Addressing overlapping water-fat peaks and water-fat chemical shift displacement effects in single-voxel MRS of bone marrow

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Introduction: Osteoporosis is a systemic skeletal disease traditionally characterized by low bone mass and micro architectural deterioration of bone tissue. However, there has recently been a growing interest in understanding the relationship between bone marrow adiposity and bone mineral density [1-3]. Specifically, it has been found that osteoporosis may be associated with increased fatty (yellow) marrow content at the lumbar spine [1-2]. Single voxel MR spectroscopy (MRS) has been previously used to measure bone marrow fat content in the vertebral bodies and the proximal femur [1-5]. However, single-voxel MRS in the presence of trabecular bone is characterized by broad linewidths for the measured water and fat peaks making the extraction of the water peak overlapping with the neighboring fat peaks challenging. Furthermore, the distribution of red marrow in certain skeletal sites (e.g. in the proximal femur) is spatially heterogeneous making the fat quantification sensitive to chemical shift displacements effects due to the finite bandwidth of the RF pulses used usually for the MRS voxel localization [4]. The present study aims to an accurate determination of bone marrow fat content by using single-voxel MRS combining (i) an a priori known model for the chemical structure of triglycerides to address the overlapping water-fat peaks (ii) an acquisition with two center frequencies to minimize the water-fat chemical shift displacement effects.

Methods: MRS measurements: The left proximal femur of seven young healthy volunteers was scanned on a 3.0 T whole-body GE scanner using an 8-channel cardiac coil. 2-5 locations were selected per subject (in the neck, trochanter or head regions) to perform single-voxel (12x12x12 mm^3) MRS resulting in a total number of 25 acquired locations. A STEAM sequence was used with TR=6, TE=15/20/25/30 ms, 9 averages per TE, 4096 data points, 5 kHz acquisition bandwidth, 2.4 kHz RF pulse bandwidth, no water suppression and no regional saturation bands. The MRS measurements were performed twice: once with the center frequency on the main fat peak and once with the center frequency on the water peak.

Fat spectrum model: Spectra were fitted using Gaussian lineshapes and frequency-based methods. The spectra with center frequency at the main fat peak and with linewidth smaller than 0.4 ppm were used to fit fat peaks A+B, C and D (Fig. 1a). The chemical structure of the triglycerides was then used to estimate the number of double bonds (ndb) and the number of methylene-interrupted double bonds (nmidb), as introduced by Hamilton [6].

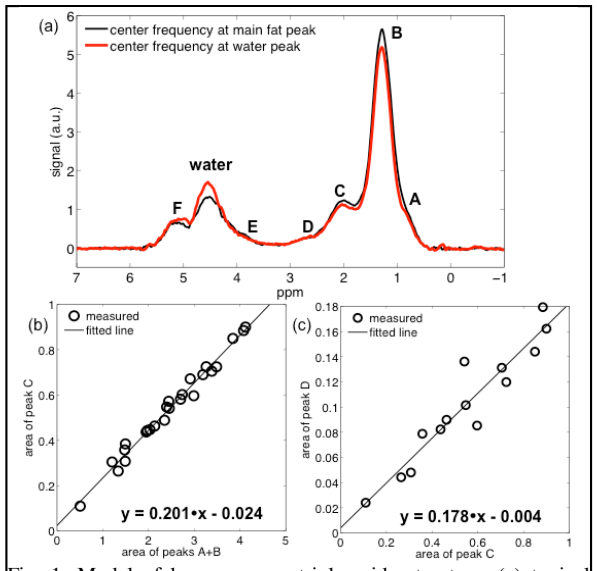

Fig. 1: Model of bone marrow triglyceride structure: (a) typical proximal femur MR spectrum (with center frequency at main fat peak and at water peak), (b) comparison of peak C area with peaks A+B area and (c) comparison of peak D area with peak C area.

Fat fraction calculation: Fat spectra minimally affected by chemical shift displacement effects were then derived by combining the spectrum centered at the main fat peak for chemical shift values lower than 3 ppm and the spectrum centered at the water peak for chemical shift values higher than 3 ppm. Peak fitting was performed by constraining the area of peaks E and F at a given ratio of peak A+B, based on the derived triglyceride chemical structure. T_2 correction was performed using non-linear least squares fitting, assuming the same T_2 value for all fat peaks. Fat fraction values were computed for the spectra with center frequency at water, at main fat peak and the combined spectra.

Results: Fat spectrum model: The ratio of area of peak C to area of peaks A+B was determined equal to 0.201 (Fig. 1b). The ratio of area of peak D to area of peak C was determined equal to 0.178 (Fig. 1c). Based on these values, assuming a triglyceride chain length CL equal to 18.4 and using the model for the triglycerides structure proposed by Hamilton [6], it was derived that ndb = 3.8 and nmidb = 1.4. Therefore, the area of peaks E and F was determined equal to 5.4% and 10.2% respectively of the area of peaks A+B.

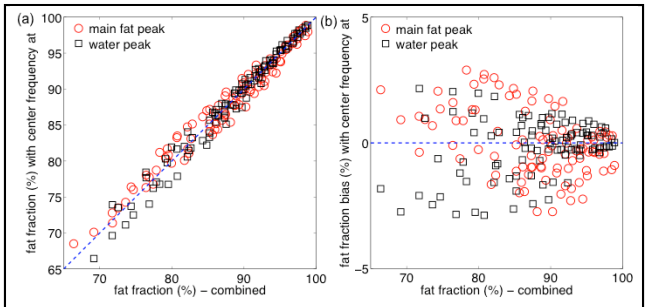

Fig. 2: Chemical shift displacement effect on non-T_2-corrected fat fraction: (a) relationship between water-centered, fat-centered and combined fat fraction and (b) corresponding fat fraction bias.

Chemical shift displacement effect: Fig. 1a shows an example of the result of chemical shift displacement effects on the bone marrow MR spectrum in the proximal femur. Fig. 2 shows the non-T_2-corrected fat fraction results for water-centered and fat-centered MR spectra. Chemical shift displacement effects induce a bias up to 3% on the non-T_2-corrected fat fraction. Fig. 3 shows the T_2-corrected fat fraction results for water-centered and fat-centered MR spectra. Chemical shift displacement effects induced a bias up to 6% on the T_2-corrected fat fraction.

Discussion: The characterization of the chemical structure of the bone marrow triglycerides makes the water peak extraction less sensitive to the occurrence of overlapping water and E and F fat peaks in the presence of thin trabecular bone structures. Although some variation could be expected in the unsaturation index across subjects [2], the assumption of a constant fat spectrum model invariant across subjects should be a good first approximation while focusing on fat fraction quantification.

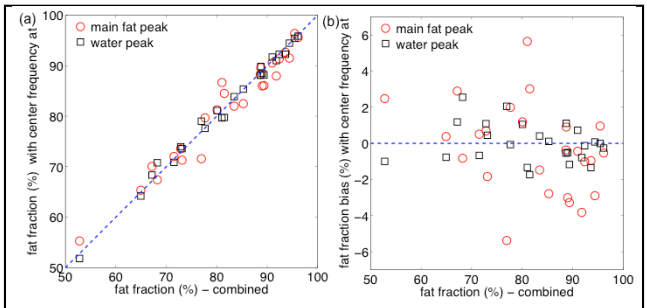

Fig. 3: Chemical shift displacement effect on T_2-corrected fat fraction: (a) relationship between water-centered, fat-centered and combined fat fraction and (b) corresponding fat fraction bias.

Chemical shift displacement effects can induce an overestimation or underestimation of fat fraction depending on the fat content distribution in the region surrounding the MRS voxel. A displacement equal to 18% of the voxel size should be expected in one dimension for the presently employed RF pulse bandwidth at 3 T. Chemical shift displacement effects induced a bias up to 6% in the fat fraction estimation of the proximal femur in the present data. An acquisition with two center frequencies is benign to water-fat chemical shift displacement effects and should be employed when applying single-voxel MRS in regions with spatially inhomogeneous fat content or close to the border between bone marrow and other tissues.

References: [1] Griffith, Radiology 236:945, 2005, [2] Yeung, J Magn Reson Imag 22:279, 2005, [3] Baum, J Magn Reson Imag 35:117, 2012, [4] Schick, Magn Reson Med 26:207, 1992, [5] Li, J Magn Reson Imag 33:974, 2011, [6] Hamilton, NMR Biomed 24:784, 2011.

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