Diffusion Tensor MRI of the remodeled living heart in multiple mechanical states: First experiments in a rat model of chronic myocardial infarction

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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. Probing the microscale diffusion of water using diffusion tensor MRI (DTI) provides information on cardiac microstructure details in a non-destructive manner [1], unlike histological methods. Importantly, cardiac DTI is the only imaging modality that allows the assessment of cardiac microstructure throughout the cardiac cycle in the same heart. Recently, assessment of the same live healthy heart in different mechanical states has been made possible thanks to the use of a custom-made MR-compatible perfusion set-up and different perfusates [2]. The aim of this study is to investigate changes in DTI parameters (i.e. apparent diffusion coefficient (ADC) and fractional anisotropy (FA) and fiber orientation) in the chronically infarcted rat heart.

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 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 was integrated in the balloon line to monitor the left-ventricular pressure. An MRI protocol for the evaluation of the cardiac structure in different mechanical states was implemented in a 9.4T horizontal MR system (Agilent Technologies, Santa Clara, CA). First, the heart was arrested using high-K^+ modified Tyrode solution and DTI was performed in slack state. The DTI experiment was repeated after induction of contracture by switching 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 [5]: G = 31 G cm^{-1}; Δ = 9.6 ms, δ = 2.5 ms, b_{max} = 679 s mm^{-2}), and ADC and FA maps were generated [5]. Furthermore, the helix angle was calculated to characterize the fiber orientation [6]. The same protocol was performed in hearts excised from healthy control animals for comparison.

Results: Example images and DTI parameters maps obtained in the healthy and remodeled hearts are shown on Figure 1a and b. In the normal heart, the average ADC in different mechanical states was: 1.81 ± 0.31 x 10^{-3} mm^2 s^{-1} (slack) and 1.84 ± 0.28 x10^{-3} mm^2 s^{-1} (contracture). The average FA at the corresponding mechanical states was: 0.29 ± 0.08 (slack) and 0.26 ± 0.07 (contracture). The average ADC obtained in the remote area (non-infarcted area) of the infarcted heart was increased (i.e. 1.91 ± 0.29 x 10^{-3} mm^2 s^{-1} (slack) and 1.93 ± 0.30 x10^{-3} mm^2 s^{-1} (contracture)), while the FA was similar (i.e. 0.29 ± 0.08 (slack) and 0.26 ± 0.07 (contracture)). In the infarct zone, ADC was increased in both states, while FA decreased.
The proportion of right-handed fibers (helix angle > 30°) was increased to 32.4% (slack) and 37.0% (contracture) in the remote area (against 28.9%, 30.6% in the normal heart, respectively), whereas disarray can be observed in the infarct zone.

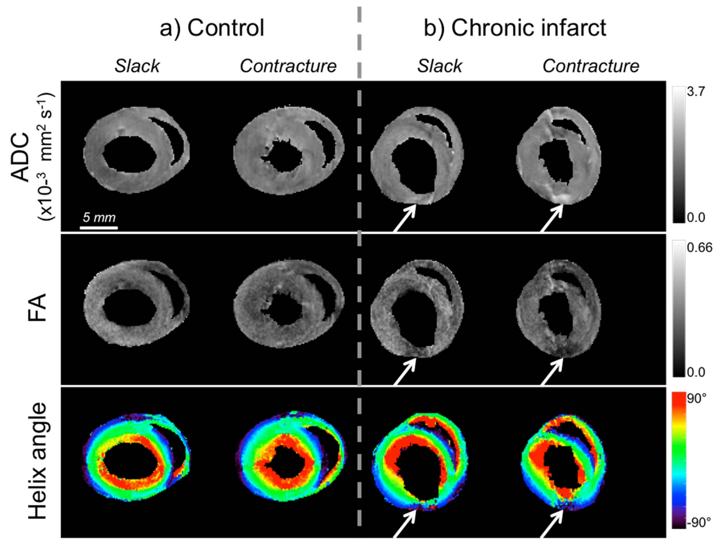

Figure 1: DTI parameters maps from a) a healthy control and b) a rat model of chronic infarct. The arrows indicate the infarct zone. Apparent Diffusion Coefficient (ADC), fractional anisotropy (FA) and helix angle maps were obtained in the same living heart in slack (left) and after induction of contracture (right).

Discussion: The present set-up allows for the determination of the histo-architecture of the same living heart in multiple mechanical states. Examples are given here in two extreme states, i.e. slack, which simulates deformation during diastole, and contracture, which represents peak systole. This provides a novel insight into the dynamics of the cardiac microstructure of the remodeled and healthy heart during the cardiac cycle: ADC appeared slightly increased in the remote zone compared to healthy tissue, which has been shown in patients in mid-systole only [7]. Conversely, FA in the remote zone seems to remain stable. Rightward shift in fiber architecture in the remote zone has been observed in patients [7] and fixed sheep hearts [8]. We have observed similar trends in both mechanical states. However, no statistical significance was reached due to the small number of experiments, since this is an on-going study. Further experiments are underway to confirm the results and to increase the number of deformation states by means of the pressure balloon.

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