DIVISION OF CARDIOVASCULAR MEDICINE

RADCLIFFE DEPARTMENT OF MEDICINE
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Oxford University Hospitals NHS
NHS Foundation Trust

PARTICIPANT INFORMATION SHEET

Assessing the Effect of Multipoint Pacing (MPP™) in Cardiac Resynchronization Therapy with AV node block on QRS duration and Exercise Capacity

We would be grateful if you would consider taking part in a clinical research trial. You have a Cardiac Resynchronization Therapy (CRT) device implanted, manufactured by Abbott. This means you may be eligible to take part in this clinical study if you wish.

To help you decide if you are interested in participating in this study, we are providing this patient information sheet. It is important for you to understand why the research is being done and what it would involve for you. Please take time to read this information and discuss it with others if you wish. If there is anything that is not clear, or if you would like more information, please ask. Remember it's your choice and you will be able to withdraw at any time should you wish.

Summary

Why are we conducting this study?

We wish to study how effective a new function available on your device called Multipoint Pacing (MPP™) is when you exercise. In particular, we want to find out whether it improves how much exercise you can carry out, how you feel during exercise, and how coordinated it keeps the contraction of the heart.

What will this entail for me?

- Your involvement in this trial will be over a period of up to 3 weeks and will involve a total of 2 visits with the study team.
- During each visit, you will have an exercise test (on a stationary bicycle) to measure your ability to perform exercise (total of two tests overall)

- Over the course of the study, you will also have eight blood samples taken from a small tube (cannula) inserted into a vein in your arm (four blood tests per exercise test)
- Before each exercise test, we will temporarily re-program your device to test how the different settings affect your ability to exercise. At the end of each test your device will be re-programmed to its original settings

Are there any risks?

- Cardiopulmonary exercise testing is extremely safe with no clinically relevant issues recorded in over 4000 tests in high risk patients. However there might a very small risk of feeling slight fatigue, breathlessness and palpitations as you would with any exercise. Please speak to your doctor if you need further details.
- There are no associated risks with the planned changes to your device settings. The same type of alterations are done routinely at clinical follow up in order to optimise the function of your device.
- There is a risk of bruising resulting from inserting a cannula to take blood samples

After reading this document, you should know why we are doing the study, what choices you have, what will happen to you if you join, and the possible risks involved. We also explain how we will protect your personal information, what to do if you have any problems and where to get more information or how to make a complaint.

Contents

What is the purpose of the study?

Your CRT pacemaker is designed to do two things. It synchronises the timing of contractions between the two bottom chambers of your heart (the ventricles). Also, it synchronises the timing of contractions between the top chambers (the atria) and the ventricles. In this way, it can improve the heart's pumping function and help to improve or limit the 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 which is present in your CRT pacemaker device is called Multipoint Pacing (MPP^{TM}), 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.

MPP^{TM} may currently already be switched on in your CRT Pacemaker. This is a decision that will have been made as part of your routice clinical care, either at the time your pacemaker was implanted or subsequently when you have been seen in the pacing clinic.

What is not clear is how effective multipoint pacing (MPP^{TM}) is when you exercise. One way we can look at this is to monitor your heart tracing (electrocardiogram) when you exercise, and see if (MPP^{TM}) makes any difference to the amount of exercise you can do. We can measure how much exercise someone can do by carrying out a cardiopulmonary exercise test (CPET), which measures the concentrations of expired gases you breathe out when you exercise on an exercise bike.

Why have I been invited?

You have been invited to take part because you have a CRT pacemaker that can deliver MPP^{TM}. You many have been informed of this study by your normal clinical team and contacted the research team yourself, or you have given verbal consent for your contact details to be securely passed to us by the pacing clinic who normally monitor your device.

Do I have to take part?

No, you do not have to take part.

It is up to you to decide whether to take part. If you decide to take part, you are free to change your mind at any time without giving a reason and leave the trial. This would not affect the standard of clinical care you receive now or in the future. If you do decide that you no longer wish to continue with the study, we would still retain any data and samples already obtained from you unless you request otherwise.

What will happen to me if I decide to take part?

If you decide to take part in this study, there will be no changes to your clinical care. You will be asked to attend 2 study visits over the course of 3 weeks. At each visit you will be asked to perform one cardiopulmonary exercise test, either with MPP^{TM} turned on or without MPP^{TM}. The order in which we perform these tests will be decided by a randomisation

algorithm. This will allow us to determine if MPP^{TM} improves your ability to exercise. Each visit will take approximately 2 hours. At the end of each visit your CRT pacemaker will be programmed back to its original settings.

Research visits

- Each visit will be the Oxford clinical research facility at the John Radcliffe Hospital in Oxford. On your first visit you will have an opportunity to go through this information leaflet with the study team who can answer any questions you have and, if you still want to take part, will ask you to sign a consent form. A member of the research team will then ask you questions about your general health, medical history, and any medications you are taking.

  The following procedures will take place during each visit:

- **CRT device setting randomisation:** We will use a randomisation algorithm to decide the order in which we perform your CPET tests. You will not be aware of the order (if MPP^{TM} is on or off), to prevent this knowledge from influencing your performance in your CPET.

- **CRT device re-programming (5 minutes):** A trained member of the research team will interrogate your CRT pacemaker and optimise its settings as much as possible. You will then have the MPP^{TM} algorithm either switched on or switched off. (NB. This will be the case whether you normally have the MPP^{TM} algorithm activated or not). You will probably not notice any immediate difference. Neither you nor the doctor running the exercise test will know which setting has been chosen until after both tests are complete (i.e. the test will be “blinded”).At the end of each visit your device will be programmed back to its original settings. This will happen even if you notice a benefit from the research settings.

- **Cardiopulmonary exercise test (up to 25 mins)**: You will then be asked to carry out gentle exercise on a static exercise bike, with increasing levels of resistance. You will wear a facemask, through which we can measure the concentrations of gases you are breathing out. You will have sticky pads attached to your chest linking you to a heart monitor so that we can measure your heart **electrocardiogram (ECG).** Whilst you are exercising, we will measure your blood pressure regularly and ask you to rate how much exertion you feel you are doing on a standardised scale. When you have carried out as much exercise as you feel capable of doing, the test will be stopped. You will have a chance to recover, and the CRT device will be reset to its original settings.

- **Blood samples:** A small tube (cannula) will be inserted into a vein in your hand or arm. We will use this to **take blood samples during your CPET test**. We will take 4 blood samples in total over the course of each CPET: one before you start your CPET, one at 3 minutes into your CTPE, one at your peak exercise, and one 15 minutes into recovery. 5ml of blood (approximately 1 teaspoon) will be taken each time. During this study you will have a total of eight bloods tests (four per CPET).

What should I consider?

- If you are pregnant, breast feeding or planning to become pregnant during this study period you may not be able to participate in the study.

- If you are involved in other research studies, you should inform the investigators prior to your enrolment in this study.

- If you have atrial fibrillation, you may not be able to take part in this study.

Are there any possible disadvantages or risks from taking part?

Your decision on whether you will participate or not will not affect in any way the quality of treatment you will receive.

There is little risk from altering your CRT pacemaker settings for the study. All the settings used in this study are also used in routine clinical care. However, some settings may work better in different individuals, especially on exercise, which is what we are investigating. In addition, you will be closely monitored throughout having the CPET.

Cannula insertion carries a very small risk of infection, which will be minimised by ensuring strict hygiene and inserting it via aseptic non-touch technique. The cannula will be removed at the end of each CTPE test. The worry associated with taking blood or inserting a cannula may cause some participants to feel unwell or faint before, during or after the procedure. Minor bruising and pain may be caused by the cannulation.

CPET is an extremely safe procedure with no clinically important complications recorded in over 4000 tests on patients with a range of high-risk cardiac conditions including congestive cardiac failure. You will be monitored throughout the CPET and a medically qualified professional will be present. You may experience mild fatigue, shortness of breath and palpitations, as with any exercise.

What are the possible benefits of taking part?

In some individual cases, a clear benefit of one setting over another may be apparent when results are analysed at the end of the study. If this is the case, we may inform your clinical care team (with your permission) so that they can improve the programming of your CRT pacemaker. This would only occur at the end of the study. However, this is not the reason the study is being performed and is not guaranteed.

A better understanding of the effectiveness of MPP pacing on exercise could lead to improved CRT response and improvement in symptoms and quality of life in other patients with severe heart failure and so this is an important study.

What happens if you find something unexpected?

In the event of any unexpected findings of clinical significance which come to light as part of the research procedures in this study, a designated clinical specialist will discuss the implications with you and may arrange for further investigations as necessary. However, it is important to note that this research is not for diagnostic purposes and is not a substitute for a clinical appointment. So if we find anything unusual, it would be appropriate for us to notify your GP so that they can arrange on-going clinical care for you. But we would only do this after we and the specialist had discussed your options and gained your permission.

What will happen to my data?

United Kingdom data protection regulation requires that we state the legal basis for processing information about you. In the case of research, this is 'a task in the public interest.' The University of Oxford is the data controller and is responsible for looking after your information and using it properly. We will be using information from you and your medical records, and will use the minimum personally-identifiable information possible.

Personal information, such as your contact details will be kept by the study investigators and accessed only by them. All data kept on university computers will be encrypted and password protected. All documents containing personal information such as your informed consent form will be stored securely in the RDM Division of Cardiovascular Medicine, University of Oxford, at the John Radcliffe Hospital and only accessible by study staff and authorised personnel.

We will store any research documents with personal information, such as consent forms, securely at the University of Oxford for 5 years after the end of the study, as part of the research record. If you agree to your samples being used in future research, your consent form will be held until the samples have been depleted or destroyed. If you agree to your details being held to be contacted regarding future research, we will retain a copy of your consent form until such time as your details are removed from our database but will keep the consent form and your details separate. We will keep any other identifiable information about you for up to 3 years after the study has finished, to allow time for full analysis and publication of results and for these to then be communicated to you if you have indicated a wish for this to happen.

Oxford University Hospitals NHS Foundation Trust will collect information from you and your medical records for this research study in accordance with our instructions. They will use your name, NHS number and contact details to contact you about the research study, make sure that relevant information about the study is recorded for your care, and oversee the quality of the study. They will keep identifiable information about you from this study – in particular, a copy of the consent form in your medical notes – in keeping with Trust policy for medical notes retention.

UK data protection regulation provides you with control over your personal data and how it is used. When you agree to your information being used in research, however, some of those rights may be limited for the research to be reliable and accurate. Further information about your rights with respect to your personal data is available at https://compliance.web.ox.ac.uk/individual-rights

You can find out more about how we use your information by contacting: neil.herring@dpag.ox.ac.uk

Will my taking part in the study be kept confidential?

Yes. All study records and samples will be identified only by a code. We will only use names, date of birth and NHS numbers where this is necessary to link to your NHS records or contact you. Information that can identify you will only be held securely by the research team at the University of Oxford for the purposes of the study.

Confidentiality will be maintained as far as it is possible, unless you tell us something which implies that you or someone you mention might be in significant danger of harm. In this case, we would have to inform the relevant agencies, but we would discuss it with you first.

Responsible members of the University of Oxford and Oxford University Hospitals NHS Foundation Trust may be given access to data for monitoring and/or audit of the study to ensure that the research is complying with applicable regulations.

Will I be reimbursed for taking part?

Participants will be reimbursed £30 for travel expenses for each visit. Light refreshments will also be available

What will happen to the samples I give?

Samples of blood collected will be analysed for this study, but your samples may also be used for other studies with appropriate ethical approval in the future if you give specific consent for this. Samples collected will be stored in secure facilities within the University of Oxford. To help keep your information confidential, your sample and any information recorded about you in this study will be assigned a study code that is used instead of your name or other identifiers. Your samples will be used in a form that does not identify you, mainly by local researchers but ethically approved research projects may take place in hospitals, universities, non-profit institutions, or commercial laboratories worldwide. Because they will be shared in a form that does not link back to you, it will not be possible to withdraw them after they are shared.

What will happen if I don't want to carry on with the study?

You are free to withdraw from the study at any time and for any reason. It will have no effect on your current or future care. If you withdraw from the study, unless you state otherwise, any blood samples which have been collected whilst you have been in the study will be used for research as detailed in this participant information sheet. You are free to request that your blood samples are destroyed at any time during or after the study. If you have agreed to their use in other research, however, these cannot be recalled once sent, since they will no longer have a link to you.

If you wish to withdraw from this study at any time please contact Professor Neil Herring Neil.herring@dpag.ox.ac.uk Tel 01865 282257 or Dr. Benjamin Bussmann ben.bussmann@ouh.nhs.uk

What will happen to the results of this study?

We hope that the results will be published in scientific journals and/or presented in scientific or other meetings for the benefit of the wider medical community. However, individual patients will not be identified in any publication or presentation and your personal and clinical details will remain strictly confidential. Any scientific publications arising from the study will be available on request to all participants. You would have no legal right to a share of any profits that may arise from the research. Some of the research being

undertaken will also contribute to the fulfilment of an educational requirement (e.g. a doctoral thesis).

What if there is a problem?

The University of Oxford, as Sponsor, has appropriate insurance in place in the unlikely event that you suffer any harm as a direct consequence of your participation in this study. NHS indemnity operates in respect of the clinical treatment which is provided.

If you wish to complain about any aspect of the way in which you have been approached or treated during this study, you should contact the Chief Investigator: Professor Neil Herring. Email: neil.herring@dpag.ox.ac.uk, or you may contact the University of Oxford Research Governance, Ethics & Assurance (RGEA) office on 01865 616480, or the director of RGEA, email Rgea.complaints@admin.ox.ac.uk

The Patient Advisory Liaison Service (PALS) is a confidential NHS service that can provide you with support for any complaints or queries you may have regarding the care you receive as an NHS patient. PALS is unable to provide information about this research study.

If you wish to contact the PALS team please contact PALS Office, Level 2, main entrance, John Radcliffe Hospital Headley Way, Headington, Oxford OX3 9DU, Tel: 01865 221473, Email: PALS@ouh.nhs.uk
http://www.ouh.nhs.uk/patient-guide/feedback/pals.aspx

Who is organising and funding the study?

This study has been designed and organised by Professor Neil Herring, British Heart Foundation Senior Clinical Research Fellow, Associate Professor of Cardiovascular Medicine and Consultant Cardiologist.

This study will contribute the the PhD thesis of Dr. Benjamin Bussmann

If you wish to know more about any aspect of the study, please contact Professor Herring (neil.herring@dpag.ox.ac.uk) or Dr Bussmann (ben.bussmann@ouh.nhs.uk).

Funding:
The research is funded by Abbott.

Who has reviewed the study?

All research in the NHS is looked at and checked by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given a favourable opinion by the South Central – Oxford C A Research Ethics Committee.

Participation in future research:

We will ask if we can contact you about future studies. This is optional, you can take part in this study but decline to be contacted again. If you consent, we will keep your contact details separately from research data you have provided. Both your details and data will carry the same unique ID. This means your data is de-identified but that we can “link” details to data. In this way we can approach patients about studies relevant to their healthcare status. You can withdraw your consent for future contact at any time.

Further information and contact details:

Please contact Professor Neil Herring Neil.herring@dpag.ox.ac.uk Tel 01865 282257 or Dr. Benjamin Bussmann ben.bussmann@ouh.nhs.uk

Thank you for considering taking part.