Efficacy and Safety of Catheter Ablation for Atrial Fibrillation in Non-fluoroscopic Cardiac Electrophysiology Lab:

A Non-Inferior, Multi-Center, Prospective Randomized Controlled Trial

(NCT06719921)

Protocol

Version V3.0

11/27/2025

PROTOCOL SYNOPSIS

Title	Efficacy and Safety of Catheter Ablation for Atrial Fibrillation in Non-Fluoroscopic Cardiac Electrophysiology Lab: A Non-Inferior, Multi-Center, Prospective Randomized Controlled Trial
Purpose	A randomized controlled trial to investigate whether catheter ablation in a non-fluoroscopy lab is non-inferior to catheter ablation in a conventional DSA lab in terms of efficacy and safety for treating atrial fibrillation (AF).
Principal Investigator	Dr. Jiang Chenyang
Coordinating Center	Sir Run Run Shaw Hospital serves as the coordinating center for this clinical study with 16 EP centers participating.
Trial Sponsor	Biosense Webster
Number of Subjects	Up to 724 patients (procedures) will be enrolled over 1 year at 16 EP centers.
Inclusion Criteria	Subjects must meet <u>all</u> the following inclusion criteria to be eligible for participation in this trial. • Age: ⩾18 years • Patients diagnosed with paroxysmal AF or persistent AF ⩽1 year, who are referred for catheter ablation. • Patients referred for catheter ablation of AF (Pulmonary Vein Isolation) as a **first-time intervention** (no prior catheter ablation or surgical procedures for AF). • The patient is able and willing to provide written informed consent

Exclusion Criteria	Subjects who meet <u>any</u> of the following exclusion criteria are not eligible for enrollment. • Patients with contraindication to anticoagulation or to right or left sided cardiac catheterization • Patients scheduled for AF ablation procedures other than PVI and requiring X-ray fluoroscopy, such as VOM ablation, epicardial ablation, LAAO, CAG, etc. • Serious known concomitant disease with a life expectancy of < 1 year • MI, CABG, or PCI within the preceding 3 months • Left atrial diameter >55 mm • LVEF<30% • NYHA class III or IV • Awaiting cardiac transplantation or other cardiac surgery within 12 months. • History of a documented thromboembolic event within the past 6 weeks. • Heart or vascular malformation that impedes catheter access or vascular puncture. • Current enrollment in an investigational study evaluating another device or drug. • Acute illness, active systemic infection, or sepsis. • Significant congenital anomaly or a medical problem that in the opinion of the investigator would preclude enrollment in this trial.
Type	A Non-Inferior, Multi-Center, Prospective Randomized Controlled Trial
Design	**Sample Size Justification**

1) The sample size calculation will be based on the primary efficacy endpoint.

Sample-size was calculated by non-inferiority log-rank test with 1:1 design. The expected recurrence rate of AF is 30% for control group based on previous studies and our experience, and a hazard ratio of 1.3 was used for establish non-inferiority. Based on a power of 80% and an alpha of 0.05, proportion lost to follow up 5%, **a sample size of 724 patients** (362 for each group) was estimated.

Non-Inferiority Logrank Tests

Numeric Results in Terms of Sample Size

Power	N1	N2	N	Equiv Haz Ratio (HR0)	Actual Haz Ratio (HR)	Ref Haz Rate (h1)	Acc-rual Pat'n	Acc-rual Time/ Total Time	Ref Loss	Trt Loss	Ref to Trt	Trt to Ref	Alp
0.8003	361	362	723	1.30	1.00	0.3000	Equal	1 / 3	0.0500	0.0500	0.0000	0.0000	0.05

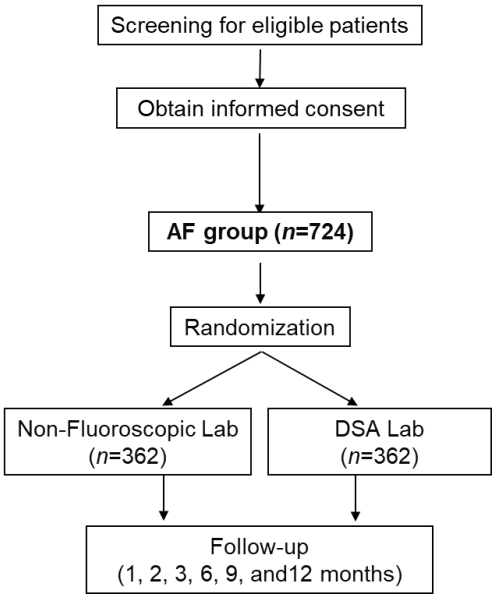
References

Jung,Sin-Ho; Kang, Sun J.; McCall, Linda M.; Blumenstein, Brent. 2005. 'Sample Sizes Computation for Two-Sample Noninferiority Log-Rank Test', J. of Biopharmaceutical Statistics, Volume 15, pages 969-979.

Lakatos, Edward. 1988. 'Sample Sizes Based on the Log-Rank Statistic in Complex Clinical Trials', Biometric Volume 44, March, pages 229-241.

2) Safety endpoints will be collected in details and analyzed for comparison between the groups, but they will not be used to determine the sample size.

Flowchart



Ablation Procedure details (study and control group)

The study will target AF catheter ablation procedures (Pulmonary Vein Isolation). After obtaining written informed consent, eligible patients will be randomized into one of the following two groups:

Group 1: Non-Fluoroscopic Lab Group

1. Ablation procedures will be performed in a catheterization lab equipped with non-fluoroscopic 3D electroanatomic mapping systems.
2. No routine fluoroscopy will be used, except if deemed necessary for safety (e.g., complications or unexpected procedural difficulties), adhering to the ALARA principle.
3. Pulmonary vein isolation (PVI) will be the sole ablation strategy, following the study protocol.

Group 2: Fluoroscopic Lab Group (DSA Lab)

	1. Ablation procedures will be conducted in a fluoroscopy-guided catheterization lab using digital subtraction angiography (DSA) for catheter navigation. 2. Radiation exposure will be recorded, and efforts will be made to minimize exposure by following the ALARA principle. 3. Similar to Group 1, PVI will be the sole ablation strategy, as per protocol. **Ablation strategy** The primary ablation strategy for both groups will be pulmonary vein isolation (PVI). Other additional ablation, including but not limited to linear ablation, complex fractionated atrial electrogram (CFAE) ablation, or superior vena cava (SVC) isolation is not recommended unless necessitated by one of the following: • Documented atrial flutter (AFL) or atrial tachycardia (AT) observed during the procedure, or • Arrhythmias originating from the specific region requiring intervention. **Energy Selection Principles** Energy modality (RF or PF) will be selected by the investigator prior to randomization according to routine clinical practice, with a population-level expectation that the proportion of PFA among newly enrolled patients will progressively increase to approximately 50–60%, without influencing individual clinical decision-making. **Recommendations** 1) The configuration of the Non-fluoroscopic Lab needs to be in accordance with the latest expert consensus

	recommendations (Jiang C, et al. Pacing Clin Electrophysiol. 2023 Sep;46(9):1035-1048). 2) The use of ICE catheter is required for both groups. The application of ICE technology includes but is not limited to: visualizing the cardiac anatomy; guiding catheter placement, transeptal puncture (if necessary); constructing the geometry; monitoring intracardiac thrombus and cardiac effusion throughout the procedure. 3) Magnetic mapping catheters (e.g. Lasso, PentaRay, or DECANAV) is recommended to create the cardiac geometry. 4) A safe, rapid, and smooth plan for transfer to the DSA lab should be established if no mobile DSA equipment is available in the Non-fluoroscopic EP Lab. In the event of an emergency requiring the use of DSA, patient transfer should be completed in a minimal period to maximize patient safety. 5) If deemed necessary, X-ray imaging may be utilized to guide catheter placement and monitor for potential complications. The use of X-ray must adhere to the As Low As Reasonably Achievable (ALARA) principle, ensuring radiation exposure is minimized while maintaining procedural safety and effectiveness.
Duration	April 22, 2025 – April 21, 2028, The study will be completed after the last enrolled subject has finished the 12-month follow-up period.
Objectives	To evaluate the efficacy and safety of AF ablation without the use of fluoroscopy.

Primary endpoint	• The primary efficacy endpoint is treatment success at 12 months without AAD, defined as freedom from recurrence of AF/AFL/AT lasting longer than 30 seconds. • The primary safety endpoint is a composite of the following prespecified procedure-related serious adverse events: death, stroke, transient ischemic attack, myocardial infarction, major vascular complication, or major bleeding within the first 7 days post procedure; development of a clinically significant pericardial effusion within 30 days; symptomatic pulmonary vein stenosis, atrial-esophageal fistula, or phrenic nerve injury within 3 months.
Secondary endpoint	• The initial success of the procedure. • The proportion of intraoperative conversion to using X-ray. • Utilization of lead personal protective equipment (PPE) and wear time. • Quality-of-life for staff at the end of each procedure. • The proportion of patients with recurrence of AF/AFL/AT during the first 90 days post-ablation. • **Early recurrence of atrial arrhythmias**, defined as any AF/AFL/AT episode lasting >30 seconds occurring during the blanking period. • **Late recurrence of atrial arrhythmias**, defined as any documented AF/AFL/AT episode lasting >30 seconds occurring after the blanking period and up to 12 months. • **Impact of early recurrence on late recurrence**, assessed through survival analysis and multivariable adjustment to evaluate whether early recurrence predicts

	subsequent late recurrence. • **AF burden,** assessed by scheduled rhythm monitoring (e.g., 7-day Holter at 3, 6, 9, and 12 months), expressed as the proportion of time spent in AF during the monitoring period. • Incidence of peri-procedural complication. • Total procedure duration, ablation time. • Changes in quality-of-life
Data Collection	Three case report forms will be used to collect essential data <u>Case Report Forms Include:</u> 1. <u>Procedure Form</u> • Patient-specific details • Procedural and ablation data, including de-identified Carto case backup data • Complications/adverse events during the procedure 2. <u>Complications/Adverse Events Form</u> • Adverse events that occur after the patient leaves the procedure room through discharge • Adverse events from the discharge date through 7 days post-procedure • Adverse events from day 8 through day 90 post-procedure 3. <u>Effectiveness Form</u> • For patients with atrial fibrillation, follow-up will be performed at 1 month, 2 months, 3 months, 6 months, 9 months and 12 months post ablation. Patients' symptoms and 12-lead ECG will be recorded at each follow-up visit to assess recurrence, and a 7-day

	Holter monitor will be used at the 1-, 2-, 3-, 6-, 9-, and 12-month visit. Pre and Post-Procedure Assessments to be documented on the CRFs include: • Baseline parameters including demographic data, TTE, CHADS2Vasc score and HAS-BLED score, OSA, AAD, OAC, interventions

Investigator's Statement

I, the undersigned, have read and understand the trial protocol described herein. I agree to perform and conduct the trial as described in the protocol and in accordance with applicable laws and regulations. I agree to maintain the confidentiality of all information received or developed in connection with this study.

_____

Investigator (Printed Name)

_____ _____

Investigator Signature Date

1. Introduction

1.1 What is the problem to be addressed?

The problem to be addressed is whether the catheter ablation procedures for atrial fibrillation (AF) in a non-fluoroscopic electrophysiology (EP) lab have the same efficacy and safety to those procedures in a digital subtraction angiography (DSA) lab, especially when new techniques -like intracardiac echocardiography (ICE), contact force catheters, Pulse field ablation (PFA), etc.-could be used in both groups.

1.1.1 Catheter ablation of atrial fibrillation and guidelines

Catheter ablation has become a standard therapy for managing AF, particularly in patients with symptomatic paroxysmal or persistent AF who have failed medical therapy. Pulmonary vein isolation (PVI) remains the fundamental strategy for catheter ablation, and PVI is endorsed by guidelines from the European Society of Cardiology (ESC), American Heart Association (AHA), and Heart Rhythm Society (HRS) as the first-line approach for AF ablation[1, 2].

New innovations such as **contact force-sensing catheters**, **3D electroanatomic mapping systems**, and **ICE** have improved catheter positioning, lesion precision, and procedural safety. In addition, Recent technological advancements have further optimized the safety and efficacy of AF ablation. **PFA**, a novel non-thermal ablation modality, uses electroporation to selectively ablate myocardial tissue while sparing adjacent structures such as the esophagus, phrenic nerve, and pulmonary veins. PFA has demonstrated potential for shorter procedure times and reduced risks of complications, offering a promising alternative to conventional thermal ablation techniques[3-6].

These advancements, combined with the established efficacy of PVI, are driving improvements in the outcomes and safety of catheter ablation procedures, addressing unmet needs in AF treatment, and broadening the scope of patients who can benefit from this therapy.

1.1.2 Fluoroscopy related health risks and occupational injuries

Historically, fluoroscopy has been the standard for guiding EP interventions; however, despite advancements that have reduced radiation exposure to safer levels[7-10], the need for heavy personal protective equipment (PPE) remains a significant concern. Prolonged use of leaded PPE has been linked to chronic occupational injuries such as back, neck, and other joint pain, as well as more serious conditions like spinal disc herniation[11, 12]. These injuries are particularly concerning for healthcare providers who perform complex and lengthy procedures, potentially limiting their career longevity[13, 14].

1.1.3 Financial and environmental burdens of fluoroscopic labs

Traditional EP labs pose substantial financial and environmental burdens. The setup of a new fluoroscopic lab, particularly one using DSA systems, involves significant initial investments—typically between 5 to 8 million yuan (¥) (687,400 to 1,100,000 dollars) per lab. Maintenance costs are also high, with annual fees reaching into the hundreds of thousands of yuan (¥) per lab. Moreover, fluoroscopic systems consume considerable energy, with each procedure requiring 60 to 70 kilowatt-hours of electricity to power X-ray machines and cooling systems. This not only drives up operational expenses but also contributes to increased carbon emissions. The sustainability of this approach is increasingly being questioned.

1.1.4 Fluoro-less/-free practices for AF catheter ablation

Non-fluoroscopic EP labs offer a feasible alternative, relying on advanced technologies such as three-dimensional (3D) mapping systems, contact-force catheters, and intracardiac echocardiography (ICE) to guide PE procedure without need for fluoroscopy. These systems not only reduce the need for heavy PPE and radiation exposure but also lower the financial and energy costs associated with traditional EP labs, making them more accessible and sustainable. Non-fluoroscopic EP labs offer a scalable and cost-effective solution, providing a more practical approach to addressing the growing demand for ablation therapies. Non-fluoroscopic EP labs, which eliminate the need for fluoroscopic imaging, have proven to be both feasible and safe[15-20]. The shift away from radiation-based guidance aligns with a growing focus on minimizing procedural risks and optimizing patient outcomes[21, 22]. While early studies suggest that non-fluoroscopic ablation techniques are feasible and effective[23-25], comprehensive data on their clinical outcomes and long-term safety are still limited. there remains a critical need for large-scale, standardized assessments to validate these findings and support broader adoption of the technology[26]. Furthermore, recent studies have suggested that the characteristics of the blanking period following PFA may differ from those after conventional RF ablation, as early recurrences of atrial arrhythmias do not necessarily predict long-term failure, and the blanking period may be substantially shorter than the traditional 3-month duration.[4, 27, 28] This highlights the need for large-scale studies to assess the real-world performance of non-fluoroscopic ablation techniques.

1.2 What are the principal research questions to be addressed?

1.2.1 Study Question and Hypothesis

We seek to assess the **efficacy** and **safety** of catheter ablation procedures for the treatment of AF, performed in a non-fluoroscopic EP lab. We hypothesize that the efficacy and safety outcomes of AF ablation in patients meeting the inclusion criteria of non-fluoroscopic EP lab will be non-inferior to those

achieved in a conventional DSA lab under identical technical conditions. The findings of this study will not only validate the feasibility of non-fluoroscopic EP labs for AF ablation but also provide a foundation for their application to emerging ablation technologies, such as pulsed field ablation (PFA), which are anticipated to gain widespread adoption in the near future.

1.2.2 Principal Research Questions

(i) **Efficacy**: Do patients undergoing catheter ablation for AF in a non-fluoroscopic EP lab achieve comparable success rates after one year or more of follow-up as those treated in a traditional DSA lab?

(ii) **Safety**: Are severe complication rates in a non-fluoroscopic lab non-inferior to those in a traditional DSA lab?

(iii) **Cost-effectiveness**: Is a catheter ablation strategy in a non-fluoroscopic EP lab cost-effective compared to traditional approaches?

(iv) **Target Population Selection**: Given that not all patients are suitable for treatment in a non-fluoroscopic EP lab, can we identify specific patient characteristics at the point of entry to determine suitability for non-fluoroscopic procedures?

2 Description Of Study Device

The following devices are included in the trial. New devices could be added to the list if they become available in the future.

2.1 CARTO® 3 System

The CARTO® 3 System is an imaging platform designed to support precise catheter navigation during cardiac procedures by generating real-time, three-dimensional maps of the heart. Utilizing electromagnetic technology, it provides accurate location and orientation of catheters, contributing to enhanced procedural safety and efficiency. The system employs magnetic sensors embedded in the catheters, along with six patient patches, to calculate catheter positioning based on electromagnetic signals. Fast Anatomical Mapping (FAM) enables the rapid creation of detailed heart maps, streamlining the mapping process and improving workflow.

2.2 SOUNDSTAR® Intracardiac Echocardiography (ICE)

ICE catheters are **8 or 10 Fr steerable phased-array devices** that provide a **90° ultrasound sector** perpendicular to the catheter tip. The catheter tip can be deflected **up to 160° in two planes** (anteroposterior and lateral), enabling four-directional movement (anterior, posterior, left, and right) to generate diverse **2D imaging**.

The CARTOSOUND® Module is a new software module that integrating real-time 3D ultrasound imaging with the CARTO® 3 System, enhancing

visualization of soft tissue during cardiac procedures. The SOUNDSTAR® catheter, equipped with a **navigation sensor**, allows its tip to be visualized on CARTO maps. This additional imaging capability allows for better catheter placement and monitoring of potential complications, such as blood clots or fluid accumulation. By improving visualization of critical structures, including the esophagus, the module helps minimize risks associated with catheter ablation procedures.

2.3 Thermocool Smarttouch® &Thermocool Smarttouch® SF (ST&STSF) Catheter

ST catheter is an irrigated-tip ablation, contact-force (CF)-sensing catheter indicated for cardiac mapping and ablation. The catheter contains a porous tip with 6 holes at the distal end. STSF catheter is a newer generation of the CF-sensing and irrigated-tip ablation catheter indicated for cardiac mapping and ablation. The catheter contains a porous tip with 56 holes at the distal end. The increased number of holes at the distal tip improves the cooling effect at the catheter-tissue interface. This newer design also requires less fluid delivery through the distal tip which could reduce the risk of volume overload. When used in conjunction with the Carto®3 system, the catheter of both kinds is able to provide real-time CF data during catheter ablation. Due to the product's indication restrictions, we suggest to use ST/STSF catheter for persistent AF patients.

SURPOINT is another new software module running with Carto 3 system. When used with ST and STSF catheter, SURPOINT is able to display AI value real-time on the Carto 3 system. The AI values can be used to guide the catheter ablation for durable lesion creation by ST and STSF catheter.

2.4 QDOT catheter

The Biosense Webster QDOT MICRO™ Catheter is a steerable multi-electrode luminal catheter with a deflectable tip designed to facilitate electrophysiological mapping of the heart and to transmit radiofrequency (RF) current to the catheter tip electrode for ablation purposes. The catheter contains force-sensing technology that provides a real-time measurement of contact force between the catheter tip and the heart wall. The location sensor embedded in the tip section transmits location and contact force information to the CARTO® 3 System.

The catheter incorporates six thermocouple temperature sensors in the tip section that can accurately monitor the catheter-tissue interface temperature and tip stability.

2.5 Varipulse Platform

The VaripulseTM platform from Biosense Webster is an innovative pulsed field ablation (PFA) system designed for treating atrial fibrillation. It uses a 7.5Fr circular catheter with 10 electrodes, each with its own irrigation pore to

improve cooling during ablation. The catheter is highly flexible, with 180° deflection in one direction and 90° in the other, making it easier to reach all pulmonary veins, including the more difficult-to-access right inferior pulmonary vein (RIPV).

The PFA energy is delivered in a bipolar pattern between alternating electrodes (e.g., between electrodes 1 and 3), as well as between adjacent pairs (e.g., electrodes 1–2 and 2–3). The system applies 1800V of pulsed energy through brief microsecond-long pulses, lasting a total of 250 microseconds per application.

During the procedure, irrigation is maintained at a flow rate both at rest and during ablation, to ensure safe and effective procedure.

3 THE TRIAL

3.1 Trial design

This is a non-Inferior, Multi-Center, Prospective Randomized Controlled Trial ((1:1 randomization) conducted in China. The study aims to consecutively enroll up to 724 procedures over the course of one year at 10 EP centers with non-fluoroscopic labs accredited by the Chinese Heart Rhythm Society. The anticipated total study duration is 36 months, with a follow-up period of 12 months for each participant. The study will be completed after the last enrolled subject has finished the 12-month follow-up period.

Following informed consent, obtained either during the pre-procedure office visit or during hospitalization for the procedure, baseline data will be collected. This data will include patient demographics, medical history, prior treatments, and laboratory test results.

The initial enrollment ratio between PFA and RF was projected to be evenly distributed at 50% each. Peri-procedural data, including procedural details, ablation strategies, acute success rates, VISITAG parameters, and any complications or adverse events, will be recorded up to the patient's discharge.

Post-discharge, participants will undergo follow-up evaluations at 1,2, 3,6,9,12 months after the procedure. The follow-up schedule will remain unchanged even if a repeat ablation procedure is required.

3.2 **Study Rationale and Objective**

This randomized controlled trial aims to evaluate the **efficacy**, **peri-procedural safety**, and **clinical outcomes** of catheter ablation performed in non-fluoroscopic EP labs compared to procedures in conventional DSA lab.

With the rapid adoption of non-fluoroscopic EP labs in China, it is essential to assess their performance to ensure safe and effective care. We hypothesize that non-fluoroscopic procedures will demonstrate non-inferior safety and efficacy to fluoroscopy-guided ablations, while offering benefits such as reduced costs, minimized radiation exposure for physicians, and improved environmental sustainability.

This study will provide evidence to guide clinical practice, improve patient care, and support the broader adoption of non-fluoroscopic EP technologies, enhancing access to advanced arrhythmia treatments and optimizing outcomes for patients with AF.

3.3 Inclusion/exclusion criteria

Inclusion criteria

Subjects must meet all the following inclusion criteria to be eligible for participation in this trial.

1) Age: ⩾18 years
2) Patients diagnosed with paroxysmal AF or persistent AF with a duration of 1 year or less, who are referred for catheter ablation.
3) Patients referred for catheter ablation as a first-time intervention (no prior catheter ablation or surgical procedures for AF).
4) The patient is able and willing to provide written informed consent

Exclusion criteria

Subjects who meet any of the following exclusion criteria are not eligible for enrollment.

1) Patients with contraindication to anticoagulation
2) Patients with contraindication to right or left sided cardiac catheterization
3) Patients scheduled for AF ablation procedures other than PVI and requiring X-ray fluoroscopy, such as VOM ablation, epicardial ablation, LAAO, CAG, etc
4) Serious known concomitant disease with a life expectancy of < 1 year
5) MI, CABG, or PCI within the preceding 3 months
6) Left atrial diameter >55 mm
7) LVEF<30%
8) NYHA class III or IV
9) Awaiting cardiac transplantation or other cardiac surgery within 12 months.
10) History of a documented thromboembolic event within the past 6 weeks.
11) Heart or vascular malformation that impedes catheter access or vascular puncture.
12) Current enrollment in an investigational study evaluating another device or drug.
13) Acute illness, active systemic infection, or sepsis.
14) Significant congenital anomaly or a medical problem that in the opinion of the investigator would preclude enrollment in this trial.

3.4 Study Endpoints

3.4.1 Primary endpoints

The primary efficacy endpoint is freedom from any documented atrial arrhythmia, including AF, atrial tachycardia or atrial flutter episodes lasting longer than 30 seconds without antiarrhythmic drugs, for 12 months after the index ablation procedure, excluding a 3-month blanking period. The continuation or reinitiation of class I or class III antiarrhythmic drugs after the 3-month post ablation blanking period, as well as electric cardioversion or catheter ablation for any atrial arrhythmias, are considered treatment failures for the primary end point.

The primary safety endpoint is a composite of the following prespecified procedure-related serious adverse events:

- Major vascular complication or major bleeding within the first 7 days post procedure.
- Development of a clinically significant pericardial effusion.
- Transient ischemic attack.
- Stroke.
- Myocardial infarction.
- Severe pulmonary vein stenosis.
- Atrial-esophageal fistula, or phrenic nerve injury within 3 months.
- Death.

3.4.2 Secondary endpoints

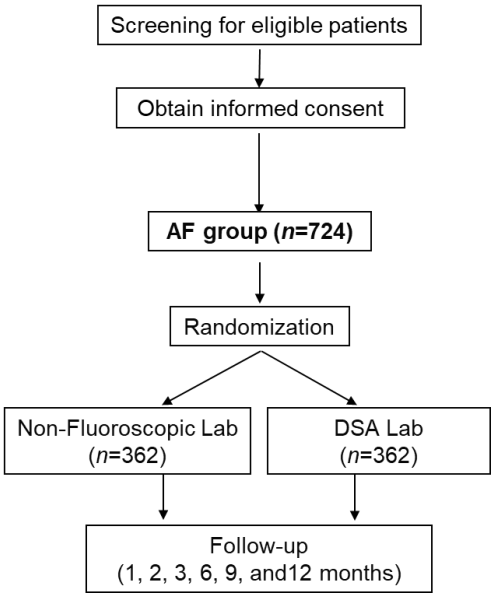
- The acute success of the procedure.
- The proportion of intraoperative conversion to using X-ray.
- Utilization of lead personal protective equipment (PPE) and wear time.Well-being survey of staff.
- The proportion of patients with recurrence of targeted arrhythmia during the first 90 days post-ablation.
- Early recurrence of atrial arrhythmias, defined as any AF/AFL/AT episode lasting >30 seconds occurring during the blanking period.
- Late recurrence of atrial arrhythmias, defined as any documented AF/AFL/AT episode lasting >30 seconds occurring after the blanking period and up to 12 months.
- Impact of early recurrence on late recurrence, assessed through survival analysis and multivariable adjustment to evaluate whether early recurrence predicts subsequent late recurrence.
- AF burden, assessed by scheduled rhythm monitoring (e.g., 7-day Holter at 3, 6, 9, and 12 months), expressed as the proportion of time spent in AF during the monitoring period.
- Incidence of peri-procedural complication.
- Total procedure duration, ablation time.
- changes in quality-of-life (using the AF Effect on Quality of Life (AFQT) and the EuroQol Health-Related Quality-of-Life 3-Level (EQ-5D-3L)).

3.5 Sample Size

For **efficacy** as the primary endpoint, sample-size was calculated by non-inferiority log-rank test with 1:1 design. The expected recurrence rate of AF is 30% for control group based on previous studies and our experience, and a hazard ratio of 1.3 was used for establish non-inferiority. Based on a power of 80% and an alpha of 0.05, proportion lost to follow up 5%, a sample size of **724 patients (362 for each group)** was estimated.

Safety endpoints will still be collected in detail and analyzed for comparison between the groups, but they will not be used to determine the sample size.

3.6 Study flowchart



3.7 Planned trial interventions

Ablation Procedure details (study and control group)

The study will target AF catheter ablation procedures. After obtaining written informed consent, eligible patients will be randomized in a 1:1 fashion to one of the following two groups:

Group 1: Non-Fluoroscopic Lab Group

1. Ablation procedures will utilize ICE and 3D mapping systems for non-fluoroscopic guidement. ICE is mandatory for real-time anatomical visualization.
2. No routine fluoroscopy will be used, except if deemed necessary for safety (e.g., complications or unexpected procedural difficulties), adhering to the ALARA principle.
3. Pulmonary vein isolation (PVI) will be the sole ablation strategy, following the study protocol.

Group 2: Fluoroscopic Lab Group (DSA Lab)

1. Ablation procedures will be conducted in a fluoroscopic lab. The use of ICE, 3D EP mapping systems, and other tools will follow the same recommendations as in the non-fluoroscopic lab group.
2. Radiation exposure will be closely monitored and minimized in accordance with the ALARA (As Low As Reasonably Achievable) principles when necessary.
3. Similar to Group 1, PVI will be the sole ablation strategy, as per protocol.

Ablation strategy

The primary ablation strategy for both groups will be **pulmonary vein isolation (PVI)**. Additional ablation, including but not limited to linear ablation, complex fractionated atrial electrogram (CFAE) ablation, or superior vena cava (SVC) isolation will not be allowed unless required in the presence of one the following:

- Documented atrial flutter (AFL) or atrial tachycardia (AT) observed during the procedure, or
- Arrhythmias originating from the specific region requiring intervention.

Energy Selection Principles

At the time of enrollment, the investigator will determine the planned ablation energy modality (radiofrequency [RF] or pulsed field [PF]) according to routine clinical practice, patient characteristics, procedural indications, device availability, and patient preference. The choice of energy modality is made prior to randomization, and the study protocol does not mandate or interfere with individual clinical decision-making.

Given the increasing adoption and availability of pulsed field ablation (PFA) in current clinical practice, and in order to maintain the external validity of the study in the future era when PFA is expected to become the predominant ablation modality, the study adopts a population-level expectation for patients enrolled after the effective date of this protocol version:

Without influencing individual clinical judgment, the cumulative proportion of PFA among subsequently enrolled patients is expected to progressively increase, with a target of achieving $\geqslant$50-60% of all newly enrolled cases.

This expectation aims to optimize the overall energy composition of the study cohort to better reflect evolving clinical practice trends. It does not impose restrictions on individual patient-level energy selection and does not apply to participants enrolled prior to the implementation of this protocol amendment.

Recommendations

1) The configuration of the Non-fluoroscopic Lab needs to be in accordance with the latest expert consensus recommendations (Jiang C, et al. Pacing Clin Electrophysiol. 2023 Sep;46(9):1035-1048).

2) The use of ICE catheter is required for both groups. The application of ICE technology includes but is not limited to: visualizing the cardiac anatomy; guiding catheter placement, transeptal puncture (if necessary); constructing the geometry; monitoring intracardiac thrombus and cardiac effusion throughout the procedure.
3) Magnetic mapping catheters (e.g. Lasso, PentaRay, or DECANAV) is recommended to create the cardiac geometry.
4) A safe, rapid, and smooth plan for transfer to the DSA lab should be established if no mobile DSA equipment is available in the Non-fluoroscopic EP Lab. In the event of an emergency requiring the use of DSA, patient transfer should be completed in a minimum period to maximize patient safety.
5) If deemed necessary, X-ray imaging may be utilized to guide catheter placement and monitor for potential complications. The use of X-ray must adhere to the As Low As Reasonably Achievable (ALARA) principle, ensuring radiation exposure is minimized while maintaining procedural safety and effectiveness.

3.8 Clinical Equipoise

3.8.1 Sample Size Justification

Since complication rates are very low (estimated at 2-3% in the ICE group, based on literature[29-32] and our prior experience), conducting a controlled study focusing on safety endpoints is not feasible. Additionally, our previous registry study has already provided supporting evidence on safety. In this study, while safety endpoints will still be collected in detail and compared between the two groups, they will not be used to calculate the sample size. Instead, the sample size calculation will be based on the primary efficacy endpoint.

3.8.2 Ablation strategy

PVI is well-established as the cornerstone strategy for AF ablation, particularly for paroxysmal AF, its effectiveness in persistent AF remains a subject of ongoing investigation. There is currently no robust clinical evidence to support that additional ablation strategies provide superior outcomes for all persistent AF patients[33]. Enhanced isolation of the vein of Marshall (EIVOM) has shown promise in improving outcomes for selected cases of persistent AF, particularly in addressing specific arrhythmogenic substrates. However, EIVOM is not universally applicable, as it often necessitates X-ray imaging and specialized techniques, which limit its use in fluoroscopy-free settings.

To maintain clinical equipoise and ensure the feasibility of this randomized controlled trial, we have chosen to focus on patients with shorter durations of persistent AF. These patients are hypothesized to have a lower likelihood of requiring EIVOM or other advanced substrate modification strategies. This

inclusion criterion allows us to evaluate the efficacy and safety of catheter ablation performed in non-fluoroscopic electrophysiology (EP) labs while minimizing the potential confounding effects of more complex ablation requirements. This approach ensures a balanced assessment of outcomes and aligns with the study's goal of evaluating PVI as the primary ablation strategy in a fluoroscopy-free context.

4 Data Collection

An Electronic Data Capture (EDC) system will be employed for the collection and secure storage of study data. The system is equipped with several built-in data integrity features, including range checks, logic checks, and mandatory data field requirements to ensure the accuracy and completeness of entries. Each investigator will be granted a unique, password-protected login to access the database, and any alterations to subject data will be logged to maintain a clear audit trail.

Primary data will be sourced from medical charts and procedural records, complemented by information gathered during structured interviews to assess quality of life (QoL) and other study-related metrics. Data collection will be managed by independent personnel who are not involved in the clinical care or procedural treatment of study subjects. Baseline, pre-procedural, and post-procedural data will be extracted from the medical record, standard questionnaires, physical examinations, and laboratory tests conducted during office visits. Physicians performing the ablation procedures will be responsible for accurate and timely documentation of relevant procedural data in the medical record.

Follow-up assessments will occur at the1-,2-, 3-,6-,9-,12-month mark and may be conducted through in-person interviews. However, in-person interviews are strongly recommended to ensure the most comprehensive evaluation. During these visits, subjects will complete standardized questionnaires, undergo physical examinations, and have laboratory tests performed as needed. A trained study coordinator will conduct the interviews, following a standardized protocol to ensure consistency across all sites.

4.1 Data Acquisition

Data will be collected prospectively at multiple time points, including baseline/pre-ablation, intra-procedural, prior to hospital discharge, and at the 3-month follow-up post-index ablation. Patient demographic and clinical characteristics, procedural details, and concomitant medications will be recorded from medical charts. Information regarding lifestyle factors, medication adherence, adverse events, redo procedures, and quality of life (QoL) - general EQ-5D and the AF specific AFEQT assessment -will be obtained through either face-to-face interview, telephone consultations, or online platforms.

At the1-, 2-, 3-, 6-, 9- and 12-month follow-up, arrhythmia recurrence will

be assessed using a 12-lead ECG and a 7-day Holter monitor. In this study, the Kapatch dynamic electrocardiogram monitor (Zhejiang Medical Device Registration Certificate No.: 20202070050) will be also utilized for cardiac rhythm monitoring at the1-, 2-, 3-, 6-, 9-, and 12-month follow-up.

4.2 Procedure of Data Collection

At each site, all subjects that meet all inclusion criteria and do not have any exclusion criteria will be enrolled non-selectively.

All subjects meeting the enrollment eligibility criteria will be recorded in a patient log. Patient logs will be kept in individual participant hospitals and do not need to be submitted to the Coordinating Center. The enrolled subjects will be compared with those who meet the inclusion/exclusion criteria but are not enrolled in the study to assess the enrollment selection bias. Only subjects who have signed the informed consent are enrolled and the follow-up data including the rhythm monitoring data collected according to the study protocol. For those who are eligible but fail to enroll due to unwillingness to sign the informed consent or due to other reasons, only baseline characteristics data, procedure data and in hospital stay outcomes (severe procedure related complications, prolonged hospital stay) will be collected. An informed consent waiver is required from EC/IRB for each participating site. The data to be collected at each time point is listed in **Table 1**.

The accuracy of data collection will be validated by comparing with the source data. At least 10% of each data variable will be randomly selected for validation by EDC system. Demographical data will be 100% SDV, and the remaining data variables will be selected for validation at various ratios depending on the criticality of the variable. SDV randomization ratio will be dynamically reset by error rate of each site and each variable.

Table 1. Data collected at different time points

	Baseline/Pre-Ablation	Ablation and Pre-Discharge	1M [Days 30±7]	2M [Days 60±7]	3M [Days 90± 14]	6M [Days 180± 30]	9M [Days 270± 30]	12M [Days 365± 45]
Informed Consent	√							
Face to Face interview/Tele-interview	√	√	√	√	√	√	√	√
Questionnaire	√				√	√		√
Socio-demographic	√							
Medical history	√							

Smoking, alcohol consumption	√		√	√	√	√	√	√
New onset medical conditions		√	√	√	√	√	√	√
Concomitant Medications	√		(√)	(√)	(√)	(√)	(√)	√
Transthoracic echocardiography	(√)	(√)	(√)	(√)	(√)	(√)	(√)	(√)
Neuroimaging of the cranium	√	√	(√)	(√)	(√)	(√)	(√)	(√)
Laboratory investigations	√	√	√	√	√	√	√	√
EQ-5D	√				√	√		√
AFEQT (for AF/AFL)	√				√	√		√
Physical examination	√	(√)	(√)	(√)	(√)	(√)	(√)	(√)
Ablation Record		√						
ECG record (Holter)	√	√	√	√	√	√	√	√
Re-ablation and ablation sites			√	√	√	√	√	√
SAEs		√	√	√	√	√	√	√
Cardiovascular related emergency visit and hospitalization			√	√	√	√	√	√

4.3 Data Elements

The following data elements will be collected in three case report forms and a site questionnaire.

Pre-procedure data

The following pre-procedure data will be collected in one of the case report forms.

Demographics	age, sex, education background, medical insurance information, etc
Medical history	medical history (congestive heart failure, hypertension, coronary heart disease, diabetes, stroke/TIA history, systemic arterial embolization, bleeding history, CHADSVASC for AF, arrhythmia history) and heart surgery history
Physical examination	blood pressure, heart rate and heart rhythm, and body weight and height

Laboratory test	CBC, Electrolytes, glucose, serum cholesterol, creatinine, INR
Echocardiogram	left ventricular ejection fraction (LVEF), left atrium diameter and volume, presence and severity of mitral and tricuspid regurgitation, LAA detection methods (CT/TEE/ICE), whether there is spontaneous echo contrast in TEE examination
Concomitant Medications	blood pressure lowering drugs, diabetic medications, lipid lowering drugs, continuous or interrupted anticoagulants, AADs
Quality of life (QoL)	general EQ-5D and the AF specific AFEQT assessment

Procedural Data

The table below lists the information documented during AF ablation and pre-discharge hospital stay. These data will be collected in another case report form.

Cardiac arrhythmia	□paroxysmal AF □persistent AF ≤1year □Others, _____
Anesthesia or sedation level	minimal sedation, conscious sedation, deep sedation or general anesthesia
Ablation and mapping catheters	list the catheters
Procedural and ablation data	total procedure time, Mapping time and points, RF application time
Ablation strategies : Ablation sites in addition to PVI including the AI value per ablation line	Circumferential pulmonary vein isolation (CPVI) Additional: Line ablation: LA roof line/LA anterior line/LA posterior line/CTI/Mitral isthmus/SVC CFAE/Rotors/Substrate modification Others
Acute success	□Yes □No, reason:_____
VISITAG® parameters	number of tags, CF, power and energy deliver time per lesion, AI value per application and per segment, impedance drop Data will be collected in the CARTO® 3 Navigation

	System during the ablation procedures for generation of left atrium ablation maps in accordance with predefined segments of anterior wall, ridge, posterior wall, roof and inferior area VISITAG® parameters source database should be exported from Carto system and saved on One Drive. Checklist will be provided to record the participants' ID, file ID and uploading information.
ACT	Max ACT during ablation _____
Pre-discharge data	• Supine time after ablation • Concomitant medications (anticoagulation, AAD, BP-lowering drugs, lipid-lowering drugs, and antidiabetic drugs) • Postprocedural complications/adverse events (device/procedure-related and any SAEs) • Length of stay in hospital

Subject Follow-Up Data

Subject follow-up data are collected in the effectiveness and safety data form and include items listed in the table below:

Patient information	weight, blood pressure, QOL, EHRA score, life style,
Concomitant medications	anticoagulation, AAD, blood pressure-lowering drugs, lipid-lowering drugs, and antidiabetic drugs
Documented AF/AFL/AT recurrence	12-lead ECG/7-day Holter, AF burden in the holter
Repeat procedure	Re-ablation and ablation sites
Emergency or re-hospitalization	Cardiovascular related emergency visit and re-hospitalization due to arrhythmia recurrence or procedure-related reasons
New onset medical conditions	hypertension, diabetes, major bleeding, renal dysfunction, etc.
Serious procedure or device related adverse events	List (Appendix A)

5. Trial/Repository Administration

The trial will be conducted in compliance with this protocol, and according to ISO 14155: 2011, Clinical Investigation of Medical Devices for Human Subjects, and the International Conference on Harmonization (ICH) Harmonized Tripartite Guideline of Good Clinical Practice (E6).

5.1 Institutional Review Board/Ethics Committee

This protocol must be reviewed and approved by the appropriate IRB/EC where the trial is to be conducted before enrollment of subjects. The IRB/EC must approve in writing any changes to the protocol that affect the rights, safety, or welfare of the subjects, or may adversely affect the validity of the trial.

A signed copy of the IRB/EC Approval Form and a signed copy of the IRB/EC approval letter addressed to the investigator must be submitted to the Coordinating Center certifying registry approval before subject enrollment. Investigators are responsible for submitting and obtaining initial and continuing review of the trial by their IRB/EC.

5.2 Responsibilities

The investigator is responsible for ensuring the trial is conducted in accordance with the procedures and evaluations described in this protocol (see Investigator Signature Page at the beginning of this protocol).

Deviations from the protocol shall not be made without discussion with the Coordinating Center. Changes to the protocol may be made only when a written protocol amendment provided by the sponsor has been signed by the investigator and approved by the IRB/EC and applicable regulatory agencies in accordance with local requirements.

5.3 Restrictions

Only staff listed in the delegation can log in the internet-based data management system with an authorized account and the unique individual password.

5.4 Confidentiality

Authentication technology is adopted to meet demands like identity authentication and non-repudiation. Sensitive data will be stored via a data encryption technology and cross-domain data transfer will be encrypted. The present trial will sign a confidentiality agreement with the staff who manage and operate the important information. Information manager should not modify or delete the existing information without authorization. Unrelated people are restricted to access to the clinical research EDC system.

Data managers will daily check all the uploaded data case by case, and if there’s a question, he/she shall raise it and send a reminder to the investigator. Data managers are served by experienced physicians from HHRC. All questions will be listed with the content, questioner, proposed date and resolved date recorded in detail.

The study team will retain all study records required by the HHRC and by the applicable regulatory bodies in a secure and safe facility for a minimum period of 15 years.

The Sir Run Run Shaw Hospital Clinical Trials Centre will function as the

coordinating centre for all aspects of this trial. The Data Management Coordinating Centre will oversee the intra-study data sharing process, with input from the Data Management Subcommittee.

All Principal Investigators will be given access to the cleaned data sets. Project data sets will be housed on the Project Web Database and/or the file transfer protocol site created for the study, and all data sets will be password protected. Project Principal Investigators will have direct access to their own site's data sets and will have access to other sites data by request. To ensure confidentiality, data dispersed to project team members will be blinded of any identifying participant information.

5.5 Private Health Information (PHI)

Subjects will be identified on the case report form by number codes only, using the criteria provided by the coordinating center. Local IRB approval is required for each participating site.

All information and data sent to the Coordinating Center concerning subjects or their participation in this trial will be considered confidential. Only authorized Coordinating Center personnel or designee, or local government authorities acting in their official capacities will have access to these confidential files. All data used in the analysis and reporting of this evaluation will be without identifiable reference to the subject.

6. Data Collection and Management

The Coordinating Center will perform all data management activities for this trial. These activities include development and validation of a clinical database into which all trial data will be entered. The Coordinating Center will be responsible for ensuring overall integrity of the data and database. Data will be stored on a secure cloud server. Only authorized study person will be able to access EDC. ID and password will be used to protect data security.

6.1 Data Collection

Case Report Forms (CRF) will be used to collect all subject data for the trial. The CRF will be developed to capture the information outlined in this protocol. Data collected on these CRFs will be entered to an Electronic Data Capture (EDC) System by individuals at the Coordinating Center and analyzed by the trial Sponsor as defined in the trial protocol.

6.2 Data Reporting

The site investigator, or a designated individual, is responsible for ensuring that trial data are properly recorded on each subject's CRF and related documents. Completed CRFs will be reviewed by Coordinating Center personnel throughout the trial.

All CRFs should be completed and submitted to the Coordinating Center using the guidelines set for by the Coordinating Center. For AE reporting,

refer to the Adverse Event Reporting Requirements and timelines within this trial protocol.

6.3 Source Documentation

Source documents will serve as the basis for validation of data entered into the EDC system. Source documents may include subject medical records, hospital charts, clinical charts, the investigator's subject registry files, admissions and discharge summaries, as well as the results of diagnostic tests such as X-rays, laboratory tests, and electrocardiograms.

If no standard hospital or office document exists to capture information that may be unique to this trial, a worksheet may be developed to record this information, which shall be signed by the PI at the given site and serve as the source document for unique trial data.

Electronic subject records will be considered source documents on the condition that the hospital's database is a validated system. If this is not the case, electronic records will have to be printed and added to the subject's paper file.

Regulations require that investigators maintain information in the subject's medical records, which corroborate data collected on the CRF.

Variables collected will be validated with source data. Demographical data will be 100% SDV, and the rest of data to be set up different randomization ratio, based on the variable priority. At least 10% of transferred data will be randomly selected by EDC system.

If there are no discrepancies, then monitor does not have to SDV anymore data for that visit. If there are discrepancies, then the amount to SDV will increase by 10% and will continue to increase until 50%. If discrepancies are still found after 50%, then all data will have to be SDV. The Site Monitor may also check the compliance of the site with the protocol and to detect issues that may be difficult to assess from remote monitoring alone.

The Project Manager – he/she will be responsible for the day to day running of the study including liaising with the individual study sites and study research co-coordinators. This individual will supervise the activities of the Study Nurses with respect to patient eligibility, data accumulation and transmission, and patient follow-up.

There will also be a separate and independent data safety and monitoring board (DSMB). The DSMB will consist of three people. All members of the DSMB have extensive clinical trials experience and were invited on the basis of their expertise and independence. The DSMB will monitor the study safety data on an ongoing basis.

6.4 Missing Data Handling

This study is a real-world study, and all the data will be recorded based on the medical routine of the hospital and the actual completed status of the subjects. If there are missing data, compliance with medical routine is not

considered as a protocol deviation.

6.5 Energy Composition Target and Monitoring

Each participating center is required to maintain complete documentation of the ablation energy modality selected for all enrolled cases. Following the effective date of this protocol version, the Coordinating Center will periodically review and summarize the energy composition of newly enrolled patients to assess whether the overall distribution aligns with the anticipated study trajectory.

To ensure that the study cohort adequately reflects the increasing clinical adoption of PFA and maintains relevance in a future PFA-dominant treatment environment, the study establishes the following population-level target for the overall energy composition during the study period:

Across the entire enrollment period, the cumulative proportion of PFA cases is expected, in principle, to reach at least 50-60% of all enrolled subjects.

This target is intended to optimize the cohort's energy structure at the population level and enhance the interpretability and external validity of study results in the context of evolving ablation practice. It does **not** impose restrictions on the energy selection for individual cases and does **not** constitute a mandatory requirement for any participating center or investigator. This monitoring process is implemented solely to support study quality control and consistency in data interpretation.

7. Adverse Event Evaluation, Record and Report

7.1 Adverse event

Adverse events (AE) mean any untoward medical occurrence during clinical trials, whether related to catheter ablation. An AE can be any adverse or unexpected sign associated with catheter ablation in time, a symptom reported by a subject, or any disease, whether or not it has a causal relationship with catheter ablation.

7.2 Serious adverse events

Serious adverse event (SAE) refers to an event or reaction that, in the view of either the investigator or sponsor, results in any of the following outcomes: death, a life-threatening adverse event, in-patient hospitalization or prolongation of existing hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or a congenital anomaly or birth defect.

7.3 Suspected Unexpected Serious Adverse Reactions (SUSARs)

SUSARS refer an adverse event that occurs in a clinical trial subject, which is assessed by the sponsor and or study investigator as being unexpected, serious and as having a reasonable possibility of a causal relationship with the ablation.

An independent Advisory Committee comprising clinical electrophysiologists, device experts, and procedural workflow specialists will provide non-binding recommendations throughout the course of the trial. This committee will offer guidance on clinical protocol development, training procedures, data interpretation, and integration of new technologies as they become available. The Advisory Committee does not have access to unblinded safety data but will work in coordination with the Sponsor and DSMB to ensure the trial remains aligned with current clinical practice standards and technological advancements.

7.4 Device defects

Device defects refer to unreasonable risks that may likely cause or contribute to a death or serious injury under common practice, such as label errors, quality problems, malfunction, etc.

7.5 Collect and report serious adverse events, device defects, and unexpected serious adverse events

7.5.1 Collection time

AE evaluation will be conducted from the signing of informed consent to the end of this trial.

7.5.2 SAE Reporting

After initial receipt of SAEs, the investigator should provide proper treatment and write to the relative facilities and sponsor immediately.

The investigator is responsible for continuing to follow all SAE reports (whether related to study drug) until resolution or until the event is considered chronic and/or stable by the investigator and/or other physician who has the responsibility for the patient's medical care. Follow-up SAE reports will be reported according to the same timelines as initial reports as soon as new significant information becomes available.

For SAE or suspected SAE-related device defects, the sponsor should report to the CFDA and the health authority at the same level and notice other sites in this trial. Study sites should report to the ethnic committee by the clinical trial management department.

7.5.3 Device defects Reporting

If any issues with the study device arise, including suspected or confirmed malfunctions related to quality, labeling, durability, reliability, or safety, please contact the designated Johnson & Johnson representative immediately.

7.5.4 SUSARs Reporting

Suspected Unexpected Serious Adverse Reactions [SUSARs] will undergo expedited reporting to relevant regulatory authorities (e.g., research ethics committees, National Medical Products Administration, and National Health

Commission of the People's Republic of China). Investigators must report all SUSARs to sponsor as soon as possible and 24h of learning of the event. These SUSARs will be centrally reviewed and reported by the sponsor as soon as possible:

For fatal or life-threatening SUSARs, sponsor must report as soon as possible and within 7 days of learning of the events. Active follow-up must be completed within the following 8 days (The first day of learning of the event is considered 0 day).

For fatal or life-threatening SUSARs, sponsor must report as soon as possible and within 15 days of learning of the events.

8. Statistical analysis

Continuous variables are expressed as mean ± SD if normally distributed or median (interquartile range [IQR]) if not normally distributed. Intergroup differences will be compared by student's t-test (normally distributed data with equal variance) or Mann-Whitney U test (failed either normality or equal variance test). Categorical variables will be presented as percentages and compared by using the Chi-square test or Fisher's exact test. The Kaplan-Meier method will be used to describe event-free rates over time. The statistical significance for all tests will be accepted at $P< 0.05$.

8.1 Sub-analyses

8.1.1 Sub-analysis 1: Comparison of PFA VS RFA

This sub-analysis will compare the 12-month efficacy and safety of PFA and RFA using data collected in the main study.

All analyses will be performed post-hoc within the predefined data framework of the primary trial; no additional interventions, visits, or consent are required.

8.1.2 Sub-analysis 2: Impact of blanking period definitions following PFA

This sub-analysis will explore the effect of different blanking period definitions (1-month, 2-month vs 3-month) on arrhythmia-free success rates after PFA, using the same dataset and follow-up schedule as the main study.

It is an exploratory analytical component of the main trial and does not involve separate randomization or data collection.

8.1.3 Sub-analysis 3: Impact of AF duration and symptom/diagnosis-to-ablation interval on ablation success

This sub-analysis will explore whether different time definitions influence the interpretation of 12-month ablation success. Two analytical models will be applied using the main trial dataset without additional interventions or visits:

- **Model A (documented AF duration model):** Patients will be stratified by AF type (paroxysmal vs. persistent ≤1 year) and analyzed according to documented AF duration based on the first recorded AF episode.

- **Model B (symptom/diagnosis-to-ablation interval model):** Patients will be stratified according to the interval from initial symptom onset or first AF diagnosis—whichever occurs earlier—to the ablation procedure, with categories defined by the actual distribution of the study population.

This exploratory sub-analysis compares analytical approaches only; it does not modify clinical management, affect randomization, or add data collection requirements.

9. Consenting Process

Local IRB approval must be obtained before patient enrollment. Informed consent form signed and dated by both investigator and subject must be obtained from all subjects prior to exporting the data from the hospital database for this study. Any modifications to the Patient Informed Consent Form must be approved by the Ethics Committee (EC). The copy of the Patient Informed Consent Form approved by EC, along with the copies of consent forms signed by every subject, must be maintained by every investigator in a designated clinical trial master file. A signed copy of the consent form must be given to each subject. It is the investigator's responsibility to ensure that the informed consent process is performed in accordance with good clinical practices (GCP).

10. Plans For Publication

We plan to submit primary safety and efficacy data for publication in a peer-reviewed journal. Additional publication plans will be discussed in consultation with the study PI and local PIs during independent publication planning meetings. Participating investigators are encouraged to propose publication ideas, which will be reviewed for suitability by the steering committee in these planning meetings.

Publication of trial results will be coordinated independently. Biosense Webster, Inc. will not interfere with the trial's conduct, data management, or authorship decisions. Authorship and publication processes will be led by the Trial Principal Investigator to uphold scientific integrity and objectivity.

References

1. Joglar JA, Chung MK, Armbruster AL, Benjamin EJ, Chyou JY, Cronin EM, Deswal A, Eckhardt LL, Goldberger ZD, Gopinathannair R, Gorenek B, Hess PL, Hlatky M, Hogan G, Ibeh C, Indik JH, Kido K, Kusumoto F, Link MS, Linta KT, Marcus GM, McCarthy PM, Patel N, Patton KK, Perez MV, Piccini JP, Russo AM, Sanders P, Streur MM, Thomas KL, Times S, Tisdale JE, Valente AM, Wagoner DRV, Krahn AD, Andrade JG, Beavers CJ, Bischoff JM, Bunch TJ, Campbell KB, Chen LY, Dharia R, Dorsch MP, Gerstenfeld EP, Jones AE, Kaluzna SD, Masha L, Nault I, Noseworthy PA, Pellegrini CN, Tzeis SE, Volgman AS, Zeitler EP. 2023 ACC/AHA/ACCP/HRS Guideline for the Diagnosis and Management of Atrial Fibrillation. Journal of the American College of Cardiology. 2024;83(1):109-279. doi: doi:10.1016/j.jacc.2023.08.017.
2. Van Gelder IC, Rienstra M, Bunting KV, Casado-Arroyo R, Caso V, Crijns HJGM, De Potter TJR, Dwight J, Guasti L, Hanke T, Jaarsma T, Lettino M, Løchen M-L, Lumbers RT, Maesen B, Mølgaard I, Rosano GMC, Sanders P, Schnabel RB, Suwalski P, Svennberg E, Tamargo J, Tica O, Traykov V, Tzeis S, Kotecha D, Group ESD. 2024 ESC Guidelines for the management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): Developed by the task force for the management of atrial fibrillation of the European Society of Cardiology (ESC), with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. Endorsed by the European Stroke Organisation (ESO). European Heart Journal. 2024;45(36):3314-414. doi: 10.1093/eurheartj/ehae176.
3. Koruth JS, Kuroki K, Iwasawa J, et al. Pulsed field ablation for pulmonary vein isolation in atrial fibrillation. JACC: Clinical Electrophysiology. 2020;6(6):764-74. doi: 10.1016/j.jacep.2020.04.005.
4. Verma A, Haines DE, Boersma LV, Sood N, Natale A, Marchlinski FE, Calkins H, Sanders P, Packer DL, Kuck K-H, Hindricks G, Onal B, Cerkvenik J, Tada H, DeLurgio DB. Pulsed Field Ablation for the Treatment of Atrial Fibrillation: PULSED AF Pivotal Trial. Circulation. 2023;147(19):1422-32. doi: 10.1161/circulationaha.123.063988.
5. Reddy VY, Dukkipati SR, Neuzil P, Anic A, Petru J, Funasako M, Cochet H, Minami K, Breskovic T, Sikiric I, Sediva L, Chovanec M, Koruth J, Jais P. Pulsed Field Ablation of Paroxysmal Atrial Fibrillation: 1-Year Outcomes of IMPULSE, PEFCAT, and PEFCAT II. JACC Clin Electrophysiol. 2021;7(5):614-27. Epub 20210428. doi: 10.1016/j.jacep.2021.02.014. PubMed PMID: 33933412.
6. Reddy VY, Gerstenfeld EP, Natale A, Whang W, Cuoco FA, Patel C, Mountantonakis SE, Gibson DN, Harding JD, Ellis CR, Ellenbogen KA, DeLurgio DB, Osorio J, Achyutha AB, Schneider CW, Mugglin AS, Albrecht EM, Stein KM, Lehmann JW, Mansour M. Pulsed Field or Conventional Thermal Ablation for Paroxysmal Atrial Fibrillation. N Engl J Med. 2023;389(18):1660-71. Epub 20230827. doi: 10.1056/NEJMoa2307291. PubMed PMID: 37634148.
7. Heidbuchel H, Wittkampf FHM, Vano E, Ernst S, Schilling R, Picano E, Mont L, Jais P, de Bono J, Piorkowski C, Saad E, Femenia F. Practical ways to reduce radiation dose for patients and staff during device implantations and electrophysiological procedures. EP Europace. 2014;16(7):946-64. doi: 10.1093/europace/eut409.
8. McCutcheon K, Vanhaverbeke M, Pauwels R, Dabin J, Schoonjans W, Bennett J, Adriaenssens T, Dubois C, Sinnaeve P, Desmet W. Efficacy of MAVIG X-Ray Protective Drapes in Reducing Operator Radiation Dose in the Cardiac Catheterization Laboratory. Circulation: Cardiovascular Interventions. 2020;13(11). doi: 10.1161/circinterventions.120.009627.
9. Eder H. X-Ray Protective Aprons Re-Evaluated. RöFo - Fortschritte auf dem Gebiet der

Röntgenstrahlen und der bildgebenden Verfahren. 2023;195(03):234-43. doi: 10.1055/a-1994-7332.
10. Guersen J, Cassagnes L, Mechin G, Ravel A, Dumousset E, Boyer L, Chabrot P. Interventional Radiologists: A Necessary Evolution of Leaded Protective Aprons Design. Journal of Vascular and Interventional Radiology. 2013;24(3). doi: 10.1016/j.jvir.2012.11.004.
11. Dehmer GJ. Occupational hazards for interventional cardiologists. Catheter Cardiovasc Interv. 2006;68(6):974-6. doi: 10.1002/ccd.21004. PubMed PMID: 17091487.
12. Jiang MR, Chen MM, Liu MQ, Fu MG, Xue MY, Fu MH, Wu MS, Ma MC, Long MD, Jiang MC. Body pain - An unheeded personal health hazard in interventional cardiologists: A national online cross-sectional survey study in China. Int J Cardiol. 2022;350:27-32. Epub 20220101. doi: 10.1016/j.ijcard.2021.12.052. PubMed PMID: 34979148.
13. Frane N, Bitterman A. Radiation Safety and Protection. StatPearls. Treasure Island (FL): StatPearls Publishing
Copyright © 2024, StatPearls Publishing LLC.; 2024.
14. Klein LW, Miller DL, Balter S, Laskey W, Naito N, Haines D, Ross A, Mauro MA, Goldstein JA. Occupational health hazards in the interventional laboratory: Time for a safer environment. Catheter Cardiovasc Interv. 2018. Epub 20180104. doi: 10.1002/ccd.21772. PubMed PMID: 29667719.
15. Khongphatthanayothin A, Kosar E, Nademanee K. Nonfluoroscopic three-dimensional mapping for arrhythmia ablation: tool or toy? J Cardiovasc Electrophysiol. 2000;11(3):239-43. doi: 10.1111/j.1540-8167.2000.tb01792.x. PubMed PMID: 10749346.
16. Novak PG, Macle L, Thibault B, Guerra PG. Enhanced left atrial mapping using digitally synchronized NavX three-dimensional nonfluoroscopic mapping and high-resolution computed tomographic imaging for catheter ablation of atrial fibrillation. Heart Rhythm. 2004;1(4):521-2. doi: 10.1016/j.hrthm.2004.07.011. PubMed PMID: 15851210.
17. Bigelow AM, Smith PC, Timberlake DT, McNinch NL, Smith GL, Lane JR, Clark JM. Procedural outcomes of fluoroless catheter ablation outside the traditional catheterization lab. Europace. 2017;19(8):1378-84. doi: 10.1093/europace/euw207. PubMed PMID: 27915262.
18. Lyan E, Tsyganov A, Abdrahmanov A, Morozov A, Bakytzhanuly A, Tursunbekov A, Nuralinov O, Mironovich S, Klukvin A, Marinin V, Tilz RR, Sawan N. Nonfluoroscopic catheter ablation of paroxysmal atrial fibrillation. Pacing Clin Electrophysiol. 2018;41(6):611-9. Epub 20180430. doi: 10.1111/pace.13321. PubMed PMID: 29566268.
19. Rodkiewicz D, Koźluk E, Momot K, Rogala K, Piątkowska A, Buksińska-Lisik M, Kwasiborski P, Mamcarz A. Efficacy of Catheter Ablation Using the Electroanatomical System without the Use of Fluoroscopy in Patients with Ventricular Extrasystolic Beats. J Clin Med. 2023;12(14). Epub 20230724. doi: 10.3390/jcm12144851. PubMed PMID: 37510966; PMCID: PMC10381465.
20. Rodkiewicz D, Momot K, Koźluk E, Piątkowska A, Rogala K, Puchalska L, Mamcarz A. Zero-fluoroscopy catheter ablation of premature ventricular contractions: comparative outcomes from the right ventricular outflow tract and other ventricular sites. Cardiol J. 2024. Epub 20240819. doi: 10.5603/cj.98002. PubMed PMID: 39158516.
21. Romero J, Patel K, Briceno D, Alviz I, Tarantino N, Della Rocca DG, Natale V, Zhang XD, Di Biase L. Fluoroless Atrial Fibrillation Catheter Ablation: Technique and Clinical Outcomes. Card Electrophysiol Clin. 2020;12(2):233-45. doi: 10.1016/j.ccep.2020.01.001. PubMed PMID: 32451107.
22. Romero J, Velasco A, Díaz JC, Alviz I, Briceno D, Grushko M, Palma E, Ferrick K, Parashar A,

Bello J, Zhang X, Gabr M, Purkayastha S, Polanco D, Grupposo V, Della Rocca DG, Lakkireddy D, Natale A, Di Biase L. Fluoroless Versus Conventional Mapping and Ablation of Ventricular Arrhythmias Arising From the Left Ventricular Summit and Interventricular Septum. Circ Arrhythm Electrophysiol. 2022;15(7):e010547. Epub 20220627. doi: 10.1161/circep.121.010547. PubMed PMID: 35759380.

23. Bulava A, Hanis J, Eisenberger M. Catheter Ablation of Atrial Fibrillation Using Zero-Fluoroscopy Technique: A Randomized Trial. Pacing Clin Electrophysiol. 2015;38(7):797-806. Epub 2015/03/20. doi: 10.1111/pace.12634. PubMed PMID: 25790320.

24. Zei PC, Quadros KK, Clopton P, Thosani A, Ferguson J, Brodt C, O'Riordan G, Ramsis M, Mitra R, Baykaner T. Safety and Efficacy of Minimal- versus Zero-fluoroscopy Radiofrequency Catheter Ablation for Atrial Fibrillation: A Multicenter, Prospective Study. J Innov Card Rhythm Manag. 2020;11(11):4281-91. Epub 2020/12/03. doi: 10.19102/icrm.2020.111105. PubMed PMID: 33262896; PMCID: PMC7685314.

25. Sadek MM, Ramirez FD, Nery PB, Golian M, Redpath CJ, Nair GM, Birnie DH. Completely nonfluoroscopic catheter ablation of left atrial arrhythmias and ventricular tachycardia. J Cardiovasc Electrophysiol. 2019;30(1):78-88. Epub 2018/09/12. doi: 10.1111/jce.13735. PubMed PMID: 30203499.

26. Jiang C, Ma C, Chen S, Chen S, Jiang C, Jiang R, Ju W, Long D, Li D, Li J, Liu Q, Ma W, Pu X, Wang R, Wang Y, Yi F, Zou C, Zhang J, Zhang X, Zhao Y, Zei PC, Biase LD, Chang D, Cai H, Chen L, Chen M, Fu G, Fu H, Fan J, Gui C, Jiang T, Liu S, Li X, Li Y, Shu M, Wang Y, Xu J, Xie R, Xia Y, Xue Y, Yang P, Yuan Y, Zhong J, Zhu W. Chinese expert consensus on the construction of the fluoroless cardiac electrophysiology laboratory and related techniques. Pacing and Clinical Electrophysiology. 2023;46(9):1035-48. doi: 10.1111/pace.14782.

27. Vio R, Forlin E, China P. Recurrences after Pulsed Field Ablation of Atrial Fibrillation: Incidence, Mechanisms, Predictors, and Comparison with Thermal Energy. Medicina (Kaunas). 2024;60(5). Epub 20240516. doi: 10.3390/medicina60050817. PubMed PMID: 38793000; PMCID: PMC11123187.

28. Mohanty S, Torlapati PG, Casella M, Della Rocca DG, Schiavone M, Doty B, La Fazia VM, Pahi S, Pierucci N, Valeri Y, Gianni C, Al-Ahmad A, Burkhardt JD, Gallinghouse JG, Di Biase L, Chierchia GB, Nair DG, Dello Russo A, Tondo C, Natale A. Redefining the blanking period after pulsed field ablation in patients with atrial fibrillation. Heart Rhythm. 2025;22(4):891-7. Epub 20240806. doi: 10.1016/j.hrthm.2024.08.011. PubMed PMID: 39117003.

29. Kewcharoen J, Shah K, Bhardwaj R, Turagam MK, Contractor T, Mandapati R, Lakkireddy D, Garg J. Catheter-related and clinical complications associated with QDOT MICROTM Ablation Catheter. Journal of Cardiovascular Electrophysiology. 2024;35(9):1874-7. doi: 10.1111/jce.16363.

30. Eckardt L, Doldi F, Anwar O, Gessler N, Scherschel K, Kahle A-K, von Falkenhausen AS, Thaler R, Wolfes J, Metzner A, Meyer C, Willems S, Köbe J, Lange PS, Frommeyer G, Kuck K-H, Kääb S, Steinbeck G, Sinner MF. Major in-hospital complications after catheter ablation of cardiac arrhythmias: individual case analysis of 43 031 procedures. Europace. 2024;26(1). doi: 10.1093/europace/euad361.

31. Winkle RA, et al. Peri-procedural complications of atrial fibrillation ablation: comparisons between radiofrequency and cryoballoon ablation. Journal of Interventional Cardiac Electrophysiology. 2015;43(1):29-36. doi: 10.1007/s10840-015-9989-6.

32. Benali K, Khairy P, Hammache N, Petzl A, Da Costa A, Verma A, Andrade JG, Macle L.

Procedure-Related Complications of Catheter Ablation for Atrial Fibrillation. Journal of the American College of Cardiology. 2023;81(21):2089-99. doi: 10.1016/j.jacc.2023.03.418.
33. Verma A, Jiang C-y, Betts TR, Chen J, Deisenhofer I, Mantovan R, Macle L, Morillo CA, Haverkamp W, Weerasooriya R, Albenque J-P, Nardi S, Menardi E, Novak P, Sanders P. Approaches to Catheter Ablation for Persistent Atrial Fibrillation. New England Journal of Medicine. 2015;372(19):1812-22. doi: doi:10.1056/NEJMoa1408288.

Appendix

Appendix A. Anticipated Adverse Events

1. Acute Respiratory Distress Syndrome (ARDS)	35. Laceration
2. Air embolism	36. Leakage of air or blood into the lungs or other organs due to perforation
3. Allergic reaction	37. Local hematoma/ecchymosis
4. Anemia	38. Mobile strands in the inferior vena cava
5. Anesthesia reaction	39. Myocardial infarction
6. Arrhythmias	40. Obstruction or perforation or damage to the vascular system
7. Atelectasis	41. Pericardial effusion
8. Atrio-Esophageal Fistula	42. Pericarditis
9. Atypical flutter	43. Phrenic nerve damage
10. AV fistula	44. Pleural effusion
11. Cardiac perforation/tamponade	45. Pneumonia
12. Cardiac Thromboembolism	46. Pneumothorax
13. Cerebrovascular accident (CVA)	47. Pseudoaneurysm
14. Chest pain/discomfort	48. Pulmonary edema
15. Complete heart block, temporary or permanent	49. Pulmonary embolism
16. Component damage to ICD or pacemaker	50. Renal Failure
17. Congestive heart failure	51. Respiratory depression/failure
18. Coronary artery dissection	52. Retroperitoneal hematoma
19.Coronary artery spasm	53. Rhabdomyolysis, including that produced by body position or propofol
20. Death	54. Seizure
21. Dislodgement of ICD or permanent pacing leads	55. Shortness of Breath
22. Endocarditis	56. Skin burns due to cardioversion, tape, etc.
23. Exacerbation of pre-existing atrial fibrillation, or other arrhythmia	57. Syncope/Dizziness
24. Expressive aphasia	58. Temperature elevation
25. Hair loss due to anesthesia	59. Thromboembolism
26. Heart failure	60. Transient ischemic attack (TIA)
27. Hematuria	61. Unintended complete/incomplete AV, sinus node or other heart block or damage
28. Hemorrhage	62. Urinary tract injury or infection related to the urinary catheter
29. Hemothorax	63. Valvular damage/insufficiency
30. Hypertension/Hypotension	64. Vasovagal reactions

31. Increase in frequency or duration of episodes of typical atrial flutter	65. Volume overload
32. Increased phosphokinase level	66. Worsening obstructive, restrictive, or other form of pulmonary disease
33. Infection, localized or systemic	67. X-ray radiation injury of skin, muscle or organ
34. Injury to skin, muscle, connective tissue due to body position, electrical cardioversion, etc.	

Appendix B. Definition of related hospitalization

Heart failure	Hospitalization event that meets ALL of the following criteria: 1. The patient was admitted to the hospital with a primary diagnosis of HF as the cause for hospitalization. 2. The patient's length of stay in hospital extended for at least 24 hours (or a change in calendar date if the hospital admission and discharge times are unavailable). 3. Diagnosis of HF by at least 1 of each of the following 3 criteria: symptom, sign, and medication (specifically for the treatment of worsening heart failure)/supportive measures/objective assessments.
Arrhythmia	When a patient was hospitalized for elective or urgent diagnosis or treatment of bradyarrhythmias, atrial, or ventricular rhythm disorders of the heart.
Transient ischemic attack and stroke	When a patient was hospitalized for elective or urgent diagnosis or treatment of TIA or stroke. TIA was defined as a transient episode of focal neurological dysfunction lasting for <24 hours caused by brain, spinal cord, or retinal ischemia, without acute infarction. Stroke was defined as an acute episode of focal or global neurological dysfunction caused by brain, spinal cord, or retinal vascular injury as a result of hemorrhage or infarction.
Myocardial infarction	When there was evidence of myocardial necrosis in a clinical setting consistent with myocardial ischemia, and required the combination of: 1. Evidence of myocardial necrosis (either a typical rise and fall in cardiac biomarkers or postmortem pathological findings); and 2. Supporting information derived from the clinical presentation, electrocardiographic changes, or results of myocardial or coronary artery imaging.
Other CV cause	A hospitalization not included in the above categories but with a specific, known cause (including but not limited to: hospitalization for unstable angina, pulmonary embolism or peripheral arterial/vascular disease, peripheral emboli, venous thrombosis, or other vascular reasons or complications).

Hospitalization for end point adjudication was defined as a nonelective admission to an acute care setting for medical therapy that results in at least a 24-hour stay (or a date change if the time of admission/discharge is not available).

Appendix C. Quality of life scale (EQ-5D-5L)

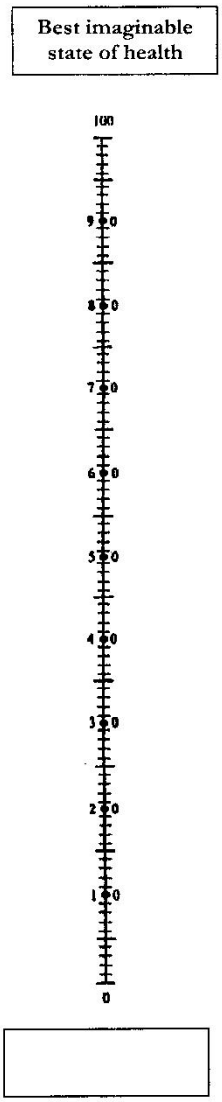
Patients will be asked to grade their Quality of Life, since the start of the study, using EQ-5D (The EuroQol Group. Health Policy 1990 December; 16(3):199-208).

	Tick one answer in each section
MOBILITY	
I have no problems in walking about	
I have slight problems in walking	
I have moderate problems in walking	
I have severe problems in walking	
I am unable to walk about	
SELF-CARE	
I have no problems washing or dressing	
I have slight problems washing or dressing	
I have moderate problems washing or dressing	
I have severe problems washing or dressing	
I am unable to wash or dress myself	
USUAL ACTIVITIES (e.g. work, study, housework family or leisure activities)	
I have no problems with performing my usual	
I have slight problems with performing my usual	
I have moderate problems with performing my usual	
I have severe problems with performing my usual	
I am unable to perform my usual	
PAIN / DISCOMFORT	
I have no pain or discomfort	
I have slight pain or discomfort	
I have moderate pain or	
I have severe pain or	
I have extreme pain or discomfort	
**ANXIETY / **	
I am not anxious or depressed	
I am slightly anxious or depressed	
I am moderately anxious or	
I am severely anxious or	
I am extremely anxious or	

Patients will also be asked to grade their state of health on the visual analogue scale.

"To help people say how good or bad their state of health has been ***on average since starting the study,*** we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.
We would like you to indicate on this scale how good or bad your health has

been ***on average since starting the study*** in your opinion. Please do this by drawing a line on the scale."



Appendix D. Atrial Fibrillation Effect on QualiTy-of-life (AFEQT) Questionnaire

Section 1. Occurrence of atrial fibrillation **Name or ID:**_____

Are you currently in atrial fibrillation? ☐ Yes ☐ No

If **No**, when was the last time you were aware of having had an episode of atrial fibrillation? (Please check one answer which best describes your situation)

__earlier today
__within the past week
__within the past month
__1 month to 1 year ago
__more than 1 year ago
__I was never aware of having atrial fibrillation

Section 2. The following questions refer to how atrial fibrillation affects your quality of life.

On a scale of 1 to 7, over the past 4 weeks, as a result of your atrial fibrillation, how much were you bothered by:
(Please circle one number which best describes your situation)

	Not at all bothered Or I did not have this symptom	Hardly bothered	A little bothered	Moderately bothered	Quite a bit bothered	Very bothered	Extremely bothered
1. Palpitations: Heart fluttering, skipping or racing	1	2	3	4	5	6	7
2. Irregular heart beat	1	2	3	4	5	6	7
3. A pause in heart activity	1	2	3	4	5	6	7
4. Lightheadedness or dizziness	1	2	3	4	5	6	7

On a scale of 1 to 7, over the past 4 weeks, have you been limited by your atrial fibrillation in your:
(Please circle one number which best describes your situation)

	Not at all limited	Hardly limited	A little limited	Moderately limited	Quite a bit limited	Very limited	Extremely limited
5. Ability to have recreational pastimes, sports, and hobbies	1	2	3	4	5	6	7
6. Ability to have a relationship and do things with friends and family	1	2	3	4	5	6	7

On a scale of 1 to 7, over the past 4 weeks, as a result of your atrial fibrillation, how much difficulty have you had in:
(Please circle one number which best describes your situation)

	No difficulty at all	Hardly any difficulty	A little difficulty	Moderate difficulty	Quite a bit of difficulty	A lot of difficulty	Extreme difficulty
7. Doing any activity because you felt tired, fatigued, or low on energy	1	2	3	4	5	6	7
8. Doing physical activity because of shortness of breath	1	2	3	4	5	6	7
9. Exercising	1	2	3	4	5	6	7
10. Walking briskly	1	2	3	4	5	6	7
11. Walking briskly uphill or carrying groceries or other items, up a flight of stairs without stopping	1	2	3	4	5	6	7
12. Doing vigorous activities such as lifting or moving heavy furniture, running, or participating in strenuous sports like tennis or racquetball	1	2	3	4	5	6	7

On a scale of 1 to 7, over the past 4 weeks as a result of your atrial fibrillation, how much did the feelings below bother you? (Please circle one number which best describes your situation)

	Not at all Bothered	Hardly bothered	A little bothered	Moderately bothered	Quite a bit bothered	Very bothered	Extremely bothered
13. Feeling worried or anxious that your atrial fibrillation can start anytime	1	2	3	4	5	6	7
14. Feeling worried that atrial fibrillation may worsen other medical conditions in the long run	1	2	3	4	5	6	7

On a scale of 1 to 7, over the past 4 weeks, as a result of your atrial fibrillation treatment, how much were you bothered by: (Please circle one number which best describes your situation)

	Not at all bothered	Hardly bothered	A little bothered	Moderately bothered	Quite a bit bothered	Very bothered	Extremely bothered
15. Worrying about the treatment side effects from medications	1	2	3	4	5	6	7
16. Worrying about complications or side effects from procedures like catheter ablation, surgery, or pacemakers therapy	1	2	3	4	5	6	7
17. Worrying about side effects of blood thinners such as nosebleeds, bleeding gums when brushing teeth, heavy bleeding from cuts, or bruising.	1	2	3	4	5	6	7
18. Worrying or feeling anxious that your treatment interferes with your daily activities	1	2	3	4	5	6	7

On a scale of 1 to 7, overall, how satisfied are you **at the present time** with:
(Please circle one number which best describes your situation)

	Extremely satisfied	Very satisfied	Somewhat satisfied	Mixed with satisfied and dissatisfied	Somewhat dissatisfied	Very dissatisfied	Extremely dissatisfied
19. How well your current treatment controls your atrial fibrillation?	1	2	3	4	5	6	7
20. The extent to which treatment has relieved your symptoms of atrial fibrillation?	1	2	3	4	5	6	7

Name or ID:_____

Appendix E. Well-being Questionnaire for Operating Room Staff

Basic Information

1. **Position:**

   ☐ Lead operator ☐ Assistant ☐ Nurse ☐ Anesthesiologist ☐ Technician

2. **Procedure duration:** _____ hours _____ minutes

3. **Order of the case today:** No. _____

4. **Personal protective equipment (select all that apply):**

   ☐ None ☐ Lead apron ☐ Lead cap ☐ Thyroid collar ☐ Lead skirt ☐ Lead glasses ☐ Dosimeter

1. Physical Discomfort and Pain Assessment

1.1 Do you experience any physical discomfort or pain?

☐ No → *Proceed to Section 2 Radiation Exposure and Protection* ☐ Yes

1.2 Please select the affected body region(s) or symptom(s):

☐ Headache ☐ Neck pain ☐ Shoulder pain

☐ Back pain ☐ Low back pain ☐ Elbow discomfort

☐ Hand discomfort ☐ Leg fatigue/stiffness ☐ Eye strain/dryness

☐ General fatigue ☐ Emotional distress/irritability ☐ Other: _____

1.3 Pain intensity (VAS 0–5): **Your score:** _____

0 = No pain 1 = Mild 2 = Moderate 3 = Severe 4 = Very severe 5 = Unbearable

1.4 Do you need to rest briefly before resuming work? (0–4 scale) **Your score:** _____

0 = Not at all, full of energy 1 = Slight, quick recovery 2 = Moderate, recovers after short rest 3 = Marked, needs clear rest 4 = Severe, must rest before continuing

2. Radiation Exposure and Protection Assessment

2.1 Level of concern about radiation exposure (0–10): **Your score:** _____

0 = Not concerned → 10 = Extremely concerned

2.2 Do you think radiation protection measures affect your health?

☐ Not at all ☐ Slightly ☐ Considerably ☐ Severely

2.3 Do you monitor radiation dose per procedure?

☐ Always ☐ Sometimes ☐ Never

2.4 If fluoroscopy-free procedures without heavy protective gear are available, would you choose them? ☐ Yes ☐ No