T_2 mapping of the mouse heart using segmented MLEV supercycle preparation

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Introduction Mouse cardiovascular disease models play an important role in cardiology research. Therefore, a continuous effort is made to improve MRI sequences for mouse cardiac imaging to provide detailed information of cardiac function and tissue status. In this respect, quantitative measurements of T_1 and T_2 are of great importance to detect and characterize cardiac pathology (edema, fibrosis, ischemia or hemorrhage) through endogenous contrast mechanisms [1,2] or by using (targeted) contrast agents [3]. While T_1 mapping of the mouse myocardium is frequently applied [3-5], T_2 mapping sequences have received much less attention [5]. **Goal:** to develop a robust method for T_2 quantification in the mouse myocardium.

Materials and Methods *Sequence* – The method was based on an ECG-triggered multi-slice FISP sequence with segmented k-space acquisition (Fig. 1). T_2 weighting was obtained prior to acquisition by an MLEV weighted [6] preparation scheme using non-selective composite pulses, thereby making the preparation insensitive to both B_1 and B_0 field inhomogeneities.

Specifically, T_2 preparation consisted of a 90˚ excitation, followed by n blocks of four MLEV weighted composite 180˚ pulses ('+': 90_x-180_y-90_x, '−': 90_{-x}-180_y-90_{-x}) and a composite -90˚ (270_x-360_{-x}) tip-up. Most importantly, different TEs were obtained by segmenting the well-known MLEV16 supercycle scheme, thereby creating the MLEV4 and MLEV8 for short TEs. With an inter-echo spacing τ of 2.3 ms, this allowed a broad range of effective TE values between 0.8 and 43.5 ms, of which the shortest echo time was reached by applying just the excitation and tip-up. The effective TE was calculated by assuming $T_2\rho$-relaxation during pulses ($T_2\rho \approx 2*T_2$) [7]. Delay Δ was varied according to the heart rate to ensure acquisition always takes place at end-diastole. The scan repetition time TR was 2s to minimize signal modulations due to respiratory triggers. Acquisition parameters were: TR_{ACQ}/TE_{ACQ} = 2.6/1.3 ms, flip angle = 30˚, FOV = 30×30 mm^2, AcqMatrix =126×126, Slice thickness = 1mm, number of slices = 3 (inter-slice distance = 2mm), number of k-lines per segment = 3, number of averages = 3, total imaging time = 4 m 30s per TE.

In Vivo – Measurements were performed on a 9.4T pre-clinical scanner (Bruker BioSpin, Ettlingen, Germany). Healthy Swiss mice (n=6) were measured to assess baseline T_2 values of the mouse. In 3 mice, measurements were repeated after 3 days to study the reproducibility of the method. T_2 values were calculated in each pixel by a two-parameter fit of the signals at different effective TEs to the formula $M_0*e^{-TE/T2}$. In each slice, the myocardium was divided into four segments (septal, posterior, lateral and anterior) based on the anatomical images. For statistical analysis, ANOVA with repeated measures was performed using SPSS 17.0 to test differences in T_2 between slice numbers, myocardial segments and measurement days.

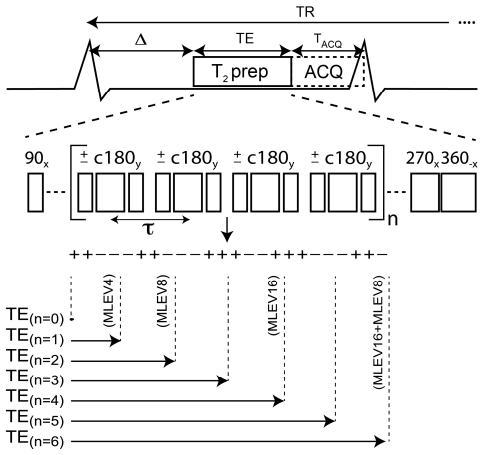

Figure 1: Mouse cardiac T_2 mapping sequence. Specific parameter values are explained in text.

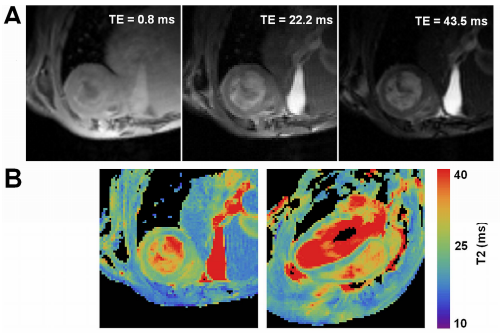

Figure 2: A) T_2-weighted short-axis images with varying echo times (n = 0, 3 and 6). B) Short-axis and long axis T_2 maps of the same mouse as in Fig 2A.

Results and Discussion Figure 2A shows anatomical images of the mouse heart with varying echo times. The start of acquisition was independent of the length of the preparation scheme, providing excellent agreement in cardiac phase for all images. Segmentation of the MLEV16 scheme proved crucial, since simply repeating MLEV4 blocks resulted in susceptibility artifacts for n > 3 at tissue interfaces. Our approach with low inter-echo spacing minimizes signal loss due to diffusion. At TE = 0.8 ms, proton density contrast was obtained, while high TEs resulted in T_2-weighted images with better blood-myocardium contrast.

Resulting short and long-axis T_2 maps are shown in Figure 2B, whose high quality reflects the agreement of the serial anatomical scans. Mean myocardial T_2 from all mice was 23.5±1.5 ms, as expected somewhat higher compared to values reported with spin-echo imaging [3], which is known to suffer more from diffusion related signal loss. The average standard deviation of T_2 estimation within a single myocardial segment was 1.7±0.5 ms, indicating a homogeneous T_2 distribution. Liver and muscle T_2 values were 16.6±1.3 and 20.4±0.5 ms, respectively. No significant differences in T_2 were found between slices or myocardial segments, however, a small but significant decrease in T_2 of 5% was found between the two measurement days. Surprisingly, T_2 maps calculated from long-axis view scans resulted in a slightly lower myocardial T_2 of 22.0 ± 2.0 ms.

In Figure 3, the mean signal of all mice (day 1) is plotted as function of TE based on both the effective echo time and the total preparation time. The use of 1, 3 and 5 blocks for the MLEV series is known to be less compensated for off-resonance effects. Therefore, measurements were performed with the same effective TE using either 2 or 4 blocks and adjusting the inter-echo time accordingly. When considering the effective TE rather than the total preparation time, almost perfect correspondence with the original dataset was achieved, which also indicates the *in vivo* validity of our assumption concerning relaxation during pulses.

Some factors that might influence T_2 estimation still need to be investigated in more detail. For example, the slight non-linearity depicted in Figure 3, which was calculated not to be a result of SNR or T_1 effects, might indicate multi-component T_2 behavior. In case of contrast-enhanced experiments dealing with lower T_1 values, T_1 effects might influence the T_2 prepared signal. We will perform Bloch simulations that will provide more insight in all these effects.

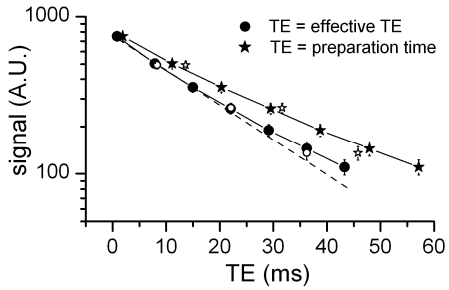

Figure 3: Myocardial signal (mean ± SEM) as function of echo-time (TE based on effective TE (circles) or preparation time (stars)) for n = 0-6 blocks, τ = 2.3ms (filled) and interleaved series (n = 2 or 4) with adjusted τ (open). The dashed line indicates the fit of the first 3 points of the effective TE data.

Conclusion In summary, we presented a method for mouse cardiac MRI enabling accurate multi-slice T_2 mapping of the mouse myocardium. We foresee numerous applications for experimental studies of cardiac disease and quantification of targeted iron-oxide based MR contrast agents.

References [1] Kellman et al. MRM 2007;57:891-897, [2] Tilak et al. Invest Radiol 2008;43:7-15, [3] Coolen et al. NMR Biomed 2010, [4] Vandsburger et al. MRM 2010;63:648–657, [5] Schneider et al. JMRI 2003;18:691:701, [6] Levitt et al. J Magn Reson 1982;50:157-160, [7] Wheaton et al. MRM 2004;52: 1223-1227.