Diffusion tensor MRI of hearts with chronic infarct in multiple mechanical states

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Target audience: Clinicians, researchers and MR technologists involved in the characterization of the myocardial tissue structure.

Purpose: Myocardial tissue structure underpins cardiac function in health and disease. Detailed knowledge of cardiac architecture and its dynamic alteration during the cardiac cycle is enhancing our understanding of its close relationship with the mechanical and electrical function of the heart. Diffusion tensor imaging (DTI) facilitates the assessment of cardiac microstructure throughout the cardiac cycle in the same heart in a non-destructive manner [1], unlike histological methods. Recently, the same live healthy heart in three different mechanical states was assessed using a custom-made MR-compatible perfusion set-up, different perfusates and a balloon inserted in the left-ventricular cavity [2]. This study investigates changes in DTI parameters in the chronically-infarcted rat heart in multiple deformation states.

Methods: All animal work was conducted in accordance with the UK Home Office Guidance on the Operation of Animals (Scientific Procedures) Act of 1986, and was approved by Oxford University's ethical review board. Permanent occlusion of the left coronary artery was induced in five female Sprague-Dawley rats [3]. Six weeks after surgery, the hearts were excised after cervical dislocation and connected to a custom-made MR-compatible perfusion rig. A balloon was inserted inside the left-ventricular cavity and a pressure sensor in the balloon line monitored the left-ventricular pressure. DTI data were acquired with a 9.4T horizontal MR system (Agilent Technologies, Santa Clara, CA) in three states as follows: First, the hearts were arrested in its relaxed state using high-K^+ modified Tyrode solution. Second, the balloon was inflated to 70 mmHg. Third, contracture was induced by switching the perfusate to Na^+-free Li^+ Tyrode. Data were acquired with a 2D diffusion-weighted fast spin echo pulse sequence (TE/TR = 15/1000 ms, ETL = 8, FOV = 20x20 mm^2 (128 x128), 13 contiguous 1-mm thick slices, 10 non-collinear gradient directions [4], G = 31 G cm^{-1}; Δ = 9.6 ms, δ = 2.5 ms, b_{max} = 508 s mm^{-2}). Mean apparent diffusion coefficient (ADC) and fractional anisotropy (FA) maps were generated [5] and values reported in manually delineated region of interest over the whole myocardium. Furthermore, the helix angle α was calculated to characterize the fiber orientation [6], and distributions of left-handed (LHF, α < -30°), circumferential (CF, 30° < α < -30°) and right-handed fibers (RHF, α > 30°) calculated. The same protocol was performed in hearts excised from five sham-operated control animals for comparison.

Results: Example parameters maps obtained in the healthy and remodeled hearts are shown in Figure 1. Average values of mean ADC and FA are listed in Table 1. No significant differences were found between the measurements in the healthy hearts and those in the remote area (non-infarcted area) of the infarcted hearts (unpaired Student T-test). In the infarct zone, FA decreased significantly, compared to the remote area, in all three mechanical states (paired T-test: relaxed: p = 0.04, volume-loaded and contractured: p < 0.01), while ADC increased significantly in the contractured state (paired T-test: p = 0.05).

The proportions of RHF, CF and LHF are shown in Figure 2. In the remote area, CF proportion decreased significantly in the relaxed state compared to healthy hearts (43.5 ± 3.2% against 49.6 ± 1.6%, unpaired T-test: p < 0.01), while RHF proportion increased (31.9 ± 2.6% against 27.7 ± 2.3%, unpaired T-test: p = 0.03). Moreover, fiber disarray was observed in the infarct zone (Figure 1).

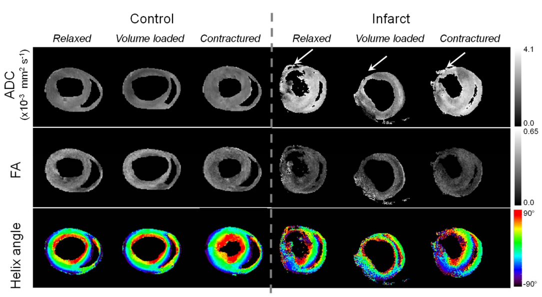

Figure 1: DTI parameters maps from a healthy control (left) and a rat model of chronic infarct (right). The arrows indicate the infarct zone. Apparent Diffusion Coefficient (ADC), Fractional Anisotropy (FA) and helix angle maps were obtained in the same living heart in tree mechanical states.

Table 1: Mean and standard deviation of DTI parameters over the myocardial volume in three mechanical states.

	Mechanical state	Control	Remote area	Infarct zone
ADC $x10^{-3}$ mm^2s^{-1}	Relaxed	1.67 ± 0.19	1.67 ± 0.24	1.74 ± 0.27
	Volume loaded	1.42 ± 0.25	1.58 ± 0.28	1.79 ± 0.41
	Contractured	1.57 ± 0.28	1.61 ± 0.32	1.77 ± 0.32 *
FA	Relaxed	0.32 ± 0.03	0.31 ± 0.03	0.27 ± 0.06 *
	Volume loaded	0.34 ± 0.01	0.31 ± 0.02	0.27 ± 0.02 †
	Contractured	0.30 ± 0.02	0.29 ± 0.04	0.25 ± 0.06 †

*Significant differences between the remote area and the infarct zone (paired T-test): *: p ≤ 0.05; †: p ≤ 0.01.*

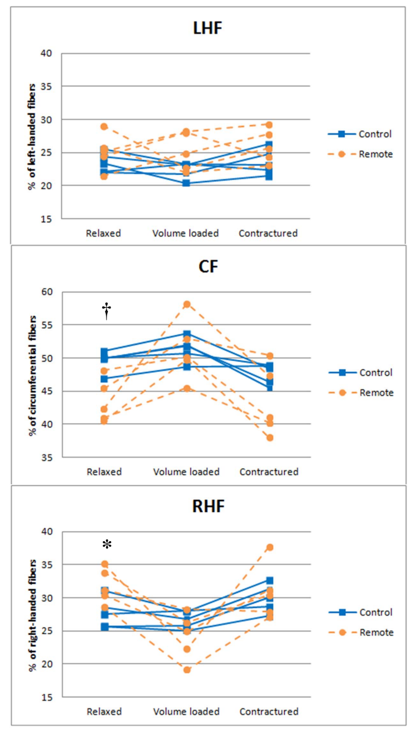

Figure 2: Changes in helix angles in three mechanical states, in healthy hearts from control animals (blue) and in the remote area of infarcted *hearts (orange). Significant changes were observed in slack state, in the proportion of CF* (†: p < 0.01) and RHF (*: p < 0.05).

Discussion: We investigated the histo-architecture of the same living heart in three mechanical states: *(i)* relaxed, which simulates deformation during diastole, *(ii)* volume loaded, which models increased venous return, and *(iii)* contractured, which represents peak systole. ADC increased slightly, although not significantly, in the remote zone compared to healthy tissue, which has been shown in patients in mid-systole [7]. Conversely, FA in the remote zone remained stable. Rightward shift in fiber architecture in the remote zone has been observed in patients [7] and fixed sheep hearts [8]. We observed a significant increase in RHF proportion in relaxed state, coupled with a significant decrease in CF proportion. However the present results represent global changes observed between healthy and infarcted hearts. A regional analysis would provide additional insight into the structural changes associated with cardiac remodeling.

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