Assessment of Lipids in Skeletal Muscle by LCModel and AMARES

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Introduction

^{1}H-MRS permits investigation of lipid metabolism. Two components of the lipid signals are distinguishable: extra- (EMCL) and intramyocellular lipids (IMCL) [1, 2]. The absolute quantification of EMCL and IMCL depends on the ability to distinguish the methylene spectral line of IMCL ($IMCL_{CH2}$) from $EMCL_{CH2}$, on relaxation corrections and on the accuracy of the constants that allow the conversion of the $EMCL_{CH2}$ and $IMCL_{CH2}$ spectral intensities to the absolute concentration (mmol/kg wet weight). Because of these difficulties, the majority of the studies used the relative measures fat-to-total creatine ratio or fat-to-unsuppressed water ratio. The goal of the present study was to develop a prior knowledge for an advanced method for accurate, robust and efficient spectral fitting (AMARES) [3] to distinguish $EMCL_{CH2}$ spectral line from $IMCL_{CH2}$ and to compare absolute concentration of muscle lipids estimated by the linear combination of model spectra (LCModel) [4] and AMARES, which is a part of the jMRUI software package [5].

Materials and Methods

Fifteen muscle spectra (calf) of five healthy men with body mass index ranged from 24.2 to 36.8 kg/m^2 were measured. The experiments were performed on a 1.5 T Gyroscan MR system (Philips). Single-voxel MRS was performed using a PRESS sequence (TR/TE 3000/25 ms, BW 1000 Hz, 1024 points). Sixteen non-water-suppressed scans were followed by 64 water-suppressed. The voxel size was 10x10x15 mm^3. Prior knowledge for AMARES was developed using the spectrum of vegetable oil with a small amount of water (Fig. 1). Water line was placed to 4.77 ppm and seven resonances of oil were fitted by Lorentzians. The position, linewidth, intensity of water and lipid methylene (CH_2) line was estimated by AMARES. The positions, linewidths and intensities of the lipid lines nos. 1-6 (Fig. 1) were defined using fixed values in respect of CH_2 line. Spectral line positions and intensities were determined using the results of high-resolution spectroscopy [6]. Fixed frequency shifts 256.9, 186.59, 95.21, 51.76, 19.81, and -25.56 Hz were used between CH_2 line and lines nos. 1-6, resp. Intensities were computed by multiplications of CH_2 intensity by fixed values 0.151, 0.06, 0.032, 0.306, 0.114, and 0.134. Linewidths were determined by multiplication of the CH_2 linewidth by fixed values 1.28, 3.0, 1, 3.05, 3, 0.92. The unsuppressed water line was fitted first. Its position was used to shift the water-suppressed spectrum to ensure that the suppressed water line was exactly at 4.77 ppm. The position of $IMCL_{CH2}$ line was fixed to 1.3 ppm. $IMCL_{CH2}$ linewidth was constrained to the interval 7.1±0.1 Hz. The position and linewidth of the $EMCL_{CH2}$ peak was constrained to the interval <1.37;1.55> ppm and <7;12> Hz, resp. The positions, linewidths and intensities of two series of EMCL and IMCL resonances nos. 1-6 (Fig. 1) were fixed in respect to the $EMCL_{CH2}$ and $IMCL_{CH2}$ lines. Baseline correction was performed by truncation of the first two points of the FID and by applying the HLSVD filter to remove residual water resonance. The zero-order phase correction was estimated by AMARES. First-order phase correction was fixed to zero. The total lipid content in the musculature was computed from the ratio of $EMCL_{CH2}$+$IMCL_{CH2}$ and unsuppressed water line. Intensities were corrected for relaxation effects using the expression: $\exp(-TE/T_2)[1-\exp(-TR/T_1)]$ and relaxation times T_1 = 1300 ms, T_2 = 28 ms for water and T_1 = 340 ms, T_2 = 85 ms for the $EMCL_{CH2}$ and $IMCL_{CH2}$. To convert the methylene-to-water spectral intensity ratio (Z) to absolute concentration, we used the equation [7]: $LC = ZWx10^6/[885.4DT(ZW+P)]$ where LC is the lipid content in mmol/kg ww, W = 0.76 represents the relative tissue water content to total weight (kg/kg) of the muscle tissue, T = 1.024 is the weighted density of the fat relative to the triolein standard (molecular weight 885.4), D = 1.05 kg/liter is the density of lean muscle tissue and P = 0.61 represents the relative CH_2 proton density (mol/mol) of tissue fat vs. water. The LCModel was customized by the manufacturer (v. 6.1-4F). $EMCL_{CH2}$ and $IMCL_{CH2}$ concentrations were computed as mM, and were corrected for T_1, T_2 relaxation effects of the water reference using LCModel's control parameter atth2o. This value was determined by the same expression and relaxation times as in AMARES. The concentration of lipid molecules was computed from $EMCL_{CH2}$ and $IMCL_{CH2}$ concentrations by division by factor 31. The value 31 is based on the assumption that the average number of CH_2 protons is 62 per triacylglycerol molecule (31 CH_2 groups) [8]. The resulting concentration was then corrected for relaxation effects of the CH_2 lines using the same equation and relaxation times as in AMARES. Division by the muscle tissue density (1.05 kg/liter) was performed to convert mM to mmol/kg ww. The correlation analysis was performed to evaluate the relationship between lipid concentrations estimated by AMARES and LCModel.

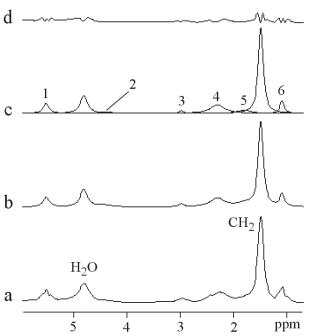

Fig. 1: Spectrum of vegetable oil processed by AMARES. (a) Measured, (b) fitted spectrum, (c) components, (d) residue.

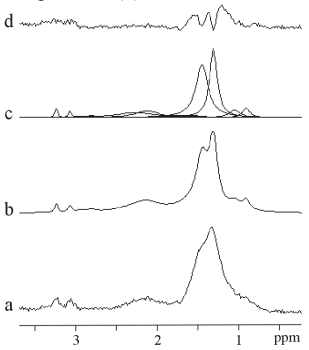

Fig. 2: Spectrum of soleus muscle processed by AMARES. (a) Measured, (b) fitted spectrum, (c) components, (d) residue.

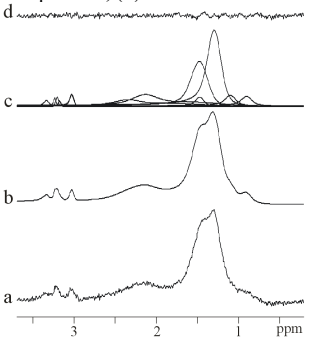

Fig. 3: Spectrum of soleus muscle processed by LCModel. (a) Measured, (b) fitted spectrum, (c) components, (d) residue.

Results

Figures 2 and 3 illustrate the spectrum of the soleus muscle fitted by AMARES and LCModel, resp. Figure 4a shows the scatter plots and regression lines (solid lines) that illustrate the correlation between total lipid concentrations estimated by LCModel and AMARES. Correlation of IMCL concentrations are shown in Fig. 4b. Number of spectra used for the correlation of IMCL was reduced to six. Nine spectra with indistinct $IMCL_{CH2}$ spectral lines due to overlapping $EMCL_{CH2}$ peaks were excluded.

Discussion

Very good correlation of the total lipid and IMCL concentrations was achieved between AMARES and LCModel data processing (Fig. 4). The correlation coefficient was 0.984 for total fat content (Fig. 4a). This result is appealing, taking into account different spectrum processing methods. Figure 4b shows the relationship between IMCL concentrations. Correlation is very good (r = 0.997), however, the slope (1.33) differs more from the identity line compared to the slope (1.12) of total lipid content shown in Fig. 4a. The correlation was probably impaired by decreased accuracy of $IMCL_{CH2}$ fits due to difficulties in separation of $IMCL_{CH2}$ spectral line from dominant $EMCL_{CH2}$. Deviations in absolute concentrations computed by LCModel and AMARES can also be explained by differences in prior knowledge, baseline corrections and by limited precision of the parameters P, D, T, and W.

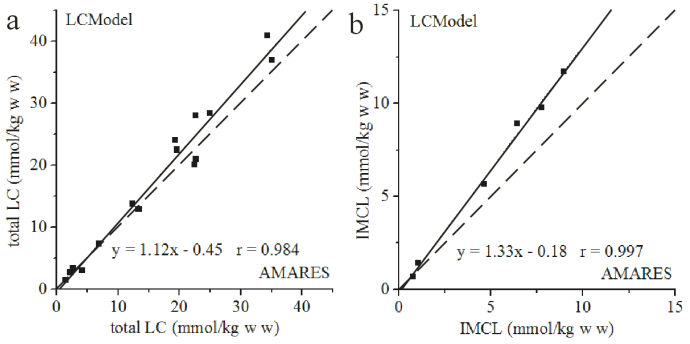

Fig. 4: Correlation of the lipid content estimated by LCModel and AMARES. Correlation of total lipid content (a), and IMCL (b). Dashed line is identity.

Conclusion

Assessment the absolute concentrations of muscular lipids by AMARES and LCModel can be performed with comparable accuracy.

References

[1] Schick F et al, Magn Reson Med 1993;29:158. [2] Boesch C et al, Magn Reson Med 1997;37:484. [3] Vanhamme L et al, J Magn Reson 1997;129:35. [4] Provencher SW. Magn Reson Med. 1993; **30**: 672. [5] Naressi A et al, MAGMA 2001;12:141. [6] Kamba M et al, J Magn Reson Imag 2000;11:330. [7] Szczepaniak LS et al, Am J Physiol 1999;276:E977. [8] Boesch C et al, Proc Nutr Soc 1999;58:841.