Characterization of iron load in rat myocardium at 7T by R2 map

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Introduction R2 mapping techniques have been used to index iron overload in the myocardium like in thalassemic subjects [1-3] or to detect edema in patients with acute myocardial infarction [4]. Some studies have shown also the possibility of using R2 measurements to track exogenously injected cells labeled with super-paramagnetic iron oxide (SPIO) in the kidneys or in the liver [5]. Applications of R2 mapping to SPIO injection in the heart also would be beneficial stem cell therapy. When working with small mammals in a preclinical environment, it becomes very difficult to perform an accurate T2 measurement of the myocardium given the very short R-R interval (100-180ms). Furthermore, the higher magnetic fields usually employed for small mammal studies increase the SNR and the sensitivity to iron load. However, higher fields introduce further image artefacts especially in the heart due to B_0 inhomogeneities. In this work we study the the possibility of performing R2 measurement in the myocardium of rats at 7T in the presence of SPIO labeled cells. Healthy and an infarcted rats are also analyzed to confirm the robustness of the methodology and its sensitivity to changes in myocardium properties.

Methods: Short axis of the heart was imaged on six healthy rats (Wistar rats, weighing 300-330 g), two rats with SPIO labeled mesenchymal stem cells injected in the myocardium (20 µl, 10^6 cells), and three infracted (cryogenic infarction). The scans were performed at 7T on an the Discovery MR901 scanner (a GE Healthcare and Agilent Technologies Ltd), using a gradient insert with 300 mT/m maximum gradient strength, 1000mT/m/ms slew rate. A 4ch surface coil array was used used for reception with a 150mm diameter quadrature transmit coil (both from Rapid Biomedical, Würzburg, Germany.). For R2 mapping we used a single phase, signle slice double inversion Black Blood Fast Spin Echo (BBFSE) sequence where the effective echo time (TE_{eff}) was varied in successive acquisitions. The co-registration and cardiac phase of all images were checked before performing a voxel-based mono-exponential curve fit on the T2 weighted images (in house algorithm MATLAB (MathWorks, Natick, MA, USA), Region of interest analysis was performed in (a) healthy myocardium (b) infarcted myocardium and (c) myocardium injected with SPIO labeled stem cells.

Results For BBFSE acquisitions the TE_{eff} ranged between 5 and 40ms in 5ms increments; echo train length (ETL) = 8; number of excitations (NEX)=6, in plane resolution 0.2x0.2mm^2, slice thickness=2mm. Figures 1 shows R2 maps of a healthy rat heart whereas Figure 2 and 3 show R2 maps of the myocardium of a rat respectively with a cryogenically induced anterolateral infarction, and SPIO labeled cells injected in the septum. Regions within the myocardium which contains elevated iron load (indicated by a white arrow in Figure 3) are clearly discernable showing higher R2 values than remote SPIO-free areas. Region of interest analysis confirmed this observation. Measured R2 values (mean ± std.dev.) were 35 ± 3 s^{-1} in healthy (n=5) and 49 ± 4 s^{-1} in myocardial areas containing SPIO loaded cells (n=2). The infarcted area also showed higher R2 values (55 ± 12 s^{-1}) (n=3). The error of the measurement within the region of the interest and across scanned subjects was small relative to the effect size, attesting to robustness of the R2 measurement.

Discussion and Conclusions:

This work has demonstrated the feasibility of consistent R2 measurements in the myocardium across animals at 7T opening the road to accurate tracking of exogenously administered SPIO labeled stem cells. Future effort will be devoted to improve the characterization of SPIO injection, using for instance R2* mapping along with R2 measurements. This would help the in-vivo myocardial cell tracking.

References:

[1] T He et al, JMRI 24: 580-585 (2006) [2] H Guo et al, JMRI 30:394-400(2009) [3] V Positano, NMR Biomed 20: 578-590 (2007) [4] S Giri et al, JCMR 11:56 (2009) [5] Y E Chung et al, JMRI 31: 1379-1386 (2010)

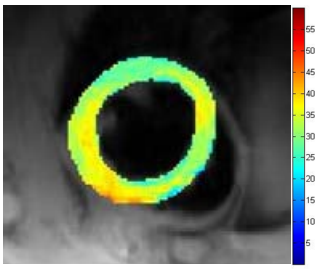

Figure 1.
R2 mapping in healthy rat

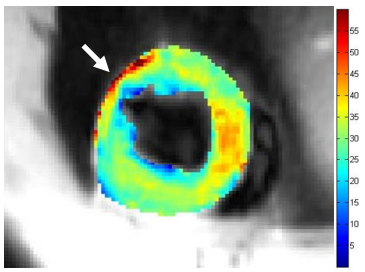

Figure 2.
R2 mapping in rat with infarct

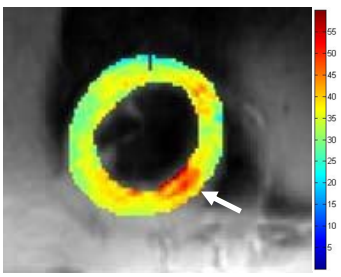

Figure 3
R2 mapping in rat with SPIO labeled cells