Improved Non-Selective T2-Prep with Adiabatic vs. Composite Pulses for Whole-Heart T2w Edema Imaging in Mice

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Introduction: An ongoing diagnostic challenge exists in quickly and reliably determining the area at risk (AR) for myocardial infarction (MI): i.e. the volume of potentially salvageable myocardium subtended by a coronary stenosis. T2w cardiac magnetic resonance (CMR) identifies the AR in large mammals by imaging post-ischemic edema. Previous T2w CMR studies have been performed in dogs, pigs and humans. However, in mice the fast heart rate, flow and motion present challenges to T2w CMR success. The typical 60 ms echo time for edema contrast occupies a large portion of the murine cardiac cycle which precludes using the same T2w methods used in larger mammals. Furthermore, a practical sequence must suppress the intraventricular bright blood and overcome the increase of B0 and B1 inhomogeneity artifacts that accompany a high-field 7T MR environment - all while imaging the entire LV in under 15 minutes. Here, we expand a T2prep approach by comparing fast adiabatic vs. composite RF refocusing pulses. After development, we applied this sequence to image the entire left ventricle (LV) in post-MI mice and jointly applied late gadolinium enhanced (LGE) CMR to assess performance and demonstrate T2w imaging of the edematous AR compared to MI size as percent LV mass.
Methods: We developed a whole-heart, multi-slice, T2w CMR sequence for mice with high immunity to flow and tissue motion artifacts and with dark-blood suppression that maintains sufficient signal-to-noise (SNR) and contrast-to-noise (CNR). Through-plane flow-sensitization gradients were applied during the T2prep to provide dark-blood capability. Through simulation, phantom and *in vivo* imaging, we developed a sequence that employed a non-selective T2prep with Malcolm Levitt-weighted (MLEV), selectable adiabatic or composite refocusing pulses, followed by a multi-slice, gradient-echo readout. We compared the performance of three refocusing pulse types: single rectangular (180_y), composite (90_x:180_y:90_x), and fast (2.4 ms) adiabatic refocusing pulses in MLEV-8 & 16 T2prep implementations. We simulated (Matlab) the three pulse types with simultaneous sweeps of ΔB0 (±1000 Hz) and ΔB1 (±50%) offset conditions with full relaxation modeling. We then imaged multiple T1 & T2 valued phantoms under manually-set ΔB0 (±2500 Hz) and ΔB1 (±50%) offsets. Finally, we performed *in vivo* CMR on post-MI mice to detect and track myocardial edema. We imaged three mice on Days 1 thru 4 after reperfused MI induced by 60-minute coronary occlusion. Imaging parameters included MLEV-8 & 16, adiabatic pulse length = 2.4 ms, TR = 3 sec, TE_{T2prep} = 60 ms, FOV = 25 x 25 mm, slice thickness = 1 mm, matrix = 128 x 128, BW = 520 Hz/pixel. LGE CMR was also performed on Day 1 to define MI size after T2w CMR was completed. All scans were performed on a Bruker 7T ClinScan to cover the entire LV in 6 or 7 contiguous short axis slices in under 12 minutes scan time.
Results: Simulation T2prep M_z output plots (Fig 1, panels A-C) show that both composite and adiabatic refocusing pulses are more resistant to B0 and B1 inhomogeneities compared to single rect refocusing pulses, where the composite and adiabatic pulses respectively gave 51.7 and 115.9 percent improvement over Single Rect pulses (change in green area, panels A-C). Separate phantom ΔB0 and ΔB1 imaging (Fig 1, panels D, E) verified that composite pulses doubled both ΔB0 coverage and ΔB1 tolerance while adiabatic pulses tripled both ΔB0 coverage and ΔB1 tolerance compared to single rect pulses. Figure 2, panels B, D present example *in vivo* Day 2 T2w myocardial edema images in mice that co-localize with LGE infarct pattern of panels A, C. These same panels also show effective flow sensitization dark-blood results and low occurrence of flow and motion artifacts. T2w image SNR was 68±4 and CNR measured between remote myocardium and AR regions was 34±2 (mean±SEM). At the whole-heart *in vivo* perspective, the composite pulses performed equally well as adiabatic pulses in both SNR and CNR with no measurable difference. However, in smaller regions of non-homogeneous B0 or B1 the adiabatic pulses are more tolerant. Overall edema tracking for 4 days post-MI gave a mean AR size of 46.7±1.5 percent LV mass. The mean MI size was 34.3±0.3, therefore, the AR was significantly (36.2%) larger than MI size ($p < 0.01$, ANOVA) with no significant change in AR size from Day 1 through 4. Likewise, the MI size was 73.4±1.2 percent of AR size.
Conclusions: Although adiabatic pulses performed best with large simulated and phantom offsets, they did not completely out-perform composite pulses *in vivo*. This may be significant since composite pulses have a much lower specific absorption rate than do adiabatic pulses. T2w CMR in mice yielded results consistent with those reported in larger mammals. MLEV-16 outperformed MLEV-8 with better image homogeneity in the fast moving mouse hearts. Through T2w CMR, we demonstrated in mice that large MI resulting from an extended coronary occlusion (60-minute) left only 25±1.2 percent of the AR as potentially salvageable myocardium. T2w CMR can now be applied in knock-out mice to study the roles of individual genes and drug interventions on MI size as percent AR. Knowledge from these pre-clinical studies may translate toward improved techniques and therapies for humans.

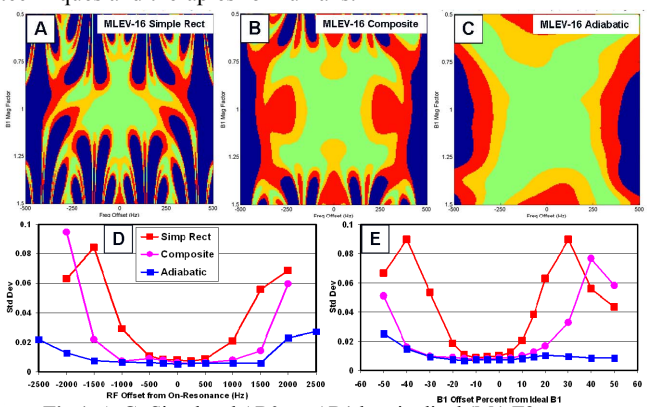

Fig 1. A-C: Simulated ΔB0 vs. ΔB1 longitudinal (M_z) T2prep output with green ≤5%, yellow ≤10%, red ≤20%, blue >20% error. **D, E:** Phantom Std Dev (artifacts) under ΔB0 and ΔB1 conditions.

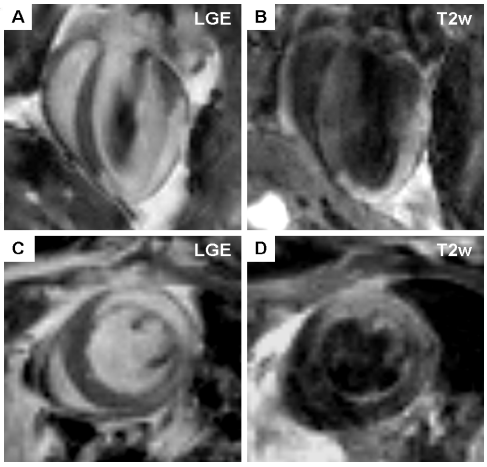

Fig 2. A-D: Same slice long and short axis sets of LGE Infarct and T2w Edematous Area at Risk with good concurrence, effective flow sensitization for dark-blood and low occurrence of flow and motion artifacts.