Comparison of High Resolution T_2^* Mapping and Quantitative Susceptibility Mapping to Investigate Myocardial Microstructure in the *Ex Vivo* Rodent Heart

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Target audience: For MR imaging scientists and radiologists interested in quantitative susceptibility mapping, heart microstructure and tissue magnetic properties.

Purpose: The structural arrangement of myocardial fibers is important to describe the contraction of the heart [1] and can be changed during cardiac diseases [2,3]. Using diffusion tensor imaging (DTI), myocardial fibers can be tracked along the most probable diffusion direction. Since DTI is very sensitive to motion, *in vivo* cardiac DTI remains a major challenge [4]. Quantitative susceptibility mapping (QSM) can provide quantitative information about local magnetic tissue properties and an excellent contrast of tissue microstructure, as demonstrated for white matter in brain [5]. QSM holds the promise to be less sensitive to bulk motion than diffusion-weighted MR of the myocardium. Since susceptibility effects increase with magnetic field strength, it is prudent to perform QSM at ultrahigh magnetic fields. This study investigates the tissue contrast in quantitative susceptibility maps of *ex vivo* rodent hearts at 9.4 T. For comparison T_2^* mapping and DTI is conducted.

Methods: Measurements were performed on a 9.4 T BioSpec 94/20 USR small animal system (Bruker, Germany) equipped with a ^{1}H mouse MRI CryoProbe (Bruker, Germany). Heart samples were harvested from a healthy adult, male Sprague-Dawley (SD) rat and from a healthy, female mouse with a genetically modified C57bl/6 background. Animals were anesthetized and 20 ml of phosphate buffered saline (PBS) was infused through the left ventricle, followed by 4% paraformaldehyde (PFA). The hearts were taken out and immersed in 4% PFA. For scanning, the rat heart was embedded in low melting agarose gel. The mouse heart was embedded in 7% gelatin. For QSM reconstruction, a 3D standard MGE technique was used. The rat heart was scanned with a spatial resolution of (94 × 94 × 94) µm^3 and an inter echo time of ΔTE = 2.85 ms for 5 echoes (TE_1 = 2.14 ms, TR = 19 ms, scan time 12 h 40 min). The mouse heart was scanned with a spatial resolution of (55 × 55 × 55) µm^3 and an inter echo time of ΔTE = 2.85 ms for 16 echoes (TE_1 = 2.14 ms, TR = 250 ms, scan time 13 h 40 min). The phase differences between the echoes were combined using a weighted least squares fit algorithm [6]. To remove background field inhomogeneities, a SHARP approach was used [7]. Susceptibility reconstruction was carried out employing spatial domain regularization [7]. T_2^* maps were calculated from magnitude images using the ARLO approach [8]. For DTI of the mouse heart, a segmented echo-planar imaging (EPI) technique with a spin echo excitation was used (b-value = 2000 s/mm^2, 30 diffusion directions, spatial resolution = (156 × 156 × 156) µm^3). DTI data was processed using DSI Studio [9]. From DTI, the angle between main diffusion direction and external static magnetic field $\mathbf{B_0}$ was calculated.

Results: QSM of the *ex vivo* rat heart yielded myocardial fiber contrast superior to magnitude images and to T_2^* maps. **Figure 1** shows a comparison of the magnitude, QSM and T_2^* contrasts for a coronal and an axial view of the rat heart wall. As a reference, a histological section from [10] is presented. The QSM shows structures matching histology. **Figure 2** depicts fiber orientation inside the mouse heart wall derived from DTI compared with QSM, T_2^* map and a histological section from [11]. The heart was oriented with its long axis parallel to $\mathbf{B_0}$. For the DTI image, an angle of 90° indicated myocardial fibers running perpendicular to $\mathbf{B_0}$, which means perpendicular to the hearts long axis. Subtle structural details can be observed in the QSM and T_2^* maps, while the contrast in the QSM is enhanced versus the T_2^* map. The QSM showed distinct transmural structural changes for the lateral wall, while T_2^* was found to be more uniform for this region.

Discussion: This study shows that QSM can provide a high contrast for myocardial fiber structures without using contrast agents. The contrast provided by QSM is assumed to be created by myocardial fibers and small spaces filled with perfusion solution, as confirmed by the histological sections. However, this is not evident in magnitude images and T_2^* maps, in which the myocardium appears more uniform. Additionally, susceptibility contrast could arise from susceptibility anisotropies resulting from highly ordered peptide bounds with a distinct orientation relative to $\mathbf{B_0}$ [12]. For the mouse heart DTI (**Figure 2**), a circular orientation of the fibers in the mid-myocardium is visible. In the mid-myocardium of the QSM of this heart, a circular pattern can be distinguished by appearing more diamagnetic. This could be associated with susceptibility anisotropies due to fiber orientation. The circular pattern could be depicted in T_2^* image, although it provides a different tissue contrast.

Conclusion: Although the relation of susceptibility anisotropy and myocardial fiber orientation needs further investigation, QSM shows a higher contrast for myocardial fiber structures than magnitude images and T_2^* maps. This observation provides encouragement that QSM might be a tool for assessing myocardial microstructure. These efforts hold the promise for better insights into myocardial fiber arrangement and myolaminar structure and might help to provide answer to the ongoing debate on the structure and role of myocardial clefts and crypts.

References: [1] Buckberg G, et al., Circulation, 2008; [2] Sutton MGSJ & Sharpe N, Circulation, 2000; [3] Tezuka F, Tohoku J exp Med, 1975; [4] Nielles-Vallespin S, et al., MRM, 2013; [5] Schweser F, et al., Neuroimage, 2012; [6] Liu T, et al., MRM, 2011; [7] Li W & Liu C, *STI Suite*, 2014; [8] Pei M, et al., MRM, 2014; [9] Yeh FC, et al., PLoS ONE, 2013; [10] Gilbert SH, et al., Am J Heart Circ Physiol, 2011; [11] Lujan HL & DiCarlo SE, Physiol Rep, 2014; [12] Worcester DL, Proc Natl Acad Sci USA, 1978.

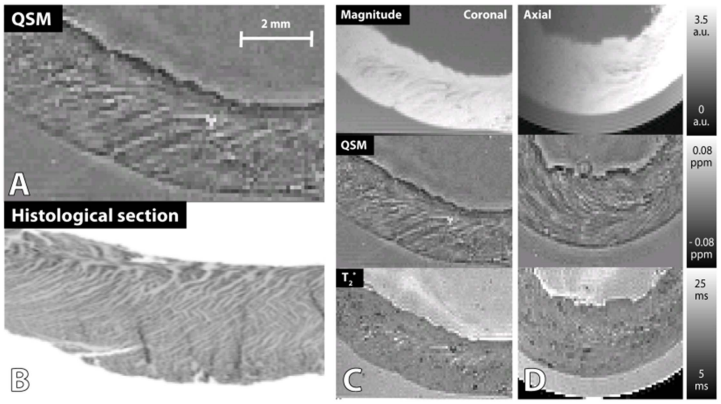

Figure 2: Images of the rat heart wall (spatial resolution = (94 × 94 × 94) µm^3). **A)** Coronal view of the reconstructed QSM showing myocardial tissue of the left ventricular wall. **B)** A comparable histological section of a rat heart taken from [10]. **C)** Coronal and **D)** axial view of the first echo magnitude image **(top)**, corresponding QSM **(middle)** and T_2^* map **(bottom)**.

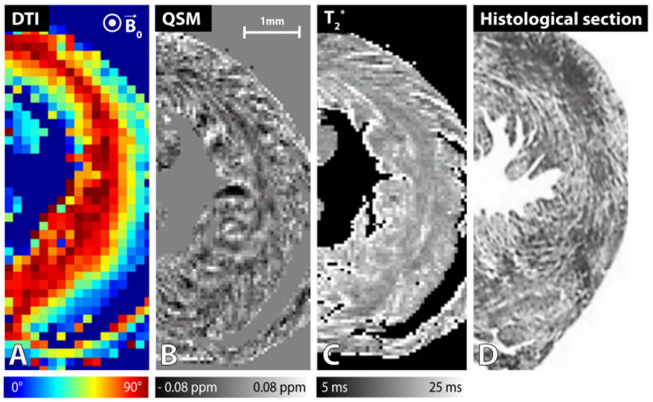

Figure 2: Axial images of the mouse heart wall. **A)** DTI image (spatial resolution = (156 × 156 × 156) µm^3) mapping the angle of the main diffusion direction relative to $\mathbf{B_0}$. It indicates that fibers run circumferentially inside the heart wall. **B)** QSM **C)** and corresponding T_2^* map (spatial resolution = (55 × 55 × 55) µm^3). **D)** A histological section taken from [11].