DETAILING MYOCARDIAL MICROSTRUCTURE IN THE *EX VIVO* RAT HEART USING HIGH ISOTROPIC SPATIAL RESOLUTION SUSCEPTIBILITY WEIGHTED MRI AND QUANTITATIVE SUSCEPTIBILITY MAPPING

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Target audience

This work is of interest for clinical scientists, imaging scientists, cardiologists and basic MR researchers interested in microstructural imaging of the heart.

Purpose

Myocardial microstructure greatly affects cardiac mechanics, plays a pivotal role in the generation of ventricular torsion and myocardial strain and provides important information about (patho)physiological conditions of the heart. *Ex vivo* histology and diffusion weighted imaging (DWI) are commonly used to assess myocardial tissue microstructure. Microstructural *in vivo* DWI of the heart remains challenging due to its propensity for cardiac and respiratory motion. Susceptibility weighted MRI has been shown to reveal myocardial microstructure in the perfused *ex vivo* rat heart [1] and holds the promise to be less sensitive to motion than DWI. Also, susceptibility weighted MRI provides excellent contrast which can be employed to investigate tissue microstructure and fiber tracking in the brain [2, 3]. Recognizing this progress, this work focuses on explorations into probing myocardial tissue microstructure using susceptibility weighted MRI. To meet this goal, this pilot study examines the feasibility of quantitative susceptibility mapping (QSM) [4] for the assessment of myocardial microstructure in the *ex vivo* rat heart using an isotropic spatial resolution as low as (94x94x94) μm^3.

Methods

Animal model: The heart of an adult male wistar rat was excised under anesthesia. Before excision, intracardiac perfusion with phosphate buffered saline (PBS) and 2% paraformaldehyde in PBS solution was carried out. ***MR Imaging:*** Experiments were performed using a 9.4 Tesla small animal scanner (Bruker Biospec, Ettlingen, Germany). A 35mm quadrature TX/RX volume coil was employed for excitation and signal reception. For data acquisition a 3D multi-echo gradient echo protocol was employed (TR = 19ms, TE = 2.14-13.54ms (5 echoes), FA = 16°, TA = 12h, FOV = (15x20x15)mm^3 covering the whole heart, matrix = 160x212x160, spatial resolution = (94x94x94)μm^3). ***Postprocessing:*** T_2^* maps were generated by fitting magnitude decay with a monoexponential function. Magnetic field perturbation was estimated from the phase images of first three echoes [5-7] and background field was removed using projection onto dipole fields [8, 9]. Susceptibility maps were reconstructed by employing a thresholded k-space division (TKD) approach [10]. Susceptibility maps were referenced to mean susceptibility in the whole heart.

Results

Figure 1 shows magnitude and phase images of a midventricular short axis view of the fixed *ex vivo* rat heart along with a quantitative susceptibility map and a T_2^* map. Small structures in the anterolateral segment (segment 6) are pronounced in the magnitude image (red arrow in Fig. 1A). These structures are also present in the phase image and can be recognized in the susceptibility map, but with less contrast (red arrows in Fig. 1B-C). Magnetic susceptibility showed relative changes across the myocardium of approximately 0.2 ppm. A transmural change in susceptibility ($\Delta\chi \approx 0.1$ ppm) was found in anterior, septal and inferior segments with higher values in subendocardial and lower values in subepicardial regions. These changes correspond to variations in T_2^* in these regions (Fig. 1D). A blood vessel (white arrow) can clearly be recognized in all four images, showing higher susceptibility and lower T_2^* which might be caused by residual deoxyhemoglobin. Myocardial T_2^* in the fixed *ex vivo* rat heart was found to range from about 10ms to approximately 25ms with substantial transmural changes.

Discussion and Conclusion

This pilot study investigated the feasibility of quantitative susceptibility mapping for the assessment of the myocardial microstructure in the fixed *ex vivo* rat heart. The preliminary results show that magnetic susceptibility varies across the myocardium with transmural changes from endo- to epicardium. Small structures within the myocardium that were observed in magnitude images were also present in phase images and showed correspondence in the susceptibility map. The reduced contrast of these structures in the susceptibility map might be explained by the employed QSM reconstruction approach, which amplifies noise. Application of more sophisticated regularization approaches could improve reconstruction quality, but requires further investigation for appropriate parameterization. While the exact biophysics of myocardial tissue magnetic susceptibility are still to be investigated, our results provide encouragement, that quantitative susceptibility mapping might be a useful tool for microstructural imaging of the myocardium and might add further scope to the armamentarium of cardiac MR. To meet this goal further research is needed to investigate the different influences on microscopic susceptibility changes in the heart muscle and its implications for clinical questions.

References:

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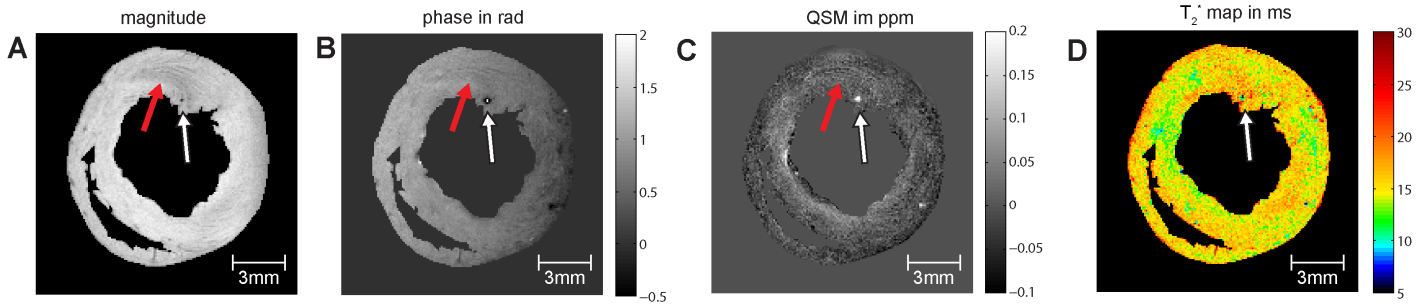

Figure 1: A) Masked magnitude image (TE 2.74ms) and **B)** phase image (TE 7.8ms) of a mid-ventricular short axis view of a fixed ex vivo rat heart. **C)** Corresponding quantitative susceptibility map and **D)** T_2^* map. Small structures are visible in susceptibility weighted magnitude and phase images and can also be recognized in the susceptibility map (red arrow). The white arrow indicates a blood vessel which can clearly be seen in all images.