BIOMIMETIC PHANTOM FOR CARDIAC DIFFUSION MAGNETIC RESONANCE IMAGING

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Target Audience Scientists with an interest in the optimisation and validation of cardiac diffusion MRI.

Purpose The rapid growth of diffusion MRI has driven demand for phantoms to aid development of novel pulse sequences and models of diffusion, and to improve quality assurance of data. Several diffusion phantoms have been proposed, mostly based on geometric arrangements of polymer fibres [1,2,3]. However, it has proven challenging to replicate the high anisotropy found in biological samples. Furthermore, many phantoms utilise solid fibres, which contrasts with the cellular structure of tissue containing a distribution of pores. One promising method based on co-electrospinning, produces hollow fibres which are perfused with an MRI-visible substrate [4]. This yields physiological values of mean apparent diffusion coefficient (ADC) and fractional anisotropy (FA) [5]. With the majority of diffusion phantoms designed to simulate brain tissue, we have developed a novel phantom designed to simulate the specific fibre orientations and diffusion properties of the heart.

Methods Fibre strips were manufactured from a polycaprolactone shell and polyethylene oxide core by co-electrospinning [4], producing strips of width = 30 mm, thickness = 0.5 mm and area-weighted pore size = 13.4 μm as measured with SEM images (Figs. 1A & 1B). Three fibre strips were infused with cyclohexane, and wound concentrically about a custom polymer spindle at different helix angles so as to simulate the left, circumferential and right-hand helical fibres of the myocardium in the left ventricle, progressing from the subepicardium to the subendocardium (Fig. 1C). Helix angles were defined as the angular projection normal to the plane perpendicular to the long axis of the spindle. The spindle and fibres were immersed in a tube containing cyclohexane, and air was excluded from the imaging volume by means of a bubble trap.

MRI was performed using a 9.4T preclinical scanner (Agilent Technologies, Santa Clara, CA). 2D spin echo diffusion tensor imaging (DTI) was performed at weekly intervals over four weeks, with TR / TE = 2500 / 17.5 ms, in-plane resolution = 150^2 μm^2, δ = 2.5 ms, Δ = 12.5 ms, b_{max} = 2000 s/mm^2, #DW directions = 30. In addition, 3D fast spin echo DTI data were acquired for fibre tracking. The diffusion data were fit with a single tensor model and a mask based on B=0 image signal intensity was applied for thresholding. The mean ADC, FA and helix angles across the simulated myocardium were measured. Fibre tracking was performed on the 3D FSE data using Diffusion Toolkit and Trackvis [6].

Results Representative mean ADC and FA maps are shown (Figs. 2A & 2B). Over the four-week period, the average mean ADC was 0.76 ± 0.02 x 10^{-3} mm^2/s, while the FA was 0.38 ± 0.02. Fibre tractography clearly illustrates how the fibres simulate the range of helix angles in the myocardium (Fig. 3). Mean helix angles of the simulated subepicardium, mid-myocardium and subendocardium were -59, 0.5 and 53 degrees respectively.

Discussion A novel phantom simulating diffusion in the heart was designed and built to serve as a tool for the development of diffusion MRI methods in the heart. The pore sizes were enlarged compared to a previous phantom [5], to account for the higher ADC and lower FA in cardiac tissue relative to brain tissue. We demonstrate here the physiological relevance and temporal stability of the phantom. ADC and FA values compare favourably to ex-vivo mouse and rat cardiac data reported in the literature, where mean ADC ranged from 0.62 to 0.89 x 10^{-3} mm^2/s, and FA ranged from 0.25 to 0.39 [7,8,9]. Further refinements could include replacing the discrete layers with a continuum of fibres with varying helix angles, and scaling up the phantom to simulate a human heart.

References [1] Fieremans E., et al. Phys Med Biol. 2008; [2] Pullens P., et al. JMRI. 2010; [3] Moussavi-Biugui A., et al. MRM. 2011; [4] Zhou F.L., et al. Appl Mats Interfaces. 2012; [5] Hubbard P.L., et al. MRM. 2014, DOI:10.1002/mrm.25107; [6] Wang R., et al. ISMRM. 2007; [7] Jiang Y., et al. MRM. 2004; [8] Strijkers G.J., et al. NMR Biomed. 2008; [9] Angeli S., et al. JCMR. 2014.

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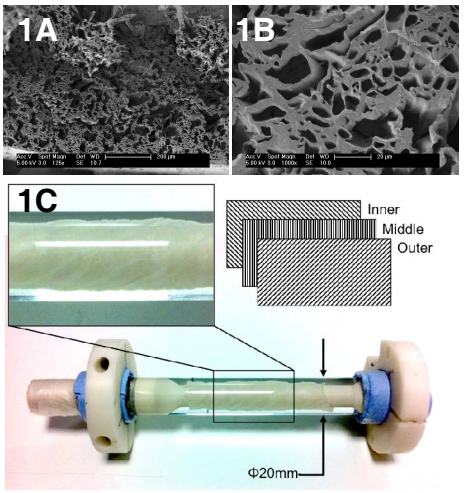
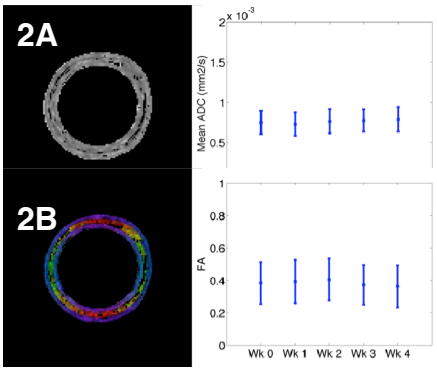
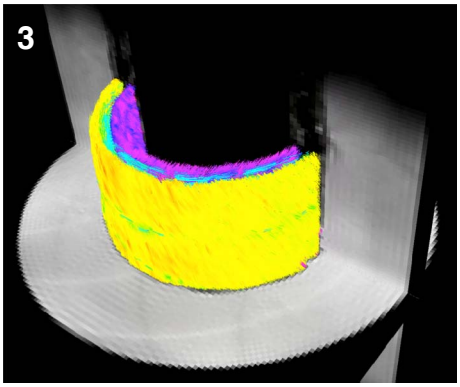


Figures 1A & 1B. SEM images at 125X and 1000X magnification; **Figure 1C.** Photograph of cardiac diffusion phantom. See inset for detail and schematic diagram of fibre orientation.





Figures 2A & 2B. Mean ADC and FA in an axial slice. Measurements over 17 slices are reported over a four week period; **Figure 3.** 3D fibre tractography superimposed on B=0 image shows the transition from negative (yellow) to neutral (cyan) to positive (magenta) helix angles of the simulated subepicardium, mid-myocardium and subendocardium.