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Ablation of both the inside and outside of the heart versus the inside of the heart only for patients with persistent atrial fibrillation

Submission date 20/07/2023	**Recruitment status** No longer recruiting	[ ] Prospectively registered [ ] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [ ] Record updated in last year
Registration date 29/08/2023	**Overall study status** Ongoing	
Last Edited 29/08/2023	**Condition category** Circulatory System	

Plain English summary of protocol

Background and study aims

Atrial fibrillation (AF) is the most common sustained abnormal heart rhythm which can increase the likelihood of other illnesses and death. This has been treated in the past with medication and resetting the heart rhythm with an electrical impulse in a process known as cardioversion, with mixed long-term success. An advance was the realisation that short-circuits in the electrical pathways in the heart that caused the abnormal rhythms could be broken by introducing a small scar across these pathways on the inside of the heart in a process known as cardiac ablation. However, symptoms can still reoccur. At present, maps of electrical activation and ablation treatment are only undertaken within the heart chamber. Some areas of heart muscle are very thick, and it can be difficult to achieve ablation through the full thickness of the muscle, which is the desired effect. In addition to this standard care, we aim to produce maps and deliver ablation treatment to the outside of the heart surface. This technique to treat both sides of the heart has been done for different heart rhythm problems with good effect.

Who can participate?

Adults over 18 who have persistent atrial fibrillation and are suitable for catheter ablation, but not enrolled in another interventional study, pregnant or considered clinically unsuitable

What does the study involve?

If suitable for the procedure the patient will have catheter ablation to both the inside and outside of the heart in areas of the upper left heart chamber where there is evidence of reconnection of abnormal pathways. The patient will have a small cardiac monitor implanted to monitor heart rhythm and be followed up at 3, 12 and 24 months to assess if there has been any reoccurrence of atrial fibrillation. An MRI scan prior to the procedure and at 12 months are optional and dependent on the participant's consent.

What are the possible benefits and risks of participating?

Patients could benefit from there being less chance of their atrial fibrillation recurring. The additional risk of taking part in this study is inflammation and pain from the mapping and ablation of the outside of the heart, called pericarditis (1-2 in 100 people). This can sometimes

occur with ablation to only the inside of the heart (1 in 200). There is also a risk of introducing infection into the outside space of the heart (1 in 100 people). We will administer antibiotics before the procedure and steroids after the procedure to minimise the risk of inflammation /pericarditis and infection.

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

When is the study starting and how long is it expected to run for?
January 2023 to May 2026

Who is funding the study?
Abbott Medical UK Ltd

Who is the main contact?
Dr John Silberbauer, john.silberbauer@nhs.net

Contact information

Type(s)
Public

Contact name
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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
325018

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 56748, IRAS 325018

Study information

Scientific Title
Pulmonary vein isolation versus endo-epicardial linear ablation for persistent atrial fibrillation: a randomized multicentre trial.

Acronym
EPIC-AF

Study objectives
The combination of exterior and interior ablation in the left atrium should lead to a reduction in the recurrence of atrial arrhythmias in patients with persistent atrial fibrillation, when compared to interior ablation of the pulmonary vein alone.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 03/07/2023, London - Hampstead Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 207 104 8227; hampstead.rec@hra.nhs.uk), ref: 23/LO/0524

Study design
Randomized interventional study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Cardiovascular disease

Interventions
The study is a randomised controlled trial, comparing current best practices against the proposed treatment strategy. The procedure will be performed by a Consultant Cardiologist or Specialist Registrar with experience in catheter ablation for AF, and experience in techniques to gain access to the outside of the heart. All patients recruited will have a clinical indication for AF ablation who have had a previous AF ablation. This involves the placement of catheters within the cardiac chamber. All procedures will be conducted under general anaesthesia.

STANDARD CLINICAL PROCEDURE: Following general anaesthesia, an ultrasound probe is inserted down the oesophagus to ensure that there are no blood clots within the heart. Small tubes will be placed in the veins in the groin to allow specialised catheters to be placed inside the chambers of the heart. Access into the left upper heart chamber (atrium), where the majority of AF ablation is undertaken, is carried out using a standard technique called a transseptal puncture. This involves a fine needle being used to create a small hole from the right atrium (right upper heart chamber) into the left atrium to allow the passage of catheters. Following this, treatment can be delivered by making a series of small burn marks to restore the normal heart rhythm. During the procedure it is common that patients require the heart rhythm to be restored to normal with a specially timed electrical shock, called a cardioversion.

RESEARCH PROTOCOL: The research protocol represents only a small modification of the standard clinical procedure. Ordinarily, access to the outside of the heart is not undertaken and would represent an additional step. To allow access to the outside of the heart, a small tube is inserted underneath the breastbone and within the space between the pericardium (sac surrounding the heart) and the heart. Specialised catheters can be introduced through this tube to allow electrical maps of the outside of the heart to be created. We will undertake internal maps of the heart to assess if the veins entering the left atrium (pulmonary veins) still have electrical signals. The electrical signals in these veins can often be the trigger for atrial fibrillation. As a result, the first ablation undertaken for the treatment of atrial fibrillation typically aims at undertaking ablation to eliminate the electrical signals from the pulmonary veins (pulmonary vein isolation). If at baseline there is pulmonary vein isolation, then the patient will be excluded from the study and they will have further ablation undertaken at the operator’s discretion. If there is electrical activity within the vein, then the patient will be randomised to either ablation to achieve pulmonary vein isolation or to achieve pulmonary vein isolation and undertake more extensive ablation both on the inside and outside of the heart. This will prolong the procedure by around 30-45 minutes. A standard procedure without the research protocol takes between 2 and 4 hours. A small implantable cardiac monitor will be implanted beneath the skin. This will help facilitate monitoring of the heart rhythm for 2 years. The device will automatically sync cardiac rhythm data to the participant's smartphone. This data will be sent securely and with pseudonyms to a specialised cardiac data processing company in Germany. This will be done in accordance with all data protection laws. This will help facilitate follow-up and assessment of primary and secondary outcomes of the different treatment arms. Patients will be blinded to knowledge of the treatment arm they were assigned to. If patients were to have another further atrial arrhythmia (irregular heartbeats), 3 months after the procedure within the study follow-up period, the knowledge of treatment undertaken would be revealed to the patient. This will allow the patient to make informed decisions regarding future therapeutic interventions.

Intervention Type
Other

Phase
Not Specified

Primary outcome measure
Time free from documented persistent atrial fibrillation at 12 months measured using patient records.

Secondary outcome measures

Measured using patient records:
1. Time free from documented persistent atrial fibrillation at 'Completed data transmission'.
2. Time free from documented AF episodes > 30 seconds at 12 months
3. Time free from documented AF episodes > 30 seconds at 'Completed data transmission'.
4. Time free from symptomatic AF episodes >30 seconds at 12 months
5. Time free from symptomatic AF episodes >30 seconds at 'Completed data transmission.'
6. Time free from regular atrial tachycardia episodes of >30 seconds at 12 months.
7. Time free from regular atrial tachycardia episodes of >30 seconds at 'Completed data transmission.'
8. Time free from symptomatic regular atrial tachycardia episodes >30 seconds at 12 months.
9. Time free from symptomatic regular atrial tachycardia episodes of >30 seconds at 'Completed data transmission.'
10. Time free from documented atrial arrhythmia episodes >30 seconds at 12 months.
11. Time free from documented atrial arrhythmia episodes of >30 seconds at 'Completed data transmission'.
12. AF burden between groups at 12 months.
13. AF burden between groups at 'Completed data transmission.'
14. AT burden between groups at 12 months.
15. AT burden between groups at 'Completed data transmission.'
16. AF and AT burden between groups at 12 months.
17. AF and AT burden between groups at 'Completed data transmission.'
18. Procedure duration.
19. Fluoroscopy time and Radiation dose.
20. Successful bidirectional linear block in "PVI + endo-epi linear ablation" arm and non-randomised arm.
21. Bidirectional linear block requiring epicardial ablation in "PVI + endo-epi linear ablation" arm and non-randomised
22. arm.
23. Incidence of peri-procedural complications.
24. Quality of life measurements (EQ-5D and AFEQT) at baseline and at 12 months after ablation.
25. Number of chemical and electrical cardioversions required in the blanking and post blanking follow-up period.
26. Number of repeat ablation procedures required in the blanking and post blanking follow-up period.
27. Estimation of the cost-effectiveness between study groups.
28. Left atrial size at 12 months after ablation.
29. LV function at 12 months after ablation.
30. PVI and linear lesion durability, as evidenced by repeat ablation in all arms of the study during follow-up.

Overall study start date
17/01/2023

Completion date
01/05/2026

Eligibility

Key inclusion criteria

1. Previous left atrial ablation with pulmonary vein isolation only
2. Indicated for repeat catheter ablation for documented symptomatic recurrent persistent AF
3. Aged > 18 years
4. Willing and able to provide informed consent
5. Willing and able to comply with the study requirements

Participant type(s)
Patient

Age group
Mixed

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 166; UK Sample Size: 166

Key exclusion criteria
1. Pregnancy or planning pregnancy
2. Previous cardiac surgery
3. Previous pericarditis
4. Previous linear ablation in the LA
5. LA diameter > 55 mm in TTE
6. Current involvement in another interventional clinical trial
7. Contraindication to anticoagulation
8. Longstanding persistent AF lasting more than 2 years in duration
9. Cyanotic congenital heart disease
10. Body Mass Index > 40
11. Unable to use a smartphone with the 'myMerlin' application
12. Failure to achieve sinus rhythm, despite a maximum of 4x cardioversions +/- IV antiarrhythmic drugs
13. Failure to achieve epicardial access, via the CO2 insufflation technique
14. Re-assessment of PVI after the 20-minute waiting period
15. Implantable cardiac monitor permanently explanted, during the blanking period

Date of first enrolment
28/08/2023

Date of final enrolment
01/04/2025

Locations

Countries of recruitment
England

Scotland

United Kingdom

Study participating centre
Royal Sussex County Hospital
Eastern Road
Brighton
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Study participating centre
The Royal London Hospital
80 Newark Street
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Study participating centre
Liverpool Heart and Chest Hospital NHS Foundation Trust
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Study participating centre
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Study participating centre
Walsgrave General Hospital
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CV2 2DX

Study participating centre
St James's University Hospital
Leeds Teaching Hospitals NHS Trust

Beckett Street
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Study participating centre
King's College Hospital
Denmark Hill
London
United Kingdom
SE5 9RS

Study participating centre
Golden Jubilee National Hospital
Agamemnon Street
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G81 4DY

Sponsor information

Organisation
University Hospitals Sussex NHS Foundation Trust

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Sponsor type
Hospital/treatment centre

Website
https://www.uhsussex.nhs.uk/

ROR
https://ror.org/03wvsyq85

Funder(s)

Funder type
Government

Funder Name
National Institute for Health and Care Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
1. Peer-reviewed scientific journals
2. Internal report
3. Conference presentation

Intention to publish date
01/06/2027

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date