Optimal IMCL/EMCL peak separation and full visibility of the dipolar coupled Cr CH3 resonance in human tibialis anterior muscle at 7T

H. E. Kan[1], M. J. Versluis[1], M. A. van Buchem[1], and A. G. Webb[1]
[1]Radiology, Leiden University Medical Center, Leiden, Netherlands

Background. Creatine (Cr) and intra myocellular lipids (IMCL) are central compounds in energy metabolism in skeletal muscle. IMCL is an important metabolite in obesity and diabetes research while Cr, as it commonly shows little inter-individual and regional variation in normal volunteers during resting conditions, is often used for internal calibration to obtain absolute concentrations for other metabolites (1). In ^{1}H MRS of skeletal muscle, the visibility of the signals of these two compounds is influenced by the angle of the muscle fibers with respect to the main magnetic field (1). Unfortunately, the optimal angle for these metabolites differs, making it difficult to reliably quantitate concentrations of both compounds in the same voxel. At the magic angle, for instance, in the soleus muscle (SOL), the signal from extra myocellular lipids (EMCL) partly overlaps the IMCL signal due to the shift of EMCL caused by bulk susceptibility effects (2). In contrast, the CH2 and CH3 resonances of Cr and phosphocreatine are easily visible at this angle, since the residual dipolar couplings that cause splitting of these signals is zero at this angle (3). At an angle of 0 degrees, however, in the tibialis anterior (TA) muscle, the separation between IMCL and EMCL is largest, but the Cr signal displays maximum dipolar splitting. Since the trimethyl ammonium (TMA) resonance commonly overlaps the upfield satellite peak of Cr at clinical field strengths (3 Tesla and below), quantification of Cr is challenging (3). In this study, we aimed to solve this issue by assessing IMCL and Cr levels in the TA at a field strength of 7T. Due to the increased spectral resolution, the full triplet of the CH3 resonance of Cr should be resolved, and IMCL and EMCL signals are separated.

Methods. ^{1}H MRS of the TA muscle was performed in 5 healthy subjects (33 ± 5 years) in a 7T Philips Achieva 58 cm clear bore scanner (Philips Healthcare, Best, The Netherlands) using a home-built, quadrature transmit and receive half-coil. To ensure optimal placement of the coil with respect to the TA muscle, the coil was rotated with its center placed directly above the TA muscle. Water suppressed STEAM spectra were acquired from a voxel (10 x 10 x 10 mm, 4 kHz bandwidth, 2048 points, TR=2 s, TE=21 ms, TM=17 ms, 64 averages) inside the TA muscle. Placement of the voxel was based on T1 weighted gradient echo images. Data were analyzed with jMrui, peaks for total Cr (TCr) and lipids were fitted to Gaussian line shapes, with prior knowledge on the line widths of the satellite peaks of the Cr CH3 resonance and the relative amplitudes of the Cr CH2 resonance. IMCL absolute concentrations were calculated using known relaxation values from the TA muscle (4) and assuming a Cr concentration of 30 mmol/kg wet weight (2).

Results. In all 5 subjects, placement of the voxel in the TA muscle resulted in almost complete separation of the IMCL and EMCL resonances, while both dipolar-coupled peaks of the Cr CH3 resonance were visible (Fig 1C,E). A voxel from the SOL muscle also acquired at 7T is depicted in Fig 1D, for comparative purposes. The separation between the satellite peaks of the CH3 resonance and the middle peak was 12.9 ± 1.5 and 12.4 ± 0.9 Hz for the upfield and downfield resonances, respectively. IMCL concentrations were 3.3 ± 1.8 mmol/kg wet weight. Other characteristics are shown in table 1.

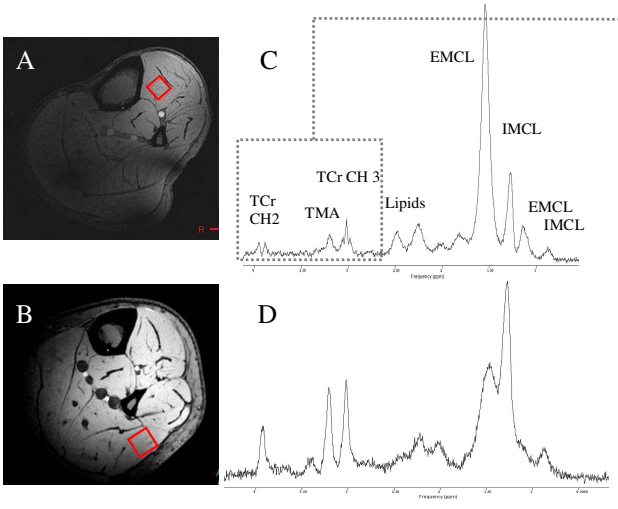

Fig 1. A .Voxel location in the TA (A) and the SOL muscle (B). Corresponding ^{1}H MR spectra are shown in C and D. Note the difference in IMCL-EMCL peak separation between the TA (C) and SOL muscle(D). In (E), the 2.8-4.0 ppm region of the TA spectrum is enlarged, with clear visibility of the dipolar coupling in the Cr signals.

Signal	Line width (Hz)	Separation (Hz)
IMCL	35 ± 14	
EMCL	56 ± 24	72 ± 11
Cr $CH3_{cent}$	18 ± 6	
Cr $CH3_{sat}$	NA	25 ± 2
Cr CH 2	17 ± 3	20 ± 2

Table 1. Characteristics of the IMCL, ECML and Cr signals in the TA muscle at 7T. Note the difference in line width between IMCL and EMCL peaks. The line width of the satellite peaks of Cr CH3 (Cr $CH3_{sat}$) was constrained to the central peak (Cr $CH3_{cent}$). Peak separations are shown between EMCL-IMCL, the two satellites of Cr CH3 and the doublet of Cr CH2.

Conclusion. In ^{1}H MR spectra of the TA muscle at 7T, almost complete separation of the IMCL and EMCL resonances can be combined with full visibility of the dipolar coupled Cr SH3 resonance. This significantly increases the possibilities for accurate quantification of both compounds, using Cr as an internal reference.

References. [1].Boesch C. *J Magn Reson Imaging* 2007;**25**(2):321-338. [2].Boesch C. et al. *NMR Biomed* 2006;**19**(7):968-988. [3].Vermathen P. et al. *Magn Reson Med* 2003;**49**(3):424-432. [4].Wang L. et al *ISMRM* 2008; **3678**