Project title: Cardiovascular Digital Twin for the Management of Valvular Heart Disease

Project reference: DT4H_04_2024

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Aim of the Project

Valvular heart disease is a life-threatening condition that affects an increasing share of the aged population. Novel developments within the clinical community in the past decade means that repair or replacement of the diseased heart valves can now be performed with minimal invasiveness. On the other hand, up to 50% of the 200k+ patients who undergo these procedures do not gain an improved cardiac function. The processes involved in the recovery are complex and multi-factorial, hinging on cardiovascular haemodynamics and myocardial mechanics.

This project aims to enable the prediction of response to interventional valve procedures using a digital twin (DT) of the patient's cardiovascular system. We will build a new DT framework, combining deep learning, multiscale biophysical modelling, and image analysis techniques. Applying this model to multimodal patient datasets, we will optimise the prediction accuracy and test on unseen datasets.

Project Description

Valvular Heart Disease (VHD) is increasingly becoming a disease of ageing. A large recent study reported that over 11% of UK individuals aged ≥65 suffer from significant VHD, while subclinical disease remained undiagnosed in over half of this population1. Severe VHD is a cause of heart failure, recurrent hospital admission, and 72% increased risk of cardiovascular mortality2. Though modern interventional techniques have radically reduced the periprocedural risk associated with repairing/replacing the valves, major questions regarding predictors of success and pathophysiology remain elusive.

Mitral Regurgitation (MR), along with Aortic Stenosis (AS) are the commonest valve disease found in the developed world. The haemodynamic response to the eradication of MR is complex, as it involves abrupt changes to the pressure and volumetric loads experienced by cardiac chambers – even with procedural success, up to 50% of the patients do not demonstrate functional or symptomatic recovery3. In the case of AS, the right ventricle-pulmonary artery coupling has been recently hypothesised to be a surrogate marker for functional recovery following aortic valve replacement – an unexpected twist, given the haemodynamic shielding provided by its isolation within the left heart. These instances demonstrate that answers to improved patient outcome lie within myocardial function and remodelling, afterload, and even the multisystemic impairments that are collectively involved in a complex interplay on the road to recovery.

The interventional cardiology lab at St Thomas' hospital is a pre-eminent UK centre for VHD research and patient care, with strong industrial links for evaluating next-gen devices. Through multiple ongoing research projects, there is a growing accumulation of patient data that far surpasses the standard-of-care including imaging, invasive, and functional, across multiple time points. Moreover, it is one of the very few centres in the UK offering tricuspid services, an emerging frontier in VHD where little is known about optimal patient selection and response to treatment.

Given the aetiological complexity and multiple modalities of patient data, there is immense potential in computational modelling for diagnostic predictions that are consistent with both physiology and observations. However, to date, VHD models (including our work in valvular 3D fluid-structure interaction) have been largely models of the valve rather than of the patient. These detailed finite element descriptions are high-fidelity but difficult to parametrise, and better suited for cross-sectional rather than longitudinal simulations due to their prohibitive computational cost. Crucially, it is often not possible to incorporate clinically relevant phenomena into such models because the underlying mechanisms remain undescribed. This limits their ability to deal with the large variation in patient trajectories and phenotype, and ultimately distances modelling from clinical research.

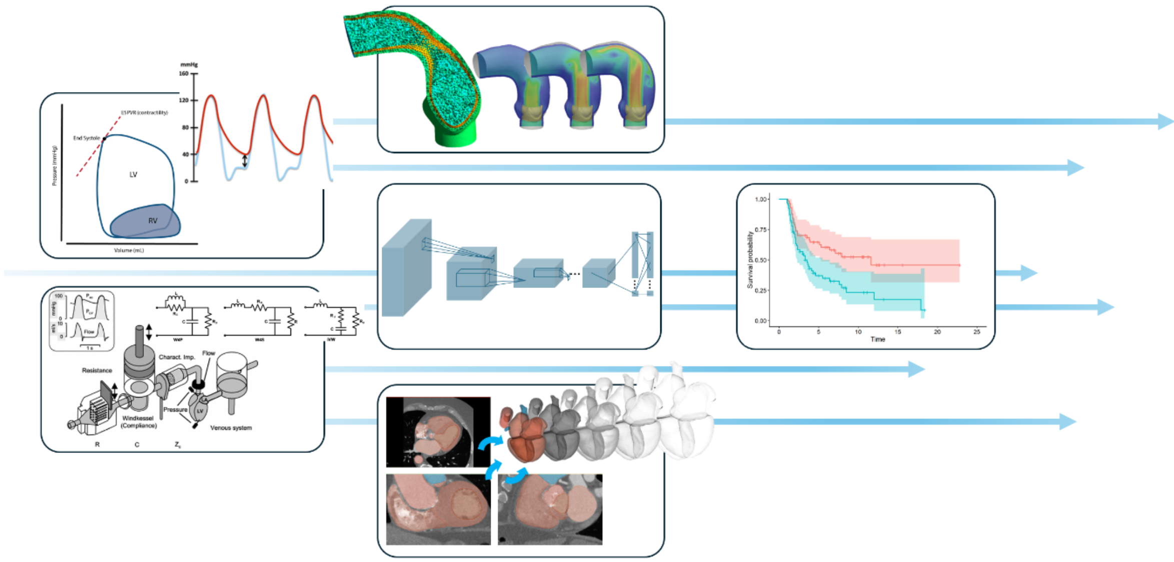
The kind of digital twin we need do not yet exist – it is our aim in this project to build a hybrid biophysical-statistical framework to follow the valvular disease progression over its history. It will leverage the well-characterised quantitative descriptions of the cardiovascular system together with the rich patient information from ongoing clinical research, within a harmonised framework. We will learn from the data to predict forward – whereby short timescale physiology will be encoded into the mechanistic model, and the longer scale evolution will be machine-learned using the patient population. As a proof-of-concept application, we will use the digital twin model to identify responders from the patients undergoing aortic, mitral or tricuspid valve intervention, using only the pre-procedural clinical data.

Requirements:

The essential qualities sought in the candidate include training in a quantitative discipline and the ability to teamwork and engage within multidisciplinary settings.

Suggested reading:

1. D’Arcy et al. 2016. Eur Hear J. 37: 3515-3522.
2. Tung et al. 2022. Open Heart 9: e002039.
3. Stone et al. 2018. N Engl J Med 379: 2307-2318.


mmHg
160
120
80
40
0
ESPVR (contractility)
End Systole
LV
RV
Pressure (mmHg)
Volume (mL)
Survival probability
1.00
0.75
0.50
0.25
0.00
0
5
10
15
20
25
Time
Resistance
Charact. Imp.
Flow
Pressure
Windkessel
(Compliance)
Venous system
R
C