

# mISIS-CPMG: a Method for Localized Multicomponent T<sub>2</sub> Measurement Immune to Very Short T<sub>2</sub> Relaxation Effects

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**Introduction:** Skeletal muscle T<sub>2</sub>, as obtained from a mono-exponential decay is a sensitive but non specific indicator of muscle activation or of disease activity. When long echo trains are acquired at high sampling rate, a T<sub>2</sub> spectrum can be calculated. In the skeletal muscle, it reveals at least four compartments, with T<sub>2</sub> values ranging from 1 to 200 ms, which have been assigned to macromolecules, intracellular, non-vascular extracellular and vascular spaces fractions [1]. It can be reasonably hypothesized that changes in spectrum of muscle T<sub>2</sub> will, to some extent, reflect the underlying mechanism and will give some specificity to T<sub>2</sub> measurements. Methods for multi-component T<sub>2</sub> measurement which combine single voxel selection (SVS) techniques with the Carr-Purcell-Meiboom-Gill (CPMG) sequence exist but give fairly accurate results only for components with long enough T<sub>2</sub> values (>10 ms) [1,2]. Fast spin-spin relaxation perturbs the response of shorter T<sub>2</sub> components to RF pulses [3]. This leads to unreliable localization and quantification results. The purpose of this study was to develop a method for multi-component T<sub>2</sub> measurement immune to relaxation effects for T<sub>2</sub> ≥ 1 ms. Image selected in vivo spectroscopy (ISIS) [4] stands out among other SVS methods as offering accurate cuboidal voxel selection independently of pulse flip angle. This offers the possibility of an optimization based on the applied RF pulses. The goal was to optimize ISIS by substituting the usual adiabatic inversion RF pulse by a very short partial inversion pulse with a large bandwidth (BW), capable of obtaining identical responses from all T<sub>2</sub> components to be measured, at the cost of smaller SNR.

**Materials and Methods:** The selection BW of Quadratic Phase (QP) pulses may be controlled independently of B<sub>1</sub> amplitude. Adiabatic pulses, usually used in ISIS, present an approximately quadratic phase modulation but the condition for adiabaticity imposes limits on minimum pulse duration. Non-adiabatic QP RF pulses, which do not present the same duration constraints, were designed using the Shinnar-Le Roux (SLR) algorithm [6] to achieve high selectivity and broad BW. In this work, QP-RF pulses were optimized and the magnetization response of both very short and long T<sub>2</sub> species was simulated from Bloch equations with MATLAB (The Mathworks, Inc.). A home-made ISIS-CPMG sequence (Fig. 1) and its optimized version, mISIS-CPMG (modified ISIS-CPMG), were implemented on a 3T whole-body scanner (Tim Trio, Siemens Healthcare). Radio Frequency pulse transmission and detection was performed with a circularly polarized transceiver coil (CP Extremity, Siemens Healthcare). Experimental slice profile of the designed QP pulse was measured over two 1 liter-phantoms with T<sub>2</sub> values of 2 ms and 100 ms, in separate experiments. The mISIS-CPMG and the conventional ISIS-CPMG with an adiabatic Hyperbolic Secant (HS) pulse were applied for T<sub>2</sub> quantification of a 300 mL rectangular volume containing three 50 mL phantoms of 4.8, 0.26 and 0.11 mM MnCl<sub>2</sub> solutions, corresponding to T<sub>2</sub>'s of 2, 36 and 83 ms and T<sub>1</sub>'s of 26, 485 and 960 ms, respectively. The excitation and refocusing pulses in the CPMG were 200 and 400 μs long, short enough to avoid relaxation effects. In both protocols, the applied echo-spacing was 1.5 ms, and 300 echos were acquired; repetition time (TR=10s) was long enough to guarantee full T<sub>1</sub> relaxation. Total acquisition lasted 160 s. Multi T<sub>2</sub> deconvolution was performed by regularized minimum least squares fitting [5].

**Results:** The designed QP RF pulse was 1.7 ms long, with BW = 10 kHz and B<sub>1peak</sub> = 31 μT (Figure 2). The simulated slice profiles obtained with this pulse were virtually identical for short and long T<sub>2</sub> components (Figure 3). The immunity of the designed pulse to transverse relaxation effects was confirmed experimentally (Figure 4). Figure 5 presents the T<sub>2</sub> decay curve obtained from the 3 phantoms with the mISIS-CPMG sequence. In Figure 6, T<sub>2</sub> spectra, obtained with the conventional and modified versions of ISIS-CPMG are compared. Playing ISIS-CPMG with an adiabatic 5 ms long HS pulse resulted in an underestimation of shorter T<sub>2</sub> components of 20%, which was almost completely prevented by the insertion of the shorter QP pulse.

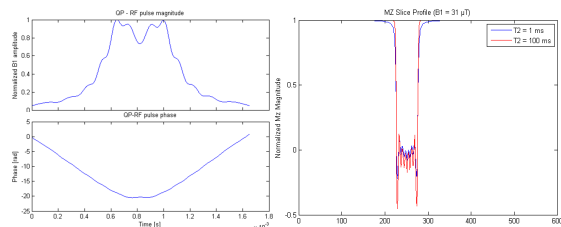


Figure 2: Magnitude and phase of the designed QP RF pulse.

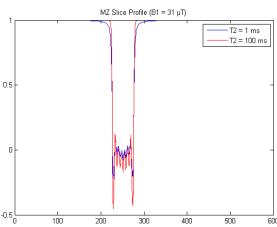


Figure 3: Simulated Mz responses of short and long T<sub>2</sub> components to the designed QP pulse.

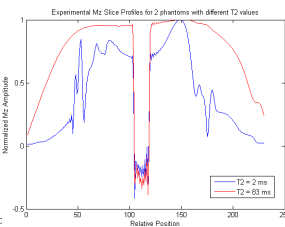


Figure 4: Normalized Experimental Mz responses of two phantoms of different T<sub>2</sub> to the designed QP pulse.

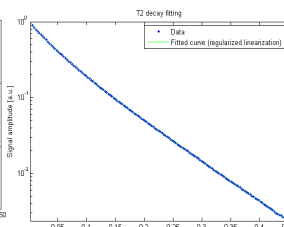


Figure 5: T<sub>2</sub> decay of the three 50 mL phantoms measured with the mISIS-CPMG

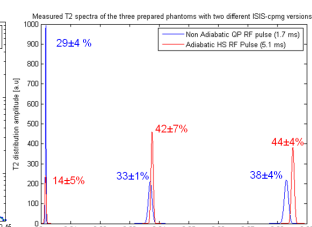


Figure 6: T<sub>2</sub> spectra obtained from both versions of ISIS-CPMG.

**Conclusion:** QP RF pulses can be optimized to obtain adequate excitation of short T<sub>2</sub> components and guarantee identical efficacy and spatial selectivity of magnetization responses over a large range of T<sub>2</sub>s.

When implemented with these pulses, mISIS-CPMG allows localized multi-component T<sub>2</sub> measurement for T<sub>2</sub>s as short as 1ms and will thus give access to more complete and reliable T<sub>2</sub> spectra, which are expected to be of great interest in evaluation of healthy and diseased skeletal muscle.

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