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A study to determine if a new pacemaker function called Multipoint Pacing (MPPTM) can improve exercise performance and heart synchronisation during exercise

Submission date
11/10/2024

Recruitment status
Recruiting

Registration date
16/01/2025

Overall study status
Ongoing

Last Edited
16/01/2025

Condition category
Circulatory System

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Cardiac resynchronisation (CRT) pacemakers are designed to do two things. They synchronise the timing of contraction between the two bottom chambers of your heart (the ventricles) and they coordinate the timing of contractions between the top chambers (the atria) and the ventricles. In this way, they can improve the heart's pumping function and help to improve symptoms and signs of heart failure, such as breathlessness. The CRT pacemaker coordinates your heart contraction by electrically stimulating the different chambers of your heart via the wires, or leads, that were placed into the heart when your CRT pacemaker was implanted. This stimulation, or pacing, is coordinated by special software, or algorithms, in the device. Some new algorithms allow your device to pace the main pumping chamber of your heart, your left ventricle, from two separate points. This may be more efficient than the traditional way of pacing the heart and could help the heart function improve even more. One such algorithm is called Multipoint Pacing (MPP™), developed by Abbott (Abbott Vascular). This algorithm can deliver two separate electrical impulses to your left ventricle per heart cycle, which provides greater options to personalise your device settings and capture more of your heart than with traditional pacing algorithms. Multipoint Pacing (MPP™) can be particularly useful in patients with heart electrical conduction disease, which limits the use of other currently available CRT algorithms. It is unknown how effective Multipoint Pacing (MPP™) is during exercise.
Cardiopulmonary exercise testing (CPET) is the gold standard test way to measure exercise performance. During a CPET we measure the volumes of gases (oxygen and carbon dioxide) you breathe in and out during exercise on an exercise bike, which tells us exactly how well your heart and lungs are working. We aim to find out if Multipoint Pacing (MPP™) can improve heart synchronisation and exercise performance during a CPET. We will do this by comparing CPET performance during Multipoint Pacing (MPP™) with performance during standard CRT programming.

Who can participate?
Patients aged 18 years and over who have heart conduction disease and a CRT pacemaker capable of delivering multipoint pacing (MPP™)

What does the study involve?
The study involves two CPET tests, one during multipoint pacing (MPP™) and the other with standard CRT programming.

What are the possible benefits and risks of participating?
In some individual cases, a clear benefit of one CRT programming setting over another may be apparent when results are analysed at the end of the study. However, this cannot be guaranteed.

Where is the study run from?
John Radcliffe Hospital (UK)

When is the study starting and how long is it expected to run for?
October 2023 to October 2027

Who is funding the study?
Abbott Medical UK

Who is the main contact?
Prof. Neil Herring, Neil.herring@dpag.ox.ac.uk

Contact information

Type(s)
Scientific

Contact name
Prof Neil Herring

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
330216

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 57233

Study information

Scientific Title
Assessing the effect of multipoint pacing in cardiac resynchronization therapy with AV node block on QRS duration and exercise capacity

Acronym
MPP-CPET

Study objectives
Multipoint pacing (MPPTM) can improve heart synchronisation and performance during exercise in patients with heart failure and electrical conduction disease.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 05/12/2023, South Central - Oxford C Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 1048144, +44 (0)207 104 8089, +44 (0) 207 104 8271; oxfordc.rec@hra.nhs.uk), ref: 23/SC/0380

Study design
Prospective single-centre randomized double-blinded crossover study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Multi point pacing in cardiac resynchronisation therapy with AV node block

Interventions
We will use a prospective single-centre randomized double-blinded crossover study to investigate our hypothesis.

Twenty participants will be enrolled and asked to attend the Cardiovascular Clinical Research Facility (CCRF) at the John Radcliffe Hospital on two occasions, approximately 1-2 weeks apart.

Each of these visits will take approximately 2 hours. Consent will be taken at the time of attendance for the study to limit the number of trips needed. A member of the research team will then ask questions about general health, medical history, and any medications being taken.

Participants will be asked to perform two separate cardiopulmonary exercise tests (CPET) with their device programmed to each of the two settings below:
1. Device set with MPP™ off, a fixed AV delay of 120 msec, and optimised biventricular pacing as per the Oxford protocol
2. As above but with MPP™ on, with the widest anatomical separation [i.e., where possible distance between cathodal LV electrodes ≥30mm—either D1–P4/P4–D1 (47mm) or D1–M3/M3–D1 (30mm) cathodal combination for LV1 and LV2] and the shortest intraventricular and interventricular timing delays of 5ms.

The order in which their device is programmed with be decided randomly. Randomization will take place by use of sealed envelopes containing allocation to the initial group. These will be prepared at the start of the study and will have no external distinguishing features. Envelopes will be randomly selected by the Investigator at the time of study enrollment. The patient and the investigators will be blinded to the order that the devices are programmed.

Cardiopulmonary exercise testing will then be carried out. We will first perform some simple breathing tests. Participants will then be asked to exercise on an exercise bike, with increasing levels of resistance whilst wearing a face mask through which we can measure the concentrations of gases being breathed out. Participants will be attached to a heart monitor so that we can measure the heart electrocardiogram (ECG). Blood pressure will be measured at 1-minute intervals and participants will be asked to rate how much exertion they feel they are doing on a standardised scale at 1-minute intervals. A small tube (cannula) will be inserted into a vein in the hand or arm to allow blood samples to be taken. Four blood samples of 5 mls each will be taken over the course of the CPET. The test will end when the participant reaches their subjective maximal capacity or if they experience arrhythmia, hypotension, severe hypertension or other cardiovascular complications that mandate termination. The researcher performing the CPET will be blinded as to which group the participant is in.

The researcher will record the participant’s concomitant medications from their recall, checking the medical notes if necessary for confirmation and specifics.

Participants will have a chance to recover, and the CRT device will be reset to its original settings.

On the second visit, the CPET will be repeated, with the participant allocated to the other device programming group.

Analysis will include measurement of VO2, VCO2, minute ventilation, tidal volume, respiratory rate and heart rate during CPET, along with rating on the Borg-RPE (6-20) scale. Venous blood samples will be taken pre-CPET, at 3 minutes, peak exertion and after 15 minutes recovery, for analysis. QRS duration (QRSd) during exercise will also be measured using either automated CPET software (manufactured by CustoMedTM (Custo Med GmbH, Maria-Merian-Str. 6, 85521 Ottobrunn, Germany) or manually, along with maximum difference in R wave amplitude. Changes in intrinsic PR interval on exercise with multipoint pacing on (measured on intrinsic beats) will also be measured.

Intervention Type
Other

Phase
Not Specified

Primary outcome(s)
QRS duration measured using an assessment of exercise ECG intervals performed automatically by the recording software (CustoMed). All beats suitable for analysis in the last 10 seconds of each exercise stage are automatically selected. QRS duration is then measured from the earliest to the latest markers on any lead of the 12-lead ECG (global QRSd). Recording occurs at baseline and through different stages of exercise up to peak VO2 during a cardiopulmonary exercise test (CPET).

Key secondary outcome(s))
1. Exercise performance will be quantified during cardiopulmonary exercise testing (CPET) using standardised measures including: VO2 max, VO2 at the aerobic threshold, VE/VCO2 slope, OUES slope, VO2/HR, heart rate, RER, and exercise duration. Blood lactate sampling will be performed at rest, peak exertion and 15 minutes into recovery.
2. Subjective effort will be quantified using the Borg-RPE scale through different stages of exercise up to peak VO2.

Completion date
01/10/2027

Eligibility

Key inclusion criteria
1. Age ≥18 years
2. Willing and able to give informed consent
3. Patients with existing CRT devices able to utilise the MPP™ algorithm, implanted ≥6 months and under follow up at OUH NHS Foundation Trust
4. Sinus rhythm and PR interval >250 ms, or higher degrees of heart block
5. Able to exercise to perform CPET

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Pregnancy or breastfeeding
2. Persistent or permanent atrial fibrillation or atrial tachycardia

3. PR interval <250 ms
4. Chronotropic incompetence, defined as the use of a rate-response algorithm or ≥80% atrial pacing
5. Any concurrent condition contraindicating the use of CPET
6. Any impediment to communication which, in the opinion of the investigator, might prevent the investigator communicating effectively with the patient during the study (including inability to speak English)

Date of first enrolment
01/09/2024

Date of final enrolment
01/10/2026

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University of Oxford
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Study participating centre
John Radcliffe Hospital
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Sponsor information

Organisation
University of Oxford

ROR

https://ror.org/052gg0110

Funder(s)

Funder type
Industry

Funder Name
Abbott Medical UK

Results and Publications

Individual participant data (IPD) sharing plan
A fully anonymised version of the dataset used for analysis with individual participant data and will be available for other researchers to apply to use 1 year after publication. Written proposals (submitted to Professor Neil Herring) will be assessed by members of the trial team and a decision made about the appropriateness of the use of data. A data-sharing agreement will be put in place before any data are shared.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 1.1	20/11/2023	25/10/2024	No	Yes
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes