Role of Cardiac Microstructure Variability on Ventricular Arrhythmogenesis

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Introduction: The propagation of cardiac electrical excitation is influenced by tissue microstructure, although quantitatively understanding this relationship presents a significant research challenge, especially during arrhythmias where excitation patterns become complex. Reaction-diffusion computational models of cardiac electrophysiology, incorporating both dynamic action potential (AP) models and image-based myocardial architecture, provide an approach to study the complex organisation of excitation waves within variable myocardial structures.

Methods: The role of tissue microstructure (cardiomyocyte and sheetlet orientations) on organ-scale normal/arrhythmic excitations was investigated. Five healthy rat ventricle datasets were obtained at 100 μm isotropic resolution using diffusion tensor MRI (DTI), from which the primary, secondary, and tertiary eigenvectors were determined. These principal eigenvectors have been shown previously to align with the myocyte, sheetlet plane, and sheetlet normal directions, respectively. The Fenton-Karma cellular activation model was modified to reproduce the rat AP duration (APD) of ~40 ms and its restitution. Localised activation and re-entrant scroll waves were initiated in the five anatomical models at prescribed locations for three different microstructure scenarios: (i) isotropic – in which electrical diffusion was equal in all directions (i.e. no microstructure); (ii) anisotropic – with reduced electrical diffusion in directions radial to the myocyte direction (i.e. myocyte but no sheetlet microstructure); and (iii) orthotropic – in which electrical diffusion in the myocyte, sheetlet plane, and sheetlet normal directions was reduced progressively (i.e. myocyte and sheetlet microstructure).

Results: Inclusion of DTI-based microstructure modulated both the ventricular activation sequence and global APD map following apical pacing. Furthermore, anisotropic and orthotropic microstructure increased the lifespan of re-entrant excitations and number of scroll wave filaments. The extent of these effects differed between the five datasets, highlighting the important role of structural variability.

Conclusion: This study shows that microstructure variability influences both specific dynamics of arrhythmias as well as properties such as lifespan and vulnerability.