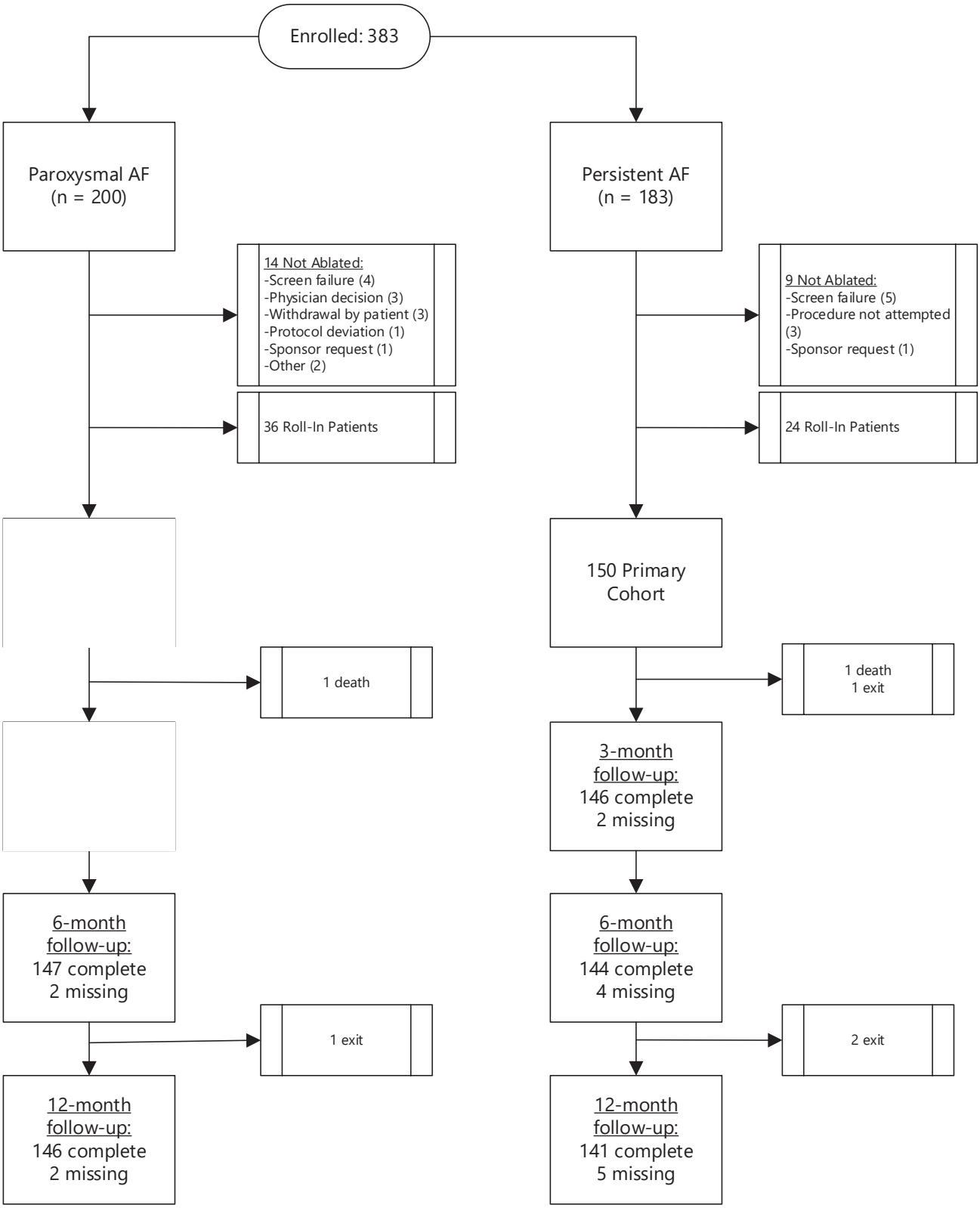
of AF on a subject's life. The endpoint for each subject was change in AFEQT score, which was the AFEQT score at 12 months minus the AFEQT score at baseline.

- The EuroQol EQ-5D questionnaire (5L version) is a standardized instrument for measuring generic health status. Composite scores for all subjects were computed based on the Pickard United States value set, regardless of their home country. The endpoint for each subject was change in EQ-5D composite score, which was the EQ-5D composite score at 12 months minus the EQ-5D composite score at baseline.

B. Accountability of PMA Cohort

Of 300 primary analysis cohort patients treated in the PMA study, 146 (97%) paroxysmal patients and 141 (94%) persistent patients were available for analysis at the completion of the study, the 12-month post-operative visit (see Figure 4).

Figure 4: Overall Subject Distribution



C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for an atrial fibrillation ablation treatment study performed in the US. The baseline demographic and health status characteristics of the treated paroxysmal and persistent AF pivotal phase subjects are shown in Table 3 below.

Table 3: Baseline Patient Characteristics*

Characteristic	Paroxysmal Atrial Fibrillation Cohort (n = 150)	Persistent Atrial Fibrillation Cohort (n = 150)
Age (year)	63.4±9.9	66.0±9.0
Male sex – no. (%)	96 (64)	113 (75)
Race – no. (%) White or Caucasian Japanese Black or African American Native Hawaiian and Other Pacific Islander Asian Indian Not reported	 115 (86) 16 (12) 0 (0) 1 (1) 1 (1) 17	 121 (88) 16 (12) 1 (1) 0 (0) 0 (0) 12
Ethnicity – no. (%) Hispanic Not Hispanic Not reported	 1 (1) 133 (99) 16	 0 (0) 139 (100) 11
Time since first atrial fibrillation diagnosis (year)	3.8±6.2	2.7±3.7
Body mass index (kg/m^2)	28.6±5.9	30.9±6.8
Left atrial diameter (mm)	38.7±5.8	42.0±5.0
Systolic blood pressure (mmHg)	130.4±17.6	130.7±17.2
Diastolic blood pressure (mmHg)	76.7±11.3	78.5±12.6
Left ventricular ejection fraction (%)	60.3±4.8†	57.6±6.4
Number of failed AADs	1.3±0.6	1.3±0.6
Cardioversions prior to enrollment – no. (%)		
Electrical	33 (22)	93 (62)
Pharmacologic	15 (10)	11 (7)
CHA_2DS_2-VASc score‡ – no. (%)		
0	33 (22)	25 (17)
1	34 (23)	27 (18)
2	38 (25)	40 (27)
3	28 (19)	32 (21)
>3	17 (11)	26 (17)
Medical characteristics – no. (%)		
Stroke	4 (3)	3 (2)
Transient ischemic attack	2 (1)	3 (2)
Myocardial infarction	7 (5)	8 (5)

Characteristic		Paroxysmal Atrial Fibrillation Cohort (n = 150)	Persistent Atrial Fibrillation Cohort (n = 150)
Coronary artery disease		31 (21)	31 (21)
Hypertension		73 (49)	97 (65)
Obstructive sleep apnea		30 (20)	47 (31)
Valve dysfunction		22 (15)	16 (11)
Diabetes		24 (16)	21 (14)
Baseline medications – no. (%)			
Antiarrhythmic		104 (69)	83 (55)
Class I	Cibenzoline	1 (1)	3 (2)
	Flecainide	43 (29)	17 (11)
	Pilsicanide	5 (3)	0 (0)
	Propafenone	6 (4)	9 (6)
Class III	Sotalol	24 (16)	11 (7)
	Amiodarone	7 (5)	26 (17)
	Dofetilide	5 (3)	2 (1)
	Dronedarone	13 (9)	15 (10)
ACE inhibitor		8 (5)	5 (3)
Beta-blocker		69 (46)	68 (45)

* Plus–minus values are means ±SD
† Data were available for 149 patients.
‡ CHA2DS2-VASc scores range from 0 to 9, with higher scores indicating a greater risk of stroke. The highest score observed in this trial was 6.

D. Safety and Effectiveness Results

1. Primary Safety Results

Among the 150 subjects in each study arm who underwent the initial pulsed field ablation procedure, there was 1 adverse event in each arm that was a primary safety event. A summary is provided in Table 4.

Table 4: Primary Safety Endpoint Adverse Event Incidence

Adverse Event	Number of Paroxysmal AF Subjects with Adverse Event (n=150)	Number of Persistent AF Subjects with Adverse Event (n=150)
Pulmonary vein stenosis (>70% diameter reduction)	0 / 150	0 / 150
Phrenic nerve injury/diaphragmatic paralysis ongoing at 6 months post-ablation	0 / 150	0 / 150
Atrioesophageal fistula	0 / 150	0 / 150
Cardiac tamponade/perforation	0 / 150	1 / 150
Cerebrovascular accident	1 / 150	0 / 150

Adverse Event	Number of Paroxysmal AF Subjects with Adverse Event (n=150)	Number of Persistent AF Subjects with Adverse Event (n=150)
Major bleeding requiring transfusion	0 / 150	0 / 150
Myocardial infarction	0 / 150	0 / 150
Pericarditis requiring intervention	0 / 150	0 / 150
Transient ischemic attack	0 / 150	0 / 150
Vagal nerve injury resulting in esophageal dysmotility or gastroparesis	0 / 150	0 / 150
Vascular access complications requiring intervention	0 / 150	0 / 150
Systemic/pulmonary embolism requiring intervention	0 / 150	0 / 150
Pulmonary edema	0 / 150	0 / 150
Death	0 / 150	0 / 150
Any PFA system-related or PFA procedure-related cardiovascular and pulmonary adverse event that prolongs or requires hospitalization for >48 h (excluding recurrent AF/AFL/AT)	0 / 150	0 / 150

The details on the two primary safety events are:

A paroxysmal AF subject experienced a cerebrovascular accident on the same day as the index ablation procedure. Six days later, the discharge NIH Stroke Scale (NIHSS) assessment revealed the subject had left anterior quad and left lateral foot numbness. A formal neurological consult with cerebral MRI was initiated, and the MRI revealed a 1.8cm acute infarct in the left superior cerebellar hemisphere.

A persistent AF subject experienced a pericardial effusion (classified by the CEC as meeting the definition of "cardiac tamponade / perforation") on the same day as the index ablation procedure. At the completion of the pulmonary vein isolation procedure, a slight decrease in blood pressure was noted. Intracardiac echo showed a pericardial effusion. The following day, ECG showed ST elevation consistent with pericarditis.

Figure 2 and Figure 3 display the Kaplan-Meier curves for the primary safety event rate through 6-months post-procedure for paroxysmal and persistent AF subjects, respectively. In both arms, the rates of primary safety events at 6 months were 0.7% (95% CI: 0.1-4.6%). The upper confidence bounds are less than the predefined performance goals of 13%, therefore, the objective is considered met in both arms.

Figure 5: Paroxysmal Arm Probability of a Primary Safety Endpoint at 6 Months

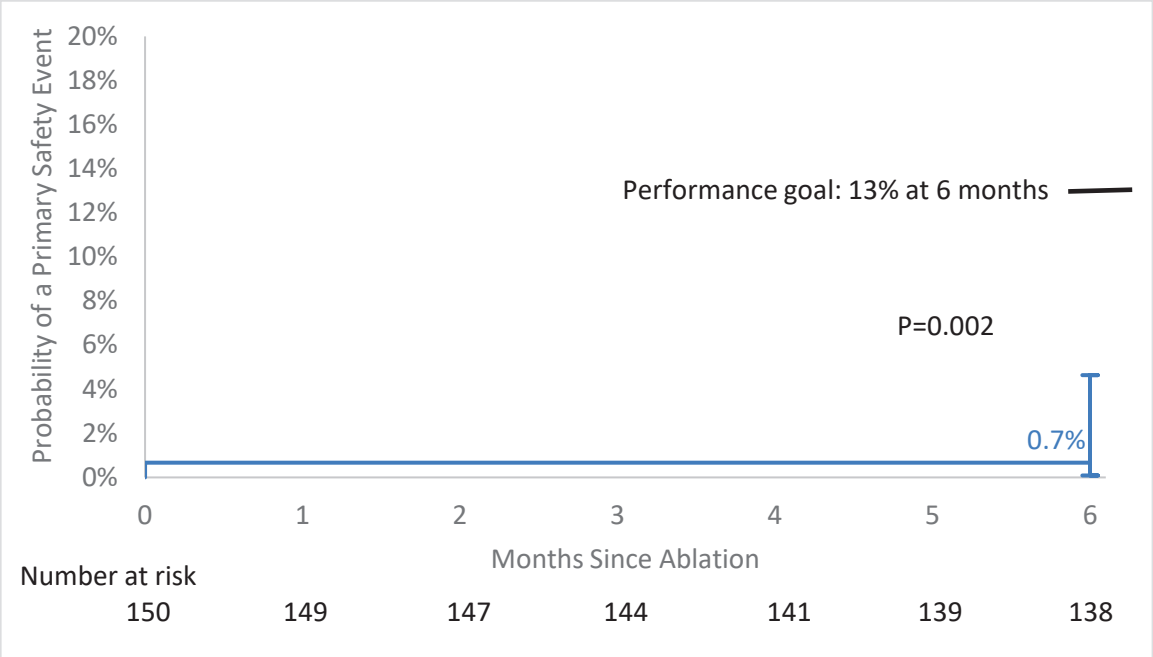
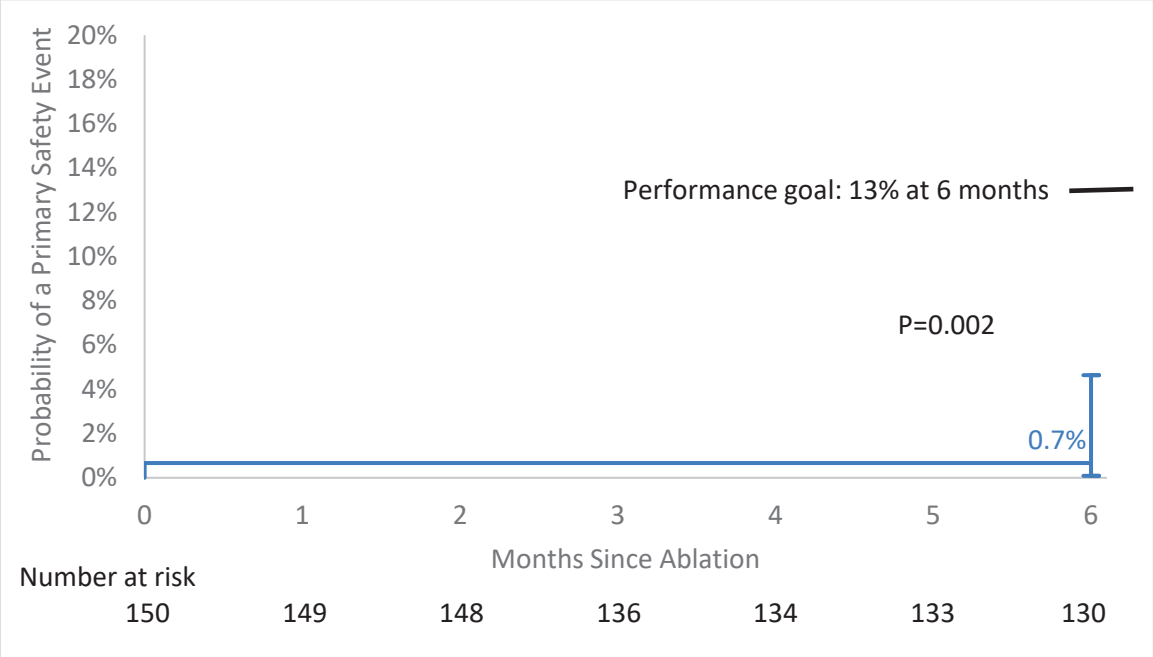


Figure 6: Persistent Arm Probability of a Primary Safety Endpoint at 6 Months



2. Primary Effectiveness Results

A total of 150 subjects underwent a study ablation in each study arm. A summary of effectiveness failures is given in Table 5, which shows the first chronological event for each subject that resulted in an effectiveness failure. The one-year Kaplan-Meier success rate was 66.2% [95% CI, 57.9 to 73.2] in the paroxysmal arm and was 55.1% [95% CI, 46.7 to 62.7] in the persistent arm (Figure 4, Figure 5).

Table 5: Summary of Effectiveness Failures

Primary Effectiveness Endpoint	Paroxysmal Atrial Fibrillation Cohort n (%) (n = 150)	Persistent Atrial Fibrillation Cohort n (%) (n = 150)
Did not have a primary effectiveness failure	100 (66.7%)	83 (55.3%)
Did not complete 12-month follow-up and did not have a primary effectiveness failure	3 (2.0%)	7 (4.7%)
Had a primary effectiveness failure	50 (33.3%)	67 (44.7%)
Acute procedural failure	0 (0.0%)	2 (1.3%)
Any subsequent AF surgery or ablation in the left atrium, except for one repeat PVI ablation using PFA within the 90-day blanking period	3 (2.0%)	2 (1.3%)
Direct current cardioversion for atrial tachyarrhythmia recurrences after the 90-day blanking period	0 (0.0%)	2 (1.3%)
Documented AF/AT/AFL on Holter/patient activated ambulatory/12-lead ECG after the 90-day post-ablation blanking period	40 (26.7%)	46 (30.7%)
Atrial fibrillation (AF)	30 (20.0%)	39 (26.0%)
Atrial tachycardia (AT)	4 (2.7%)	0 (0.0%)
Atrial flutter (AFL)	6 (4.0%)	7 (4.7%)
Class I or III antiarrhythmic drug (AAD) dose increase from the historic maximum ineffective dose (prior to the ablation procedure) or initiation of a new Class I or III AAD after the 90-day blanking period.	7 (4.7%)	15 (10.0%)

Figure 7: Paroxysmal AF Treatment Success at 12 Months - Primary Effectiveness Events

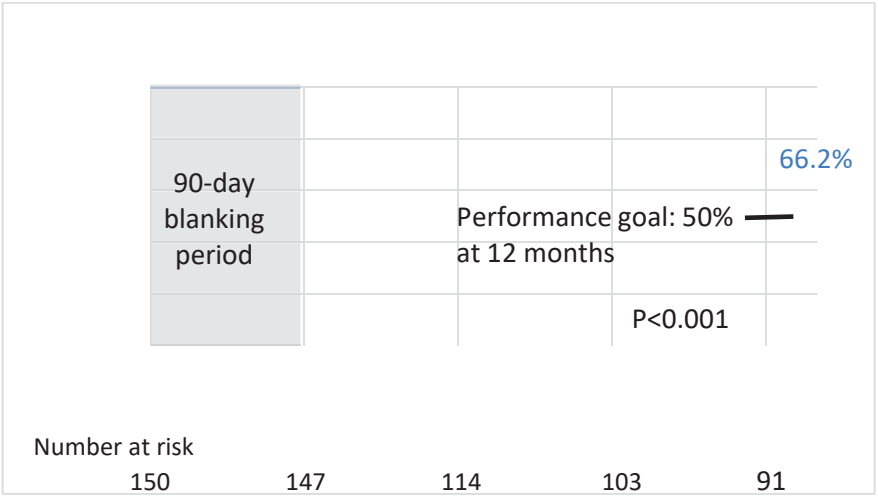
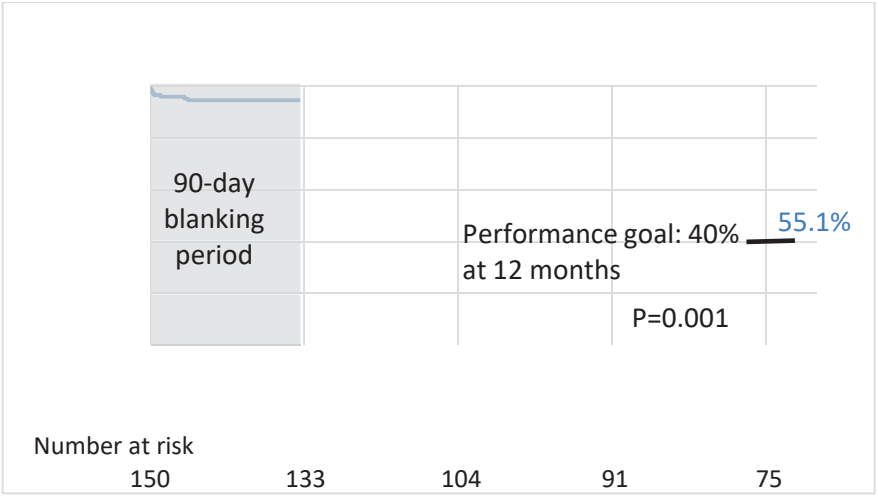


Figure 8: Persistent AF Treatment Success at 12 Months - Primary Effectiveness Events



Arrhythmia Monitoring Compliance

A major component of the primary effectiveness endpoint was documented AF/AT/AFL after the 90-day post-ablation blanking period. Subjects were required to use multiple methods of arrhythmia monitoring, including ECG at each study visit, 24-hour holter at the 6- and 12-month visits, and patient-activated ambulatory trans-telephonic monitor (TTM) weekly and whenever symptoms occurred from discharge through 12-month follow-up.

The tables in this section display a summary of the ECG, Holter, and TTM compliance of the 150 paroxysmal and 150 persistent subjects. TTM compliance was calculated on a week-to-week basis for each subject (number of weeks with ≥ 1 TTM divided by the number of weeks in the blanking or post-blanking period).

Table 6: 12-Lead ECG Compliance

Visit Name	Paroxysmal AF ECGs Expected	Paroxysmal AF ECG Compliance n (%)	Persistent AF ECGs Expected	Persistent AF ECG Compliance n (%)
Baseline	150	147 (98.0 %)	150	145 (96.7 %)
30-Day Follow-Up	150	146 (97.3 %)	150	138 (92.0 %)
3-Month Follow-Up	149	144 (96.6 %)	148	139 (93.9 %)
6-Month Follow-Up	149	147 (98.7 %)	148	140 (94.6 %)
12-Month Follow-Up	148	140 (94.6 %)	146	135 (92.5 %)

Table 7: 24-Hour Holter Compliance

Visit Name	Paroxysmal AF Holter Visits Expected	Paroxysmal AF Holter Compliance	Persistent AF Holter Visits Expected	Persistent AF Holter Compliance
6-Month Follow-up	149	125 (83.9 %)	148	124 (83.8 %)
12-Month Follow-up	148	129 (87.2 %)	146	116 (79.5 %)

Table 8: Weekly TTM Compliance

Timeframe	Paroxysmal AF TTMs Expected	Paroxysmal AF Subjects with TTM	Persistent AF TTMs Expected	Persistent AF Subjects with TTM
Days 0-90	1950	1577 (80.9 %)	1943	1463 (75.3 %)
Days 91-363	5795	4100 (70.8 %)	5755	4132 (71.8 %)

3. Secondary Endpoint Results

Of the 150 paroxysmal subjects, 144 subjects completed both questionnaires at both the baseline and 12-month visit. Of the 150 persistent subjects, 140 subjects fully completed both questionnaires at both the baseline and 12-month visit.

AFEQT

The Atrial Fibrillation Effect on Quality-of-Life (AFEQT) score is a quality of life measure with a range of 0 (complete disability) to 100 (no disability).

Table 9 shows the AFEQT questionnaire results at baseline and 12 months. There was a significant mean increase in score from baseline to 12 months of 29.4 points ($p<0.0001$) in the paroxysmal arm and 29.0 points ($p<0.0001$) in the persistent arm.

Table 9: Composite Score AFEQT Results Through 12 Months

AFEQT Results	Paroxysmal AF	Persistent AF
N	144	140
Baseline (Mean ± SD)	60.4 ± 19.8	62.0 ± 21.6
12-Month Visit (Mean ± SD)	89.8 ± 15.4	91.0 ± 12.9
Difference (95% CI)	29.4 (25.8 - 33.1)	29.0 (25.5 - 32.5)
Paired t-test p-value	<0.0001	<0.0001

EuroQol EQ-5D

The EuroQol EQ-5D questionnaire has a composite score based on the 5-question survey that ranges from 0 (least healthy) to 1 (most healthy).

Table 10 displays the EQ-5D questionnaire results at baseline and 12 months. There was a statistically significant improvement of 0.05 ($p=0.001$) in the paroxysmal AF arm and 0.06 ($p<0.0001$) in the persistent AF arm.

Table 10: Composite EQ-5D Results Through 12 Months

Composite EQ-5D Results	Paroxysmal AF	Persistent AF
n	144	140
Baseline (Mean ± SD)	0.86 ± 0.19	0.86 ± 0.19
12-Month Visit (Mean ± SD)	0.91 ± 0.16	0.92 ± 0.15
Difference (95% CI)	0.05 (0.02 – 0.08)	0.06 (0.04 – 0.09)
Paired t-test p-value	0.001	<0.0001

4. Ancillary Objective Results

Ancillary Objective — Acute Procedural Success

In the paroxysmal arm, all 150 subjects had acute procedural success for a success rate of 100.0%. All pulmonary veins attempted were isolated.

In the persistent arm, all 150 subjects had acute procedural success for a success rate of 100.0%. Two subjects had ablation in the left atrium for a non-PVI target with a non-study device. However, for the ancillary objective results, all pulmonary veins attempted were isolated with the study device only.

Ancillary Objective — Single Procedure Success

The results here match results of the primary effectiveness objective, except that any repeat PVI ablation with the PulseSelect™ PFA system within the blanking period was considered a failure.

In the paroxysmal arm, when repeat ablations within blanking are counted as failures, the single procedure success rate is 63.5% (95% CI: 55.2 - 70.7%).

In the persistent arm, when repeat ablations within blanking are counted as failures, the single procedure success rate is 50.0% (95% CI: 41.7 – 57.8%).

Ancillary Objective — Procedural Parameters

The procedural characteristics are shown in Table 10 below.

Table 11: Procedural Characteristics

Parameter	Paroxysmal (n = 150)	Persistent (n = 150)
Skin-to-skin procedural time (min)*	134±50 125 (102-157)	145±60 133.5 (107-173)
Device left atrial dwell time (min) †	65±29 58.5 (46-76)	70±31 62.5 (51-84)
Time between first and last application (min) †	58±28 53 (40-68)	64±28 60 (45-77)
Fluoroscopy time during procedure (min)	26±17‡ 21 (15-31)	29±21 23 (14-38)
Total pulsed field ablation energy delivered (sec)	25±8 23 (19-28)	29±10 27 (23-34)
Number of applications per procedure	48±15 43.5 (37-54)	57±20 52.5 (44-67)
Type of anesthesia used – no. (%) General anesthesia Deep sedation Conscious sedation	 134 (89) 8 (5) 8 (5)	 126 (84) 10 (7) 14 (9)
Neuromuscular blockade use – no. (%)	7 (5)	11 (7)
Isoproterenol and/or Adenosine used to assess PVI – no. (%)	26 (17)	33 (22)
Intra-procedural cardioversions – no. (%)	25 (17)	98 (65)
Esophageal temperature change from baseline (°c)	0.4±0.5§	0.3±0.4‖

Parameter	Paroxysmal (n = 150)	Persistent (n = 150)
	0.3 (0.1-0.5)	0.2 (0.0-0.5)
Mapping / Navigation system used – no. (%)		
CARTO	39 (26)	35 (23)
EnSite	86 (57)	88 (59)
Rhythmia	17 (11)	15 (10)
None of the above	8 (5)	12 (8)
Ablation Targets		
Pulmonary Vein Isolation (PVI)	150 (100.0)	150 (100.0)
Non-PV Left Atrial (LA) Triggers	0 (0)	0 (0)
LA Roof Line	0 (0)	0 (0)
LA Posterior Wall	2 (1.3)	4 (2.7)
Mitral Valve Isthmus Line	0 (0)	1 (0.7)
Other Ablation within LA	0 (0)	1 (0.7)
Atrioventricular nodal reentrant tachycardia (AVNRT) Ablation	1 (0.7)	0 (0)
Cavo-Tricuspid Isthmus (CTI) Ablation	29 (19.3)	43 (28.7)
Other Ablation**	2 (1.3)	3 (2.0)

Plus–minus values are means ±SD, with median (interquartile range) also presented.

* Skin to skin procedure time is from first sheath inserted to last sheath pulled out – this includes transfer time to recovery room and sheath pulling time

† Left atrial dwell time and time from first to last application includes the protocol-mandated 20-minute wait period and any post-ablation mapping time

‡ Data were available for 149 patients.

§ Data were available for 67 patients.

‖ Data were available for 74 patients.

** Other ablations are “atypical a-flutter/tachycardia” and "Right atrial tachycardia” (paroxysmal); “Focal AT,PAC”, “atypical flutter”, and "SVC” (persistent).

Ancillary Objective — All Reported Adverse Events

All adverse events were collected starting at the time of signing the informed consent form through the duration of the subject’s participation in the study. There were no unanticipated adverse device effects reported in the study. All adverse events were reviewed and adjudicated by an independent Clinical Events Committee (CEC). Adverse events are reported per the Medical Dictionary for Regulatory Activities (MedDRA) preferred term. A summary of adverse events is below for each arm.

Paroxysmal Arm

A total of 231 adverse events were reported. Six adverse events were reported prior to the procedure in paroxysmal pivotal subjects. Of the 225 adverse events reported which occurred either during or after the ablation procedure, 48 were classified as serious. 65 events were deemed related or possibly related to the PFA system and/or procedure of which 9 were serious (of note, the events are not mutually exclusive as an event can be related to the procedure and system). The 9 serious adverse events related to procedure or device during or after index ablation are in Table 11.

Table 12: Paroxysmal Arm Serious Adverse Events Related to a Procedure or Device During or After the Index Ablation Procedure Summary

Serious Adverse Event Related to the Procedure or Device	Days Post-Ablation	Procedures or Components to which the Adverse Event is Related (noted if only possibly related)
Urinary retention	0	Other Study Procedure (Index Procedure, Overall ablation procedure)
Hypoaesthesia	0	Other Study Procedure (Index Procedure, arterial line: Peripheral vascular access)
Cerebrovascular accident	0	PFA Procedure (Index Procedure) PFA System - PFA Generator (possible) PFA System - CEDS (possible) PFA System - Remote Control (possible) PFA System - Cable, Generator to Remote Control (possible) PFA System - Cable, Generator to CEDS (possible) PFA System - Cable, CEDS to EP Recording System (model 990027) (possible) PFA System - Catheter Connecting Cable, CEDS to EP Recording System (model 2ACHC) (possible) PFA System - Catheter Interface Cable (possible) PFA System - PVAC GOLD PFA System - Cardiac Trigger Monitor (possible) PFA System - Power Cord (possible) PFA System - Uninterruptible Power Supply (possible) PFA System - C14M-C13F Power Cord (possible) PFA System - Cardiac Trigger Monitor Accessories (possible)
Atrial flutter	16	PFA Procedure (Index Procedure, Overall ablation procedure) (possible)
Atrial flutter	26	PFA Procedure (Index Procedure, Overall ablation procedure) (possible)
Atrial flutter	93	PFA Procedure (Index Procedure) (possible)
Atrial flutter	222	PFA Procedure (Index Procedure, Overall ablation procedure) (possible)
Atrial flutter	297	PFA Procedure (Index Procedure)
Atrial flutter	319	PFA Procedure (Index Procedure, Overall ablation procedure) (possible)

One death occurred in the paroxysmal arm in the primary analysis cohort. 99 days after the subject's index ablation procedure, the site became aware of an adverse event with primary diagnosis of abdominal ascites. Six days later, the site updated the adverse event primary diagnosis to liver failure, indicating the subject died 99 days after the subject's index ablation procedure. The death was classified as a non-cardiac death. The CEC adjudicated the death event as not related to the overall ablation procedure, not related to the PFA procedure, and not related to any PFA system components.

Persistent Arm

A total of 239 adverse events were reported. Five adverse events were reported prior to the procedure in persistent pivotal subjects. Of the 234 adverse events reported which occurred either

during or after the ablation procedure, 76 of these were classified as serious. 62 events were deemed related to the procedure and/or PFA system, of which 15 were serious (of note, the events are not mutually exclusive as an event can be related to the procedure and system). The 15 serious adverse events related to procedure or device during or after index ablation are in Table 12.

Table 13: Persistent Arm Serious Adverse Events Related to a Procedure or Device During or After the Index Ablation Procedure Summary

Serious Adverse Event Related to the Procedure or Device	Days Post-Ablation	Procedures or Components to which the Adverse Event is Related (noted if only possibly related)
Pericardial effusion	During Procedure	PFA Procedure (Index Procedure, Overall ablation procedure) (possible) PFA System - PFA Generator (possible) PFA System - PVAC GOLD (possible)
Atrioventricular block	During Procedure	PFA Procedure (Index Procedure) PFA System - PFA Generator
Vascular access site haemorrhage	0	Other Study Procedure (Index Procedure, Femoral vascular access)
Hypotension	0	Other Study Procedure (Index Procedure, Overall ablation procedure)
Pneumonia	1	Other Study Procedure (Index Procedure, Overall ablation procedure)
Urinary tract infection	2	Other Study Procedure (Index Procedure, Other: Overall ablation procedure)
Bronchial hyperreactivity	3	Other Study Procedure (Index Procedure, Overall ablation procedure) (possible)
Atrial flutter	26	PFA Procedure (Index Procedure)
Atrial flutter	43	PFA Procedure (Index Procedure, Overall ablation procedure) (possible)
Atrial flutter	56	PFA Procedure (Index Procedure) (possible)
Sudden cardiac death	76	Other Study Procedure (Repeat Ablation, Overall ablation procedure)
Vascular access site haemorrhage	81	Other Study Procedure (Repeat Ablation, Femoral vascular access)
Atrial fibrillation	123	PFA Procedure (Index Procedure) (possible)
Atrial flutter	128	PFA Procedure (Repeat Ablation)
Atrial fibrillation	267	PFA Procedure (Index Procedure, Overall ablation procedure) (possible)

Serious Adverse Events Following Repeat Ablation

In the paroxysmal arm there were 17 repeat ablations among 16 subjects. These resulted in no serious adverse events that were related to either the PFA procedure or PFA system.

In the persistent arm there were 25 repeat ablations among 25 subjects, 16 treated with the PFA system and 9 treated with a non-study device. These resulted in 2 serious adverse events that were related to a repeat ablation with the PFA system. One subject had a vascular access site

hemorrhage on the day of the repeat ablation, which was adjudicated as related to the overall ablation procedure, not related to the PFA procedure, and not related to any PFA system components. One subject had a sudden cardiac death in the persistent arm in the primary analysis cohort 14 days after repeat ablation, and following Dofetilide loading. The death was not counted as a primary safety event because it was adjudicated by the CEC as not PFA procedure or PFA system related, and because it followed a repeat ablation procedure.

5. Subgroup Analyses

Subgroup analyses were performed to assess the consistency of the primary effectiveness outcome across the following preoperative characteristics: Age, sex, and race (Table 13, Table 14). Subgroup analysis on age was performed by dividing age into quartiles.

Table 14: Paroxysmal Arm Primary Effectiveness Objective by Demographics

Subgroup	Number of Subjects	Number of Failures (%)
Age		
18-56	38	8 (21.1%)
57-64	38	15 (39.5%)
65-69	36	12 (33.3%)
≥70	38	15 (39.5%)
Sex		
Male	96	31 (32.3%)
Female	54	19 (35.2%)
Race		
White	115	38 (33.0%)
Other	18	4 (22.2%)
Not Stated	17	8 (47.1%)

Table 15: Persistent Arm Primary Effectiveness Objective by Demographics

	Number of Subjects	Number of Failures (%)
Age		
18-60	36	13 (36.1%)
61-66	35	12 (34.3%)
67-71	42	22 (52.4%)
≥72	37	20 (54.1%)
Sex		
Male	113	50 (44.3%)
Female	37	17 (46.0%)
Race		
White	121	54 (44.6%)
Other	17	7 (41.2%)
Not Stated	12	6 (50%)

6. Sub-study Results

Pulmonary Vein Stenosis Sub-Study Results

A total of 83 Pivotal subjects consented to the PV stenosis sub-study. Among these subjects, 8 were exited from the study prior to receiving an ablation. Among the 75 sub-study subjects who were ablated, 67 completed both the baseline and 3-month imaging and 63 had analyzable data. An independent core laboratory adjudicated pulmonary vein stenosis diameters as moderate (50% to 70%) or severe (≥70% reduction. Table 15 provides a summary of results. There were no subjects with moderate or severe reduction in PV diameter.

Table 16: Summary of Change in PV Diameter

Vein	n	Baseline Diameter (mm) (Mean ± SD)	3-Month Visit Diameter (mm) (Mean ± SD)	Diameter Change (mm) (Mean ± SD)	Moderate Change n (%)	Severe Change n (%)
All	275	17.7 ± 4.1	17.5 ± 4.0	-0.2 ± 1.3	0 (0)	0 (0)
RIPV	63	17.6 ± 3.1	17.5 ± 3.1	-0.1 ± 1.4	0 (0)	0 (0)
RSPV	62	19.7 ± 3.2	19.3 ± 3.0	-0.4 ± 1.4	0 (0)	0 (0)
RMPV	9	10.5 ± 2.2	10.0 ± 2.0	-0.5 ± 1.5	0 (0)	0 (0)
RCPV	0	N/A	N/A	N/A	N/A	N/A
LIPV	63	15.3 ± 2.6	15.2 ± 2.5	-0.1 ± 1.1	0 (0)	0 (0)
LSPV	63	17.3 ± 3.0	17.3 ± 3.1	-0.0 ± 1.4	0 (0)	0 (0)
LMPV	0	N/A	N/A	N/A	N/A	N/A
LCPV	15	25.6 ± 4.6	25.4 ± 4.9	-0.2 ± 1.4	0 (0)	0 (0)

Cerebral Magnetic Resonance Imaging Sub-Study Results

A total of 59 subjects consented to the cerebral MRI sub-study. Among these subjects, 9 were exited from the study prior to receiving an ablation. Among the 50 sub-study subjects who were ablated, 45 completed both the pre-procedure and post-procedure cerebral MRIs. The mean lag time for post-procedure cerebral MRIs was 30.3 ± 15.0 hours after the ablation. All MRIs were reviewed by 2 independent neuroradiologists to identify new silent cerebral events (SCEs) on post-procedure MRI scan. SCE detection was defined as below:

> SCE detection = Diffusion positive (DWI hyperintense) + apparent diffusion coefficient (ADC) reduced

Among the 45 subjects undergoing pre and post-procedure cerebral MRI, 12 (26.7%) had an observed SCE (Table 17).

Table 17: Summary of Silent Cerebral Event Rate

		n (% of subjects)		
Arm	n	No SCEs	At least one SCE	95% Confidence Interval
Paroxysmal	26	21 (80.8%)	5 (19.2%)	6.6-39.4%
Persistent	19	12 (63.2%)	7 (36.8%)	16.3-61.6%
Total	45	33 (73.3%)	12 (26.7%)	14.6-41.9%

The same MRIs were also reviewed by 2 independent neuroradiologists to identify new silent cerebral lesions (SCLs) on the post-procedure MRI scan. SCL detection was defined as below:

> SCL detection = Diffusion positive (DWI hyperintense) + ADC reduced + Fluid-attenuated inversion recovery (FLAIR) positive

Among the same 45 subjects undergoing pre- and post-procedure cerebral MRI, 4 (8.9%) had an observed SCL (Table 18). It is important to note that all of the SCLs identified in this study were also categorized as SCEs by definition.

Table 18: Summary of Silent Cerebral Lesion Rate

		n (% of subjects)		
Arm	**n**	**No SCLs**	**At least one SCL**	**95% Confidence Interval**
Paroxysmal	26	24 (92.3%)	2 (7.7%)	1.0-25.1%
Persistent	19	17 (89.5%)	2 (10.5%)	1.3-33.1%
Total	45	41 (91.1%)	4 (8.9%)	2.5-21.2%

Participation in the cerebral MRI sub-study also required subjects to complete the Mini-Mental Examination (MMSE) before the procedure and at the 30-day post-procedure visit. The MMSE is an 11-question measure that can be used to assess cognitive impairment. The maximum score is 30, indicating good cognitive function; any score below 24 is considered abnormal, indicating possible cognitive impairment. No subject in the cerebral MRI sub-study had a score below 25 pre- or post-procedure.

7. Pediatric Extrapolation

In this premarket application, existing clinical data was not leveraged to support approval of a pediatric patient population.

E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 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 pivotal clinical study included 111 investigators of which one was a full-time employee of the sponsor (however, employment by sponsor began after last day as an electrophysiologist at a participating study site) and eight 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: 0
- Significant payment of other sorts: 8
- Proprietary interest in the product tested held by the investigator: 0

- Significant equity interest held by investigator in sponsor of covered study: 0

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. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

None.

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

In accordance with the provisions of section 515(c)(3) 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 demonstrates that the pertinent issues for safety and effectiveness of a pulsed field ablation system have been vetted through comprehensive bench and clinical evaluations.

XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The PULSED AF Clinical study met its primary efficacy endpoint which was freedom from a composite endpoint of acute procedural failure, arrhythmia recurrence, repeat ablation, cardioversion or antiarrhythmic drug escalation through 12 months, excluding an initial 90-day blanking period to allow procedural recovery. Using statistical survival methods, the efficacy success rate at 12 months in the paroxysmal arm is 66.2% (95% confidence interval: 57.9-73.2%), which is statistically significantly ($p=0.0003$) higher than the pre-specified performance goal of 50% success. The efficacy success rate at 12 months in the persistent arm is 55.1% (95% confidence interval: 46.7-62.8%), which is statistically significantly ($p=0.0006$) higher than the pre-specified performance goal of 40% success.

Both the AFEQT and EQ-5D hypotheses resulted in p-values <0.025 ($p<0.001$ for both) in both paroxysmal and persistent arms, therefore the Hochberg multiple testing procedure is met and a statistically significant improvement in quality of life from baseline to 12-months post-ablation can be claimed.

B. Safety Conclusions

The risks of the device are based on nonclinical studies as well as data collected in a clinical study conducted to support PMA approval as described above.

The primary safety end point in the PULSED AF clinical study was freedom from a composite of serious procedure- and device-related adverse events.

Among the 150 paroxysmal subjects who underwent the initial pulsed field ablation,

there was one adverse event determined by the CEC to be a primary safety event. It was a cerebrovascular accident on the day of the index PFA procedure. The rate of primary safety events at 6 months is 0.7% (95% CI: 0.1-4.6%). The upper confidence bound is less than the predefined performance goal of 13% (p=0.002), therefore, the objective is considered met.

Among the 150 persistent subjects who underwent the initial Pulsed Field Ablation, there was one adverse event determined by the CEC to be a primary safety event. It was a pericardial effusion during the index PFA procedure. The rate of primary safety events at 6 months is 0.7% (95% CI: 0.1-4.6%). The upper confidence bound is less than the predefined performance goal of 13% (p=0.002), therefore, the objective is considered met.

C. Benefit-Risk Determination

The probable benefits of the device are based on data collected in a clinical study conducted to support PMA approval as described above. The benefits of treatment using the device include a high probability in freedom from atrial arrhythmia recurrence and clinically significant improvement of quality of life. Based on the PULSED AF clinical study, 66% of the paroxysmal AF patients and 55% of the persistent patients were free from all primary efficacy failure events (including atrial arrhythmia recurrence) through 12 months after treatment with the PulseSelect™ PFA system. A post-hoc analysis also showed that 79.7% of paroxysmal patients and 80.8% of persistent patients were free from recurrence of symptomatic atrial arrhythmias, as documented on trans-telephonic monitoring. Further, paroxysmal and persistent patients experienced a clinically significant increase in quality of life assessed using the AFEQT and EQ-5D from baseline to 12 months post ablation.

The probable risks of the device are also based on data collected in a clinical study conducted to support PMA approval as described above. Among 300 subjects treated with the PulseSelect™ PFA system, 1 of 150 paroxysmal subjects (0.7%) and 1 of 150 persistent subjects (0.7%) had a CEC-adjudicated adverse event that contributed to the primary safety endpoint. These events included a cerebrovascular accident in one paroxysmal subject and a pericardial effusion in one persistent subject. No new or unanticipated adverse events or patient risks were identified in the PULSED AF clinical study.

Patient Perspective

The submission did not include specific information on patient perspectives for this device.

In conclusion, given the available information above, the data support that the probable benefits outweigh the probable risks for the catheter ablation treatment of atrial fibrillation with the PulseSelect™ PFA system.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and

effectiveness of this device when used in accordance with the indications for use. The PULSED AF clinical study met its primary safety and efficacy objectives. The PulseSelect™ PFA system demonstrated a reasonable assurance of effectiveness and safety for the treatment of drug refractory, recurrent, symptomatic paroxysmal atrial fibrillation and persistent atrial fibrillation (episode duration less than 1 year).

XIV. CDRH DECISION

CDRH issued an approval order on December 13, 2023. The final clinical conditions of approval cited in the approval order are described below:

You must obtain approval of your post-approval study (PAS) protocol(s) within 60 days from the date of this order. Within 30 days of your receipt of this letter, you must submit a PMA supplement that includes a complete protocol of your post-approval study described below. Your PMA supplement should be clearly labeled as a "PMA Post-Approval Study Protocol" as noted below and submitted to the address below. Please reference the PMA number above to facilitate processing. If there are multiple protocols being finalized after PMA approval, please submit each protocol as a separate PMA supplement.

In addition to the Annual Report requirements, you must provide the following data in post-approval study (PAS) reports for each PAS listed below.

The PULSED AF Post Approval Study (PAS) is a prospective, global, multi-center, non-randomized, observational study to evaluate the long-term effectiveness and safety of the PulseSelect™ Pulsed Field Ablation (PFA) System for the treatment of drug-refractory, recurrent, symptomatic, paroxysmal atrial fibrillation (AF) and persistent AF (episode duration less than one year). Approximately 530 adult patients (including additional patients to account for expected attrition during the first 3 months of follow-up) who intend to undergo their de novo pulmonary vein isolation procedure using the PulseSelect PFA system to treat symptomatic paroxysmal AF or persistent AF (episode duration less than one year) refractory or intolerant to at least one Class I or III antiarrhythmic medication will be enrolled and ablated using the PulseSelect PFA system, with at least 50% of patients treated in the United States and at least 200 patients in the paroxysmal AF cohort and at least 300 patients in the persistent AF cohort. The study will include a diverse (i.e., race, ethnicity, gender) patient population. All subjects will get a transthoracic echocardiogram performed at baseline and 12 months post-ablation to detect new left ventricular wall motion abnormality. A 12-lead ECG will be performed at baseline and 12 months post- ablation in all subjects. Follow up clinical data will be collected at discharge and 3, 6, 12, 24 and 36 months post-ablation.

The primary objectives of the PAS will be the following:

1) Estimating the rate of major procedural complications;
2) Estimating freedom from AF/atrial flutter (AFL)/atrial tachycardia (AT) recurrence post-90-day blanking through 36 months post-ablation using the PulseSelect PFA system in each cohort.

The secondary objectives will include but not limited to the following:

1) Estimating the rate of procedure-related mortality of the AF ablation procedure using the PulseSelect PFA system;
2) Estimating the rate of early mortality after ablation using the PulseSelect PFA system through 3 months post-procedure;
3) Estimating the rate of cardiac arrest that occurs during or after the AF ablation procedure using the PulseSelect PFA system;
4) Estimating the rate of new ventricular wall motion abnormality seen on echocardiogram at 12 months post-ablation;
5) Estimating the rate of serious device or serious procedure related adverse events for catheter ablation using the PulseSelect PFA system through 12 months post-procedure;
6) estimating freedom from AF/AFL/AT recurrence post-90-day blanking through 12 months post- ablation using the PulseSelect PFA system in each cohort;
7) estimating freedom from symptomatic AF/AFL/AT recurrence through 36 months post-ablation using the PulseSelect PFA system in each cohort;
8) Estimating change in quality-of-life through 36 months post-ablation.

You are also required to report any early mortality (through 3 months post-procedure) and any cardiac arrest that occurs during or after the AF ablation procedure using the PulseSelect PFA system within 10 days after you first receive notice of the event.

From the date of study protocol approval, you must meet the following timelines for the PULSED AF PAS:

- First subject enrolled within 6 months
- 20% of subjects enrolled within 12 months
- 50% of subjects enrolled within 18 months
- 100% of subjects enrolled within 24 months

In addition, you must submit separate periodic reports on the progress of the PULSED AF PAS as follows:

- PAS Progress Reports every six (6) months until subject enrollment has been completed, and annually thereafter, from the date of the PMA approval letter, unless otherwise specified by FDA.
- If any enrollment milestones are not met, you must begin submitting quarterly enrollment status reports every 3 months in addition to your periodic (6-month) PAS Progress Reports, until FDA notifies you otherwise.
- Submit the Final PAS Report three (3) months from study completion (i.e., last subject's last follow- up date).

Each PAS report should be submitted to the address below identified as a "PMA Post-Approval Study Report" in accordance with how the study is identified above and bearing the applicable PMA reference number.

The applicant's manufacturing facilities have been inspected and found to be in

compliance with the device Quality System (QS) regulation (21 CFR 820).

XV. 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.

Post-approval Requirements and Restrictions: See approval order.

XVI. REFERENCES

None.