Angular Dispersion and Average Orientation of Bulk Triglycerides: Influence on the Proton Lineshape from Extramyocellular Fat

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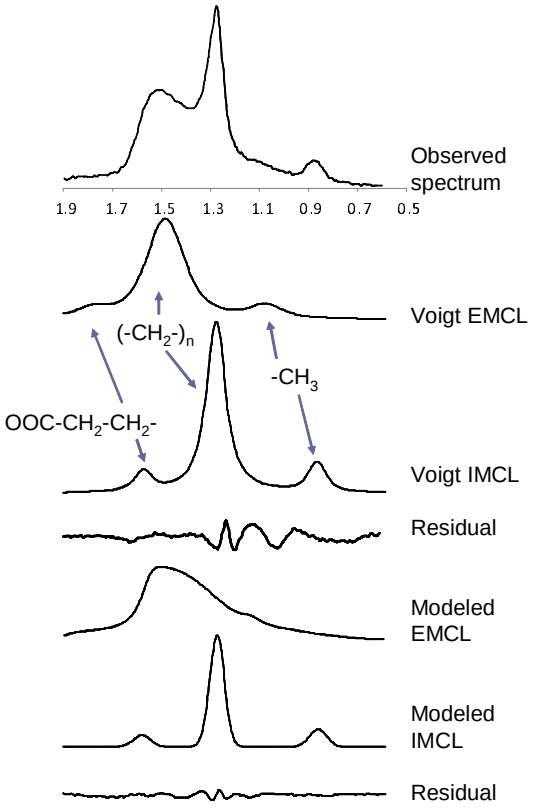
Background: Storage and oxidation of fatty acids play a central role in skeletal muscle metabolism, so it is not surprising that a major research topic in proton NMR spectroscopy is analysis of triglyceride concentration in the intra- and extracellular compartments (1). Extramyocellular lipids (EMCL) may be approximated as strands or cylinders parallel to one another, and intramyocellular lipids (IMCL) are thought to be spherical droplets. The dominant orientation of muscle fibers and possibly EMCL varies between muscles. Chemical shift differences result from small differences in magnetic susceptibility of fat compared to water and the difference in susceptibility of two different geometric structures. However, the signal from the EMCL compartment often overlaps the IMCL signal. Conventional fitting methods assume that both the IMCL and EMCL signals can be represented as single Lorentzian, Gaussian or Voigt lines. In reality, the EMCL signal is often asymmetrical (2, 3). The EMCL lineshape has been estimated by acquisition of reference spectra from bone marrow or extracellular fat and post-processing. We explored an alternative to assess lineshape of the extracellular resonance from single-voxel spectra without acquisition of reference spectra from other anatomical regions.



Methods: The fraction of cylinders at any angle 0 to 90° relative to Bo was described by a Gaussian function centered at specific angle and a width representing the dispersion of orientations. The angular term that governs the relative chemical shift ω of each cylinder was determined from $\omega=3\cos^2\theta - 1$, where θ is the angle between the EMCL and the applied field. The maximal shifts at 0° and 90° were determined in experiments with phantoms. Simulations were generated using muscle fiber orientations reported previously (4) and fit using Voigt, Lorentzian or Gaussian lineshapes. A least-squares fitting algorithm was used to estimate the six overlapping components of the region of interest, the IMCL and EMCL resonances from protons in the $-CH_3$ groups, $(-CH_2-)_n$ groups, and the $-CH_2-$ group β to the carbonyl. Under IRB approval, single-voxel STEAM spectra were acquired from soleus and gastrocnemius muscle of healthy human subjects at 7T (Philips Medical Systems, Cleveland, Ohio).

Results: In simulations with a dominant angle of 0° relative to the applied field and little dispersion of orientations, the Voigt lineshape accurately determined the relative IMCL/EMCL resonance areas over a wide range of linewidths from both compartments. Increasing dispersion of orientations caused an overestimation of IMCL / EMCL, up to 3 fold, when fit using Voigt, Lorentzian or Gaussian lineshapes. This error was reduced using the least-squares algorithm which accurately returned the central orientation and dispersion of EMCL strands in analysis of simulated spectra. The improvement in curve fitting is illustrated in the Figure from the soleus of a healthy volunteer. The observed spectrum from 0.5 - 1.8 ppm is shown in the upper panel. The estimated EMCL and IMCL signals from methyl, bulk methylene $(-CH_2-)_n$ and CH_2 β to COO, as well as the residual, are shown assuming Voigt lineshape. Results from the alternative fitting method are shown. Both the residual and estimated IMCL / EMCL are reduced. In this example the average orientation of extracellular triglycerides was 35° relative to Bo with a dispersion width of 24°.

Conclusion: Markedly asymmetrical signals from EMCL may overlap with IMCL resonances. The significance of this interaction for quantitation of IMCLs varies with average bulk orientation and dispersion of orientation of lipid strands in the extracellular compartment. The use of symmetric lineshapes to fit the EMCL and IMCL signals tend to overestimate IMCL/EMCL but the effect is negligible if essentially all strands of extracellular fat are parallel to one another. A smoothly-varying function describing orientation and angular dispersion of extracellular fat improves line fitting.

References: 1) Boesch et al. NMR Biomed. 2006; 19: 968-88. 2) Steidle et al. J Magn Reson. 2002; 154: 228-35. 3) Boesch et al. NMR Biomed 2006; 19: 968-88. 4) Vermathen et al. Magn Reson Med. 2003; 49: 424-32.