

Robust Detection of Lactate by STEAM in Human Skeletal Muscle at 7T

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Introduction Despite its pivotal role in energy metabolism and pathology, to physicists and physiologists, lactate remains a challenge for *in vivo* quantitative detection using ¹H MRS. This is mainly due to a combination of the J-modulation of lactate resonances and the interference from the large overlapping lipid and water signals. Various spectral editing techniques have been proposed and tested with lactate phantom at low fields, using zero- or double-quantum coherence (ZQC/DQC) filtering (1-4). Some have been applied to *in vivo* measurements, mostly in the brain. However, it is not clear that whether such an approach holds true for lactate in oriented skeletal muscle where the presence of residual dipolar coupling (RDC) dramatically alters the resonance pattern of lactate. At high fields, the increased ZQC/DQC modulation could potentially lead to dramatic loss of lactate signal. For example, at 7T, the ZQC effect is expected to have a phase-modulation frequency of 834 Hz, which means that, for a STEAM sequence (90°-TE/2-90°-TM-90°-TE/2-Acq) at intermediate TEs (135 - 144 ms), even a variation in mixing time (TM) as small as 0.6 mSec will cause inversion of the signal with implications for lactate quantification *in vivo*. The lactate may be present but not visible because of such modulation if the spectrum is measured with the wrong TM.

Purpose The present study is to demonstrate a strikingly different lactate resonance pattern between phantom and skeletal muscle *in vivo*. High-quality quantifiable ¹H MR spectrum can be obtained for lactate and other metabolites in human skeletal muscle using STEAM sequence without spectral editing.

Methods The protocol was approved by the Institutional Review Board. Four studies were performed in two subjects. The right forearm of each subject was placed on a partial-volume T/R surface coil, parallel to B₀ or at an orientation angle of ~20°. Localized single-voxel ¹H MR spectra were obtained from the flexor digitorum profundus (FDP), before and after 2-min hand-grip exercise, using a 7 Tesla Achieva scanner (Philips Medical Systems) and a STEAM sequence with TR = 1186 ms, 16 average, TE = 140 or 100 ms. TM was varied from 13.0 to 14.5 ms in 0.1 ms step, or 13.0 to 28.0 ms in 1.0 ms step. The same STEAM sequence was also used to acquire spectra from lactate in aqueous solution (50 mM). In addition, for lactate phantom, TM dependence was also measured at long TE 280 ms and short TE 20 ms conditions.

Results and Discussion Lactate in solution showed a doublet at the methyl resonance and a quartet at the methine resonance, and both resonances were sensitive to TM modulation with a periodicity of 1.2 ms (Fig 1a), as predicted by ZQC theory. But this occurs only at intermediate TEs (100 and 140 ms), not at short TE 20 ms or long TE 280 ms, due to very little development or decayed ZQC. In sharp contrast, at intermediate TEs, no phase modulation was observed for lactate signals in the forearm muscle under identical STEAM sequence condition (Fig. 1b). Such TM insensitivity was also observed in a much larger TM range 13 – 28 ms (data not shown) and the effect was completely reproducible. Although the mechanism is unknown, it is possible that the ZQC is somehow quenched by RDC in skeletal muscle under the condition studied. The presence of RDC was evidenced by the decrease in the splitting of lactate CH and CH₃ resonances, from ~20 Hz to ~14 Hz, as the forearm orientation was changed from parallel to 20° (data not shown). Lactate produced after exercise was comparable to total creatine (30 mmol/kg ww), and all metabolite are in-phase without spectral editing.

Conclusion We demonstrated that, for the weakly-coupled lactate resonances, the lesson learned from phantom cannot be applied to skeletal muscle *in vivo*. STEAM sequence without spectral editing offers a simple yet robust means to measure lactate signal in muscle.

References: 1) Sotak CH, MRM 1988,7:364-70; 2) Kingsley PB, Magn Reson Med 1994, 31:315-9; 3) Sotak CH, Alger JR. Magn Reson Med 1991,17:533-8; 4) Kmiecik JA, et al. Magn Reson Med 1997,37:840-50.

Fig. 1. ¹H MR spectra of lactate phantom **a)** and human forearm muscle after exercise **b)**, acquired using STEAM sequence, at varying TM from 13.0 to 13.5 ms, with forearm parallel to B₀ and TE = 140 ms. Note that, lactate signals are sensitive to TM in phantom but not in skeletal muscle *in vivo*. The later showed RDC effect with splitting of 20 Hz at both CH and CH₃ signals. Abbreviation: Acetyl, acetyl group of acetylcarnitine; TMA, trimethylamine group; Cr2/Cr3, total creatine methylene/methyl; IMCL/EMCL, intra- or exa-myocellular lipid.

