# $^1$H-MRSI Measurements in Human Thigh Muscles – Measurement of Metabolite Distribution and Fiber Orientation and Determination of Reproducibility

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**Introduction:** Determination of metabolite concentrations, including intramyocellular lipids (IMCL), creatine / phosphocreatine (Cr) and trimethyl-ammonium groups (TMA) in human muscles by $^1$H-MRS has been performed mostly in calf muscles by single voxel (SV) techniques. Few SV studies have estimated these metabolites or the fiber orientation with MRS in quadriceps (m. rectus, vastus lateralis, medialis, intermedius). Since quadriceps muscles are of physiological interest and preferred location for biopsies, we determined metabolites and fiber orientation simultaneously in different thigh muscles by MRSI and evaluated the reproducibility.

**Methods:** The thigh of five healthy subjects was measured twice with the subject leaving the magnet between scans. Measurements were performed on a 1.5T system (SIGNA, GE) using a flexible surface coil. A 2D-MRSI sequence with PRESS volume pre-selection was used (transverse orientation, thickness=15mm, Matrix=36×36 (circular sampling), FOV=20cm, TR/TE=1200/35ms). Processing included spatial zerofilling, apodization, chemical shift artifact correction, B0 shift correction, and lipid extrapolation to reduce signal bleeding from EMCL. The spectra were fitted using "TDFDFIT" employing prior knowledge. Metabolites and fiber orientation (obtained from dipolar splittings of Cr and Tau resonances) of each voxel were assigned to one of seven muscles using segmentation (Fig. 1). MR images were acquired with the same sequence (replacing one phase-encoding with a readout gradient) and served as individual references for receive profile intensity corrections. A SV spectrum from bone marrow served as internal reference.

**Results:** Spectral quality was very good in four of five subjects for both, initial and repeated scans. While spectra from one subject (S3) were poor, they were not excluded from the subsequent analysis. Fig. 2 shows a correlation between IMCL contents obtained from the first and second measurements. The linear fit showed a slope and intercept close to 1 and 0, respectively. The correlation coefficient was 0.97. Large IMCL differences were observed between individuals (high between-subject coefficients of variation, CVb, Table). Within subjects, vastus muscles showed only small differences for IMCL levels. Reproducibility of IMCL estimation was good for the vastus muscles: within-subject coefficients of variation (CVw) ranged from 4.5% (VM2) to 14.3% (VL). IMCL determination for other muscles in the thigh (RF, AM) was less reproducible (Table). TMA levels were different between muscles. TMA reproducibility was similar to IMCL (CVw, Table). Cr levels were very similar between muscles. In addition, between subjects only very small Cr differences were noted (low CVb) and reproducibility was high (low CVw). Fiber orientations were different between some muscles. Reproducibility (CWw) was good and between subjects differences were relatively low for fiber orientations.

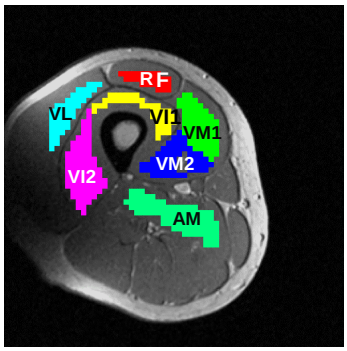


**Fig 1:** Manual segmentation of the thigh, overlaid on a co-registered MR image. Segmented muscles included m. rectus femoris (RF), m. vastus medialis (VM), intermedius (VI), lateralis (VL), and m. adductor magnus (AM). VM and VI were divided into two parts, each.

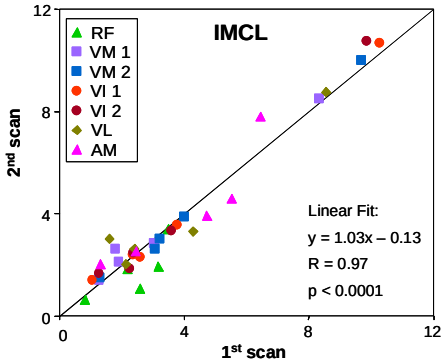


**Fig 2:** Correlation between IMCL levels [a.u.] from the 1st and 2nd scan. Different symbols denote different muscles. Abbreviations for muscles as in Fig.1. The solid line is the identity line.

**Discussion:** Simultaneous determination of IMCL levels and other metabolites in different thigh muscles is possible by MRSI methods with sufficient reproducibility to measure clinically relevant changes. Large interindividual IMCL differences confirmed previous observations. Between the three vastus muscles, differences in IMCL were relatively small. Cr was very similar within and between subjects for all muscles.

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| Muscle | IMCL | | | TMA | | | Cr | | | Fiber orientation | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | mean | CVw | CVb | mean | CVw | CVb | mean | CVw | CVb | mean | CVw | CVb |
| RF | 211 | 30.6 | 49.8 | 14.5 | 30.4 | 38.2 | 46.4 | 8.9 | 8.5 | 14.3 | 14.4 | 15.0 |
| VM 1 | 338 | 8.5 | 85.0 | 26.2 | 11.0 | 29.5 | 47.4 | 5.5 | 6.2 | 23.9 | 8.2 | 15.6 |
| VM 2 | 423 | 4.5 | 77.6 | 25.2 | 6.3 | 26.3 | 45.7 | 2.1 | 9.1 | 25.6 | 4.7 | 8.3 |
| VI 1 | 404 | 5.1 | 91.8 | 33.9 | 4.7 | 22.9 | 46.5 | 2.3 | 5.4 | 34.4 | 7.1 | 12.8 |
| VI 2 | 394 | 8.6 | 92.1 | 43.2 | 5.6 | 17.6 | 48.9 | 6.7 | 10.6 | 38.2 | 4.9 | 6.5 |
| VL | 388 | 14.3 | 72.1 | 49.9 | 11.4 | 22.5 | 45.0 | 11.1 | 10.5 | 34.6 | 12.5 | 25.2 |
| AM | 413 | 15.0 | 53.5 | 38.7 | 10.7 | 25.9 | 44.6 | 8.7 | 7.4 | 30.6 | 4.7 | 17.5 |

**Table:** IMCL, TMA, Cr and Fiber orientation in different muscles of the thigh. Mean values [arbitrary units] for the repeated measurements on 5 subjects ± 1sd. Coefficients of variation [%] within subjects (CVw) and between subjects (CVb) are also given. Abbreviations for muscles as in Fig. 1.