Separating water and olefinic fat peaks using diffusion-weighted MRS and diffusion constraint fitting to measure vertebral bone marrow fat unsaturation

Stefan Ruschke[1], Michael Dieckmeyer[1], Hendrik Kooijman[2], Axel Haase[3], Ernst J. Rummeny[1], Jan S. Bauer[4], Thomas Baum[1], and Dimitrios C. Karampinos[1]

[1]Department of Diagnostic and Interventional Radiology, Technische Universität München, Munich, Bayern, Germany, [2]Philips Healthcare, Hamburg, Hamburg, Germany, [3]Zentralinstitut für Medizintechnik, Technische Universität München, Garching, Bayern, Germany, [4]Neuroradiology, Technische Universität München, Munich, Bayern, Germany

Target audience: Scientists interested in MRS of bone marrow and clinical researchers interested in biomarkers of bone health

Purpose: There is a growing interest in measuring metrics of bone marrow fat composition due to their recently shown association with bone health [1]. Specifically, vertebral bone marrow fat unsaturation has been previously shown to decrease in patients with osteoporosis [2], in patients with diabetes [3] and in patients with diabetes and prevalent fragility fractures [4]. Bone marrow fat unsaturation is traditionally determined by measuring the area of the olefinic fat peak at 5.3 ppm in the MR spectrum from a single-voxel STEAM or PRESS MRS experiment. However, the broad peaks in the bone marrow MR spectrum and the presence of a strong water peak can hinder a reliable extraction of the olefinic fat peak in the spine. Previous work has shown relatively large reproducibility errors in measuring fat unsaturation in the spine using short-TE PRESS [5]. STEAM at TE= 100 ms has been proposed to suppress the water peak in bone marrow, but it can suffer from T_2 relaxation-induced signal loss [6]. Recent work has shown the potential of DW-MRS to measure fat unsaturation with high SNR efficiency in tissues with low fat content and high water diffusion coefficient, relying on the large difference of the diffusion coefficient between water and fat [7]. The present work aims to separate water and olefinic fat peaks in bone marrow MRS in order to measure vertebral bone marrow fat unsaturation *in vivo*.

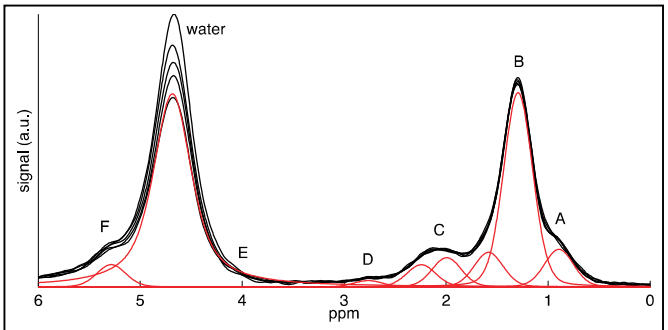

Fig. 1: DW-MRS series of the bone marrow: Measured spectra (black) for b-values of 0 / 200 / 400 / 600 / 800 s/mm^2. The red curves show the fitted peaks for the b-value of 800 s/mm^2. Notice the stronger diffusivity of the water peak at 4.7 ppm compared to the fat peaks.

Methods: In-vivo measurements: The lumbar spine of 4 young healthy subjects was scanned on an Ingenia 3.0 T scanner (Philips Healthcare, Best, Netherlands). Single-voxel MRS measurements were performed in the L3 and L5 vertebral bodies using a DW-STEAM sequence with the following parameters: b-values = 0 / 200 / 400 / 600 / 800 s/mm^2, TE = 25 ms, TM = 32 ms, TR = 6 s, VOI = 15x15x15 mm^3, 4096 sampling points, sweep width = 3000 Hz, 16 averages. Half of the signal averages were performed by reversed polarity of the diffusion-weighting gradients [8]. Furthermore, the lumber vertebra L5 of one additional subject was scanned three consecutive times with the same setting (except TR = 3.5 s). Spectra processing: The spectra were processed using in house-built MATLAB routines. The data from the two diffusion gradient polarities was first combined to compensate for eddy-current effects [8]. After standard routines, including apodization and phase correction, the signal was Fourier transformed and in fitted in the frequency domain using the non-linear Levenberg-Marquardt algorithm. All five spectra of a b-value series were jointly fitted using one diffusion coefficient for water and one for all fat peaks. One water and eight fat peak areas were fitted, namely: Peak A (methyl) at 0.90 ppm; B1 (methylene) at 1.30 ppm and B2 (β–carboxyl) at 1.59 ppm; C1 (α-olefinic) at 2.00 ppm and C2 (α-carboxyl) at 2.25 ppm; D (diallylic methylene) at 2.77 ppm; E (glycerol) at 4.20 ppm and F (glycerol and olefinic) at 5.29 ppm. (Fig. 1) Pseudo-Voigt line-shapes were assumed with a fixed Lorentzian factor of 0.2 and 0.8 for fat and water peaks, respectively. Furthermore, linewidths and peak locations were allowed to vary once for water and once for all fat peaks together leading to a total number of 15 parameters.

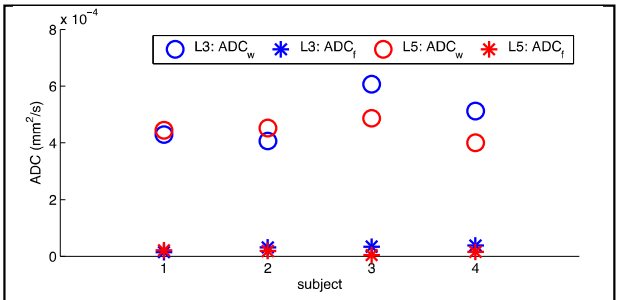

Fig. 2: ADC of water and fat peaks in the scanned subjects as a result of the joint fitting routine.

Results: A characteristic bone marrow spectrum shows broad linewidths (Fig. 1) and a strong difference in the diffusion coefficient with a measured mean (± standard deviation) ADC of 2.2 ± 1.1 x 10^{-5} and 4.7 ± 0.8 x 10^{-4} for fat and water (Fig. 2), respectively. The extracted peak area ratios F to B for the L3 and L5 vertebrae show only little variation with mean values of 0.097 and 0.092, respectively (Fig. 3). Results of the three consecutive measurements show a mean peak area ratio F to B of 0.098, a standard deviation of 0.003 and a coefficient of variation of 0.029.

Discussion & Conclusion: The proposed DW-STEAM acquisition combined with the proposed diffusion constraint fitting shows promising results for extracting the peak area ratio F to B as a measure of fat unsaturation. Specifically, the proposed constraint fitting on the acquired b-value-series data can overcome the difficulties in extracting the olefinic fat peak overlapping with the water peak due to the much higher diffusion coefficient of water compared to fat. Fat peaks A to D serve as penalty in the optimization routine for the fitting of peaks E and F using the relation of a common diffusion coefficient for all fat peaks. Additionally, the use of a b-value series instead of a TE-series assures the same J-coupling behavior for all processed spectra making the joint fitting process more robust. However, further work would be necessary to characterize the repeatability of the proposed technique in a larger scale study, including both controls and patients with bone disease. **In conclusion, DW-MRS combined with diffusion constraint fitting constitutes a powerful alternative for measuring *in vivo* vertebral bone marrow fat unsaturation.**

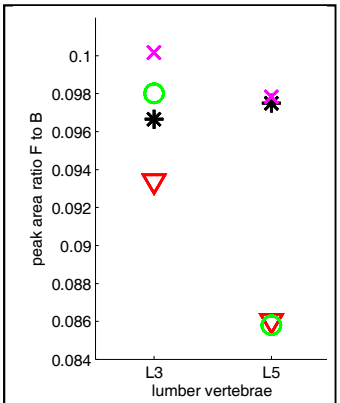

Fig. 3: Fat unsaturation measured as a peak area ratio F to B in the L3 and L5 vertebrae. Symbols of same color and shape belong to the same subject.

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