Measurement of Intramyocellular Lipids in Obese Subjects Using Spectroscopic Imaging with High Spatial Resolution

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Introduction: Intramyocellular lipids (IMCL) quantification in obese subjects by single voxel ^{1}H spectroscopy and conventional MRSI fails often due to overlap of IMCL by a strong extramyocellular lipids (EMCL), and by strong signal contamination from subcutaneous fat and bone marrow. EMCL signals are typically 1 to 2 orders of magnitude larger than IMCL signals, they often cause artefacts or bleed into IMCL peak even if proper EMCL apodizations are applied. Several methods have been reported to eliminate these problems with post-acquisition processing [1,2]. None of the methods offers general solution. Conventional high-resolution spectroscopic imaging (MRSI) with large number phase encoding steps (e.g. 128x128 or more) can be efficient in removing those obstacles. However, it requires unacceptable long acquisition time to acquire all k-space encodings. High-resolution spectroscopic imaging with the read gradient during acquisition [3] is capable to solve the problem of long acquisition time. The goal of our study is to test whether this method can generate ^{1}H spectra of well resolved IMCL and EMCL in calf muscle of obese subjects.

Materials and Methods: Six healthy sedentary (BMI = 20.7 ± 1.6 kg/m^2, mean ± SD), and five obese non-diabetic female subjects (BMI = 38.7 ± 3.8 kg/m^2) were studied. All data were acquired on a 1.5 T Gyroscan Intera (Philips) whole-body clinical scanner using a knee coil. Multi-slice T1 weighted spin echo images were first acquired to guide positioning of the measured slice and VOIs (Fig. 1). MRSI technique consisted of a 2D, rf spoiled gradient echo sequence with step increment of TE ($\Delta TE/TE_1/TR$ = 2.6/8/150 ms) [3]. Image matrix (256, 256), FOV = 180 mm and 128 phase encoding steps led to resolution in the plane of 0.7x1.41 mm. The slice thickness was 15 mm and bandwidth per pixel 135.7 Hz. Spectral bandwidth 6 ppm and spectral resolution 0.125 ppm was achieved with 48 image records. The net measurement time was 15 minutes 22 seconds (1 acquisition). Slice selection was performed by using the fat selective binomial $1\bar{1}$ excitation pulse ($\alpha = 40^o$). The bandwidth for full excitation was in the range of <0; 3> ppm, i.e., in the range of methylene and methyl protons of fatty acids. We emphasize that the broad fat excitation bandwidth and moderate water suppression were the reasons for using $1\bar{1}$ excitation pulse. The sensitivity to low IMCL signals was sufficiently improved and the muscle's water lines remained higher than fat lines (Fig. 1c). It was then possible to compute the magnetic field distribution $\Delta B(x, y)$ in the slice either from the spectral position of the methylene EMCL line or residual water line in each pixel (voxel). A post-detection data processing scheme was used which permits spectral artifact corrections caused by chemical-shifts, spectral line aliasing and magnetic field inhomogeneities $\Delta B(x, y)$ [3]. The magnitude spectra were calculated by summation of the thousands (10^3 - 10^4) of voxel spectra. Figures 1a, b, c show irregularly shaped VOIs and the correspondent spectra. To improve IMCL detection, the voxels with large amount of EMCL were removed (Fig. 1c). The magnitude spectra were processed by the Magnetic Resonance User Interface (MRUI) software package [4]. The input time domain data were computed by inverse FFT. The even and odd points of the magnitude spectrum were used in inverse FFT as the real and imaginary data, respectively. Methylene EMCL and IMCL peak areas (Fig. 1d) were determined with AMARES [5], which is implemented in the MRUI. Prior knowledge was proposed in [3]. Fat content was assessed using methylene spectral intensity of the central part of tibial bone marrow as the internal reference with 100 % fat content.

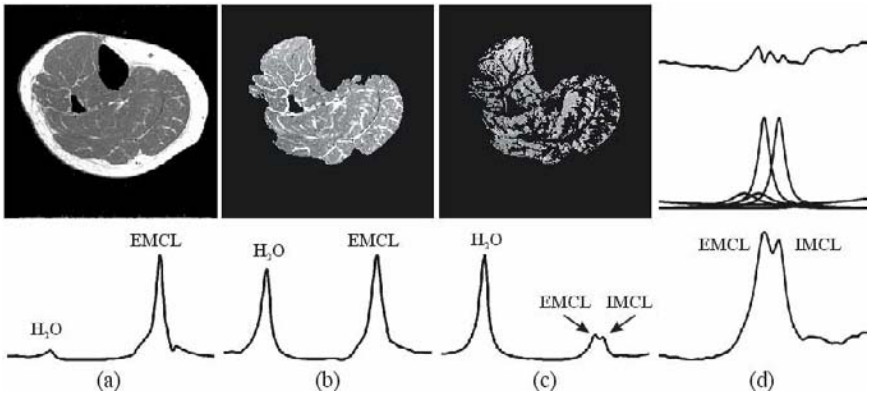

Fig. 1 Calf of the obese subject. VOIs and water suppressed magnitude spectra. (a) The whole slice without bones and bone marrows. (b) Soft tissue with the muscles and interstitial fat. (c) Muscles with partial elimination of the interstitial fat. This VOI was obtained by thresholding of the MRSI fat image. (d) MRUI analysis of the fat lines from (c), fitted Lorentz lines and residuals.

Results: Fig. 1 shows VOIs and the correspondent water suppressed spectra of the representative obese subject (BMI = 41.2 kg/m^2). Spectra of lean muscles of all subjects show good IMCL and EMCL separation (Fig. 1c, d). Table 1 presents mean lipid content and ± standard deviations of the whole study group. Multiplication by 10.1 is needed to convert our volume % into mmol/kg wet weight [6]. At the baseline study, control subjects have lowered both EMCL and IMCL concentrations then the obese subjects. The lowest differences are, surprisingly, in the total fat content of the whole slice (Fig. 1a). The most significant differences are in EMCL and IMCL concentrations of the muscles (Fig. 1b, c). Lipid content has been relatively stable for the control subjects.

Table 1. Mean lipid content (volume %)

	EMCL		IMCL
VOI	Fig. 1a	Fig. 1b	Fig. 1c
obese	33.6 ± 5.1	5.0 ± 1.5	0.47 ± 0.16
control	21.8 ± 4.6	1.3 ± 0.5	0.21 ± 0.11

Discussion and Conclusion: To our knowledge, this is the first time that a MRSI with high spatial and relatively high spectral resolution was used for evaluation of IMCLs of obese subjects. The technique do not requires shimming and VOIs are defined in the post processing. The use of a large number (128) of phase encoding steps minimizes contamination of the spectra due to signal bleeding from subcutaneous or interstitial fat and bone marrow. The method offers possibility to study different muscle groups and the variation of lipids within one muscle. The small voxels that can be achieved facilitate differentiation between EMCL and IMCL.

References: 1. Haupt CI et al, Magn Reson Med 35:678 (1996). 2. Vermathen P et al, Magn Reson Med 51:253 (2004). 3. Weis J et al, Magn Reson Med 54:152 (2005). 4. http://www.mrui.uab.es. 5. Vanhamme L et al, J Magn Reson 129:35 (1997). 6. Boesch C et al, Proc. Nutr. Soc. 58:841 (1999).

Acknowledgements: Supported by Swedish Research Council (K2003-71X-06676-21A). The authors thank to F. Ortiz-Nieto for data processing.