ISRCTN14850730 https://doi.org/10.1186/ISRCTN14850730

A study testing two treatments for a type of irregular heartbeat (paroxysmal atrial fibrillation): one using standard vein isolation, and the other combining that with a new technique that targets nerve clusters on the heart using pulsed energy

Submission date 03/06/2025	**Recruitment status** No longer recruiting	[ ] Prospectively registered [ ] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [ ] Record updated in last year
Registration date 22/10/2025	**Overall study status** Ongoing	
Last Edited 22/10/2025	**Condition category** Circulatory System	

Plain English summary of protocol

Background and study aims
This study examines a novel heart treatment called Pulsed Field Ablation (PFA), a precise method for correcting irregular heartbeats associated with atrial fibrillation (AF). Unlike older techniques, PFA works from inside the heart but may not affect the nerves on the heart's outer surface, which can trigger AF. This study aims to determine whether adding external nerve ablation (treatment on the outside of the heart) enhances long-term outcomes. The goal is to see if combining internal and external ablation works better for patients with paroxysmal AF (episodes of irregular heartbeat that start and stop suddenly). This could lead to more effective, longer-lasting treatments.

Who can participate?
Adult patients aged 18-80 years who have paroxysmal AF.

What does the study involve?
Participants will be randomly assigned to either standard treatment (PFA inside the heart only) or Research treatment (PFA inside + nerve ablation outside the heart). All procedures will be done under general anaesthesia by expert heart specialists in Brighton. Patients won't know which group they're in. To track results, a small loop recorder (a heart monitor implanted under the skin) will record heart rhythms, and a 24-hour ECG will check nerve function three months later.

Control group: Endocardial GP mapping, then Endocardial PVI performed with PFA
Intervention Group: Endo-Epicardial GP mapping, Endocardial PVI with PFA, GP Mapping, then Epicardial PFA ablation of GPs

What are the possible benefits and risks of participating?
Benefits:
• PFA has safety benefits with reduced risk of oesophageal and phrenic injury.
• There may also be benefits from more accurately defining GP locations in the restriction of ablation delivery to prevent unnecessary myocardial destruction.
• In a smaller study, targeting of the GPs in addition to PVI has shown 85.3% freedom from recurrent atrial arrhythmia compared with 60.6% with PVI alone.

Risks:
• The risk of death from an AF ablation procedure is about 1 in 1000 people.
• Risk of developing inflammation and pain due to the mapping and ablation of the outer layer of the heart, known as pericarditis. This condition may occur in 1 to 2 out of every 100 individuals.
• There is also a risk of introducing infection into the outside space of the heart (1 in 100 people).
• The period under general anaesthetic for the procedure poses little additional risk, and specialised cardiac anaesthetists will deliver the anaesthesia itself.
• Small risk of complications that may occur after you go home; this could require you to return to the hospital. For patients randomised to have ablation on the inside and outside of the heart, there are additional risks associated with inserting the tube under the breastbone. These risks include bleeding around the outside of the heart, an air leak around the outside of the lung, bleeding and injury to the liver, and inflammation or infection around the outside of the heart. These complications often do not require any treatment. Occasionally, a small drain may need to be inserted, but it is rare for an emergency operation to be necessary. These risks are in addition to those already present with standard clinical treatment.

Where is the study run from?
Royal Sussex County Hospital, UK

When is the study starting and how long is it expected to run for?
June 2025 to October 2027

Who is funding the study?
Abbott Laboratories

Who is the main contact?
Jagan Muthurajah, jagan.muthurajah4@nhs.net

Contact information

Type(s)
Principal investigator

Contact name
Dr John Silberbauer

Contact details
Royal Sussex County Hospital
14 Kemp Town Place
Brighton
United Kingdom

BN2 1NE
+44 (0)7901713440
john.silberbauer@nhs.net

Type(s)
Scientific

Contact name
Dr Jagan Muthurajah

Contact details
Royal Sussex County Hospital
14 Kemp Town Place
London
United Kingdom
BN2 1NE
+44 (0)7784763985
jagan.muthurajah4@nhs.net

Type(s)
Public

Contact name
Dr Ian Mann

Contact details
Royal Sussex County Hospital
14 Kemp Town Place
Brighton
United Kingdom
BN2 1NE
+44 (0)7779224567
ian.mann2@nhs.net

Additional identifiers

Integrated Research Application System (IRAS)
349665

Protocol serial number
65216

Study information

Scientific Title
Pulsed ganglionic plexi (GP) atrial fibrillation (AF) study: a randomised trial comparing pulmonary vein isolation (PVI) versus pulmonary vein isolation plus epicardial ganglionic plexi ablation using focal pulsed field ablation (PFA) for paroxysmal atrial fibrillation

Acronym

Pulsed GP AF

Study objectives
This study aims to identify whether epicardial ablation of the Ganglionic Plexi, in addition to endocardial pulmonary vein isolation, results in greater autonomic effects and freedom from recurrent paroxysmal AF compared to endocardial pulmonary vein isolation alone using focal pulsed field ablation.

Hypotheses
The proposed hypothesis posits that the ablation of epicardial ganglionated plexi (GPs) in conjunction with pulmonary vein isolation (PVI) will result in a significant alteration in autonomic measures, as assessed by a 24-hour electrocardiogram (ECG) monitor.
Null Hypothesis: There will be no significant change in the mean heart rate (HR) at three months post-treatment for patients undergoing PVI combined with GP ablation.
Alternative Hypothesis: There will be a significant change in the mean HR at three months post-treatment for patients receiving PVI and GP ablation.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 01/09/2025, London – Brighton and Sussex Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 104 8202, (0)207 104 8055, (0) 207 104 8140; brightonandsussex.rec@hra.nhs.uk), ref: 25/LO/0555

Primary study design
Interventional

Study design
Single-centre 1:1 parallel-group randomized trial

Study type(s)
Screening, Treatment, Safety, Efficacy

Health condition(s) or problem(s) studied
Atrial fibrillation treatment using new pulsed field ablation

Interventions
This study will be conducted at the Royal Sussex County Hospital. A single-centre, 1:1 parallel-group randomised study will be conducted to explore the effect of PVI alone compared to PVI plus epicardial mapping and ablation of ganglionated plexi (GPs) using PFA in patients with paroxysmal AF. All recruited patients must have a clinical need for AF ablation. The patients will be recruited by the Research fellow from the waiting list for AF ablation at Brighton, screened against the listed inclusion and exclusion criteria. Patients will have baseline demographics documented; echocardiography and 24 ECG monitor performed as per standard of care before the day of the procedure.

The team consulted patient groups and members of the public in both the drafting and adaptation of the protocol and patient information leaflet. After several iterations, the research champions expressed satisfaction with the content of both documents.

It aims to compare two treatments for patients with paroxysmal atrial fibrillation (AF): Standard treatment (PVI ablation) vs Standard treatment plus an additional procedure to map and treat nerves on the outside of the heart using a new technology called PFA.

The mean heart rate increase was chosen as the ablation of GPs will remove the parasympathetic input to the heart and therefore lead to reduced heart variability and increased AERP acutely. The primary endpoint is chosen to have a clear quantitative value measured from a 24-hour ECG monitor. The outcome will be taken as a continuous variable, and analysis will be performed accordingly.

The control arm was chosen to represent the current standard of treatment for AF with PVI.

Sample size
The forthcoming Pulsed GP AF study aims to investigate the impact of GP ablation in enhancing the efficacy of PVI as the primary method for addressing paroxysmal atrial fibrillation. The power calculation indicated that the study is adequately powered to detect a difference with a total sample size of 40. Specifically, assuming a baseline heart rate (HR) of 65 ± 9 bpm and an 8 bpm increase in the treatment group, with an alpha of 0.05 and power of 80%, a total sample size of 40 patients (1:1 enrolment), assuming a common standard deviation of 9 bpm and a normally distributed heart rate, is required. The sample size has been increased to 42 to account for participant attrition. Dr Saskia Eddy, Assistant Professor in Medical Statistics, has verified this calculation.

Patient Recruitment and Enrolment [over 12 months]:
Patients will be contacted by a Research Fellow who will explain the procedure and research elements.
Interested patients will receive a patient information leaflet and have the opportunity to discuss the study in person at a dedicated research clinic. Patients who agree to participate will be randomly assigned to one of the two ablation procedures (standard PVI or PVI plus GP ablation) using block randomisation.
Patients will not be informed of their group assignment to maintain study blinding.
Before the procedure, patients will complete quality-of-life questionnaires. They will have an echocardiogram [heart scan performed using ultrasound], and a 24 ECG monitor as standard of care for patients with AF.

On the Day of the Ablation Procedure:
Patients will sign the consent form on the day of the procedure.
General anaesthesia will be administered, and the assigned ablation procedure will be performed by experienced heart doctors.
At the end of the procedure, a small device called an implantable loop recorder (ILR) will be placed under the skin to monitor heart rhythm over time.
Participants will be sent home on the same day or the next day.

Follow-Up After Ablation [total duration of follow-up 12 months for each patient]:
1st Follow-Up at 3 months: Patients will visit the clinic to discuss symptoms, review medication, and arrange 24-hour ambulatory ECG monitoring.
2nd Follow-Up at 12 months: Another clinic visit to discuss symptoms, review medication, and arrange 24-hour ambulatory ECG monitoring.

After the study, patients will have routine follow-ups as needed.
The loop recorder will be removed at the patient's discretion after the study is completed.

Intervention Type
Procedure/Surgery

Primary outcome(s)
Mean heart rate increases measured using a 24-hour ECG monitor at 3 months

Key secondary outcome(s)
1. Mean heart rate increases measured using a 24-hour ECG monitor at 12 months
2. Acute change in atrial effective refractory period measured using an ECG monitor during the procedure
3. Heart rate variability changes (SDNN, rMSSD, HF power) measured using a 24-hour ECG monitor at 3 and 12 months
4. Atrial fibrillation (AF) burden at 1 year following a 2-month blanking period, defined as the percentage of time in AF, measured using an implantable loop recorder (ILR) between 2 and 12 months of follow-up
5. AF burden during the 2-month blanking period, defined as the percentage of time in AF, measured using an ILR during the first 2 months
6. Atrial tachycardia (AT) burden at 1 year, following a 2-month blanking period, defined as the percentage of time in AT, measured using an ILR between 2 and 12 months of follow-up
7. Number of Ganglionated Plexi (GPs) identified at different pacing thresholds during high-frequency stimulation (HFS) [fixed pulse width of 10ms and variable current 1- 25mA] in the endocardium versus the epicardium during the procedure
8. Significant procedural-related complications (phrenic nerve palsy, atrial-oesophageal fistula, vascular injury requiring intervention, significant blood loss resulting in Hb drop >2g, cardiac tamponade, stroke or TIA, coronary vasospasm) were measured using patient medical records at discharge

Completion date
01/10/2027

Eligibility

Key inclusion criteria
1. Adults aged 18-80 years
2. Paroxysmal AF (episodes terminating spontaneously within 7 days)
3. Clinical indication for ablation
4. Left atrial size <5.5mm
5. Absence of significant structural heart disease or other contraindications to catheter ablation

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
80 Years

Sex
All

Key exclusion criteria
1. Female participants who are pregnant, lactating or planning pregnancy during the study
2. Current enrolment in another interventional trial
3. Considered clinically unsuitable
4. Patients lacking capacity
5. Declined Loop recorder implant/24-hour ECG monitor
6. Contraindication to anticoagulation.
7. Body Mass Index >40
8. Unable to use a smartphone with the ‘myMerlin’ application or mobile transmitter
9. Allergy to Steroids or multiple antibiotics

Date of first enrolment
01/10/2025

Date of final enrolment
01/10/2026

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University Hospitals Sussex NHS Foundation Trust
Worthing Hospital
Lyndhurst Road
Worthing
United Kingdom
BN11 2DH

Sponsor information

Organisation
University Hospitals Sussex NHS Foundation Trust

ROR
https://ror.org/03wvsyq85

Funder(s)

Funder type
Industry

Funder Name
Abbott Laboratories

Alternative Name(s)
Abbott, Abbott U.S., Abbott Alkaloidal Company, The Abbott Alkaloidal Company

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan
Patients will be identified by the Research Fellow at the Royal Sussex County Hospital, who has completed GCP training, using the hospital's waiting lists.

Only members of the patient's existing clinical care team will access patient records without explicit consent to identify potential participants, check inclusion criteria, or make the initial approach. The Research Fellow is a doctor specialising in cardiac electrophysiology, experienced in performing standard AF ablation and CO2 insufflation epicardial access.

The study team will access clinical records available on NHS systems to ensure the patient population meets the inclusion and exclusion criteria.

To ensure there is no breach of confidentiality during the process of identifying potential participants, the following measures will be taken:

Access Control: Only members of the patient's existing clinical care team, who have a legitimate need to access patient records, will be involved in identifying potential participants. This includes the Research Fellow and Research Nurses who are part of the clinical care team.

Training and Compliance: All personnel involved in the study will have completed Good Clinical Practice (GCP) training, ensuring they are fully aware of their responsibilities regarding patient confidentiality and data protection.

Secure Systems: Patient records will be accessed and stored using secure NHS systems, which comply with data protection regulations. This ensures that all patient information is handled securely and confidentially.

Anonymisation: Where possible, patient data will be anonymised to protect their identity. This means that any identifying information will be removed or coded to ensure that individuals cannot be easily identified.

Monitoring and Auditing: Regular monitoring and auditing will be conducted to ensure compliance with confidentiality protocols. Any breaches or potential breaches will be promptly addressed and rectified.

By implementing these measures, we aim to protect the confidentiality of patients, service users, and any other individuals involved in the study.

Dataset will be generated and analysed in a non-publically available repository, but can be provided upon request to the CI of the study, Dr Ian Mann [ian.mann2@nhs.net]. The dataset is not expected to be made available publicly, but will be provided for peer review.

IPD sharing plan summary

Stored in non-publicly available repository, Available on request