A Computational Model of Brugada Syndrome in 3D Heterogeneous Cardiac Tissue

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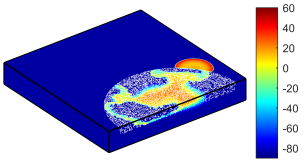
Background: The Brugada syndrome (BrS) is an inherited cardiac disorder associated with ventricular arrhythmias and sudden cardiac death. There are two classical interpretations of the ECG features and pathophysiological mechanism of the BrS: the repolarization disorder theory and the depolarization disorder theory. The repolarization disorder theory attributes the ECG changes to nonuniform alteration of the epicardial right ventricular action potential duration, whereas the depolarization disorder theory explains the pathological phenotype as a result of slow and discontinuous conduction. However, arrhythmogenesis in BrS may be due to a combination of electrophysiological and structural factors (e.g, fibrosis).



Membrane potential during reentry in BrS

Methods: We adapted our previously published phenomenological model of ventricular epicardial cells to reproduce the characteristics commonly associated to BrS action potentials. We incorporated the phenomenological model in the monodomain formulation to simulate the electrical activity of cardiac tissue in a 3D transmurally heterogeneous slab ($7 \times 7 \times 1\ cm$). A BrS region showing both electrophysiological abnormalities and diffuse fibrosis was introduced inside the epicardium. We employed our model to assess the insurgence of sustained reentry as a function of electrophysiological alterations and fibrosis distribution. For each simulation, we also computed simulated epicardial and endocardial monopolar electrograms.

Results: Our computational study suggests that both electrophysiological and structural alterations are important factors in the induction of sustained reentry associated to BrS. Furthermore, our results suggest that neither dispersion of repolarization nor structural abnormalities are sufficient on their own to induce sustained reentry. Moreover, electrograms simulated with our model are comparable to clinical recordings and reproduce the characteristics of BrS electrocardiographic pattern.

Conclusion: This computational study suggests an arrhythmic mechanism that unifies the repolarization and depolarization hypothesis of the pathophysiology of BrS. In addition, we believe that our model offers an additional framework for the computational investigation of BrS and its arrhythmic behaviour.