From Men to Mice: Theoretical Considerations for Edema Imaging at Ultra-High Magnetic Fields

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Introduction: T_2-weighted magnetic resonance imaging (T2w-MRI) has been shown to visualize and to quantify edema in the acutely infarcted myocardium (AIM) in humans (e.g. [1, 2]), and in animal models such as pigs [3] or dogs [4]. The contrast in T2w-MRI is based on the increase in T2 in the injured area of the heart compared to normal ('remote') myocardium. Ischemia-reperfusion injury mouse models allow for reproducing and studying conditions found in AIM patients. While humans and large animals are studied at a magnetic field strength of 1.5-3 T, mice are typically imaged at dedicated ultra-high field MR systems, equipped with magnets ≥ 7T. The change in magnetic field strength and species may result in an altered T_2 contrast, which may directly impact on the visibility of the acutely injured myocardium and the accuracy of its area assessment. Based on relaxation time measurements, we sought to quantitatively investigate the achievable contrast between normal and ischemia-reperfusion injured myocardium in mice at 9.4T and to compare it to the clinical scenario at 3T.

Materials & Methods: T_2-measurements were performed in 9 C57/Bl6 mice (26 ± 4 g) one day post ischemia-reperfusion injury (ischemia time: 45 min) using a spin echo (SE) sequence with variable echo times, the T_1 times were taken from [5]. Relaxation time experiments in four patients with acute myocardial infarction were conducted at 3 T using *ShMOLLI* for T_1 [6] and T2p-SSFP sequences for T2 [7]. Based on these measurements, computer simulations of a SE sequence in steady-state were performed using purpose written software in *idl*. The signal intensity *nSI*, normalized to the proton density, which then only depends on the respective T_1- and T_2-relaxation times, was calculated as a function of the flip angle α of the excitation pulse, the echo time TE, and the repetition time TR. The theoretical contrast *C* between remote (i.e. normal) myocardium and AIM, based on T_1- and T_2-differences only, was calculated as $C = |nSI_{AIM} - nSI_{Remote}|$.

Results: The T_2-measurements in mice at 9.4T yielded values of 21 ± 2.0 ms for normal versus 27.9 ± 2.4 ms for injured myocardium. For the remote human myocardium at 3T we obtained T_1= 1263 ± 41 ms and T_2= 39 ± 3 ms, and these values were elevated in AIM (T_1= 1492 ± 29 ms and T_2= 56 ± 6 ms). Figure 1 shows the result of the simulations in mice, i.e. contrast *C*, as a function of TE for different excitation flip angles and a fixed TR of 0.5s. Based on the combination (α, TE) that maximizes the contrast, C_{max} as a function of TR is shown in Figure 2 for mice and humans. Figure 3 shows examples of T2w-images acquired humans (T2p-SSFP– Fig. 3a) and in mice (2D-SE – Fig. 3b). The arrows indicate the area of increased signal intensity.

Figure 1:

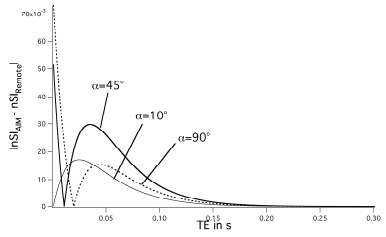


Figure 2:

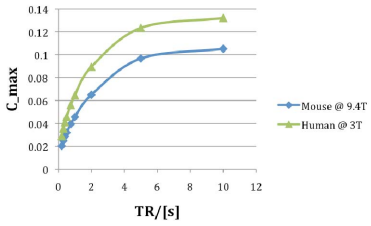
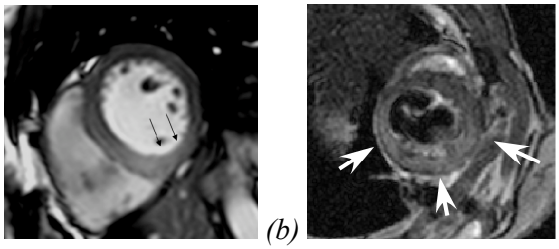


Figure 3:



Discussion: The contrast between injured and remote myocardium has been simulated as a function of T_1 and T_2. The difference in proton density between the two compartments was neglected for these considerations, as clinical T2w images may be normalized to proton density maps to correct for coil sensitivity. Under these assumptions, the differences in T_1 and T_2 between both compartments were found to be more favourable in humans at 3T compared to mouse hearts at 9.4T. More specifically, while the T_1 values are closer together, the differences in T_2 are larger in humans than in mice, whereas T_1 in AIM of mice is also increased by ~40%. Hence, the optimal achievable contrast for T2-weighting was about 40% larger in humans than in mice, where a theoretical difference of only ~10% can be achieved. This agrees with our practical experience as shown in Fig. 3. **Conclusion**: High field animal studies yield less T2W contrast in myocardial infarction than lower field strength. Hence, T_2-mapping rather than T2w imaging might be required for an accurate quantification of edema in mice at ultra-high magnetic fields.

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