Optimization of spectroscopy-based diffusion measurements of intramyocellular lipids

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Introduction: ^{1}H MR spectra of skeletal muscle feature two distinct contributions from lipids, intramyocellular lipids (IMCL) stored as lipid droplets inside the cytoplasm of the muscle cells and extramyocellular lipids (EMCL) located in fascia along the muscle fibers [1]. It has been established that IMCL play an important role in energy metabolism and are linked to insulin resistance [1]. The diffusion properties of these lipid pools have however only rarely been studied [2], but might add relevant information to lipid characterization. Several factors make diffusion measurements of lipids difficult: rather low diffusion coefficients (ADC) necessitate large b-values, which in turn imply long echo times (TE) and long mixing times (TM), while lipids feature short relaxation times. In addition, use of large b-values causes artifacts induced by strong gradients, such as eddy currents and gradient switching induced motion. Last but not least, the motion of the limbs due to cardiac pulsation leads to additional signal reduction. The current work was aimed at optimizing parameters for diffusion measurements of lipids in muscle and to minimize motion-induced signal variations by application of physiologic gating.

Methods: All spectra were acquired on a clinical 3T system (Trio, Siemens Medical, Germany) using a modified STEAM sequence. (I) Measurements to optimize trigger delays were performed on eight healthy volunteers. For triggering a standard pulse oximetry sensor was used. A ROI of 8 ml, covering mainly EMCL, was placed in the vicinity of a vessel. Parameters for the triggering data: TE 105 ms, TM 150 ms, TR 1000 ms, diffusion gradient amplitude 26 mT/m and duration 25 ms, b-value ~ 16000 s/mm^2. For each triggering delay 16 single scans were acquired with no water suppression applied and separately stored. (II) Measurements on IMCL were performed on two volunteers with and without pulse triggering (trigger delay of 100 ms). The ROI with volume of ~ 5 ml was carefully placed in the tibialis anterior muscle and 128 single scans were recorded (TE, TM, TR as above, no water suppression, diffusion gradient amplitudes of 15, 25 and 32 mT/m with a duration of 30 ms; resulting in b-values of ~ 2000, 21000 and 35000 s/mm^2. Spectra were processed and averaged with and without individual phase correction in MRUI [3].

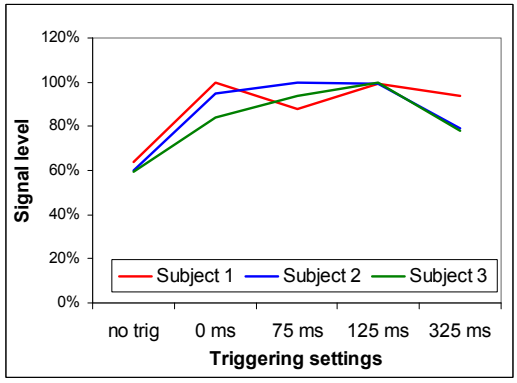

Fig. 1: *Effect of gating and choice of trigger delay on signal amplitude of lipids near a vessel.*

Results: Spectra obtained with large b-values showed large phase variations in phantoms and in vivo. Fig. 1 illustrates the signal gain associated with physiologic triggering (optimal delay was found to be around 100 ms). Even with proper triggering delay the signal phase was found to vary by up to 180°, necessitating storage and phasing of individual acquisitions. Results of IMCL measurements with different protocols are portrayed in Fig. 2, while Fig. 3 summarizes these results in terms of amplitude decay as a function of b-value for the different acquisition and processing strategies.

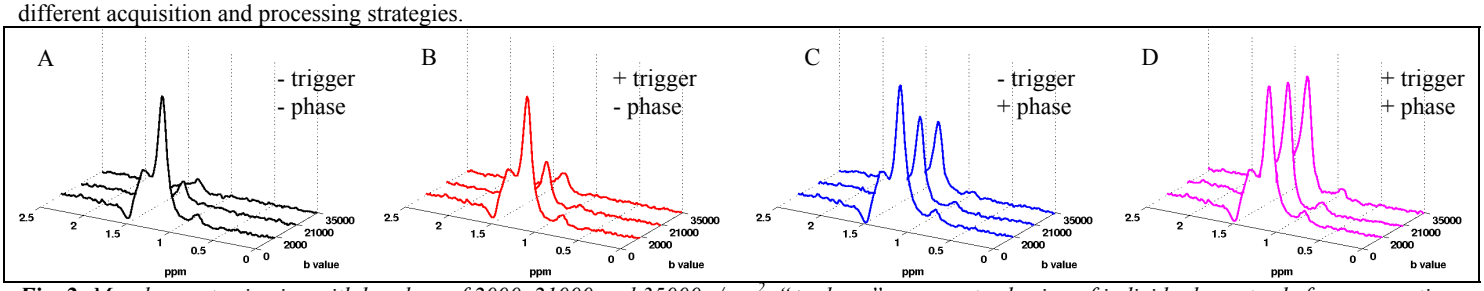

Fig. 2: *Muscle spectra in vivo with b-values of 2000, 21000 and 35000 s/mm^2. "+ phase" represents phasing of individual spectra before summation, "- phase" represents averaging without individual phasing, "+ trigger" stands for triggering enabled, "- trigger" represents cases where triggering was not used*

Discussion: Even though modern clinical MR scanners can deliver strong gradient pulses, diffusion measurements of lipids require long mixing times as well as long diffusion pulses. Gradient induced vibrations appear to lead to large phase shifts that can be corrected by individual phasing of each acquisition. Furthermore, local motion in muscle due to cardiac pulsation needs to be considered when diffusion measurements with large b-values in muscle are performed. If these motion effects are not taken into account, ADC estimation from peak area measurements at different b-values will be systematically flawed and ADC's will be significantly overestimated. As is visible in Fig. 3, the triggering itself is not a satisfactory countermeasure to unwanted signal decay, however, together with individual phase corrections of separate spectra it allows to obtain more reproducible IMCL diffusion measurements *in vivo*.

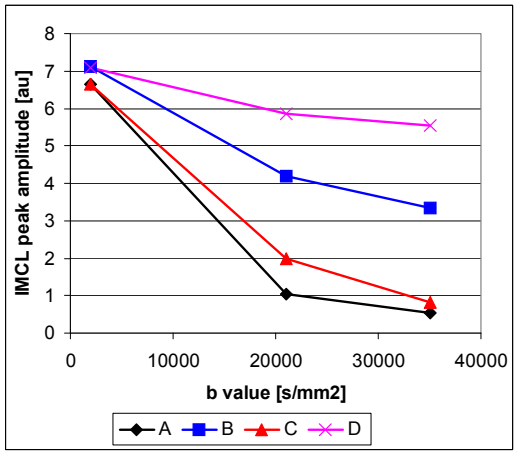

Fig. 3: *IMCL peak area vs. b-value (colors and labeling correspond to those in figure 2)*

References:

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