Imperial College London

[insert trust/hospital logo here]

[Insert Hospital address]

PROTECT HF

PROTECT-HF: Physiological versus Right ventricular pacing Outcome Trial Evaluated for bradyCardia Treatment

(ECHO sub study Cohort)

Participant Information Sheet

We would like to invite you to consider taking part in this research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish.

Please ask us if there is anything that is not clear or if you would like more information. Take your time to decide whether or not you wish to take part. This PIS includes information regarding our main study as well as an optional echo research sub-study which we are undertaking in a smaller group of patients.
Thank you for reading this.

PART 1

What is the purpose of the study?

The PROTECT-HF trial will compare two different pacing approaches for treating patients at risk of, or who already have slow heart rates.

We will compare the standard approach for pacing, which involves placing a pacing lead into the right ventricle “RV pacing”, with a new form of pacing, “physiological pacing”.

Both approaches utilise the same pacemaker device, the difference in this study is the location within the heart that one of the leads will be positioned.

With right ventricular pacing the pacemaker lead is positioned on the heart muscle in the right ventricle (the chamber of the heart which pumps blood to the lungs). This method has been the

standard approach for more than 60 years and is very effective at treating slow heart rates, however it produces an abnormal sequence in the way the ventricles (the main pumping chambers of the heart) are activated. This abnormal activation can be less efficient and can lead to impairment in heart function in some patients.

With physiological pacing, the pacemaker lead is positioned on the heart's natural electrical conduction system at one of two locations; high up on the His bundle or a little lower along the Left bundle branch – these approaches allow a normal and more efficient pattern of ventricular activation, which may well mean less impairment of heart function results.

This trial will aim to establish whether preserving the heart's normal activation sequence using physiological pacing results in an improvement in heart function and also fewer deaths when compared to standard RV pacing.

The study is important as it will allow us to know what the best pacing approach is for people with slow heart rates in the future.

Why have I been chosen?

You have been invited because you have been identified by your doctor to require a pacemaker as a treatment for slow heart rates or potential slow heart rates. We will be undertaking this research in 2600 patients.

Do I have to take part?

No. Your decision to participate (or not) in this study is completely free and voluntary. If you decide that would like to participate, you will be asked to sign a consent form.

We will discuss the study with you either face-to-face or via telephone before any consent (whether electronic or paper) is signed. This written information leaflet details the known risks and potential risks. You may take time to consider whether you would like to participate in the trial and ask us questions if they so wish.

You have the right to refuse or withdraw your participation at any time (even if you agree today) without giving a reason. If you decide not to participate or to withdraw, it will not affect the quality of your care or treatment, nor the relationship you have with your doctor and nursing team. However, the research team would retain data already collected after consent and continue to use it confidentially for the purpose of the study. No further data will be collected, or any other research procedures carried out on or in relation to the study after you withdraw.

What will happen to me if I take part?

Once you have agreed to take part in the study, you will attend the hospital and undergo implantation of a pacemaker as clinically required. You will be randomly assigned to receive either right ventricular pacing (standard approach for pacing) or the new physiological pacing approach. This means that you cannot chose which group you join. This will be decided by chance by a computer. You have an equal chance of being in either group.

As part of the design of the study, you will not be told which pacing approach you have received.

If you agree to take part the following will take place:

1. We will ask for details about your demographics, past medical history and medication and your best contact details (we will also ask for contact details of a nominated person if you're happy for us to contact someone close to you. This will enable someone else to help provide details on your heart health if we cannot get hold of you or if you prefer that we contact them)
2. We will record details of your ECG and heart pump function (this information will come from scans of your heart you may have had recently)
3. We will record details of your measurements for heart rate, blood pressure, height, and weight. These measurements will be taken when you come into hospital for the implantation of your pacemaker. These are measurements taken as part of your routine standard of care.
4. We will ask you to complete questionnaires about your current quality of life.
5. If you are a female patient of childbearing age, as per standard of care, you will undergo a pregnancy test prior to your procedure. If this test is positive, you will not be eligible to participate in the trial. Any changes to your clinical procedure will be discussed with you by your clinical team directly.
6. You will undergo implantation of your pacemaker in an operating room called a cardiac catheterisation laboratory. This typically takes about one to one and a half hours.
7. After your pacemaker you will typically undergo a non-invasive check of your pacemaker and an xray of your chest
8. You will probably be given a small monitoring device by the medical team looking after you to monitor the pacemaker and your heart's function whilst you are at home and no longer in the hospital
9. Details of your pacemaker implant will be passed to the coordinating trial team based at Imperial College in London. This will include the x-ray images following your procedure if routine post implant X-ray is performed as part of your standard of care at your local hospital.
10. Routine clinical follow up will continue for your heart; this will probably include visits to the hospital for your pacemaker to be checked once or twice a year.
11. Members of the research team from Imperial College London will have access to your contact details so that they can contact you or your nominated other every6-months a member of the trial team will make contact with you or your nominated other either by phone or email to ascertain details on how you are, whether you have had any problems with your heart health requiring trips to hospital and to repeat the questionnaires with you that assess your quality of life. Some of the questionnaires can be answered via an online survey (the link to this survey will be sent via email). Your contact details will be stored on the study database. We will also ask you about how much health resources you have needed to use over the past 6 months. This assessment will take approximately 15-20minutes to complete. (You do not need to visit any hospital once the pacemaker has been implanted to contribute to the clinical trial). For many patients this assessment will go on for 4 years, however this will range from 3 to 6.5 years.
12. Every month, we will also send you an email with a link to a questionnaire asking how you are feeling on a scale of 0-100; this will only be done if you have provided an email address at the time of enrolment or an email address of your nominated other.
13. The trial team will obtain data about how your pacemaker is functioning (for example what percentage of your heart beats are paced beats and how much activity you do on a daily basis) from the pacemaker directly – this data communication is the same as for your routine clinical care and is fully encrypted and secure. If your hospital uses Medtronic remote home monitoring for your pacemaker device, "Cardiac Compass data" (CCD) from Medtronic's CareLink system, this is shared with the coordinating study team. We will gain your consent for this data to be shared. This is the same data your clinical care team has access to; it is fully encrypted, and secure and no personally identifiable data is shared with Medtronic for this to occur. You do not need to take any action for this to occur. This data will be sent to the research team and also to the clinical team looking after you. If you do not have this

"remote monitoring" set-up your clinical team will provide this data to the research team after your in-house pacemaker checks.

14. The study team may also make contact with you if they have been made aware of you having an adverse event by either your clinical team, local study team or your nominated other to find out how you are doing and the outcome of the adverse event, as well as to obtain further information to report this event.
15. Once the study is completed, should you wish, you will receive written communication detailing the results of the trial once all the data has been analysed.

Echocardiogram Sub Study Details

A sub-study of our research involves additional scans of the heart, called echocardiograms. This is part of our research protocol and in addition to your usual care.

An echocardiogram, a non-invasive ultrasound scan of your heart will be performed within 6 weeks of your pacemaker implantation. This will be scheduled after the pacemaker implantation.

The scan involves you lying on a couch with clothes removed from your upper body but wearing a hospital gown. A technician will perform a scan providing a detailed evaluation of your heart function utilising ultrasound. This harmless evaluation takes approximately 30 minutes.

You will be invited to return for a repeat scan approximately 2 years later to assess for any changes in your heart function over this time period. The images from these scans will be assessed by a group of experts to help better understand how pacing the heart impacts heart function.

Are expenses available?

We will reimburse costs incurred for attending echocardiogram appointments up to a total value of £30 per participant. Unfortunately, we are not able to offer further expenses for the study. With the exception of your pacemaker implantation (which you require clinically) the study has been designed so that you do not need to make long and extra visits to a hospital or clinic for extra follow-up. All remaining study follow up is conducted remotely.

If you want to take part

If you decide you would like to take part in the study please let a member of the research team know (contact details below) or a member of your normal clinical care team. After this we will confirm that you are eligible to take part in the study. You will have the opportunity to discuss the study in detail and ask any questions you have. If you decide you would like to take part we will ask you to sign a consent form and you will then be formally entered into the study.

You do not need to decide immediately, if you wish you can take more time to decide and if you do decide to enter the study you can return at a subsequent date to provide consent.

You will be asked to sign an additional clinical consent form giving specific permission for the pacemaker insertion at the time of implantation of the device; this is usual standard clinical practise.

What are the possible disadvantages or side effects of taking part?

All pacemaker implant procedures carry a small risk (in the order of 1%) and these include the below: Bleeding, bruising, damage to blood vessels, damage to the lung that sits underneath the vein where the leads are passed through (pneumothorax), damage to the wall of the heart and bleeding around the heart

(tamponade), infection (this risk is lowered by the use of antibiotics during the procedure), the leads placed may move position sometimes requiring repeat procedures to reposition them and the placement of pacing wires requires the use of X-rays to guide their positioning.

The placement of pacing wires is part of your routine care. If you take part in this study you will not undergo any additional pacing procedures. These procedures use ionising radiation to form images of your body, provide treatment and provide your doctor with other clinical information. Ionising radiation may cause cancer many years or decades after the exposure. The chances of this happening to you are the same whether you take part in this study or not.

These risks are not unique to the study but rather apply to the clinical procedure being undertaken. The clinical team are highly experienced in these procedures and will be available to address complications which arise within the specialist setting of the catheter laboratory which is well-equipped for this.

It is possible that if you receive physiological pacing it could lead to worse outcomes than conventional right ventricular pacing. We do not expect this to be the case, as physiological pacing appears to be safe in 1000s of patients already studied in non-randomised studies which have already been performed. However, we cannot be certain of this finding without a randomised trial being performed.

Occasionally, promising treatments are found to be harmful when they are tested in formal randomised trials even when early non-randomised studies have been encouraging. For this reason it is vital that we perform this study. If physiological pacing results in worse outcomes than right ventricular pacing, the patients in the physiological pacing group could be harmed by taking part in the trial.

What are the possible benefits of taking part?

The aim of taking part in the research study is to improve medical knowledge and inform future clinical practice. The reason we are conducting the study is to find out whether physiological pacing results in improvements in outcomes compared to conventional right ventricular pacing. It is possible that you could benefit if you receive physiological pacing and it proves to have better outcomes than right ventricular pacing.

The ultimate aim would be to establish whether pacing the heart in this more physiological way should be the standard of care for all patients in the future.

The study may not directly help you but the information we get may well help improve the treatment of people with bradycardia in the future.

What if something goes wrong?

Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. The detailed information on this is given in Part 2.

Participants should be aware that in the unlikely event of a loss of capacity (ability to make decisions for oneself), the research team would retain data collected and continue to use it confidentially for the purpose of the study. You will not be withdrawn if you have already had your pacemaker implantation and lose capacity afterwards. If you lose capacity after giving informed consent, but before you have your pacemaker implantation, you will be withdrawn from the study, but will still receive your pacemaker as clinically indicated and part of your standard of care. The follow-up following loss of capacity will be limited.

We will no longer contact you or your nominated other directly to obtain any information and will stop sending you the study related questionnaires to complete, both the monthly and six-monthly questionnaires. We will only collect information about your health status from your clinical and research teams directly, including information from your pacemaker device and if you have attended hospital for any heart failure related reasons. If you have remote monitoring for your pacemaker device from Medtronic's CareLink system, we will continue to collect this information.

Will my taking part in this study be kept confidential?

If you agree, we would contact your GP to inform them you are participating and will provide them with information regarding the study. Any significant health related findings discovered either during your study echocardiograms, for example left ventricular thrombus (blood clot in one of the chambers of your heart) or from one of your pacemaker device checks, for example atrial fibrillation (irregular heartbeat), will be relayed to your GP.

All the data measurements which are made as part of the study will be analysed and stored on a secure University computer in an pseudonymised format. Any information obtained from this investigation that would allow you to be identified will remain confidential.

Contact details

If you have any further questions, please do not hesitate to contact:

Dr Daniel Keene on 07749576830.

You may also contact your local study team (details at the end of this information sheet) to discuss any further questions.

Or if you would like an independent contact for further information, please contact the hospital's Patient Advice and Liaison Service (PALS 020 3313 0088)

This completes Part 1 of the Information Sheet.

Thank you for taking the time to consider participating in this study.

If the information in Part 1 has interested you and you are considering participation, please continue to read the additional information in Part 2 before making any decision/

PART 2

What if relevant new information becomes available?

If the study is stopped for any reason, we will tell you. Your clinical care continues regardless of whether the study continues or stops.

What happens when the research study stops?

You can decide to withdraw from the study at any point without needing to give a reason. Withdrawing from the study will not affect your clinical care in any way.

After the study ends, we will inform you which pacing location you received pacing from and we will communicate the findings of the study to you directly.

The research protocol will not affect your clinical management in any way either during or after the clinical protocol.

What if something goes wrong?

In the unlikely event that a complication occurs, as a result of participating in the research, we have procedures in place to promptly and efficiently treat complications. A Consultant cardiologist will be present while you have your procedure. The department is fully equipped and staff members are trained to confidently deal with any emergency which might arise.

Imperial College London holds insurance policies which apply to this study. If you experience harm or injury as a result of taking part in this study, you will be eligible to claim compensation without having to prove that Imperial College is at fault. This does not affect your legal rights to seek compensation.

If you are harmed due to someone's negligence, then you may have grounds for a legal action. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been treated during the course of this study then you should immediately inform the Investigator (Dr. Daniel Keene - 07749576830). The normal National Health Service complaints mechanisms are also available to you and often the first point of contact is the hospital Patient Advice and Liaison service (020 3313 0088). If you are still not satisfied with the response, you may contact the Imperial College, Research Governance and Integrity Team.

How will we use information about you?

Imperial College London is the sponsor for this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it appropriately . Imperial College London will keep your personal data for:

- 10 years after the study has finished in relation to data subject consent forms.
- 10 years after the study has completed in relation to primary research data

We will need to use information from you and from your medical records for this research project.

The study is expected to finish in November 2029.

For more information / confirmation regarding the end date please contact the study team, see **'Where can you find out more about how your information is used'** for contact information.

We will need to use information from you and from your medical records for this research project. This information will include your:

- NHS number
- Name
- Contact details

People within Imperial College London and study team (see section sharing your information with others and section what will happen to me if I take part) will use this information to do the research

or to check your records to make sure that the research is being done properly and the information held (such as contact details) is accurate.

Members of the research team from the College will have access to your contact details so that they can contact you every 6 months for the duration of the study (between 3 to 6.5 years) to conduct the remote study follow-ups.

People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead.

We will keep all information about you safe and secure.

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

Legal basis

As a university we use personally-identifiable information to conduct research to improve health, care and services. As a publicly-funded organisation, we have to ensure that it is in the public interest when we use personally-identifiable information from people who have agreed to take part in research. This means that when you agree to take part in a research study, we will use your data in the ways needed to conduct and analyse the research study. Our legal basis for using your information under the General Data Protection Regulation (GDPR) and the Data Protection Act 2018, is as follows:

- Imperial College London - “performance of a task carried out in the public interest”); Health and care research should serve the public interest, which means that we have to demonstrate that our research serves the interests of society as a whole. We do this by following the UK Policy Framework for Health and Social Care Research.

Where special category personal information is involved (most commonly health data, biometric data and genetic data, racial and ethnic data etc.), Imperial College London relies on “scientific or historical research purposes or statistical purposes.

International transfers

There may be a requirement to transfer information to countries outside the United Kingdom (for example, to a research partner, either within the European Economic Area (EEA) or to other countries outside the EEA. Where this information contains your personal data, Imperial College London will ensure that it is transferred in accordance with data protection legislation. If the data is transferred to a country which is not subject to a UK adequacy decision in respect of its data protection standards, Imperial College London will enter into a data sharing agreement with the recipient research partner that incorporates UK approved standard contractual clauses or utilise another transfer mechanism that safeguards how your personal data is processed.

Sharing your information with others

We will only share your personal data with certain third parties for the purposes referred to in this participant information sheet and by relying on the legal basis for processing your data as set out above.

Other Imperial College London employees (including staff involved directly with the research study or as part of certain secondary activities which may include support functions, internal audits, ensuring accuracy of contact details etc.), Imperial College London agents, contractors and service providers (for example, suppliers of printing and mailing services, email communication services or web services, or suppliers who help us carry out any of the activities described above). Our third party service providers are required to enter into data processing agreements with us. We only permit them to process your personal data for specified purposes and in accordance with our policies.

Potential use of study data for research

When you agree to take part in a research study, the information collected either as part of the study or in preparation for the study (such as contact details) may, if you consent, be provided to researchers running other research studies at Imperial College London and in other organisations which may be universities or organisations involved in research in this country or abroad. Your information will only be used to conduct research in accordance with legislation including the GDPR and the UK Policy Framework for Health and Social Care Research.

This information will not identify you and will not be combined with other information in a way that could identify you, used against you or used to make decisions about you.

Commercialisation

Data from the study may also be provided to organisations not named in this participant information sheet, e.g. commercial organisations or non-commercial organisations for the purposes of undertaking the current study, future research studies or commercial purposes such as development by a company of a new test, product or treatment. We will ensure your name and any identifying details will NOT be given to these third parties, instead you will be identified by a unique study number with any sample / data analysis having the potential to generate 'personal data'.

Aggregated (combined) or anonymised data sets (all identifying information is removed) may also be created using your data (in a way which does not identify you individually) and be used for such research or commercial purposes where the purposes align to relevant legislation (including the GDPR) and wider aims of the study. Your data will not be shared with a commercial organisation for marketing purposes.

What are your choices about how your information is used?

You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have because some research using your data may have already taken place and this cannot be undone.

We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you if this could affect the wider study or the accuracy of data collected.

Where can you find out more about how your information is used

You can find out more about how we use your information at www.hra.nhs.uk/information-about-patients/

- by asking one of the research team

- by sending an email to protect-hf@imperial.ac.uk or imperial.protect-hf@nhs.net

Complaint

If you wish to raise a complaint about how we have handled your personal data, please contact the research team first by sending an email to protect-hf@imperial.ac.uk, or by ringing us on 020 7594 9776.

Following our response, if you are not satisfied please contact Imperial College London's Data Protection Officer via email at dpo@imperial.ac.uk, via telephone on 020 7594 3502 and/or via post at Imperial College London, Data Protection Officer, Faculty Building Level 4, London SW7 2AZ.

If you remain unsatisfied with our response or believe we are processing your personal data in a way that is not lawful you can complain to the Information Commissioner's Office (ICO)- via www.ico.org.uk. Please note the ICO does recommend that you seek to resolve matters with the data controller (us) first before involving them.

What will happen to the results of the research study?

Scientific data from this study will be presented at scientific meetings and published both as internal reports and in scientific journals so that the information can be used to help others. Your participation in the study will be kept strictly confidential. If you are interested, we can provide you with a summary of the findings from this research once the study has been completed. Please let us know and we can organise this.

Who is organising and funding the research?

This research is sponsored by Imperial College London. This research is funded by the British Heart Foundation. Your doctor is not being paid to include you in this study.

Who has reviewed the study?

The study has been reviewed by independent experts as part of the review by the British Heart Foundation.

The study has also been reviewed by a Research Ethics Committee which is independent of the British Heart Foundation and Imperial College London.

This study has been reviewed and given favourable opinion by the North East - Newcastle & North Tyneside 2 Research Ethics Committee.

Study Investigators Contact details:

Study Investigator	
Study Nurse/ Coordinator	
Day time Telephone	
Email	

Thank you for taking the time to consider participating in this study.
If you accept to participate a copy of this information sheet and of the consent form will be given to you.