Diffusion Weighted MRI of the Mouse Heart In Vivo Following Ischemia-Reperfusion Injury

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Introduction: Diffusion weighted MRI (DWI) plays a major role in the study of neurological disease but its application in the heart has been limited by technical challenges. The motion of the heart complicates DWI significantly, and most studies in the heart have thus been performed ex vivo. Here we present our preliminary experience with diffusion weighted MRI (DWI) of the mouse heart in vivo. The mouse heart beats at 400-600 beats per minute and two DWI schemes were thus tested to minimize motion artifact: 1) TE-min scheme in which the TE was minimized and, 2) a Flow-Comp scheme in which the diffusion encoding gradients were velocity compensated. Both schemes exploited the ability of a 1500 mT/m gradient insert to achieve high b-values with a bipolar diffusion-encoding gradient lasting less than 4.5 ms.

Materials and Method: C57BL6 mice with ischemia-reperfusion (left coronary artery occlusion for 30 minutes followed by reperfusion) were studied. DWI was performed on a 9.4T small animal scanner (Bruker Biospin) with a 1500 mT/m gradient (Resonance Research Inc). A fat-suppressed single-shot spin echo EPI sequence was used. In the TE-min scheme, a bipolar gradient was placed between the 90^0 and 180^0 RF pulses. Imaging parameters were: TR/TE: 2000/11.5ms, Matrix size: 80 x 80, FOV: 2.0 x 2.0 cm^2, maximum b-value: 480 sec/mm^2. Cardio-respiratory gating (SA Instruments Inc) and 4-16 signal averages were used. The trigger delay was carefully chosen using a FLASH cine with a high temporal resolution (movie frame every 2.6 ms) to avoid obvious cardiac motion. In the Flow-Comp scheme an identical bipolar diffusion encoding gradient was placed on the other side of the 180^0 RF pulse for flow compensation. Mice were imaged with both sequences 6 and 24 hours after the ischemic insult.

Results: Image quality with the TE-min sequence was more consistent than with the Flow-Comp sequence but required careful selection of the trigger time. Several 5ms windows (longer than the 4.5 ms bipolar diffusion encoding gradient) were identified in the cardiac cycle where motion was negligible and the TE-min sequence could thus perform robustly. The echo time of the Flow-Comp sequence was 3ms longer than the TE-min sequence, which significantly reduced image quality at times. In addition, the spatial resolution and maximum b-value of the Flow-Comp sequence were also lower. 24 hours after ischemia-reperfusion, an increase in the apparent diffusion coefficient (ADC) was observed in the anterior and lateral walls of the left ventricle (Fig. 1). In contrast, there was only a slight increase in the ADC in the injured myocardium within 6 hours of ischemia reperfusion (Fig 1), which was similar in amplitude in both the TE-min and Flow-Comp sequences (Fig. 1).

Conclusion: We present here, to the best of our knowledge, the first diffusion weighted MR images of the mouse heart in vivo. We show, moreover, that DWI can provide a non-invasive readout of cell death in acute ischemic injury. We have previously shown that most cardiomyocytes remain intact within the first 6 hours of ischemia-reperfusion, explaining the only slight increase in the ADC seen at 6 hours. By 24 hours, however, significant amounts of cell death/rupture occur, accounting for the significantly increased ADC. Despite the rapid heart rate of the mouse, the feasibility of tailored DWI schemes to avoid motion artifact is demonstrated is this study. The incorporation of parallel acquisition into future DWI schemes will be a major advance and allow the TE, which significantly influences image quality in mice at high fields, to be significantly shortened.

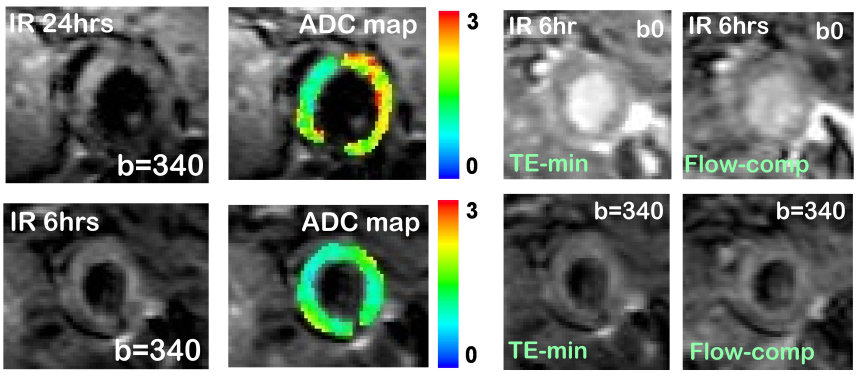

Fig. 1: Diffusion-weighted images, acquired with both DWI schemes, and the corresponding ADC maps of the mice.

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TE-Min	Infarct	Remote
IR 24 hours	2.13	1.24
IR 6 hours	1.30	1.20
Flow-Comp		
IR 6 hours	0.99	0.82

Table 1: Apparent diffusion coefficient calculated from TE-min and Flow-Comp diffusion-weighted MRI.