PROTON MAGNETIC RESONANCE SPECTROSCOPY (1H-MRS) OF TIBIALIS ANTERIOR MUSCLE: INTRA-INDIVIDUAL VARIATION OF METABOLITE RATIOS IN HEALTHY VOLUNTEERS

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OBJECTIVE: To determine the short-term intra-individual variation of tibialis anterior metabolite ratios in healthy volunteers measured by 1H-MRS at 1.5T and 3.0T.

METHODS AND MATERIALS: ***Subject selection –*** Thirty-seven healthy subjects (17 males and 20 females; mean age 26 years, age range 19-50 years) with no history of endocrine or metabolic disorders and taking no medications were recruited. Subjects with abnormal fasting glucose and/or lipid profile were excluded. Eligible volunteers were divided in two groups. Twenty-seven subjects (12 males and 15 females; mean age 25 yrs) were scanned at 1.5T, and 10 subjects (5 males and 5 females; mean age 28 yrs) were scanned at 3.0T. No subjects were scanned at both magnetic fields. 1H-MRS of tibialis anterior muscle was performed after 8-hour fasting and repeated on a separate day (mean, 12-day interval; range 4-56 days). ***1H-MRS Technique –*** On each visit, localizer images and 1H-MRS were obtained before and after repositioning of subject in the magnet. All subjects were required not to change usual physical activity and dietary habits for the duration of the study, avoiding physical effort or high-fat diet 72 hours prior to scanning. 1H-MRS data at 1.5T was acquired using PRESS (TR/TE) 3000/25ms at 1.5T, and 3000/30ms at 3.0T. In all cases, a voxel measuring 3.4 mL was placed avoiding visible fat using a rigorous method based on osseous landmarks. Automated and/or manual shimming was performed for each voxel placement, obtaining water line widths of ~11 Hz. Water presaturation was used for metabolite acquisition and unsuppressed water spectra of same voxel were obtained for each scan. ***Quantification –*** All spectra were quantified using jMRUI and AMARES;[1] and LCModel with a new fitting algorithm developed specifically for analysis of muscle 1H-MRS.[2] Intramyocellular lipid CH_2-protons (IMCL, 1.3 ppm) and total creatine (TCr, ~3.0 ppm) were quantified relative to unsuppressed water peak (W, 4.7 ppm) of same voxel. IMCL was also quantified relative to TCr. Intraday (i.e., same-day) and inter-visit (i.e., repeat scan on separate day) coefficients of variation for all ratios were obtained.

RESULTS AND DISCUSSION: A total of 144 spectra were obtained, of which 127 were utilized for statistical analysis (96 at 1.5T, 31 at 3.0T). Seventeen spectra were discarded due to poor residuals after peak fitting. Results are shown in Table 1. The most significant variability arose from inter-visit IMCL/W and IMCL/TCr, which reflect biological changes, instrumental instability, and positional factors. Metabolite quantification in muscle is also influenced by angular dependence of lipids and creatine resonances, which affect peak resolution, linewidths and reliable detection of TCr neighboring peaks.[3] A slightly higher inter-visit CV was noted at 3.0T, which may be secondary to small sample size. Intraday CVs for IMCL/W were similar regardless of software or magnetic field. Intraday variability is affected by technical factors (system stability, patient and voxel positioning) and no influence from biological change is expected. Our results indicate that despite rigorous positioning and careful pre-scanning adjustments, technical factors may obscure intraday changes of IMCL-CH_2 within the 10% range. For same-day studies of IMCL at 1.5T, our results suggest that IMCL/W is preferable to IMCL/TCr, regardless of data analysis software. At 1.5T, LCModel allows more consistent measurement of TCr/W as it accounts for neighboring TCr signals.[2] At 1.5T, jMRUI shows higher CVs for TCr/W and IMCL/TCr probably due to suboptimal model assuming similar linewidths for choline (3.2 ppm) and TCr. This is partially improved at 3.0T due to enhanced spectral resolution. For the purpose of longitudinal studies, there appears to be no significant benefit of employing higher fields to decrease variability, and IMCL/W or IMCL/TCr measured with LCModel could be employed interchangeably. CVs for these ratios (17-22% range) may not negatively affect longitudinal observation in IMCL-accumulating diseases such as type 2 diabetes, obesity and HIV-lipodystrophy, which show increased IMCL concentrations in the 25-210% range when compared to controls. Physiologic variation of IMCL could be further decreased by prescribing strict diet and enforcing limited physical activity for subjects involved in longitudinal studies.

Table 1.

		1.5 T (n=27 pts, 96 spectra)		3.0 T (n=10 pts, 31 spectra)	
	Parameter	**LCModel**	**jMRUI**	**LCModel**	**jMRUI**
IMCL/W	Intraday CV	9%	9%	9%	9%
	Inter-visit CV	18%	17%	20%	23%
TCr/W	Intraday CV	5%	8%	5%	5%
	Inter-visit CV	3%	8%	5%	5%
IMCL/TCr	Intraday CV	11%	14%	9%	10%
	Inter-visit CV	17%	22%	19%	25%

CONCLUSION: Variability of 1H-MRS IMCL and TCr ratios in tibialis anterior muscle allows for quantitative estimates of biologically relevant changes occurring in IMCL-accumulating states.

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