Breakdown of re-entry caused by transmural APD dispersion and fibre orientation

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1 - Introduction

Ventricular fibrillation (VF) is a deadly cardiac arrhythmia, and one route to VF is breakdown of a re-entrant wave. Several mechanisms underlying breakdown have been proposed including steepness of the action potential duration (APD) restitution curve and the effect of rotational anisotropy in the ventricular wall.

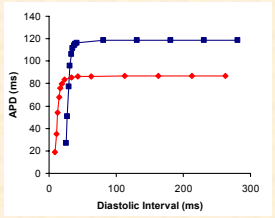
The ventricles are electrically heterogeneous, and endocardial tissue has a longer APD than epicardial tissue. As a result, re-entry has a shorter period in epicardial tissue, and the transmural difference in period could pull apart a transmural re-entrant wave. The aim of this study was to use a computational model to investigate the relative roles of rotational anisotropy and transmural APD differences in destabilising re-entry.

We used both a simplified model of cellular cardiac electrophysiology in a slab of tissue representing part of the LV free wall, and a biophysically detailed model in anatomically detailed models of the LV and RV free walls.

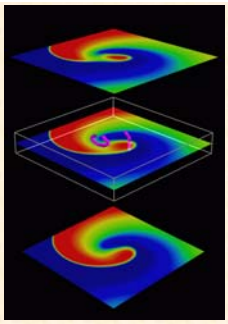
2 – Simplified model

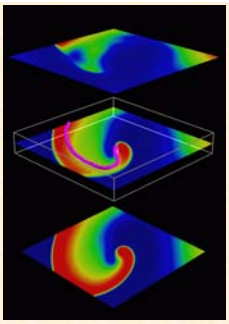
In our first group of simulations we simulated action potential propagation in a 60 x 60 x 10 mm monodomain with and without 120º rotational anisotropy, with no-flux boundaries, and with excitability described by the Fenton Karma (FK) model [Chaos 1998;8:20-47].

We approximated transmural differences in APD changing the parameter u^{si}_c from 0.85 to 0.5 along the short axis of the slab. APD restitution curves for u^{si}_c = 0.85 (red) and u^{si}_c = 0.5 (blue) are shown right. A linear change in u^{si}_c resulted in a linear change in APD with a total ΔAPD of around 25%. Re-entry in slabs with uniform u^{si}_c of between 0.85 and 0.5 was stable, so we could use this model to assess independently the effects of rotational anisotropy and transmural APD differences on the stability of re-entry with a transmural filament.

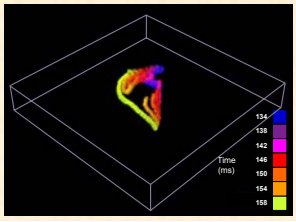


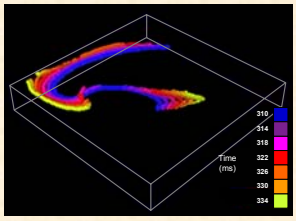
The figure shows snapshots of activation on the top, middle and bottom surfaces of isotropic (left) and anisotropic (right) simulations, 150 ms after initiation of re-entry.



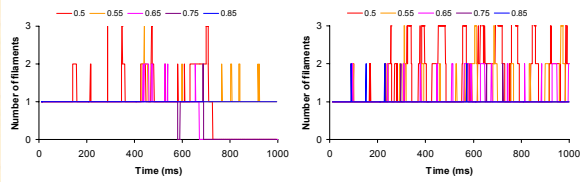


The figure below shows filament behaviour in isotropic (left)and anisotropic (right) simulations. In the isotropic simulations breakdown tended to be short-lived. Rotational anisotropy produced longer and more persistent filaments.





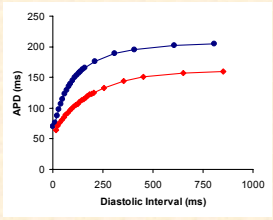
The figures below show the number of filaments for slabs with no (blue), modest (purple, pink, and orange) and large (red) APD differences. The extent of breakdown depended on the transmural difference in APD. In some of the isotropic simulations re-entry self terminated, but in the anisotropic simulations breakdown was persistent.



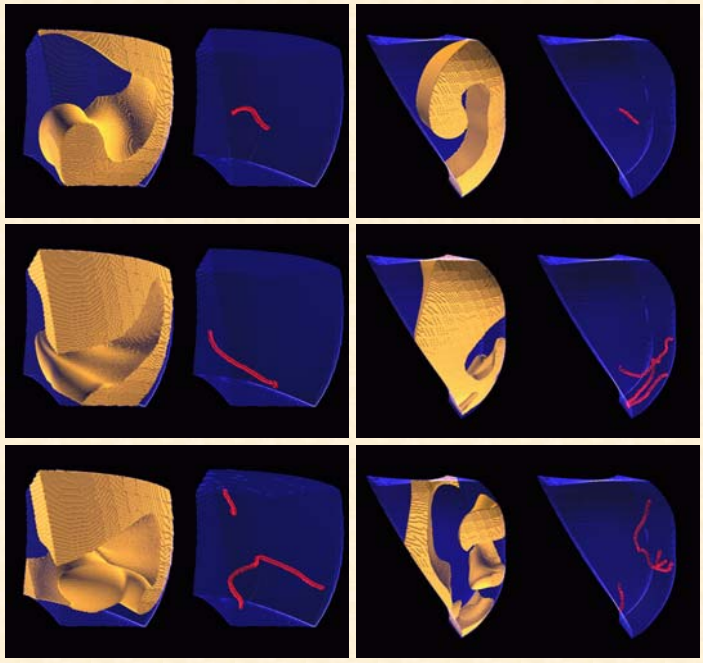
3 – Biophysically detailed model

In our second group of simulations we simulated re-entry in LV and RV wedges from the Auckland canine ventricles, with and without rotational anisotropy, with no-flux boundaries, and with excitability described by the Luo-Rudy phase 1 model [Circulation 1991;68:1501-1526].

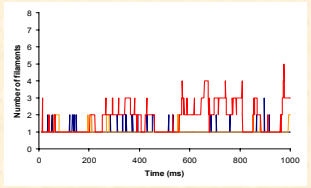
Transmural differences in the expression of several ion channels contribute to differences in the shape and duration of the action potential. We approximated these differences by changing only the K^+ conductance gK of the LR1 model. APD restitution curves for the endocardial layer (gK = 0.2 mS/cm^2, blue) and epicardial layer (gK = 0.4 mS/cm^2, red) are shown. The Ca^{2+} conductance gCa was set to 0.03 mS/cm^2 to give stable re-entry for this range of gK.

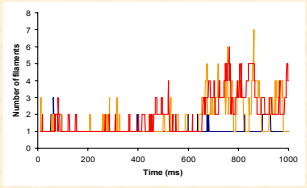


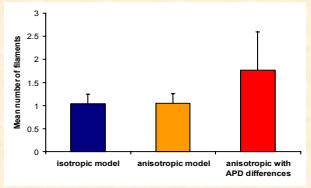
The figures below show snapshots of activation and filaments 750 ms after initiation of re-entry in the LV (left) and RV (right) for the uniform isotropic (top), uniform anisotropic (middle), and nonuniform anisotropic (bottom) models.

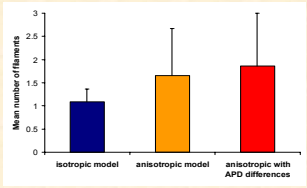


The figures below show the number of filaments for the isotropic (blue), anisotropic (orange), and nonuniform anisotropic (red) models. All six models showed breakdown, but the number and persistence of filaments was greater for the RV simulations.









4 – Conclusions

Transmural differences in APD are able to destabilise re-entry both in simplified and in biophysically detailed models. Regional differences in APD act synergistically with rotational anisotropy to break a single re-entrant wave into multiple wavelet VF. This effect was more potent in the RV, where the gradient of both APD and fibre rotation is higher than in the LV.

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