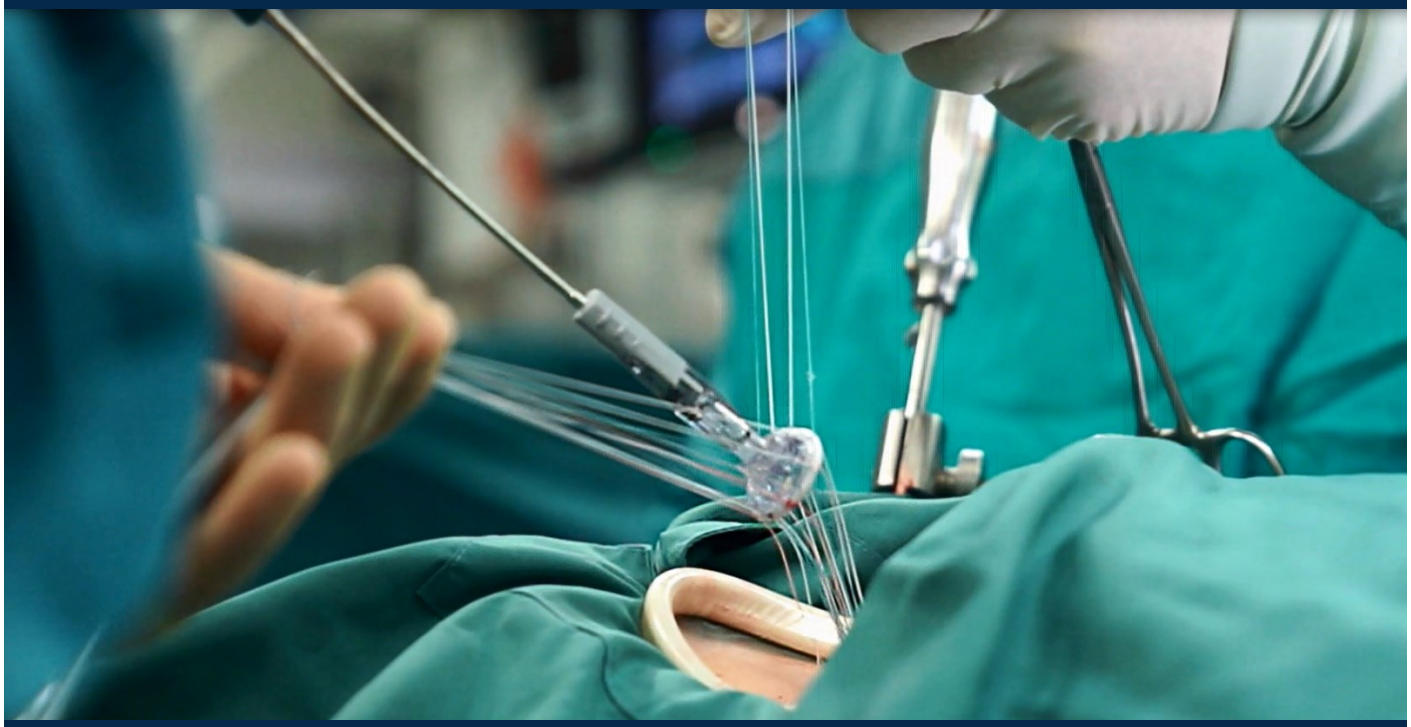
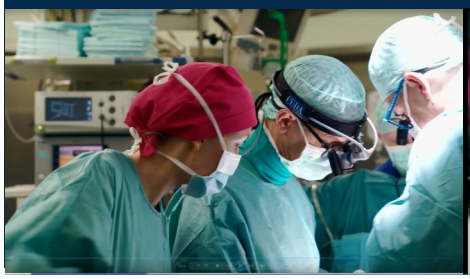
EurValve

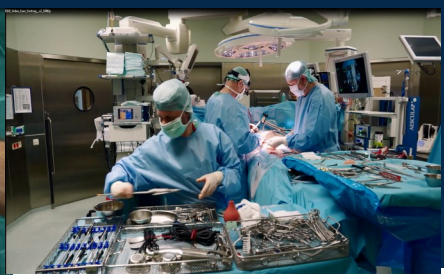
Personalised Decision Support for Heart Valve Disease

Newsletter 5 Final Issue — March 2019



NEWS. UPDATE. PUBLICATIONS. EVENTS.

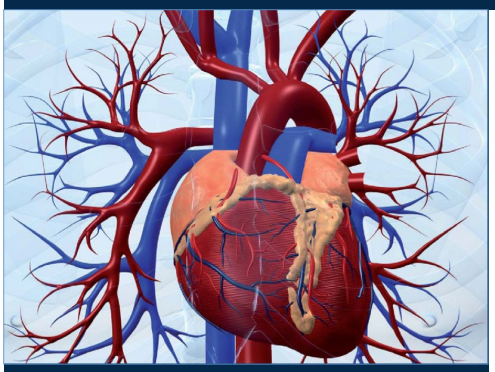




Editorial

Professor Rod Hose – EurValve Scientific Coordinator

Professor of Computational Biomechanics,
University of Sheffield, Department of Infection, Immunity and Cardiovascular Disease, Insigneo Institute for *In Silico* Medicine



At the end of an exciting and challenging 3 years, the EurValve project is drawing to a close.

The project had the goal of constructing a stand-alone, clinically-compliant multi-component Decision Support System (DSS) for Heart Valve Disease. It includes a number of important developments and innovations, presenting clinical guidelines, computational model-based diagnostic and prognostic indications and case-based reasoning. The DSS provides quantitative measures of disease severity and patient impairment, complementary to those gathered in the current clinical pathway, and predicts changes under candidate interventions. The potential of the DSS for improving the management and interventional planning was confirmed by a group of independent clinical users in a randomised controlled experiment. There has been particular clinical interest in the use of activity monitoring to provide a measure of the degree to which the disease might affect everyday living, and to inform the physiological state in the core computational models.

The design of a practical tool for use by cardiovascular clinicians has been a significant step forward in bringing VPH technology close to the clinic. From the translational perspective, there are significant innovations in the integration of clinical data into the computational workflow and the personalisation of model parameters, and in the streamlining of the analysis process so that it is operable, with acceptable accuracy, in timescales of a few minutes. The process from medical image through data integration to computational results is automated, although there is the facility for inspection and manual correction of valve anatomies for difficult cases. Each case of the 120 cases in the EurValve cohort was processed in approximately four minutes.

The onward exploitation trajectory for EurValve is well-identified, and the prospects for a product with appropriate regulatory approval reaching the market in the foreseeable future are good. It is the intention of the developers to continue with this work, and to bring an enhanced EndoSize® product with Decision Support to the market.

The final project review will take place in Eindhoven at the end of March 2019. We are looking forward to demonstrating what EurValve has achieved to the Project Officer and the reviewers. We give our thanks to Carmen la Plaza Santos who was our Project Officer for the first two years and to Milan Popovic who took her place in September 2018.

Rod Hose

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Facts on Cardiovascular Disease

Prevalence of Aortic Stenosis is 3% in the elderly

Mitral Regurgitation is the second most frequent indication for valve surgery

Cardiovascular disease (CVD), is a term covering diseases of the heart and blood vessels. CVD conditions include:

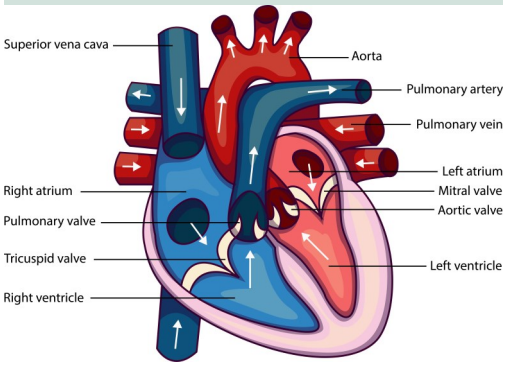
- Coronary artery disease
- Abnormal heart rhythms
- Heart failure
- **Heart valve disease**
- Congenital heart disease
- Cardiomyopathy
- Pericardial disease
- Aortic disease
- Vascular (blood vessel) disease

The heart has 4 valves:
The mitral and tricuspid valves, which control blood flow from the atria to the ventricles.
The aortic and pulmonary valves, which control blood flow out of the ventricles.

When one or more of your heart valves become diseased or damaged, if can affect and disrupt the flow of blood through the heart. This can put extra strain on it and cause symptoms such as chest pain, difficulty breathing and tiredness. Heart valve disease can vary from mild to severe. Sometimes it can be life-threatening and need urgent treatment.

Heart valves can develop one or both of these problems:

- The valve opening becomes narrow (stenotic) – limiting the amount of blood pumped to the rest of the body.
- The valve does not close completely (valve insufficiency or regurgitation) – blood can flow backward instead of only forward reducing the heart's ability to pump blood to the rest of the body.



Definitions

Aortic Stenosis (AS) is obstruction of blood flow across the aortic valve due to pathological narrowing. It is a progressive, fatal disease that presents after a long subclinical period with symptoms of decreased exercise capacity, exertional angina, syncope, and heart failure.

Mitral Regurgitation (MR) is leakage of blood backward through the mitral valve each time the left ventricle contracts. Leakage can increase blood volume and pressure in the area. The increased blood pressure in the left atrium can increase pressure in the veins leading from the lungs to the pulmonary veins. Severe regurgitation pressure may result in congestion in the lungs.

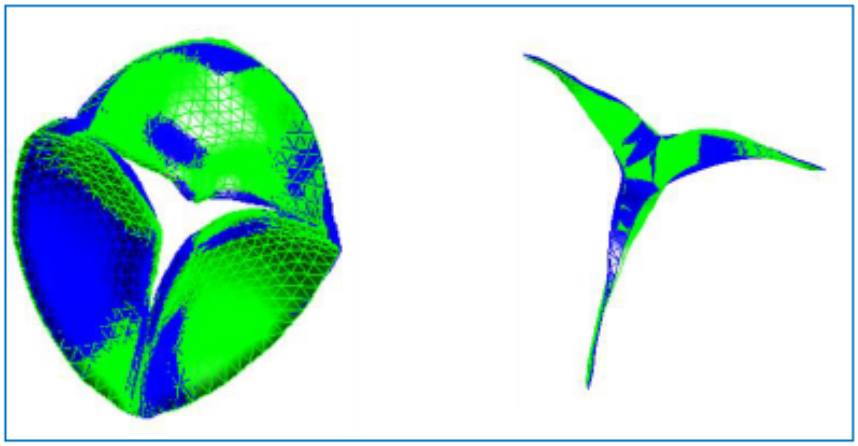
Source: The World Health Organization. www.who.int. http://www.ehnheart.org/cvd-statistics/cvd-statistics-2017.html
Lindroos M, Kupari M, Heikkila J, Tilvis R. Prevalence of aortic valve abnormalities in the elderly: an echocardiographic study of a random population sample. J Am Coll Cardiol 1993;21: 1220-5.
McCann G. Surgery in asymptomatic aortic stenosis. BMJ. 2004 Jan 10; 328(7431): 63–64.
Ancona R, Pinto SC. Mitral valve incompetence: epidemiology and causes. Vol. 16, N° 11 - 16 May 2018
https://www.bhf.org.uk/heart-health/conditions/heart-valve-disease

The Hypothesis and Focus of EurValve

- The major focus of EurValve was to develop, test and validate a Decision Support System (DSS) for aortic and mitral valve diseases that integrated data with the model to improve the management of heart valve disease.
- The study aimed to show that a personalised computational model can predict the outcome of heart valve replacement surgery.
- The modelling was intended to provide information on the haemodynamics in the affected vessels, such that the haemodynamic effects of an intervention can be simulated and optimised for an individual patient.
- The essential purpose of the observational clinical study was to determine the degree to which the computer prediction matches the surgical outcome.

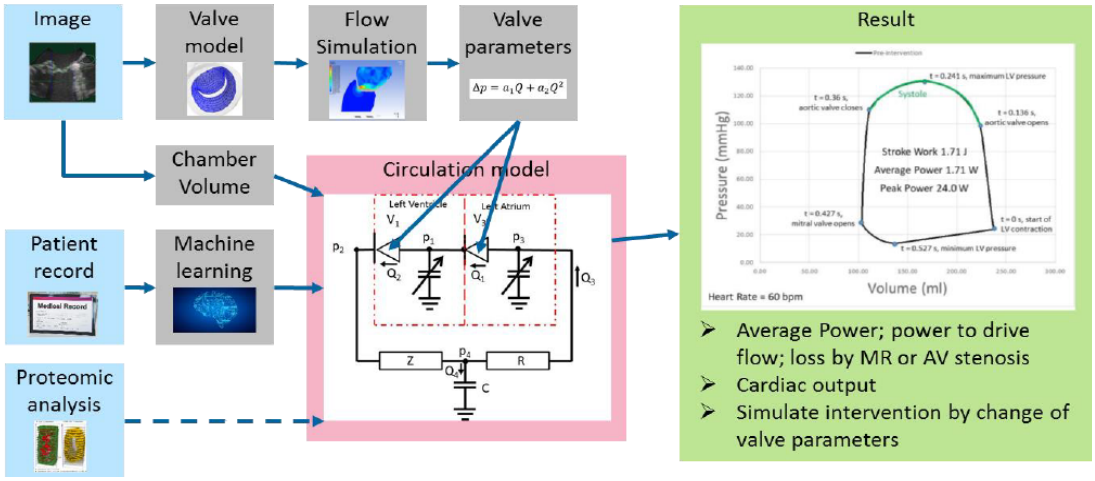
Whole heart model

EurValve developed, provided and evaluated software components enabling the simulation of the heart and systemic circulation for a valve DSS. The software components comprise components for machine learning of model input parameters, heart and valve segmentation, systems model of the heart and circulation, uncertainty quantification and sensitivity analysis, proteomics data analysis, and reduced order modelling for blood flow simulations.



Aortic example (Green segmented aortic valve, Blue Reconstructed aortic valve)

The Decision Support System



Data Sources

Patient cohorts
Retrospective
Prospective
- Electronic Health Records
- Image data
- Pervasive monitoring data

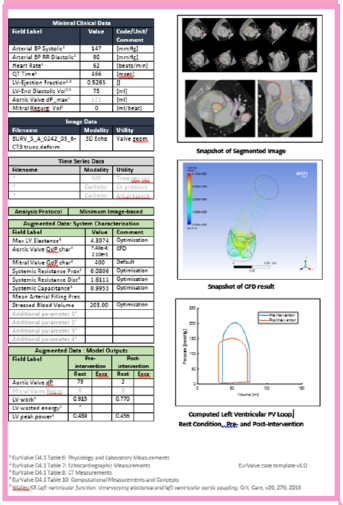
Public Databases
Literature data

Challenges of Integration of Models with Clinical Data

- To identify directs inputs to models in data captured in the clinical process
- To tune model parameters to reproduce clinical observations for test cohort (optimisation)
- To associate tuned model parameters with wider data in clinical record (machine learning)
- To develop a principled approach to representation of physiological envelope for individual patients
- To validate outputs from personalised models.

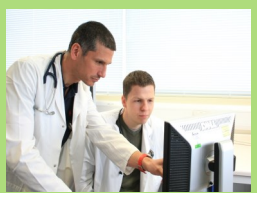
Outputs

Valve pressure gradient
Systemic pressure
Flow distribution
Ventricular afterload
End diastolic volume



Decision Support System

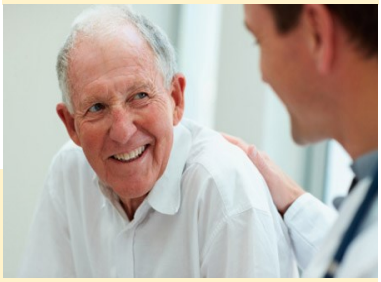
Built on an existing decision support tool for heart valve disease, the DSS tool integrates different concepts and patient-specific measures to improve the management of heart valve disease. The DSS helps the clinician find the best treatment strategy, whether and when to intervene, type of intervention, whether open surgery or transcatheter interventions, how to select the best prosthesis and its optimum sizing and, for catheter-based interventions, how to choose the most suitable access route.



Scope: to develop a Decision Support System that integrates data with the model to improve the management of heart valve disease.

Challenge: to develop a digital patient, specifically in the context of heart valve disease, which integrates heterogeneous patient data, complemented by population data where appropriate.

Optimal Treatment



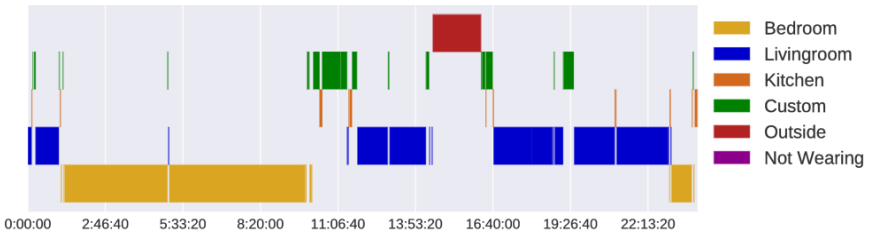
The **target user** of this DSS is the **healthcare professional**, the surgeon or cardiologist, who will make the decision on the nature and timing of the intervention. The major advance of this system over current practice is that it **integrates and interprets all heterogeneous data available about the patient, integrates population data where needed, and provides a consistent, repeatable, quantitative and auditable record of the information that contributes to the decision process.**

EurValve Activity Monitoring

EurValve addressed clinical interest in the patient's daily life over the course of their interventions by deploying a home-based activity and location system (the University of Bristol kit) in its patients in Sheffield. The metrics derived from these measurements were used as one of the inputs of the development of the DSS, helping to predict outcomes in particular patients. Many questions can be investigated; one hypothesis could be that people that are more sedentary prior to intervention may have worse outcomes in terms of mortality and function. EurValve also used the Philips Health Watch which provides measurements of heart rate, respiration rate, step count, active energy expenditure and total energy expenditure for data collection in all three clinical centres.

The combination of both devices collecting data over time in free living conditions provides an opportunity to study how movement influences heart rate, and how this relationship can be exploited via machine learning to predict heart rate from the acceleration alone. Numerous findings of value to clinical practice have been identified. In each case, the information provided by the devices offers a glimpse into the patients' behaviours outside a clinical environment that could be of significant utility to medical professionals. Trends in the recovery of the patient will be identifiable and potentially will illuminate - for example - whether patients should be readmitted. An additional value is in the selection of the ideal time to perform an intervention, so minimising the risks associated with an already complex procedure.

The integration of these activity-monitoring technologies into a Decision Support System seems to be a very promising strategy. Initial results have demonstrated both the practical capabilities, and the potential for developing characterisations of each patient's physiological activity envelope, which in most interventional decision-support processes would be a valuable, perhaps an invaluable, source of data.



A day in the life of a patient

Randomised Controlled Experiment

A randomised controlled experiment was run in order to assess the efficiency and effectiveness of a DSS. Forty five clinicians across the 3 clinical centres performed this exercise. In this second step a comparison between virtual decision making using a DSS and current clinical decision making was carried out. Once the simulated models (based on known interactions and newly acquired from machine learning tools) have been validated against the actual patient specific outcome they will provide the opportunity to simulate several (virtual) options of post-interventional outcome.

EurValve Innovations

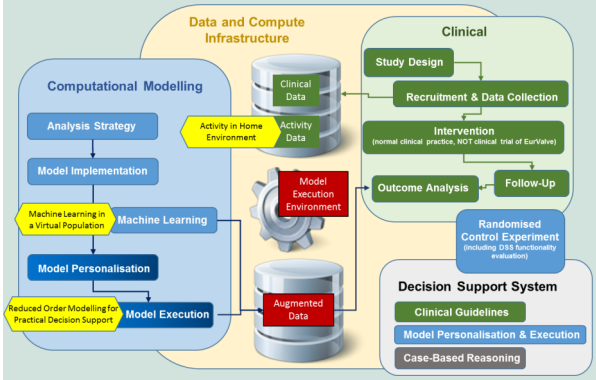
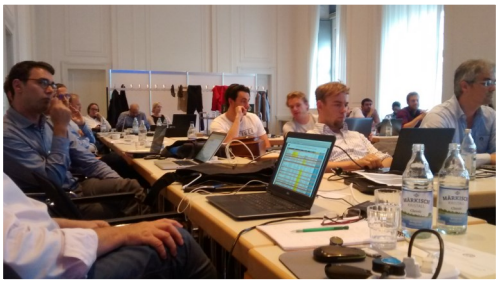
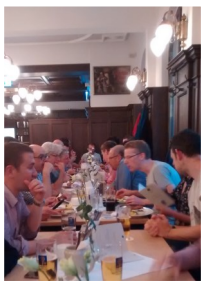


Photo Roundup





News and Events

MDC conference: EurValve sponsored two speakers at the MDC conference—*The Heart by Numbers*. This meeting, organized jointly by the Biophysical Society (BPS), the Max Delbrück Center for Molecular Medicine Berlin (MDC), the German Center for Cardiovascular Diseases (DZHK), and the Berlin Institute of Health, was a great success. Over 120 participants from 15 countries with common interest in cardiology and biology attend the meeting to share their research. The focus was on mathematical and biophysical models coupled with experiments. Topics included subcellular structures, excitation-contraction coupling, metabolism, contraction, organ electrophysiology, heart mechanics, total heart function, disease modelling and therapy from combined modelling and experimental perspectives.

Krakow Workshop: *Personalised medicine for heart diseases - Computational Models for the Clinic: Cardiac/Cardiovascular Application***.** This meeting was organized by CYFRONET AGH to coincide with the final Project Board meeting in Krakow in January 2019. The workshop reported on the output of the EurValve project and related subjects. It explained the challenges and opportunities of a model; an explanation of FFR; machine learning; Reduced Order Models; activity monitoring in a cohort of patients and many other aspects.

Publications

Authors	Journal	Title
Weese, J.et al	Medical Physics	CFD- and Bernoulli-based pressure drop estimates: A comparison using patient anatomies from heart and aortic valve segmentation of CT images.
M Kasztelnik et al	Computer Methods and Programs in Biomedicine	Support for Taverna workflows in the VPH-Share cloud platform
P. Nowakowski et al	Journal of Computational Science	Cloud computing infrastructure for the VPH community
X Fafoutis et al	EAI Endorsed Transactions on Pervasive Health and Technology	Designing Wearable Sensing Platforms for Healthcare in a Residential Environment
A. Crozier et al	Annals of Biomedical Engineering	Image-Based Personalization of Cardiac Anatomy for Coupled Electromechanical Modeling
R McConville et al	Data in Brief	A dataset for room level indoor localization using a smart home in a box
C J McWilliams et al	BMJ Open	Towards a decision support tool for intensive care discharge
Niall Twomey et al	Informatics	A Comprehensive Study of Activity Recognition Using Accelerometers

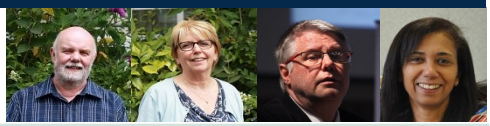
Project Details and Contact Information

EurValve — Personalised Decision Support For Heart Valve Disease

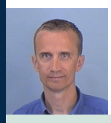
Dates: 1 February 2016 - 31 January 2019

Website: www.eurvalve.eu
Project Officer: Carmen Laplaza Santos and Milan Popovic
Coordinator: University of Sheffield
Scientific PI: Professor D R Hose, (d.r.hose@sheffield.ac.uk)

Partners: EurValve was a collaboration between 13 partners from industry, academia and healthcare.



University of Sheffield: Rod Hose, Pat Lawford, Keith McCormack, Karen El-Arifi



Philips Eindhoven: Herman ter Horst

ANSYS: Michele Rochette

Philips Hamburg: Juergen Weese

German Heart Institute Berlin: Titus Khüne, Markus Kelm

University of Rennes1: Pascal Haigron

Catharina Hospital: Pim Tonino, Jo Zelis

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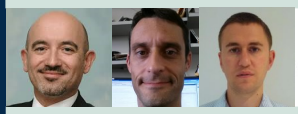
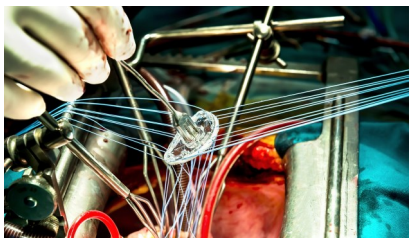


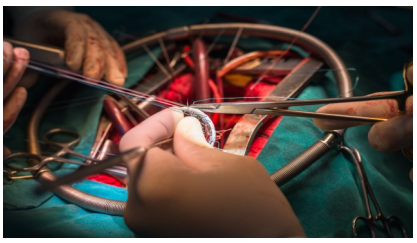
Sheffield Teaching Hospitals NHS Foundation Trust: Norman Briffa, Steven Wood, Gareth Archer

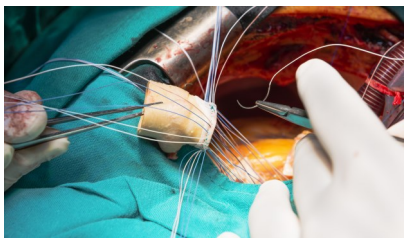
Max Delbrück Centre for Molecular Medicine: Martin Falke

University of Bristol: Ian Craddock

Technical University of Eindhoven: Frans van der Vosse







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https://ec.europa.eu/digital-single-market/ehealth