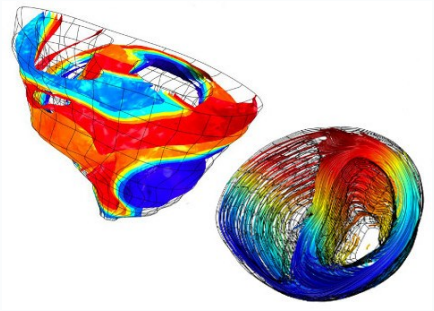
EurValve Project Newsletter

January 2017

Background to the EurValve Project



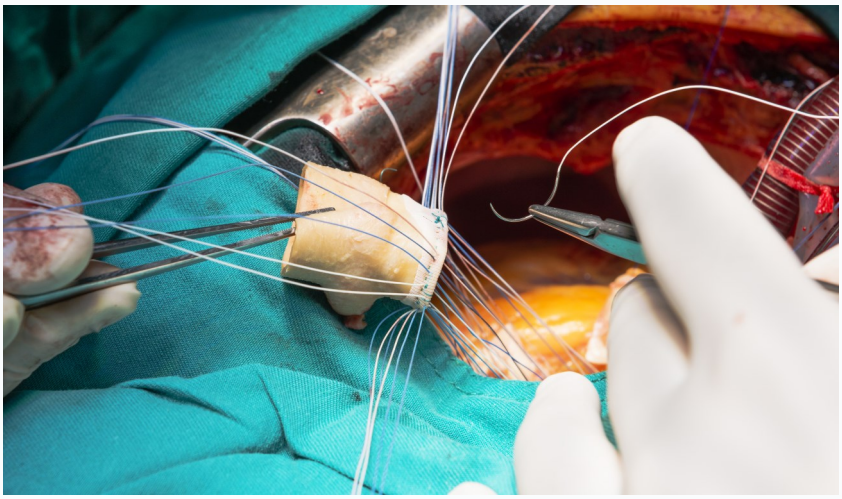
Valvular Heart Disease currently affects 2.5% of the population, but is overwhelmingly a disease of the elderly and consequently on the rise. The prevalence is up to 13% in those over the age of 75, and the population beyond the age of 85 is set to nearly double in 2028. It is dominated by two conditions, Aortic Stenosis and Mitral Regurgitation - both associated with significant morbidity and mortality, yet which pose a truly demanding challenge for treatment optimisation.

EurValve is a research group that plans to implement, test and validate a modelling based Decision Support System (DSS) for aortic and mitral valve diseases that allows simulating, comparing and understanding the effects or outcomes and risks of different treatment strategies. In addition, the DSS will improve knowledge of disease mechanisms by applying a holistic assessment of cardiovascular function that includes haemodynamic data at all cardiovascular compartments—ventricle, valve, vessels and multiscale components that couple organ with cell function.

The DSS will have major impact on patients with:

- Borderline indications for treatment
- Complex haemodynamic conditions such as combined aortic-mitral valve disease
- Valve geometries that are subject to valve repair

By combining multiple complex modelling components developed in recent EC-funded research projects, a comprehensive, clinically-compliant DSS will be developed to meet this challenge, by quantifying individualised disease severity and patient impairment, predicting disease progression, ranking the effectiveness of alternative candidate procedures, and optimising the patient-specific intervention plan.



Inside this Issue

WWW

Check out the EurValve website at Eurvalve.eu

The EurValve Consortium

Academic Partners

The EurValve consortium, coordinated by the University of Sheffield, has 13 partners. Six are academic, 3 are clinical and 4 are industrial. The primary aim of the Consortium is to develop and to deploy a Decision Support System to assist the clinician to provide the optimal treatment strategy for the individual patient. The concept is to use all of the data that is available about the patient, augmented by population data, by literature data and by types of data that are currently sparsely used in the clinical process, including activity data measured on the individual. Computational models serve to provide improved characterisations of patient physiology and, critically, to predict the effects of potential interventions. The central innovation of advanced modelling will be assembled from existing systems already available, and the substantial cluster of processing tools will be developed and refined by the project's academic technology partners below. The specialised inclusion of activity monitoring assessment will be contributed by the University of Bristol.

ROD HOSE

The University Of Sheffield.

MARIAN BUBEK

CYFRONET

FRANS VAN DE VOSSE

TU/e Technische Universiteit Eindhoven University of Technology. Where innovation starts

MARTIN FALKE

MDC MAX DELBRÜCK CENTER FOR MOLECULAR MEDICINE IN THE HELMHOLTZ ASSOCIATION

PASCAL HAIGRON

UNIVERSITÉ DE RENNES 1

IAN CRADDOCK

University of BRISTOL

Management

KEITH MCCORMACK

The University Of Sheffield.

The Coordinator, the University of Sheffield, has the overall responsibility for the progress of the Project. The Coordinator will be supported by the Project Manager, who will be responsible for the daily coordination and scientific steering of the project.

KAREN EL-ARIFI

The University Of Sheffield.

The EurValve Consortium

Clinical Partners

Two clinical trials will be conducted. The Retrospective Study will acquire data from a large patient group across EurValve's three clinical centres—Sheffield, Eindhoven and Berlin, to facilitate the development of the mechanism to infer missing data, and to provide evidence for the generation of the rule sets that will drive the detailed decision support process. This study will therefore gather data to inform a 'machine learning' process. The Prospective Study will compare computer predictions of the outcomes of heart valve replacement surgery with the actual results obtained in normal clinical practice. A total of 120 patients across the three centres will be signed up for the study. The enrolled patients will be investigated before valve intervention by ECG, MRI, laboratory tests, anthropometrics—blood pressure, body weight, clinical status. These data will be used for modelling. In the Sheffield cohort there will be an extra observation of the patients' level of activity before and after the intervention, yielding additional information relevant to CV disease: lifestyle, behaviour, risk and recovery. In Berlin myocardial biopsies will be obtained for the purpose of analysing proteomic information.

TITUS KÜHNE

GERMAN HEART INSTITUTE BERLIN

PIM TONINO

catharina ziekenhuis

NORMAN BRIFFA

Sheffield Teaching Hospitals NHS
NHS Foundation Trust

Industrial Partners

The four industrial partners of EurValve will pool their resources to develop the Decision Support System that will be a practical and philosophical advance on existing tools, as it combines powerful mechanistic modelling of patient physiology with a comprehensive level of personalisation, based on maximal information about and relevant to the patient.

HERMAN TER HORST

PHILIPS

CEMIL GÖKSU

Therenva
Share medical innovation

Philips Research Hamburg will provide models and software to compute biomarkers relevant to valve disease that are the basis for patient specific simulations. Refinement and performance optimisation of the main computational system will be conducted by partner ANSYS. Philips Research Eindhoven will provide a software module, based on machine learning and on clinical knowledge obtained from the literature, to infer data that is not available but is required for using computational, physiological models for personalised valve disease decision support. The concept will build on an existing software solution already available from partner Therenva.

JUERGEN WEESE

PHILIPS

MICHEL ROCHETTE

ANSYS

Beneficiary Profiles

Each edition of the EurValve newsletter will contain profiles on the beneficiaries. In this edition, we feature the coordinator of the project, the University of Sheffield and the lead clinical centre, the German Heart Institute, Berlin.

Beneficiary Profile – The University of Sheffield

The **University of Sheffield** has been confirmed as a world leading university in the latest national research assessment. In clinical medicine it is in the top 10 for combined world-leading and internationally excellent research outputs. The University is a member of the UK's prestigious Russell Group of research-intensive institutions. It has a formidable record in computational life sciences research and has collaborated in pan-European EC-funded projects since the earliest Framework Programmes.

Research in the Department

The Faculty of Medicine, Dentistry and Health is one of the major UK centres for education and research in health and related subjects. With origins dating back to 1828, the faculty has a long-standing tradition of excellence in clinical education and research.

Having recently established the 140 plus member Insigneo Institute for *in silico* Medicine – a joint venture between the faculties of Medicine and Engineering together with the Sheffield Teaching Hospital NHS Foundation Trust – it is able to provide unified access to all aspects of simulation-based medical research. The STH NHS is also a partner in EurValve. As an important leader in the *in silico* research community, Sheffield has overseen the increasing maturity of mathematical modelling activities within medicine, developing sophisticated framework-based approaches to many aspects, including collaborative development environments, formalised multiscale technologies, secure data-sharing mechanisms, structured algorithmic development processes and generalised sharable workflow technologies.

The Eurvalve Coordinator and PI in Sheffield is **Rod Hose**. Rod is Professor of Computational Biomechanics and was a co-author of the White Paper that launched the Virtual Physiological Human initiative. He was the PI for VPH-Share, and was workpackage leader for valvular disease in euHeart, both EC funded projects. After graduating in Mathematics from the University of Manchester, he joined Lucas Aerospace as a graduate apprentice engineer, working as a stress engineer and a consultant structural analyst in the aerospace, motor vehicle and general engineering sectors. He completed his PhD in Applied Mechanics at the University of Manchester Institute of Science and joined the University of Sheffield in 1994, where he was responsible for the development of undergraduate teaching in medical physics and had a primary research interest in the computational analysis of heart valve prostheses.

Sheffield.ac.uk

The University Of Sheffield.

Beneficiary Profile – The German Heart Institute, Berlin

Deutsches Herzzentrum Berlin (German Heart Institute Berlin, DHZB) is one of Europe's largest Heart Institutes. The research activities of DHZB cover almost all fields of cardiac diagnostic and therapy. One major research focus is on non-invasive cardiovascular imaging of patients in all age groups. Research of imaging based modelling has been successfully introduced and is currently applied in several clinical conditions (including heart failure in mitral and aortic valve disease, pulmonary stenosis, aortic coarctation). In addition, modelling of blood flow in new valve substitutes is part of DHZB research. DHZB has been the leading clinical partner in a recent modelling validation trial—EU FP7 "Cardioproof" where mechanical valve simulations and virtual treatment have been key aspects. The imaging science group covers the full spectrum of cardiovascular research that ranges from the development of hardware and software, the conduction of small and large animal research, translational science and the lead in clinical multicentre studies.

The DHZB has close international ties and long standing collaborative projects with some of Europe´s leading research institutes. In EurValve, DHZB has the role of the leading clinical partner. DHZB will provide expertise and will be responsible for the building of a clinical research database that will include a digital image repository. It will also define digital patient data, assembly data for the clinical cohort and coordinate the clinical phase of the project with the other hospitals involved and identify clinically relevant literature. DHZB will be responsible for a randomised controlled experiment that evaluates the efficiency against current clinical guidelines and involves clinical professionals from the field of Cardiology.

Professor Dr Titus Kühne is the clinical leader of the EurValve project. Titus is formally affiliated with DHZB and the Charité, Medical University Berlin where he is the director of the recently founded Institute for Computational and Imaging Science.

dhzb.de

Hypothesis

The study concerns the model-based simulation of the haemodynamic and myocardial consequences of a replacement heart valve in patients with valvular heart disease, including image-based—echo, CT, MR data, cell physiology data and clinical information.

- EurValve aims to show that a personalised computational model can predict the outcome of heart valve replacement surgery, for both the aortic and mitral valves.
- The modelling is intended to provide information on the haemodynamics (the flow patterns and pressure fields) in the affected vessels, such that the haemodynamic effects of an intervention can be optimised for an individual patient.
- The modelling of cell physiology should also provide information on the mechanisms of myocardial remodelling which are connected to heart valve replacement and to enable a holistic view of cardiovascular function, the results of the haemodynamic and cell physiology models will be combined.
- The study will combine data from 3D and 0D models to yield a system that can predict responses to the effects of haemodynamic changes in the cardiovascular system. The essential purpose of this observational clinical study is to determine the degree to which the computer prediction matches the surgical outcome.

Centralised Data Concept

The concept underpinning EurValve is the digital patient, in which all available data on a patient are combined and interpreted through the operation of a computational model. The outputs, novel disease characterisations and intervention alternatives are provided to the cardiologist to support their decision. The pathway from data to information is illustrated below.

The patient's physiological status can be described by a computer model, with two important consequences:

- The model can provide quantitative measures that are able to characterise the physiological status and contribute to diagnosis.
- Changes in the components of the system, or of the 'forces' on the system, are reflected in physiological changes that can be predicted by operation of the model.

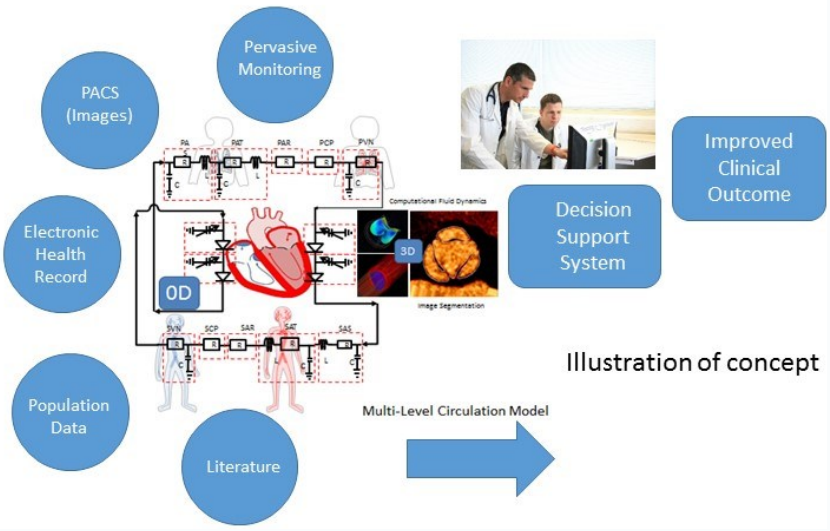


Illustration of concept

It is assumed that there is an association between the physiological status and the biological response, including for example the remodelling of the heart under the loads that it generates and to which it is subjected. This biological response might be described by specific pathways and mechanistic models, and it might be evaluated in terms of individual propensity to particular outcomes based on population studies.

The Outcome of EurValve

"The algorithmically-driven process will dramatically improve outcomes and consistency across Europe in this fast growing patient group, maximising individual, societal and economic outcome"

The automated Valvular Heart Disease workflow will provide an assessment of an individual patient, guiding a clinician through the established clinical guidelines for their condition, and making available a maximal array of data on pre-operative and predicted post-operative cardiac performance in an easily-assessable form to enable the clinician to make the best-informed judgement possible.

Health and Activity Monitoring

Why are we conducting this study?

In cases of aortic stenosis or mitral regurgitation heart muscle—the myocardium may increase in size to try to maintain the required function, but this additional work will eventually damage it. The increased load is usually accompanied by some degree of heart muscle weakening or heart failure. Replacing the defective valve with a new mechanical or tissue valve allows the myocardium a chance to recover.

University of Bristol Location Sensor

Philips Health Watch

Activity Monitoring

To understand how people's daily lives change after surgery, each patient in the Sheffield cohort will wear two Wristbands (one to monitor their activity , the Bristol Activity Watch, the other, the Philips Health Watch to measure their heart rate). The degree of physical activity at home, both before and after surgery will help us to understand how this relates to their condition.

Data collection and scientific analysis

As part of our prospective study, we will evaluate the data collected routinely during each patient's treatment for example, age, results of ultrasound, MRI and echo etc and use it to perform a personalised computer simulation of their valve surgery. When their treatment is complete we will compare the computer prediction with 'real life' outcomes from the data.

How many patients will participate in the study?

A total of 120 participants will be involved in the overall trial across all three centres.

When facing challenges such as the timing and nature of interventional treatment, clinicians naturally seek additional data on which to base their judgements, and a new technology - the Decision Support System (DSS) - is emerging in which computerised processes combine to assemble the information on an individual patient in an optimal way. The latest addition to the DSS 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 a computer model for Valvular Heart Disease which 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 complex future patients, to help select their optimum treatment. The results of the study will contribute to our future ability to advise and treat patients with valvular heart disease, especially regarding

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

EurValve Information

Project title	**EurValve—Personalised Decision Support for Heart Valve Disease**
Project Number	**689617** **Total cost: €4 998 012,51**
Start date	**01/02/2016** **End Date: 31/01/2019**
Coordinator	**The University of Sheffield**
Partners	**ANSYS** **Catharina Hospital** **Cyfronet** **The German Heart Institute Berlin** **University of Rennes 1 - LTSI** **Philips Eindhoven** **Max Delbrück Centre for Molecular Medicine** **Philips Hamburg** **Sheffield Teaching Hospitals NHS Foundation Trust** **Therenva** **Technical University of Eindhoven** **University of Bristol**

Find out more about EurValve on our website: www.eurvalve.eu

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Contact

For further information on the EurValve project, please contact:
the Project Manager, Karen El-Arifi: karen.el-arifi@sheffield.ac.uk
or the Project Co-ordinator, Professor Rod Hose: d.r.hose@sheffield.ac.uk

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