CompBioMed Conference 2019 Abstract Template – Computational Modelling of Ischemia, Myocardial Infarction and Hypokalaemia in a Human Heart Model Demonstrate High Fidelity between Clinical Data and Simulation

Aguado-Sierra, J.[1], Iles, T.L.[2], Iaizzo, P.A.[2], Vazquez, M.[1,3], Butakoff, C.[3]

[1]Barcelona Supercomputing Center, Spain.

[2]University of Minnesota, MN, USA.

[3]Elem Biotech S.L., Spain.

1. Background

The human heart is a complex organ that may beat more than 2-3 billion times in one's lifetime, it adapts and remodels itself based on physiologic needs. Currently, computational modelling aims to reproduce a snapshot of the cardiac function for both diagnostic or treatment assessment purposes. Given that patient-specific, ion-channel cardiomyocyte functional descriptions are impossible to measure clinically, without highly invasive methods, we propose to computationally resolve multiple disease scenarios utilizing a variety of ion-channel functional phenotypes. From a modelling point of view, in order to reasonably represent the evolving physiologic states throughout one's lifetime, e.g., due to hormonal changes and aging induced alterations in ion channel phenotypes. Such variations can be incorporated within computational models in order to analyze a spectrum of responses for a defined single subject under a variety of clinical scenarios: e.g., ischemia, myocardial infarction or hypokalemia.

2. Objective

The primary objective of present project was to provide preliminary validations for a novel methodology capable of reproducing multiple cardiac disease states under a variety of ion channel functional expressions for a give human heart model.

3. Methodology

Human hearts were obtained fresh from organ donors whose hearts are not viable for transplant; appropriate consents for research were obtained. Next, each specimen was carefully perfusion fixed and maintained with the Visible Heart® Laboratories at the University of Minnesota; their Institutional Review Board approved these research protocols. High-resolution MRI scans of these hearts were used for generating computational models: including volumetric finite element mesh models used to solve for electrophysiological propagations. The ventricular cardiomyocyte model of O'Hara-Rudy was employed to reproduce the electrophysiological propagation. Three pseudo-ECG leads were computed to quantify the QRS and QT durations. The spectrum of phenotypes of the normal population was determined by employing experimentally-calibrated, single cardiomyocyte normal variability data. A total of 64 subjects, 32 male and 32 female hearts were created as baseline. A myocardial infarction was imaged using a 3D MRI, gadolinium-enhanced sequence. The segmented infarct was registered within the human heart mesh. To model ischemia, we assume that the same region irrigated by the coronary that suffered the infarct, would be similarly affected by an ischemic condition when CAD is present. Hypokalemia was modelled

by modifying the baseline potassium concentration in the whole heart to a 3.2 mol K^+ concentration. A total of 64 phenotype-, gender-specific simulations were run for each pathology, totalling 192 unique models.

4. Results

QRS duration and QTc interval values obtained from the virtual population showed agreement with published clinical data corresponding to each pathology modelled. All responses exist within the clinically observed behaviour of all three pathologies. One heart can present several outcomes according to its present functional phenotype. Ultimately this research provides the capability to map the spectrum of normal cardiac condition to a range of pathological responses to predict multiple possible realities. Furthermore, it provides a methodology to reproduce a virtual population, which can be employed to assess a variety of treatments including pharmacological and devices.