Project title: Basal septal curvature as a transformative imaging-based biomarker in hypertensive and metabolic heart diseases

Project reference: DT4H_08_2022

1st supervisor – Alistair Young - School of Biomedical Engineering & Imaging Sciences

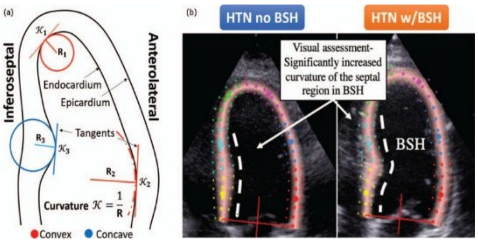
2nd supervisor – Pier-Giorgio Masci– School of Biomedical Engineering & Imaging Sciences

Aim of the project

To delve into the pathophysiological correlates, model the mechanical contraction function, and define the clinical significance of the presence and extent of basal septal hypertrophy (BSH).

Project description

Fig.1 (a) An intuitive explanation of convex and concave curvature of the left ventricular endocardium, as seen in the four-chamber echocardiography view. The curvature is a reciprocal of the radius of circle adjacent to the endocardium. (b) The comparison of the septal wall in hypertensive patients with and without the basal septal hypertrophy (BSH). The visual assessment differentiating the two can be quantitatively compared with the curvature metric.



Basal septal hypertrophy (BSH) represents a localized thickening of the basal interventricular septum, which constitutes a marker of early structural remodelling in hypertensive heart disease (HHD) and metabolic (MHD) heart diseases.

We have recently developed an innovative approach to probe BSH, named basal septal curvature (BSC), which is calculated as the inverse radius of each point of the endocardial contour along the inferior septum interventricular septum **(Fig.1)**, [1]. The BSC is more reproducible and correlates better with functional parameters than the standard ratio between interventricular septum and lateral wall thickness (ThickRatio), as adopted in clinical practice so far [1]. Thus, we postulate that BSC has the potential to better gauge early remodelling patterns in HHD and MHD, improve the understanding of their pathophysiological underpinnings and predict the clinical outcome.

Recent progress in *digital twin* technologies has enabled the construction of computational replicas of the heart, and the systematic in-silico study of the mechanisms underlying cardiac function. For instance, statistical shape modelling allows a thoughtful description of the anatomical features in patients through novel descriptive variables associated with the modes of variation. Studying the impact on the function of the anatomical changes by each mode is a systematic and transformative approach to studying the interplay between anatomy and function. An early study of this interplay has revealed the importance of the anatomical mode containing BSH [2].

Therefore, we aim to:

I) Develop a fully automatic solution to characterise BSH from cardiovascular magnetic resonance (CMR), combining our novel BSC and statistical shape modelling.

II) Uncover the relationship between functional (i.e., contraction), structural (aim -I), myocardial tissue composition and phenome-wide association analysis in subjects with

BSH vs. controls in the largest population-based biobank ever created, the UK BioBank (UKBB);

III) Formulate novel hypotheses on the pathophysiological implications of BSH by building a digital twin of the anatomy and electro-mechanical coupling of the heart.

IV) Validate hypotheses by testing the model predictions (aim III) against the empirical evidence (aim-II), and iterate in the generation of hypotheses and evidence generation.

The starting point in this research is that we hypothesize that

1) Novel descriptors of BSH, BSC and those uncovered by a statistical shape model, will explain better functional parameters, genetic background and cardiovascular risk factors than traditional ThickRatio measures (higher AUC by de Long test). This is based on our preliminary data extracted from a large cohort of patients affected by hypertrophic cardiomyopathy, an inherited cardiomyopathy associated with marked LV wall thickness and other remarkable structural changes of the left ventricle.
2) The BSH is an adaptive remodelling process that is associated with decreased contractility in the basal septal region but a global increase in mechanical contraction function and efficiency.

<u>Candidate profile:</u>
This project would suit a student with experience in computational modelling, data science and medical imaging.

References

[1] Septal curvature as a robust and reproducible marker for basal septal hypertrophy
[2] Linking statistical shape models and simulated function in the he
[3] The 'Digital Twin' to enable the vision of precision cardiology