Spatially resolved measurement of bone marrow fat content and unsaturation index via spectroscopic MR imaging

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Introduction

Fatty acid triglycerides are ubiquitous in nature. They are the major components of fatty marrow dominant in long bones, a generic chemical structure and proton MR spectrum being shown in Fig 1. The major constituent of hematopoietic marrow, found in the ribs, trunk and proximal femur, is water. Osteoporosis has been shown to be associated with changes in marrow composition, particularly increased fat content (FC) and decreased fat unsaturation index[1] (UI, the fraction of olefinic protons) at sites of hematopoiesis such as the vertebrae[2]. The primary manifestation of osteoporosis, however, is reduced in trabecular density and altered architecture resulting in decreased spectral linewidth (often quantified by R_2* or R_2') of the fatty acid mid-chain methylene protons). Spatially resolved measurement of these three indicators of bone quality are potentially obtainable from a single chemical shift imaging (CSI) scan. Previously, a rapid CSI technique has been reported for measuring R_2*, R_2 and R_2' of the mid-chain resonance[3]. In this work the potential of the IMGE-CSI[4] sequence to measure marrow UI and FC is examined.

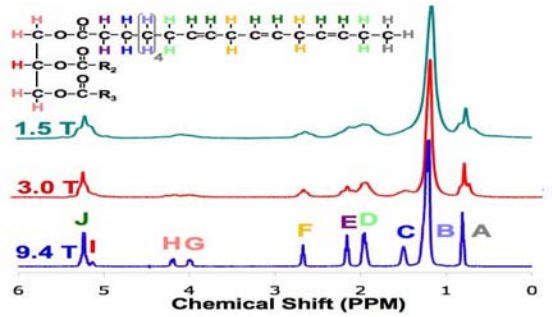

Fig. 1 Corn oil proton MR spectra acquired at 1.5 T, 3.0 T, and 9.4 T. Inset: structure of a typical triglyceride (fatty acid R_1 has be set to Linolenic acid). Note color coding of protons on chemical structure and assignments on 9.4 T spectrum: terminal methyl (A), mid-chain (B), β-carboxy (C), allylic (D), α-carboxy (E), diallylic (F), glycerol (G,H), methine glycerol (I), olefinic (J).

Materials and Methods

Unsaturation Index: A "gold standard" UI measurement of five model triglycerides of varying fatty acid composition (peanut, canola, corn, olive, safflower oils) was obtained from spectra acquired at 9.4 T (Bruker DMX 400). UI was calculated as: $UI = I_{olefinic} / I_{total}$, where $I_{olefinic}$ is the integral of the olefinic resonances, and I_{total} is the integral of the entire spectrum. Spatially resolved proton spectra of the same vegetable oils were acquired at 1.5 T (Siemens Sonata) and 3.0 T (Siemens Trio) using the IMGE-CSI[4] sequence implemented in the SequenceTree[5] environment: flip angle = 90°, TR = 2 s, slice thickness = 5 mm, in-plane resolution = 2.5 × 2.5 mm^2 (FOV = 180 × 180 mm^2, acquisition matrix = 72 × 72), number of echoes = 50, echo spacing = 6 ms, and number of interleaves = 6, providing an effective ΔTE of 1 ms (spectral bandwidth = 1 kHz). Data processing was performed in IDL. FT was performed in the 2 spatial dimensions and the interleaves reordered to provide a matrix of spatially resolved FIDs. Individual FIDs were zero-filled to 1 second and Fourier transformed to produce proton spectra for each pixel. Because the olefinic and methine glyceryl resonances are not resolved at 1.5 T or 3 T, and because the ratio of methine glyceryl to terminal methyl protons in these fully relaxed spectra is 1:9, UI was estimated as: $UI = [I(4.5\text{-}6.0) - \frac{1}{9}I(0.5\text{-}1.05)] / I(0.0\text{-}6.0)$ where I is the integral over the ppm range specified by the parentheses. A 3 T proton spectrum was acquired at the mid tibia of a healthy 30 year-old male volunteer where the marrow is entirely fatty and the UI estimated to demonstrate the feasibility of this approach.

Model of trigylceride proton spectrum: In hematopoietic marrow, the olefinic and water resonances are not resolvable, confounding estimates of *UI* and *FC*. Line broadening due to the presence of trabeculae exacerbates this problem. Construction of a model triglyceride proton spectrum enables coefficients representing the resonance integrals to be obtained via a non-linear least squares regression. An approximation, adequate for data fitting at 1.5 T and 3.0 T, was constructed on the basis of literature data[6] and from comparisons of the corn oil spectra acquired at 1.5, 3 and 9.4 T, and is summarized in Table 1.

Fat content: Fat content of marrow is usually presented as fat volume fraction[4] which is typically in the range from 0.2 to 0.7 in the L2-4 vertebrae[2]. However, for the simulation performed here it is convenient to define fat content (FC) as: $FC = I_{Triglyceride} / (I_{Triglycerid} + I_{Water})$[1], where $I_{Triglyceride}$ is the integral of all triglyceride resonances and I_{Water} is the integral of the water resonance. Using this definition, and to evaluate our method, a fictitious water resonance was added to the 1.5 T and 3 T corn oil spectra (Fig. 1) so that FC varied from 0.3 (representing young healthy controls[1]) to 0.6 (representing older subjects or osteoporotics[1]) in increments of 0.05. The resulting spectra were then fit to a multi-Lorentzian model.

Effect of spectral line broadening and Gaussian noise on UI and FC estimates: Field gradients due to the magnetic susceptibility difference between bone and marrow causes broadening of the proton resonances which complicates *in vivo* UI and FC measurements. To investigate the robustness of the model fitting technique, a synthetic mixed marrow proton spectrum was constructed with UI of 0.06 and FC of 0.45. Line broadening and noise corruption was applied to the model, and UI and FC estimated from coefficients obtained from a non-linear regression. The "signal" was defined as the total integral under the spectrum and "noise" as the standard deviation of the array of uniformly distributed random numbers added to the model spectrum. Line broadening was quantified by R_2': linewidth = $(R_2 + R_2')/\pi$, where R_2/π is the linewidth of a resonance in the absence of trabeculae. The R_2' value of the model spectrum was varied from 0 s^{-1} to 100 s^{-1}.

Results

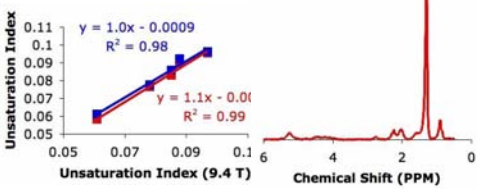

Fig 2. UI measured at 1.5 T (red) and 3 T (blue) Vs "gold standard" UI measurement at 9.4 T

Fig. 3 Bone marrow spectrum at mid tibia of a 30-year old male volunteer 3.0 T, UI = 0.059.

Res.	PPM	*J* values (Hz)
A	0.85	6.57 (triplet)
B	1.25 1.27	
C	1.54	
D	2.01	
E	2.21	7.33 (triplet)
F	2.71	4.21 (triplet)
G	4.03	
H	4.24	
I	5.17	
J	5.28	5.20 (triplet)

Table 1 Model spectrum. Integrals (I) were normalized so: $I_A = 9$, $I_C = I_E = 6$, $I_G = I_H = 2$, $I_I = 1$. Normalization factor, each res. linewidth were variable.

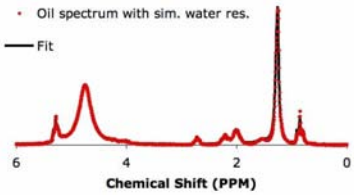

Fig. 4 Corn oil spectrum (3 T) with fictitious water peak inserted (FC = 0.45), together with multi-Lorentzian line fit. Regressions were successful at 1.5 T also.

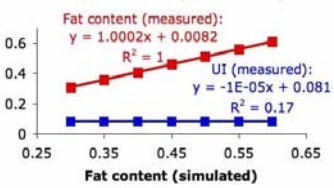

Fig. 5 Measured FC and UI vs simulated FC (3 T). Similar plots were generated for 1.5 T.

Fig. 2 shows the correlation between UI measured at 1.5 and 3 T and the "gold standard". An *in vivo* measurement of 0.059 for UI was obtained for bone marrow of a volunteer (Fig. 3). The model spectrum summarized in Table 1 was successfully used to describe the spectrum with fictitious water peak via non-linear regression (Fig. 4) to enable reliable measurements of UI and FC (Fig. 5). Line fitting was robust in the presence of line broadening but required adequate SNR.

Conclusions: The data suggest that spatially resolved unsaturation index and fat content of bone marrow can be measured using the IMGE-CSI pulse sequence and multi-Lorentzian line fitting. The method may provide a new tool for assessing multiple indices of bone quality non-invasively.

References: 1) Yeung et al., JMRI, 22:279 (2005). 2) Wehrli et al., Radiology, 217:527 (2000); 3) Jones et al., Proc ISMRM, 1709, (2006). 4) Hilaire et al., MRI, 18:777 (2000). 5) Magland et al., Proc ISMRM, 3032, (2006). 6) Lie Ken Jie et al., Chem. Phys. Lipids, 77:155 (1995).

Acknowledgements: NIH grants RO1AR49553, RO1 AR41443, RO1 AR53156