

**Project title: Fetal Cardiac Digital Twin**

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### **Aim of the project**

An embryo's heart starts to beat at week 5-6 of gestation. As the embryo develops the heart is continually changing. The size and shape of the heart alter to accommodate different cardiovascular requirements associated with growth and length of gestation. In parallel, proteins expressed in the cardiac myocytes change, as do blood ionic concentrations. The connective tissue orientation and make up can also alter at different stages of fetal development. All of these changes can impact cardiac electrophysiology and have implications for fetal wellbeing and subsequent cardiovascular health. Furthermore they may be adversely affected by maternal (or fetal) genetic or metabolic disorders. There remain questions on how best to measure cardiac electrophysiology, what factors impact the fetal ECG and how the ECG signal may change through gestation. This study will create digital twins of fetal hearts at different stages of gestation to investigate how different factors, measurement techniques and time impact fetal ECG signals.

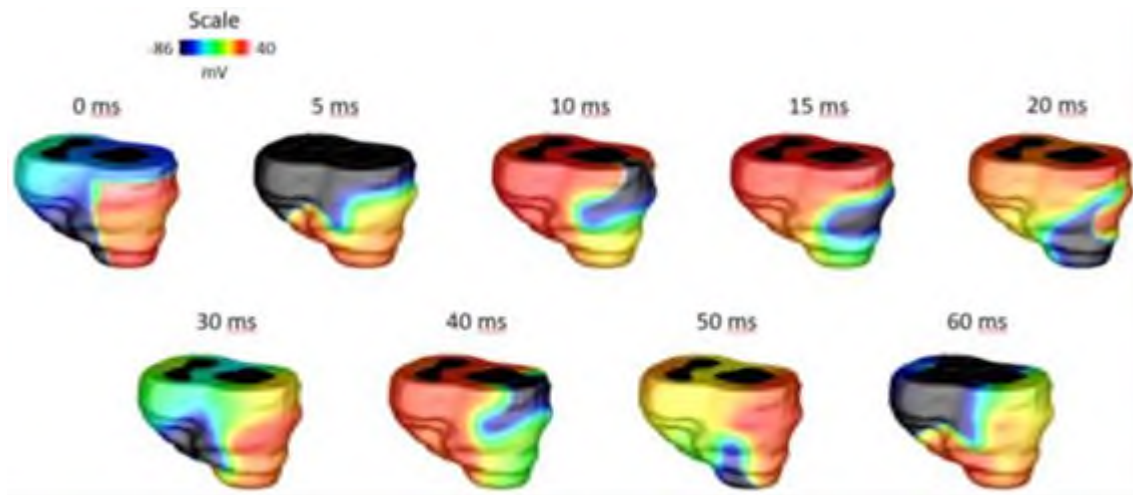
### **Project description**

Fetal death is defined as miscarriage when it occurs before 24 gestational weeks (gw); early miscarriage, occurring in the first 12 gw, affects approximately 25% of pregnancies in high-income countries and late miscarriage affects 1-2% pregnant women. In particular, stillbirth, defined as fetal death occurring after 24 gw, occurs in 1 in 200 pregnancies among the general population of high-income countries, but it can be higher in certain ethnic subgroups (it has been estimated to be around 12/1000 in African Americans). The risk of stillbirth increases towards term with about 65% of stillbirths occurring after 28 gw and fetal death accounting for 50% of all perinatal deaths. Despite the high emotional distress that such events cause to both family and clinicians, there remain questions about the specific causes of second and third-trimester pregnancy loss. Pregnancy loss can be sudden and unexpected, and in many cases fetal death occurs before symptoms or indications from clinical monitoring. In more than 10% of cases, stillbirth remains unexplained, with this rate increasing to 24% after 38 gw\*. There still remains a medical need and need to provide peace of mind to expectant parents for improved monitoring during pregnancy to enable prediction and prevention of stillbirths.

Fetal ECG's can be recorded routinely. However, linking changes in ECG to underlying mechanisms in the fetal heart is technically challenging. We propose to leverage the excellence in fetal cardiac imaging at GSTT and KCL with the expertise in cardiac modelling and simulation at KCL to create a digital twin of the fetal heart. This will provide an environment for testing hypotheses, optimising measurements and developing new measurement techniques.

KCL has an excellent track record in the development and implementation of cardiac models for clinical applications. We have an international reputation for development and application of novel MRI techniques for measuring the fetal heart. We have an excellent track record in making software

for extracting cardiac anatomy and function from images and using this to create patient cardiac digital twins. We have developed these workflows focusing on the adult population but there is an acute need to apply these approaches to the fetus.



Simulation of electrical activation, linking cellular electrophysiology to whole heart activation patterns, derived from foetal MR cardiac images.