Title of the project - A holistic approach to unravel the problem of unfavourable ventriculo-arterial coupling: merging hemodynamic and molecular data

Primary PI - Dr G Biglino (Lecturer of Cardiovascular Bioinformatics and Medical Statistics) g.biglino@bristol.ac.uk

Secondary PI - Prof M Caputo (Professor of Congenital Heart Surgery) m.caputo@bristol.ac.uk

Keywords (from list) - Biomedical Engineering; Medical/Clinical Science; Medical Imaging; Physiology

Assessing ventricular function in young patients with repaired congenital heart disease (CHD) remains challenging. Adult echocardiographic parameters and ranges do not apply to children, particularly in CHD, where ventriculo-arterial (VA) coupling can be unfavourable. In fact, normal VA coupling, defined as the natural connection between a systemic left ventricle (LV) and the aorta, can be compromised ("mismatched") in CHD. Conductance catheters, outputting pressure-volume loops, represent the gold standard for measuring VA coupling, but are invasive and technically challenging, particularly in young patients. Therefore, non-invasive alternatives are desirable. Wave intensity is a hemodynamic index assessing the working condition of the heart in conjunction with the vasculature, i.e. directly assessing VA coupling. Recent work has rendered the analysis suitable for cardiovascular magnetic resonance (CMR) imaging data, but its clinical significance in relation to outcomes is lacking.

This project wiith aim to prospectively measure VA coupling non-invasively in three CHD scenarios with differences in aortic distensibility and systemic ventricle, and healthy controls, based on the hypothesis that any mismatch with respect to the normal physiological arrangement results in compromised coupling. This project will also allow to investigate the correlation with clinical outcomes and exercise performance, verifying the clinical significance of any observed changes in relation to functional data derived from cardiopulmonary exercise testing (CPET) in the same patients. As such, research carried out in the context of this project will also allow to assess the value of wave intensity as a possible predictive biomarker of ventricle adaptation. Furthermore, it will be of great interest to correlate haemodynamic data with genomics, epigenomics (DNA methylation) and RNA expressional data (at mRNA and miRNA level) on patients' tissue and blood samples, exploring possible causative mechanisms of abnormal VA coupling, possibly identifying other biomarkers of ventricular function and vessel stiffening.

Improved success in CHD repair is leading to more patients reaching adulthood, but anatomical arrangement following complex surgical repairs can lead to difficult adaptation of the systemic ventricle. Ventricular function can be hugely affected by the status of the vasculature and their interaction, and repaired CHD anatomy can disfavour coupling, impinging on the pumping function of the systemic ventricle. However, how clinically significant is such an unfavourable arrangement? How energetically inefficient? Does it translate to overall poor ventricular performance? These questions warrant further investigation.

This work will have an important imaging and image-processing component, with possible exploration of improvements to the currently available analytical tools, as well as handling clinical data, creating clinical databases, and performing statistical analyses, with an overall strong translational potential.