Cellular Variability within the In-Silico Atria and its Impacts on Conduction Velocity in Healthy and AF Remodeled Tissue

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Background

Atrial models are increasingly relied upon to understand the mechanisms behind atrial arrhythmias such as atrial fibrillation. In order to represent the behaviour of the atria, it is important to create representative models of the human atria. Due to difficulties incorporating cellular variability, models typically assume cellular coupling masks the impact of electrophysiological variability on the cellular level. Electrophysiological models typically only vary at a regional level. Recent studies have shown that cellular variability may have a larger impact on electrophysiological behaviour than previously expected.

Objective

The objective of the study is to determine the impact of cellular variability on the propagation across isolated tissue and whole atrial models for both healthy and AF remodeled tissue. This is completed through observing the impact on conduction velocity and the atrial depolarization and repolarization.

Methods

A population of unique cellular models was created using the Courtemanche cellular model. Published experimental data was used to divide the population into 8 regional populations based on 5 biomarkers (RMP, APA, APD20, APD50, APD90). Regionally homogenous and heterogeneous tissue samples were separately calibrated to target experimental CV values. The variability in CV across 10 heterogeneous models were compared for each atrial region. Activation maps and APD maps were calculated for whole atria simulations of the regionally homogenous and heterogeneous models.

Results

Isolated heterogeneous tissue results using the same tissue conductance showed the standard deviation in CV ranged from 0.19cm/s to 2.4cm/s depending on atrial region. Similar variability in CV was observed between healthy and AF remodelled tissue samples. Figure 1 shows the regional variability in CV across the 10 heterogeneous models. In the healthy atria, whole atrial simulations showed heterogeneous models resulted in a similar average total activation times (TAT) compared with the regionally homogenous model (117ms), varying between 117ms and 118ms. Depolarization across the regionally homogenous model and the variable models remained consistent for both the healthy and AF remodelled atria. Repolarization in the variable atrial models was faster than in the homogenous model.

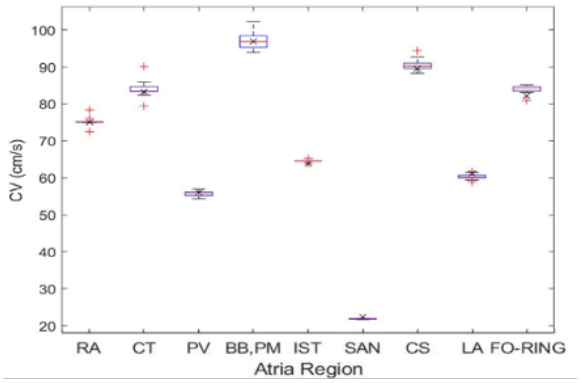

Figure 1: Boxplot showing variability in CV across AF remodeled atrial regions due to cellular variability.

Discussion

Cellular variability across isolated tissue results in CV variation of up to 4cm/s. Unsurprisingly, electrophysiological variability has a negligible impact on depolarization across the atria. Most of the observed variability in activation times is caused by anatomical variability. Electrophysiological variability results in an earlier and faster repolarization phase for both the healthy and AF remodelled atria. This could have a significant impact on the susceptibility to the maintenance of AF episodes. Accounting for cellular variability could result in models better representing healthy atrial behaviour and that of different arrhythmias.