Cardiac Diffusion Tensor Magnetic Resonance Imaging for High Resolution Reconstruction of Individual Whole Hearts

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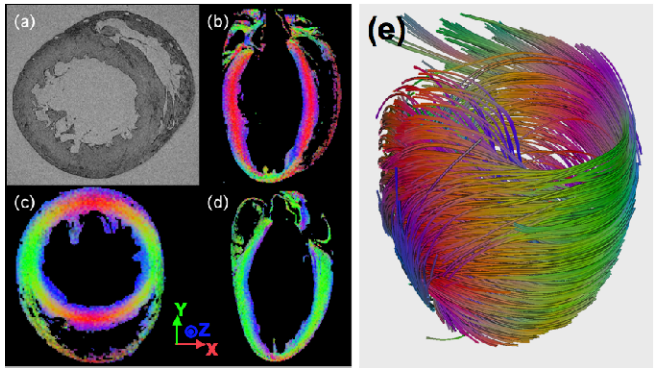
Introduction

In-silico research is playing an increasingly important role in the integration of multiple experimental findings into a single, comprehensive model. Once built, 'virtual experimentation' on these models allows one to test a single parameter in isolation, while monitoring its effects at high resolution and over a large volume, which would not always be possible in the 'wet-lab'. Data obtained using high resolution 3D diffusion tensor imaging (DTI) can be integrated into these models to provide information regarding myocardial fibre architecture, allowing us to create a tool to accurately study the electrophysiological and mechanical behaviour of the heart. We present the progress to date of the '3D Heart' project, which aims to develop an efficient methodology for the acquisition and co-registration of high resolution cardiac anatomical- and DT-MRI data with serial histology, in order to produce highly detailed computer models of individual whole hearts.

Materials and Methods

Hearts have been excised from a series of Sprague Dowley rats, and one New Zealand white rabbit. These were fixed in Karnovsky's for 12 hours (2% formaldehyde, 2.5% glutaraldehyde mix) and embedded in 1% agarose gel doped with gadodiamide contrast agent (2 mM concentration for rabbit, 4 mM for rat), inside a glass NMR tube. All MRI data has been acquired using a Varian 9.4 T (400 MHz) MR system (Varian Inc, Palo Alto, CA), comprising of a horizontal magnet (bore size 210 mm), a VNMRS Direct Drive console, and shielded gradient system (1 T/m, rise time 130 µs). A birdcage coil with an inner diameter of 28mm (Rapid Biomedical, Wurzburg, Germany) was used to transmit/receive the NMR signals. Anatomical MRI scans were performed on all ex-vivo hearts, using a 3D T_2* weighted gradient echo pulse sequence [1]. The highest resolution data sets acquired were 21.5 µm isotropic for rat and 26.4 µm× 26.4 µm in plane, 24.4 µm out-of-plane for rabbit. Following this, the gadodiamide was washed out of two of the rat hearts, which were then re-embedded in 1% agarose. These hearts were scanned using a 3D fast spin echo diffusion weighted pulse sequence, with 6 diffusion gradients (mean *b*-value = 785 s/mm^2), to acquire DTI data at 101.6 µm isotropic resolution. Following acquisition, the diffusion tensor was calculated on a voxel-by-voxel basis via a weighted linear least squares fit method, using in house software developed in IDL (Interactive Data Language, ITT Corporation, Colorado, USA). Once MRI was complete, serial histology was performed on the rabbit heart and one of the rat hearts, using a protocol similar to that described in [2], to produce data sets with a slice thickness of 10 µm, and in-plane resolution up to 0.55 µm.



Results

Slices from 3D anatomical and diffusion weighted MRI data sets are shown in Fig. 1. The mean value of fractional anisotropy in the total myocardial volume was 0.37 ± 0.11 for the heart shown in Fig.1, and the average transmural range in left-ventricular helix angle was (87 ± 9)° for an apical slice, (98 ± 9)° at the mid-ventricular level, and (104 ± 7)° for a basal slice. These values are similar to those reported in previous DTI studies of the rat heart [3].

Figure 1 (a) Short axis section from a 3D anatomical scan of an ex-vivo rat heart. Voxel resolution is 21.5 µm in-plane. (b) Four chamber, (c) axial, and (d) two chamber sections from a 3D, 101.6 µm isotropic resolution DTI scan. Figures (b)-(d) are colour coded according to the XYZ – RGB scheme shown in (c), with colour determined by the direction of the primary eigenvector at a given voxel, and magnitude modulated by the fractional anisotropy. (e) Visualization of the fibre structure in the left ventricle from fibre tracking, based on primary eigenvector data (visualization created using MedInria software).

The anatomical MRI data of the rabbit heart has been combined with the histological data via a series of 3D rigid and 2D non-rigid registration algorithms, in order to produce a computer model of the ventricles, consisting of 4.3 million vertices and 24 million tetrahedral elements. As no DTI data were available for this heart, fibre structure data was incorporated on a per rule basis using a-priori knowledge [4].

Discussion

The 3D DTI data collected for the rat heart will provide an accurate, high resolution model of myocardial fibre architecture, which is essential for realistic modelling of cardiac electrophysiology and mechanics. Future work will focus on the development of methods to interpolate the DTI tensor data from the rat hearts into the co-registered anatomical MRI / histological data stack, and techniques for acquiring DTI data from Langendorff-perfused and in-vivo hearts. We also aim to address the significant challenges posed by the automated segmentation and co-registration of MRI and histological data, and the computation difficulties of managing these large (> 1.6 TB for one rabbit heart) data sets.

Acknowledgements

This project is supported by the Biotechnology and Biological Science Research Council, grant reference BBE0034431.

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