The University Of Sheffield.

Sheffield Teaching Hospitals NHS
NHS Foundation Trust

Academic Directorate of Cardiology and Cardiothoracic Surgery
Chesterman Wing, Northern General Hospital, Herries Rd, Sheffield S5 7AU

'EurValve'

Model-based simulation of a replacement heart valve and its effect on the heart muscle

Principal Investigator: Mr Norman Briffa 0114 22 66786

Patient Information Sheet

Dear Patient,

At your recent appointment you will have been informed that you require a replacement heart valve in a procedure which your surgeon will have discussed with you. You are receiving this information sheet because your doctor has spoken with you about this procedure and its associated risks, and believes you would be eligible to take part in a worthwhile research project called 'EurValve'. Your doctor has asked you whether you would consider participating in this project and has additionally provided you with this information sheet. Please read this carefully and consider whether you wish to participate in this trial.

Background

Valvular Heart Disease (VHD) affects around 2.5% of the population and is on the rise. It is dominated by two conditions of the circulation, 'Aortic Stenosis' and 'Mitral Regurgitation', and both are associated with significant morbidity and mortality, yet they pose a truly demanding clinical challenge, as the timing and nature of interventional treatment is crucial.

When facing such challenges, Clinicians naturally seek additional data on which to base their judgements, and a new technology - the 'Clinical Decision Support System' - is emerging in which computerised processes combine to assemble the information on an individual patient in an optimal way. The latest addition to the Decision Support method is **predictive computer simulation**, in which a 3D computer model is constructed that matches the patient's anatomy and physiology, and can be interrogated about possible courses of action.

The 'EurValve' project is building such a computer model for Valvular Heart Disease, and the model will be able to simulate the operation of an individual's heart, quantifying the pressures and flows of blood through the Mitral and Aortic valves, throughout the cardiac cycle, in conditions of rest and exercise, and with the patient's own valve or a prosthetic replacement.

The result will be an individualised set of data describing the consequences of a possible intervention, and will allow the clinician to have unprecedented insight into the patient's prognosis. If the system is successful it would be the intention to operate this model on all future patients, to help select their optimum treatment.

What happens if I participate in the study?

If you would like to participate in the study the first step will be to sign the Consent Form. Your participation in the study includes the following activities:

Data collection and scientific analysis

Your treatment is exactly as standard practice with two exceptions: activity monitoring and a repeat of some assessments ***after*** your routine treatment (discussed next). We will evaluate the data collected routinely during your treatment (for example, age, weight, sex, results of ultrasound etc.) and use it to perform a personalised computer simulation of your valve surgery. The aim of this project is that when your treatment is complete we will compare the computer prediction with 'real life' outcomes from your data; if the modelling process is effective, we hope to include this in clinical practice in the future. The data collection covers the period from your next visit until the repeat assessment, typically no later than 20 weeks after surgery.

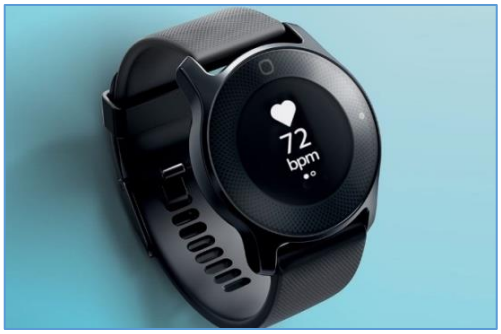
Activity Monitoring

We are interested to understand your degree of physical activity at home, both before surgery and afterwards, to understand how this relates to your condition. We will therefore provide you with two wrist-worn sensors (pictured below) that will measure your movement and heart rate, and we'll ask you to wear these for three periods, each of around two weeks at a time. The length of time will be explained to you by your doctor or a member of the research team. The devices are not known to be uncomfortable and are easily worn with no major input required from you to monitor the collection of data. We ask you please to wear the devices as much as you can: as sleep is an important part of health we would like you to try and continue wearing the devices throughout the day and night except when bathing or showering.

The devices will be allocated to you around week 3-6 after your consent. These will have base stations that will help with motion tracking. We will provide a leaflet to use as a guideline to set these up in your home, or a member of the research team can set this up on your behalf at a convenient time for you. We ask you to position the three Access Points around your house. Please put one in your bedroom, one in your main living room and one in another commonly used room (your kitchen), but preferably a room quite far from the other two. Data is stored in one of the base stations, and you will be asked to bring this with you each time you visit. On completion of the study, arrangements will be made for the return of the devices to the study team.

Along with wearing the devices, you will be asked to complete a number of short questionnaires to assist with capturing as much relevant information as possible.

University of Bristol Location Sensor



Philips Health Watch

Post-operative Assessment

We'd like to understand your condition after your surgery in the same detail as before your operation, so we'll invite you back for a second visit in line with your routine appointment. At this time we will repeat a few of the assessments and give you a second MR scan like your first scan; this will be considered to be a 'research' scan, as it is outside of your routine care.

Do I have to take part in the study?
No. You are free to refuse to join the study and may withdraw at any time or choose not to answer certain questions. Your child will receive the same quality of care at the hospital whether you join the study or not.

How is participation organised?
The study was submitted to the UK NHS Ethics Authority and received a favourable opinion. It is performed in accordance with all applicable legal requirements (for example Privacy and Good Clinical Practice Regulations).

Participation in the study is voluntary and is independent of your medical treatment. You can refuse to participate, and can withdraw at any time without giving a reason, and at no disadvantage. You will continue to receive your normal routine care under your clinician.

Why are we conducting this study?
Because of your condition, your heart muscle (the 'myocardium') has increased in size to try to maintain the required function, but this additional work is permanently damaging the myocardium itself. The increased load is usually accompanied by some degree of heart muscle weakening (heart failure). After the replacement of your defective valve with a new mechanical or tissue valve, the myocardium has a chance to recover.

Our study focuses on two questions: Can we predict the outcome of your treatment using a specially-developed computer model, and can we use data about your level of personal activity to help understand how well you will respond?

The results of the study will contribute to our future ability to advise and treat patients with valvular heart disease, especially regarding the question of the best timing of their surgery.

How many patients will participate in the study?
40 patients will complete the study at Sheffield Teaching Hospital NHS Foundation Trust.

Who is carrying out the study?
Mr Norman Briffa will be conducting the study alongside Professor Rod Hose who works at the University of Sheffield. The study will primarily be conducted at the Northern General Hospital where you will receive most of your standard care treatment. Once you have ceased activity on the trial, study analysis of your data will then commence alongside all other participant data collected. The data will be anonymised and only accessible by delegated research team members through this project.

Other centres within the EU are also conducting a similar project under the same funding stream. The team will gather the data from Sheffield where the data will be collated from numerous EU sites with the transfer of the anonymised data to a study specific database. The large password protected and encrypted database will hold anonymised data from all EU participants where data can be analysed. This analysis of all the information will be used to develop the future modelling tool.

Are there advantages from participating in the study?
Participation in the study will not bring you any immediate benefit. In the medium to long term, however, you may well benefit from the findings of the investigation if, for example, you need further valve surgery in the future, regarding the best timing and type of intervention for you.

Are there any special risks associated with the study?

Data collection and scientific analysis

The potential risk of data abuse is minimised by our strict compliance with the guidelines of data protection. Please see also below 'How are privacy, data protection and data verification ensured'.

Activity Monitoring
The wrist-worn devices are similar to watches and pose minimal risk.

Second Visit
No invasive procedures take place. The MR scan poses minimal risk.

Costs and fees?
The study is funded by the European Commission. No organisations or participants face costs or receive compensation for their participation.

Is there special insurance coverage?
NHS bodies are legally liable for the negligent acts and omissions of their employees. If a research subject is harmed whilst taking part in a clinical research study as a result of negligence on the part of a member of the study team this liability cover would apply.

Non-negligent harm is not covered by the NHS indemnity scheme. Sheffield Teaching Hospitals NHS FT, therefore, cannot agree in advance to pay compensation in these circumstances. In exceptional cases an ex-gratia payment may be offered.

In order not to invalidate any the insurance cover, please inform the principal investigator (telephone number on page 1) as soon as possible of any possible undesirable side effects or deterioration in your health.

How are privacy, data protection and data validation ensured?
Should you agree to participate, your data collected under this project will be processed as follows:

- Your personal data (name, first name, sex, date of birth and address) will be obtained by the consenting clinician and noted on the consent form. This unencrypted information remains only with the the study clinician. A copy of the form will be added to your medical file.
- The clinical data collected for the project is stored against a pseudonym and electronically processed only in this form.
- The key that is used to create the pseudonym is stored on a separate computer from the other information and is only accessible to the immediate clinical team directly involved in the study.
- It is planned to publish the study results in special journals, but this is done anonymously so that you cannot be identified.
- The pseudonomised records are maintained according to statutory requirements (at least 10 years) but are then destroyed or deleted.
- At the end of the study a fully-anonymised version of your data will be created for use indefinitely by researchers working in cardiovascular medicine or related fields.
- At any time you can ask that we stop using your pseudonymised data. In this case, no new data will be collected and the stored information will be deleted from the research system, unless this is prevented by legal retention requirements. Data once anonymised cannot be deleted (as we can no longer identify that it is yours).
- If you wish, you have the right at any time to request information about your existing personal data, and to correct any inaccuracies. Please contact the principal investigator to arrange this.
- Your signature will not release the doctor from his duty of confidentiality.

Where can I obtain more information?
If, today or in the future, you would like more information, please contact the principal investigator at the telephone number listed on the first page of this information sheet.They will be able to advise on whether the study was published and inform you of the overall outcome of the project. Thank you for considering participating in the study.

What if I wish to complain about the way in which this study has been conducted?
If you have *any* cause to complain about *any* aspect of the way in which you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms are available to you and are not compromised in any way because you have taken part in a research study:

Patient Advice and Liaison Service
- Tel: 0114 271 2400
- Email: PST@sth.nhs.uk

The study doctor is: - Mr Norman Briffa
Contact phone numbers: - 0114 22 66777 (secretary Alex Rose)

Thank you for considering participating in the study.

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EurValve Consent Form

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[Patient Stickers go here]

	Patient to initial
I have read and understood the current REC approved information sheet provided (Version 1v6, 18-Nov-16) and spoken to a delegated research team member about the objectives, nature and risks of the above-named study. I have no further questions at the time of consent.	
I understand that participation in the study is voluntary and I can withdraw my consent, without giving a reason, at any time, with no disadvantage.	
I give permission for my medical records to be accessed for the duration of the trial relating to the research project by a delegated research team member.	
I give permission for my data to be transferred outside of the UK in line with the project's EU partners for data analysis.	
I agree for my data to be accessed by regulatory bodies and sponsor representatives if required for monitoring purposes.	
I have been informed about the relevant insurance coverage and the related obligations of the study sponsor.	
I have been given a copy of the patient information sheet and consent form for my records.	
I agree that the data collected in this study may be stored in de-identified form. I also agree that the data collected in this study may be stored in fully anonymised form indefinitely, for use by researchers in cardiovascular and related research.	
I agree to take part in the 'EurValve' project.	

Participant: _____ _____ _____
Print Name Signature Date

I, the undersigned, have fully explained the relevant details of this study to the patient named above

Name of Person Taking Consent: _____ _____ _____
Print Name Signature Date

Reminder: Copies of this form must be given to the participant, the researcher and one kept in the notes.