Computational investigation of the role of structural remodelling in atrial fibrillation

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Background

Atrial fibrillation (AF) is the most common heart rhythm disturbance and its prevalence increases with age and in heart disease. Treatment of AF is an increasing economic burden in healthcare. However, the long term success of treatment for persistent and permanent AF has been disappointing, in part because the mechanisms which underlie the initiation and maintenance of AF are not well understood.

Computer models that incorporate key features of atrial structure provide a powerful means of investigating how the electrical and structural remodelling that occurs with ageing and heart disease increases the risk of AF. However, while detailed image-based models of the normal atria have been implemented[1,2], this approach has not yet been used to investigate the effects of heart disease.

The objectives of my PhD research proposal are:

1. To develop an image-processing pipeline to extract and quantify information regarding structural remodelling in suitably paced sheep atria.
2. To develop anatomically realistic 3D atrial models incorporating regional heterogeneity and anisotropic fibre orientation.
3. To perform model-based analysis to compare the paced sheep atria with control and to validate the results using electrophysiological data acquired.

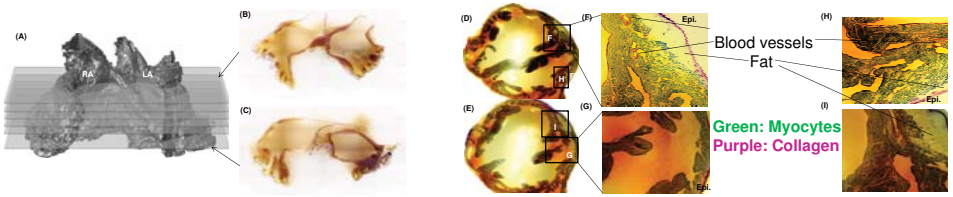

Fig. 1: *Surface images of normal sheep atria. (**A**) 3D computer reconstruction of the whole atria from anterior view. (**B-C**) Samples from the previous set[1,2] (8x8x50 μm³) (**D-I**) Samples from the new set (6x6x24 μm³) with zoomed out views.*

Methods

Experimental studies are being carried out in sheep 2 weeks after 2 or 4 weeks of high rate pacing and also in control sheep. Electro-anatomic maps are acquired in sinus rhythm (SR) during atrial tachypacing and induced AF with an Ensite NavX™ system (St Jude Medical) using a Constellation basket catheter.

Structural studies

3D atrial geometry is reconstructed from high field MR images (0.2x0.2x0.5 mm³) using a suite of image processing tools. Atrial chamber and tissue volumes will be estimated as an initial assessment of atrial structural remodelling in animals undergoing high rate pacing. Gadolinium (Gd) is perfused prior to fixation to simulate late Gd enhancement MRI.

A subset of atria from paced and control sheep will undergo extended volume surface imaging[3] to generate high resolution image sections (Fig. 1(D-E)) for detailed analysis.

Image based modelling

3D geometry of the whole atria will be reconstructed from high resolution serial images (6x6x24 μm³). Local fibre orientations will be estimated by eigen-analysis of the structure tensor[1,2]. A family of cell models representing the regional electrical heterogeneity will be incorporated to analyse the role of fibrosis and to quantify the various mechanisms underlying atrial arrhythmogenesis.

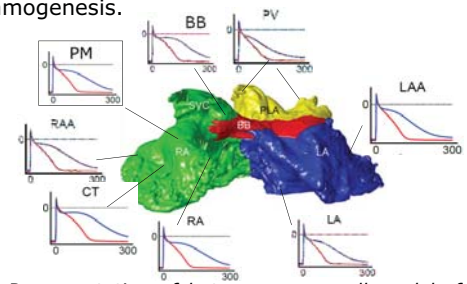

Fig. 2: *Representation of heterogeneous cell models for control(blue curves) and paced(red curves) atria.*

Model analysis will be compared with experimental electrophysiological data acquired using Ensite NavX™ mapping system.

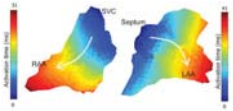

Fig. 3: *Activation time maps for RA and LA during sinus rhythm.*

Initial Results

Activation patterns were characterised in SR and atrial pacing for normal and chronic pacing hearts Reproducible atrial flutter was induced and mapped in the latter.

MRI images of atria from normal and chronic pacing hearts were further processed using Matlab/ImageJ and then segmented with Amira. Atrial dilatation was evident in the paced heart (see Fig. 4) and atrial tissue volume was substantially greater (48.2 cm³ vs 35.2 cm³). No evidence of fibrosis was found in normal hearts using Gd-MRI imaging.

Extended volume surface imaging is ongoing.

Cell activation models developed for PVs and PLA are currently being extended to other atrial regions.

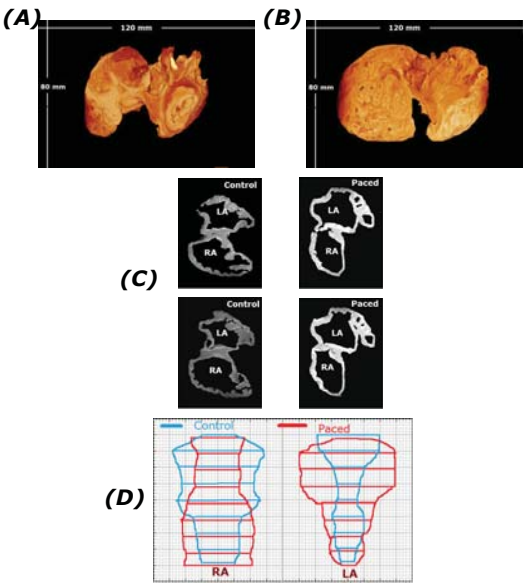

Fig. 4: *MR imaging of atrial surface geometry in normal hearts and following chronic high rate pacing:*

(A) *3D reconstruction of atria for normal heart.*

(B) *3D reconstruction of atria following chronic pacing.*

(C) *Comparison of typical short axis sections of atria from normal and paced hearts.*

(D) *Estimated leading dimensions from representative stack of short axis sections in anterior/posterior view for both RA and LA.*

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References

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