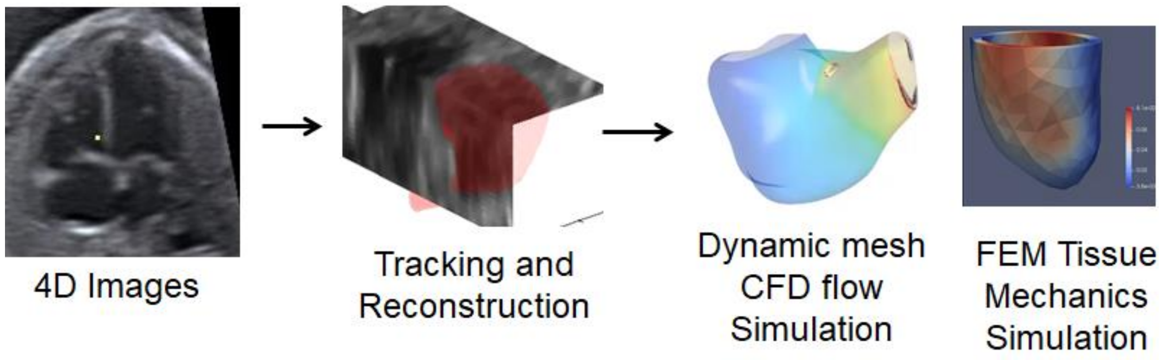
Title: Biomechanics of the Foetal and Embryonic Heart

Abstract:
The developing foetal / embryonic heart is a fascinating organ, being the first organ to form, and undergoing tremendous amount of growth over gestation. In 0.6-1.9% of pregnancies, however, it can be congenitally malformed, resulting in diseases such as Tetralogy of Fallot (TOF) or Hypoplastic Left Heart Syndrome (HLHS). During pregnancy complications such as Intrauterine Growth Restriction (IUGR), cardiac mal-remodelling and functional deterioration can also occur and persist after birth, elevating mortality and morbidity rates. Studies have shown that the prenatal heart's development is responsive to its biomechanical environment, and abnormal biomechanics may lead to malformations, but the details of the prenatal heart biomechanics and its impact on cardiac growth and remodelling is unclear. Paediatric cardiologists have attempted minimally invasive, catheter-based foetal heart interventions can rescue the foetal cardiac biomechanical environments, which can prevent malformations at birth. However, the biomechanics of these malformed hearts, and that of the intervention are not understood, and is a bottleneck to advancements. My lab and I are interested in developing greater understanding of the prenatal heart biomechanics in health, disease, and across foetal heart interventions, and to understand the mechanobiological pathways abnormal forces can lead to malformations.

To these ends, we have performed studies in both small animal embryos, and with clinical images of human foetal hearts. With the chick embryonic model of hypoplastic left heart syndrome (HLHS) via left atrial ligation, we developed 4D high-frequency ultrasound imaging techniques, and performed image-based computational fluid dynamics (CFD) simulations to understand the embryonic heart biomechanics, and found that low and oscillatory wall shear stresses at the left free wall, and high fluid retention in the same region may be causing the left ventricle to be hypoplastic. Single-cell sequencing in this disease model provided clues to the mechanobiological pathways leading to this malformation. For human foetal hearts, we developed algorithms to model cardiac motion and measure myocardial strains, and techniques to perform image based CFD of blood flow and Finite Element Modelling (FEM) of myocardium, to understand foetal heart biomechanics in health and disease. We characterized the vortex dynamics of the normal foetal heart, discovered an energy saving feature of the wave-like contractile motion of the right ventricle, and found that elevated flow stresses instead of pressures appear to correlate to right ventricle wall thickening in Tetralogy of Fallot Hearts. FEM modelling showed that in evolving HLHS human foetal heart, aortic obstruction is likely to hypertrophy, suffer from reduced contractility, and remodel it fibre orientation, but fibroelastosis is unlikely to affect heart function to cause heart failure. Our future work includes investigating the biomechanics of foetal heart intervention and building predictive models to help physician accurately select patients for the interventions.

Biography:
Dr. Yap Choon Hwai graduated with PhD from Georgia Institute of Technology and worked as a postdoctoral scholar in University of Pittsburgh School of Medicine, and as an Assistant Professor in the Department of Biomedical Engineering in the National University of Singapore, before joining Imperial College as a Senior Lecturer. His research focus is on the mechanics of prenatal cardiovascular system, with the focus of understanding how blood flow and myocardial biomechanical forces affects heart development and contribute to congenital malformations, and how foetal heart intervention can rescue the biomechanical environment to avoid malformations. His group has made pioneering contributions in this area. Another part of his research is to use novel materials strategies to modulate thrombosis in cardiovascular medical devices.



Caption: Workflow of image-based biomechanics studies of the foetal / embryonic heart