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Comparing three types of specialist pacemakers to improve heart function and reduce rhythm problems in heart failure

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Registration date 11/11/2025	**Overall study status** Ongoing	
Last Edited 04/12/2025	**Condition category** Circulatory System	

Plain English summary of protocol

Background and study aims

Some patients with heart failure experience delays in electrical signals, causing the left and right sides of the heart to beat at slightly different times. This reduces the heart's effectiveness as a pump and can cause symptoms and shorten life expectancy. Specialist pacemakers can be put in by doctors to improve the timing of the left and right sides of the heartbeat, which can improve symptoms and life expectancy. Traditionally, these pacemakers have one lead placed directly into the heart muscle on the right side, and one lead which sits in a vein on the outside of the left side of the heart. These devices are called biventricular pacemakers. Whilst these pacemakers can improve the timing of the right and left-sided heartbeat, the pattern in which electricity spreads through the heart is abnormal, which can cause abnormal heart rhythms.

A new type of pacemaker has been developed, where instead of two leads on opposite sides of the heart, a single lead is placed into the middle of the heart, where it can reach the natural wiring of the heart to both sides (conduction system pacing). This study will compare biventricular pacing to conduction system pacing to try and find out which is better for patients. It will assess symptoms, physical capability, heart-pumping function and the risk of developing abnormal heart rhythms. The study will also assess a combined approach of the two pacemakers, called left bundle optimised cardiac resynchronisation (LOT-CRT), to see how this compares to each of the individual pacemaker setups. The main aims of the study are to compare the effects of conventional biventricular pacing (BVP), conduction system pacing (CSP) and left-bundle optimised CRT (LOT-CRT) on heart failure symptoms and heart rhythm problems over six months. The study will also explore how these pacing methods affect heart muscle strength, electrical activity, and overall heart function.

Who can participate?

Adult patients referred from a cardiologist for a specialist type of pacemaker called cardiac resynchronisation (CRT), which improves the pumping of the heart.

What does the study involve?

All patients will be asked to attend four hospital visits over six months. All visits will be at

Hammersmith Hospital, Imperial College Healthcare NHS Trust. Refreshments will be available at all visits.

Participants will undergo several routine tests as part of standard preparation for a pacemaker, whether they agree to be part of this research study (or not). However, if they consent to be part of the study, the test results will be used as part of the research. In women <65 years, a pregnancy urine test will be included. If pregnancy is confirmed, they will be excluded from the study.

Visit 1 – Consent & Pre-Implant Tests
If deemed eligible to be recruited to the study, a research team member will provide a brief explanation of the study before inviting you to attend for informed consent to be obtained, research tests and smartphone application onboarding. Reasonable travel costs to the hospital via taxi will be reimbursed for Visit 1 (as this is solely for research purposes).

Research-specific measurements are undertaken at this visit: ultra-high frequency ECG, 6-minute walk test and heart failure questionnaires. If more than 6 weeks have passed since the last transthoracic echocardiogram, blood test (B-type natriuretic peptide, BNP) and 12-lead ECG, these will be repeated at this visit. All blood tests will be processed as per the standard NHS laboratory throughout the study.

A web-based symptom recording application will be set up on the participant's smartphone. During setup, the participant will be asked to choose the symptom they recognise to be most associated with their heart failure. During the study, they will be asked to record the severity of this symptom from the previous day by placing a tab on a sliding scale. This will be required every day from the point the application is set up (before the pacemaker implant) through until the end of the study, 6 months after the pacemaker implant. The application will serve solely as a research tool, and the data generated will be pseudonymised and only accessible to the research team. Training in the application will be provided by a research team member at the first visit. Throughout the study period, a member of the research team will be available to help troubleshoot any issues with the application. After the 6-month period of symptom recording, the application will be deleted from participants' phones. If a participant does not own a smartphone, a nominated proxy (relative/friend) can be set up with the application and input daily data as per the participant's instructions. No identifiable data will be collected from the proxy. If this is not possible, a member of the research team will call the participant daily and input the data.

Visit 2 – Randomisation & Implant
Sometimes, when the best way of treating patients is unknown, comparisons are made. To do this fairly and to avoid potential bias, people included in comparisons are put into groups randomly. The allocation will be selected by a computer, with no information about the individual (i.e. by chance). Subjects in each group have different treatments, which are compared.

On the day of pacemaker implant, participants will be randomly allocated to one of the following groups, with an equal chance (1 in 3):
• Traditional biventricular pacing (BVP)
• Conduction system pacing (CSP)
• Combined approach (LOT-CRT)
The study is double-blind, meaning that both the participant and the researchers taking measurements and analysing the data will not know which treatment group the participant has been allocated to. This information will become available to the participant after the 6-month study period (unblinding), or earlier if they request to leave the study. If members of the clinical

team require this information before the completion of the 6-month study period, it can be released, but this may result in discontinuation from the study.

During the pacemaker implantation procedure
Participants will be admitted for a day case procedure in the cardiac catheter laboratory at Hammersmith Hospital, where pacemaker implantations are performed. The pacemaker procedure will vary depending on the treatment group to which the participant is allocated.

• Biventricular pacing (BVP, current standard care):
o A lead may be put into the right atrium (as per the clinical team)
o A right ventricular lead directly into the muscle of the heart
o A left ventricular lead that sits directly on the outside of the heart in one of the veins

• Conduction system pacing (CSP)
o A lead may be put into the right atrium (as per the clinical team)
o A lead into the middle of the heart, into the natural wiring of the heart
o If there are concerns regarding the effectiveness of the lead into the middle of the heart, a left ventricular lead that sits directly on the outside of the heart in one of the veins may be put in. This lead will be switched off for the first 6-months of the study period. It may be switched on subsequently at unblinding, if it is felt to be beneficial by the clinical team.

• LOT/HOT-CRT (combined approach)
o A lead may be put into the right atrium (as per the clinical team)
o A lead into the middle of the heart, into the natural wiring of the heart
o A left ventricular lead that sits directly on the outside of the heart in one of the veins. This lead will be switched on for the first 6-months of the study period. It may be switched off subsequently at unblinding, if it is felt to be beneficial by the clinical team.

Several measurements will be taken at the time of implant. This will involve non-invasive electrical mapping (described below), measurements of blood pressure using either a finger-cuff device or a small tube inserted into an artery at the wrist under local anaesthetic and ultra-high frequency ECG.

Non-Invasive Electrical Mapping
This will involve patients being fitted with a vest containing multiple electrodes on the cardiac day-ward before the pacemaker implant. Once fitted with the vest, patients will undergo a low-dose CT scan of the chest to confirm the heart position. Assessments of the electrical patterns will be made throughout the pacemaker implant using the specialist vest, which can be expected to be worn for 2-4 hours on the day of the procedure.

The hospital visits after the pacemaker implant are part of normal care; however, they will be longer than normal care (55-75 minutes) to allow us to take additional measures purely for the purposes of this research.

Visit 3 – 12-week Follow-up
The visit after 12 weeks will involve the usual standard of care tests.
• Device checks
• Transthoracic echocardiogram
• 12-lead ECG
• Blood test (BNP)
As well as research specific measurements;
• 6-minute walk test

• Heart failure questionnaires
• Ultra-high frequency ECG
• Fitting of 24h ECG monitor (Holter) - required to be returned at Visit 4

Visit 4 – 6-month Follow-up (and beyond)
The 24h ECG monitor will be returned to the hospital. The visit after 6-months will involve the usual standard of care tests.
• Device checks
• Transthoracic echocardiogram
• 12-lead ECG
• Blood test (BNP)
As well as research specific measurements;
• 6-minute walk test
• Heart failure questionnaires
• Ultra-high frequency ECG
• Low-dose CT scan of the chest
• Assessments of the electrical patterns within the heart using the same specialist vest described at Visit 2. The expected total time of wearing the vest is 75 minutes.
• Measurements of blood pressure using a finger-cuff device
If an ultrasound scan of the heart (TTE), 12-lead ECG or blood test (BNP) have been done via clinical care teams within 2 weeks before visits 3 & 4, these will not be repeated.

After the 6-month follow-up visit, there will be no further research burdens or in-person visits. Participants will be told of the type of pacemaker they have (un-blinded), and further programming of the pacemaker will be made on clinical grounds. Ongoing follow-up will be solely remote assessment via surveillance of electronic records until the end of the study (maximum 3 years from recruitment). If the information is not on the electronic records, a research team member may telephone their care providers to obtain this.

What are the potential benefits and risks of participating?
There may be no direct benefit from participating in the study. The study aims to gain more information about understanding the impact of the type of pacemaker on the risk of developing abnormal heart rhythms and improving heart function. It is hoped that the information gained will help people with this condition in the future receive the best-suited pacemaker therapy.

The risks during the procedure are similar to those during routine pacemaker insertion. A conduction system branch pacing wire is not known to have a higher complication rate compared to a conventional pacing wire. Conduction system pacing wires are as effective as conventional pacing wires at preventing slow heart rates and improving heart pumping. If a conduction system pacing wire cannot be implanted or does not perform as expected during follow-up, a procedure will be performed to either replace the conduction system lead or convert their pacing system to a conventional biventricular pacing system.

Patients allocated to the conduction system pacing and LOT-CRT groups with a defibrillator function will have devices requiring specialist approval and review for future MRI scans.

The insertion of the small tube into the (radial) artery at the wrist carries a risk of complication of <1% (including damage to the artery, bleeding/bruising, infection or a reaction to the local anaesthetic).

If a participant takes part in this study, they will undergo two low-dose CT chest scans and fluoroscopy as part of the device implant procedure. These procedures use ionising radiation to

form images of the body and provide the clinical team with relevant information. The CT scans will result in additional radiation exposure compared to standard care. Ionising radiation can cause cell damage that may, after many years, become cancerous. Everyone is at risk of developing cancer during their lifetime, with the general population risk estimated at around 50%. Participation in this study will increase that risk by approximately 0.03%.

There are small risks of pain, minor bleeding, bruising and infection associated with the venepuncture process to obtain the blood samples – these would be taken as part of normal clinical care.

The questionnaires (HeartQol, Kansas City Cardiomyopathy Questionnaire and Minnesota Living with Heart Failure Questionnaire) may contain some questions which patients may find sensitive. The data from these questionnaires will be pseudonymised and kept for research purposes only.

Where is the study run from?
The research team responsible for the study are based at Imperial College London, who also sponsor the study. All clinical visits will be at Hammersmith Hospital, Imperial College Healthcare NHS Trust.

When is the study starting and how long is it expected to run for?
October 2024 to October 2028.

Who is funding the study?
British Heart Foundation, UK

Who is the main contact?
1. Dr Jack Samways, RIPCORD-CRT Study Manager, j.samways@nhs.net
2. Prof Zachary Whinnett, RIPCORD-CRT Principal Investigator, zachary.whinnett@nhs.net

Contact information

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Integrated Research Application System (IRAS)
342311

Central Portfolio Management System (CPMS)
61755

Protocol serial number
EDGE 172375, BHF funding FS/CRTF/25/24768

Study information

Scientific Title
Randomised investigation of physiological, conventional and optimised resynchronisation therapy in heart failure with prolonged QRS Duration

Acronym
RIPCORD-CRT

Study objectives
1) To compare the clinical impact of conduction system pacing, conventional biventricular pacing and hybrid optimised cardiac resynchronisation therapy (LOT/HOT-CRT) on clinical heart failure (HF) and arrhythmia outcomes at six-months.
2) To explore the impact of these modalities on mechanistic contractility, arrhythmia and global function outcomes.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 02/10/2025, Greater Manchester South Research Ethics Committee (3rd Floor, 3 Piccadilly Place, London Road, Manchester, M1 3NB, United Kingdom; +44 02071048014; gmsouth.rec@hra.nhs.uk), ref: 25/NW/0269

Study design
3-arm parallel (1:1:1) study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Heart failure with reduced ejection fraction and electrical dyssynchrony

Interventions
This is a 3-arm parallel (1:1:1) randomised study of cardiac resynchronisation therapy devices in patients with heart failure with reduced ejection fraction and electrical dyssynchrony.

Randomisation will be done using a dedicated randomisation software and stratified based on 12-lead ECG QRS morphology assessed by the Strauss criteria. Ensuring an equal distribution of Strauss' positive left bundle branch block patients between study arms.

Patients will be randomised equally to 1 of the 3 following arms:
- Biventricular pacing (BVP); the current standard treatment
- Conduction system pacing (CSP)
- LOT-CRT (Left-bundle optimised CRT); a combination of CSP and a coronary sinus left ventricular lead

Intervention Type
Procedure/Surgery

Primary outcome(s)
1. Primary outcome: Daily ordinal symptom score with clinical over-rides measured using a daily ordinal scale with mobile application-based assessment of quality of life (using visual analogue scale), with clinical over-rides as detailed below, from randomisation to 6-months post-device implant:
1.1. Death

1.2. Intractable symptoms leading to trial exit/unblinding
1.3. Heart failure hospitalisation
1.4. Non-heart failure hospitalisation
1.5. Appropriate implantable cardioverter defibrillator therapy (anti-tachycardia pacing or shock, deemed appropriate as per the clinical care team interrogating the device)
1.6. Symptom score
2. Primary arrhythmia outcome: Ordinal arrhythmia scale using clinical endpoints as detailed below from randomisation to 6-months post-device implant:
2.1. Death
2.2. Appropriate implantable cardioverter defibrillator therapy (anti-tachycardia pacing or shock, deemed appropriate as per the clinical care team interrogating device)
2.3. Sustained ventricular arrhythmia (VA) (>30s of rhythm determined to be ventricular in origin by clinical team on device interrogation)
2.4. Sustained atrial arrhythmia
2.5. Non-sustained VA
2.6. >10% ventricular ectopy on 24h ECG
3. Primary contractility outcome: Ordinal contractility scale using clinical endpoints as detailed below from randomisation to 6-months post-device implant:
3.1. Death
3.2. Intractable symptoms leading to trial exclusion/unblinding
3.3. HF hospitalisation
3.4. Non-HF hospitalisation
3.5. LVEF

Key secondary outcome(s))

1. Death from any cause will be measured using an appraisal of electronic health records and contacting the primary care providers if that is not available, by occurrence of death, from randomisation up to 36 months or until death, whichever occurs first.
2. Intractable symptoms leading to trial exit/unblinding will be measured using an appraisal of electronic health records and contacting the primary care providers if that is not available, by occurrence of intractable symptoms, from randomisation up to 36 months or until trial exit /unblinding, whichever occurs first.
3. Heart failure hospitalisation will be measured using an appraisal of electronic health records and contacting the primary care providers if that is not available, by adjudicated unplanned heart failure acute care (hospital admissions or ambulatory diuretic therapy), from randomisation up to 36 months.
4. Non-heart failure hospitalisation will be measured using an appraisal of electronic health records and contacting the primary care providers if that is not available, by adjudicated unplanned non-heart failure acute care (hospital admissions or ambulatory emergency clinic), from randomisation up to 36 months.
5. Appropriate implantable cardioverter defibrillator device therapy will be measured using an appraisal of electronic health records and contacting the primary care providers if that is not available, by adjudicated anti-tachycardia pacing or shock for ventricular arrhythmia, from randomisation up to 36 months.
6. Daily heart failure symptom score, measured by mobile app-based daily ordinal score (0–600 scale), from randomisation up to 36 months.
7. Sustained ventricular arrhythmia, measured by adjudicated device interrogation showing arrhythmia >30 seconds, from randomisation up to 36 months.
8. Sustained atrial arrhythmia, measured by adjudicated device interrogation showing arrhythmia >30 seconds, from randomisation up to 36 months.
9. Non-sustained ventricular arrhythmia, measured by adjudicated device interrogation showing

arrhythmia <30 seconds, from randomisation up to 36 months.
10. > 10% ventricular ectopy, measured by 24-hour ECG, at 12 weeks post-implant.
11. Left ventricular ejection fraction (LVEF), measured by echocardiogram, within-group differences, from baseline to 6 months post-implant.
12. Left ventricular repolarisation heterogeneity, measured by ECGi-derived repolarisation time and gradient, from implant to 6 months.
13. Left ventricular activation, measured by ECGi-derived activation time and recovery interval, from implant to 6 months.
14. QT dispersion, measured by 24-hour ECG, from randomisation to 6 months post-implant.
15. Left ventricular end diastolic volume (LVEDV), measured by echocardiogram, within-group differences, from baseline to 6 months post-implant.
16. Left ventricular end systolic volume (LVESV), measured by echocardiogram, within-group differences, from baseline to 6 months post-implant.
17. Functional exercise capacity measured using a six-minute walk test within-group comparison, from baseline to 6 months post-implant. This is performed for research purposes only at visits 1, 3 and 4 of the study.
18. Serum B-type natriuretic peptide (BNP) will be measured from venepuncture samples using standard laboratory procedures, obtained at visits 1, 3, and 4 post-implant.
19. Quality of life, measured by HeartQoL questionnaire, from baseline to 6 months post-implant.
20. Quality of life, measured by Kansas City Cardiomyopathy Questionnaire 12 (KCCQ-12), from baseline to 6 months post-implant.
21. Quality of life, measured by the Minnesota Living With Heart Failure Questionnaire (MLWHFQ), from baseline to 6 months post-implant.
22. Heart failure status, measured by Cardiologist assessment at visits 1, 3 and 4, using the New York Heart Association classification.
23. Patient activity level, measured by device-derived pacemaker data, at 6 months post-implant.
24. Atrial fibrillation burden, measured by device-detected rhythm proportion, at 6 months post pacemaker implant.
25. Thoracic impedance, measured by device, at 6 months post pacemaker implant.
26. Blinding index, measured by Bang Blinding Index responses, from device implant to 6 months post-implant.
27. Safety endpoints, measured by occurrence of device-related complications (e.g. infections, lead revision, generator change), from device implant to 36 months post-implant.

Completion date
01/10/2028

Eligibility

Key inclusion criteria
Patients referred/scheduled for a CRT procedure (new implant or upgrade) who have:
1. Symptomatic heart failure (NYHA II-IV)
2. Reduced ejection fraction (LVEF≤40%)
3. Prolonged QRS duration (≥130ms) and left bundle branch block ECG morphology, or very prolonged QRS duration (>150ms) and non-left bundle branch block ECG
4. Optimal medical therapy for HF

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
99 years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Unable to provide informed consent
2. <18 years old
3. Pregnant patients (with female patients of childbearing age requiring a negative urine BHCG)

Date of first enrolment
12/11/2025

Date of final enrolment
01/10/2028

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Imperial College Healthcare NHS Trust
The Bays
St Marys Hospital
South Wharf Road
London
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Sponsor information

Organisation
Imperial College London

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Charity

Funder Name
British Heart Foundation

Alternative Name(s)
the_bhf, The British Heart Foundation, BHF

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a non-public available repository (REDCap, https://projectredcap.org) and will be published as a supplement to the results publication.

• The process for requesting access (if non-publicly available): The RIPCORD-CRT REDCap page is accessed using Imperial College London usernames and passwords, of which only personnel nominated by the Trial Manager (Dr Jack Sawmays) will be granted access
• Whether consent from participants was required and obtained: Consent from all participants will be required and obtained. Please see the attached consent form
• Comments on data anonymization: All data with be pseudonymised with allocated study ID numbers. A Study Key file, which allows identification of patients to their study ID, will be accessible only by the Trial Manager and Principal Investigator and stored securely in line with sponsor agreement and NHS practices.
• Any ethical or legal restrictions: No

IPD sharing plan summary

Published as a supplement to the results publication, Stored in non-publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Other files	version 5		10/11/2025	No	No
Participant information sheet	version 8		10/11/2025	No	Yes
Protocol file	version 1.2	27/10/2025	10/11/2025	No	No