Focussing on characterising the properties of the heart that provide the substrate for arrhythmias

The central hypothesis is that the determinants of arrhythmic risk including atrial and ventricular fibrillation lie within the heart itself and that much of this risk is genetic. Our team's core activities are therefore concerned with linking genetic alterations determining fibrillation syndromes to arrhythmogenic phenotypes through the use of mouse and human induced pluripotent stem cell (iPSC) models.

My clinical research involves electrophysiological phenotyping and is firmly based on the laboratory models. A large, wide-ranging referral base allows the efficient delivery of this translational limb of the program. I have also developed links with industry based on translational principles that provide novel approaches (drugs and devices) for patient management - largely based on the insights obtained through the pre-clinical programmes.

The heart is an efficient, generally reliable mechanical pump driven by electricity. On occasion the usually smooth electrical activation breaks down and when this occurs electrical chaos ensues and can manifest as ventricular fibrillation that leads to a failure of contraction and the sudden death of an individual. There is a substantial body of data indicating there is a predisposition amongst certain individuals to ventricular fibrillation and furthermore that this susceptibility can be detected through an examination of the passage of electrical signals through the chambers when the person is in normal rhythm.
The project will involve the analysis of electrograms (electrical signals from the heart) obtained directly from heart disease patients being managed at Royal Papworth Hospital and then annotated with colleagues in the Department of Engineering in the University of Cambridge.

Doctors managing these patients routinely place catheters in the heart and record electrical signals. The recordings are the result of complex activation processes and reflect the characteristics of the underlying tissue. The signals are recorded either during normal rhythms or during artificial pacing over a range of frequencies from multiple sites.
Data will be analysed and characteristics highlighted. A training set will be established and the responses of signals to differing interventions (pacing rates, premature stimulation etc.) will be explored.

The objective is to generate an algorithm based on statistical inference and probabilistic data modelling to allow a model of cardiac activation under different conditions to be predicted.

We have great hopes that we will be able to develop a test that will predict patients at risk and on that basis provide them with protection through the use of an implanted defibrillator. The work should be ground-breaking and have substantial impact in improving risk prediction and thereby helping both involved individuals and their families.