A Multi-scale Computational Model of Calcium-mediated Ectopy in the Human Post-infarction Heart

Fernando O. Campos*, Joao F. Fernandes, Yohannes Shiferaw, Titus Kuehne, Martin J. Bishop and Gernot Plank

School of Biomedical Engineering and Imaging Sciences, King's College London, London, United Kingdom

Background: A variety of malignant arrhythmias are implicated with ectopic beats (EBs) resulting from spontaneous calcium (Ca) release (SCR) events at the subcellular level. However, investigation of these arrhythmias is hampered by the lack of adequate techniques to assess with certainty abnormalities at the subcellular scale and arrhythmogenic events at the organ level.

Objective: The aim of this study was to construct a multi-scale computational model to investigate SCR-mediated ectopy within the infarcted human heart.

Methods: An experimentally based phenomenological model of SCR events was integrated in the equations for Ca cycling of a state-of-the-art model of the human ventricular action potential (AP). Key parameters of the cell model were modified to represent remodeling conditions known to occur in heart failure (HF). This augmented myocyte model was employed in in-silico experiments on a post-infarction biventricular (BiV) model. Magnetic resonance (MR) imaging data from a patient who suffered myocardial infarction was used to build the BiV model in this study. The infarct scar and border zone were segmented by thresholding the voxel intensity within the ventricular wall. These were then used to build a tetrahedral finite element mesh.

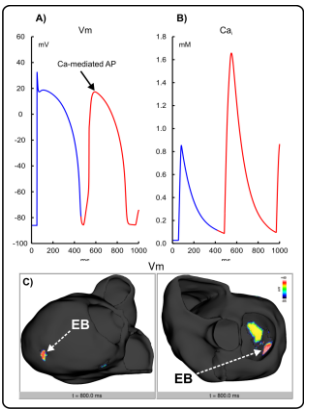

Figure 1: A) Triggered AP resulting from a SCR event. B) Spontaneous Ca transient. C) Ca-mediated PVC on the BiV model.

Results: In single-cell experiments, stochastic SCR events were shown to become more likely as the cell was overloaded with Ca. These SCRs caused triggered APs in HF experiments (Fig. 1A-B). In the human BiV model, cells exhibiting SCRs within the infarcted border zone were capable of overcoming local source-sink mismatches to trigger an EB (Fig. 1C).

Conclusions: The results presented here are the first to show that EBs resulting from abnormalities at the subcellular level can be studied using highly detailed human heart models.