Project title: Integrated Novel Computed Tomography Metrics into Cardiac Digital Twins to Optimally Guide Catheter Ablation of Ventricular Tachycardia

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Aim of the project

Digital replicas of a patient's heart, termed cardiac digital twins, are playing an increasingly important role in cardiovascular medicine. The aim of this project is to use state-of-the-art cardiac imaging and analysis software to derive high fidelity structural and functional cardiac information from computed tomography (CT) data to generate personalised cardiac models. This novel imaging and analysis pipeline will shed new light on tissue structural and functional properties across different cardiomyopathies, augmenting the accuracy of the models created. Corresponding simulation of electrophysiological dynamics within these models will provide enhanced guidance for optimal targets for invasive catheter ablation therapy of ventricular tachycardia.

Project description

Catheter ablation of ventricular tachycardia (VT) represents a challenging clinical procedure, primarily due to the difficulty in accurately identifying the optimal sites to target for durable arrhythmia elimination. Procedure times are often long, with a relatively high risk profile and high rates of VT recurrence (up to 50% 1 year following the procedure). Novel pre-procedural image-based strategies which aim to more accurately characterise the region of myocardial tissue remodelling (fibrosis, scar) which represents the substrate for VT are gaining clinical interest. The increased use of highly detailed pre-procedural imaging has also facilitated the application of - computational simulation, using image-based patient-specific 'digital twin' replicas of a patient's heart, which permit pre-procedural planning based on non-invasive prediction of critical arrhythmia sites to guide selection of ablation targets.

Cardiac computed tomographic angiography (CTA) represents an appealing pre-procedure imaging modality for VT ablation, due to its short acquisition times, the high spatial resolution and relative robustness in the presence of cardiac implantable electrical devices (CIED). However, CTA has previously been limited in its ability to accurately identify regions of tissue remodelling in the ventricle, in comparison with cardiovascular magnetic resonance (CMR) imaging, which represents the reference standard for cardiac tissue characterisation.

However, recent advances in CCT have demonstrated its ability to effectively identify ventricular remodelling through the identification of changes in tissue thickness, tissue enhancement on late-phase imaging and the assessment of tissue extracellular volume, a quantitative measure of fibrotic remodelling. These techniques enable an extension from a binary categorisation of tissue as 'scar' or 'healthy 'to a multiparametric evaluation of the myocardial architecture. Furthermore, recent methodologies have been developed which allow automated analysis of specialised CCT sequences for the quantitative analysis of myocardial strain. This will characterise in detail the local functional properties of both diseased myocardium which retains some contractile function, as well as patterns of dyskinesia in areas of frank scar. Tissue characterisation with this level of detail will permit the incorporation of biologically realistic tissue structure and functional properties into image-based personalised cardiac electromechanical models, providing an accurate representation of the complex substrate underlying the VT to be targeted. The generation of such models will be critical to understand the impact of identified structural and functional changes on the arrhythmogenicity of the tissue.

In this project, we will perform both retrospective and prospective analysis of comprehensive CCT datasets using bespoke software to identify late iodine enhancement, myocardial ECV and myocardial strain. These data will be compared with existing analysis techniques to understand their detailed relationships with left ventricular wall thickness, as well as characteristics of endocardial electrograms recorded from corresponding tissue locations during VT ablation procedures. Following this analysis, patient-specific models will be constructed from the CT data, to reflect both the quantitative fibrotic remodelling and myocardial strain patterns identified on CCT. Simulations will be conducted of the detailed electrophysiological dynamics during VT to mechanistically understand to role of these image-based characteristics, and the importance of them in successfully matching to the clinically measured VT dynamics.

<u>Expected Background</u>: This project would be best suited to a candidate with a physical science undergraduate (maths, physics, computer science, engineering) who has a strong interest in medicine, physiology, computer simulations, signal and image processing, along with experience in coding (Matlab, C++, Python).

