

Rapid Chemical Shift Imaging Method and Processing for Quantification of Bone Marrow Fat Fraction in the Vertebrae

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INTRODUCTION

Proton MR spectroscopy is a useful method for evaluating bone marrow composition in disorders affecting bone mineral homeostasis since both osteoblasts and adipocytes are derived from the same cell lineage [1 - 3]. In order to assess changes in bone marrow adiposity over time in response to intervention reproducible measurement is critical. The goal of this pilot study was to assess the performance of a rapid, multi-echo, based chemical-shift imaging technique for *in vivo* marrow fat fraction quantification in the lumbar vertebrae, a site of hematopoiesis where mixed marrow is typically present.

METHODS

Five healthy females (mean age = 44.4 ± 16.3 (SD), ranging from 27 to 67 years, BMI = 22.7 ± 3.9) were recruited. The study was approved by the Institutional Review Board and all volunteers signed informed consent. Four subjects were imaged twice on two different days and one on the same day (2 hours apart) with repositioning of the subject in between. A 2D interleaved multiple-gradient-echo chemical-shift imaging (IMGE-CSI) sequence [4] was implemented to quantify lipid content in vertebral bone marrow on a 3T scanner (Siemens TIM Trio) using the manufacturer's Spine and Body Matrix coils. The sequence consisted of a 90°-180° pulse pair, followed by 16 equal-polarity gradient echoes and six interleaves, each offset in time by 0.6 ms. Three saturation bands were placed outside the region of interest to minimize artifacts from abdominal motion. The sequence parameters were: TR/TE (spin echo)=1000/8ms, FOV=30x60cm², 60x120matrix, Slice Thickness (STh)=10 mm, Scan Time (ST)=12.8 mins, Spectral Bandwidth (SBW)=1.7 kHz, Spectral Resolution (SRes)=17 Hz. A spatial FFT was first performed for each of the echoes, which were subsequently ordered in time to obtain a spectral FID (96 data points) in each of the imaged voxels. The FID signal was zero filled to 256 points, apodized prior to Fourier transformation and phase corrected. The spectra obtained for each of the coils were then combined as sum of squares. Subsequently, the spectra were integrated from 0-3ppm (region I_h) and from 3.5-6ppm (region I_f). I_h accommodates all aliphatic protons except glycerol protons that, together with olefinics, resonate in I_f along with water. The empirical formula of marrow lipid (C_mH_nO₆) was derived from [5], yielding m=55.5, n=101.3 and a mean number of unsaturated hydrogens U=5.7. The marrow fat volume fraction $\chi_f = V_f / (V_f + V_w)$ was calculated for five different vertebral bodies (L1-L5) as the average of the four central voxels.

Quantities V_f and V_w are the voxel volumes of fat and water, given by Eqs 1 and 2. Here, $d_{f,w}$ and $M_{f,w}$ are the densities and molecular weights of the two constituents with the numeral 5 accounting for the 5 glycerol protons in I_h , and $E_{1f,w} = 1 - \exp(-TR/T_{1f,w})$ representing saturation factors for fat and water protons. In order to estimate fat and water T₁ relaxation times (T_{1f}, T_{1w}), a 90°-180°-180° double spin-echo excitation (PRESS) sequence preceded by an adiabatic pulse was implemented, with TR/TE=5000/15ms, TI=50-3000ms (10 increments), voxel size=1.5x1.5x1.5cm³, ST=50s, SBW=33kHz, SRes=8Hz, 10 averages. The voxel was placed in the center of L3 in each of the scans. The resulting FID signal was zero filled to 8196 points, and the final spectrum corresponding to each TI was obtained using the same processing steps described earlier. T_{1f} and T_{1w} were estimated by fitting experimental data to Eq. 3 for water and fat components respectively. Experimental data were measured in two different ways: 1) The respective signal intensity of the peaks at 4.7 (water) and 1.3 (fat) ppm and 2) The peak integrals corresponding to I_f (water) and I_h (fat). T_{1f,w} values based on the peak integral fit were averaged across both scans in each subject and used for individual marrow fat fraction calculation. Coefficients of variation (CV) and intraclass correlation coefficients (ICC) for marrow fat volume fraction quantification were determined to evaluate reproducibility and reliability. Mean CVs were calculated as the mean of the CVs computed per subject at one vertebral level reflecting the global reproducibility at L1-L5.

$$\text{Eq. 1 } V_f = \frac{I_h \cdot M_f}{d_f(n-U-5)E_{1f}}; \quad \text{Eq. 2 } V_w = \frac{I_l - (d_f V_f / M_f)(U+5)E_{1f}}{(d_w / M_w) \cdot 2E_{1w}}; \quad \text{Eq. 3 } S(TI) = S_o \cdot [1 - 2e^{-TI/T_1} + e^{-TR/T_1}] \cdot e^{-TE/T_2}$$

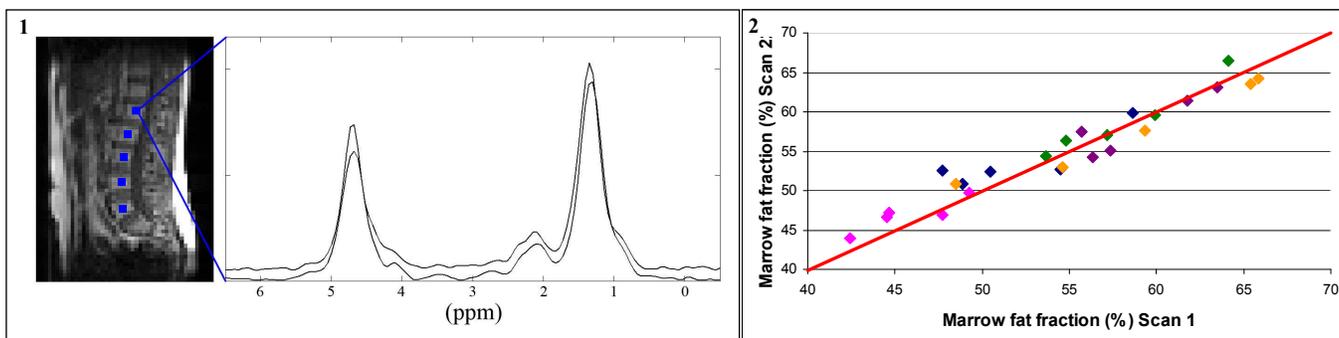


Fig 1. *Left.* 2D image reconstructed from the first of the 96 echoes. Detailed spectral information may be derived at each imaged voxel. Multi-voxel ROIs (blue) from which fat fraction was evaluated in each lumbar vertebra. *Right.* Spectral reproducibility for voxel located at L1 acquired on two different days in one of the subjects. **Fig 2.** Test-retest plot for marrow fat fraction evaluated in five subjects in all five lumbar vertebrae. ICCs ranged from 0.95 (L1) to 0.99 (L5). Each subject is displayed in a different color with the red line representing the line of identity.

RESULTS AND DISCUSSION

Quantification of *in vivo* marrow fat fraction was highly reproducible. Fig 2 shows the consistency of measurements obtained on the same subject. The mean CV averaged across subjects at each vertebral level was 2.88%, 2.08%, 2.05%, 2.23% and 1.46% (L1 to L5 respectively) and the ICC was 0.95, 0.95, 0.96, 0.99 and 0.99 (L1 to L5). The results suggest the method to be able to reliably detect changes in the marrow fat fraction on the order of 4% in 95% of the cases. We note that no prospective registration method was applied for subject repositioning in the repeat scan. Implementation of such an algorithm [6] might further improve precision. Reproducibility of T_{1w} and T_{1f} was also assessed for each of the fits performed. A 5 or 10% variation in T_{1w,f} would have introduced an error on the order of 1.2 and 2.3%, respectively, in the fat fraction calculation. The peak integral fitting method, which is less sensitive to spectral line broadening, yielded a more reproducible T_{1w} measurement (CV=5.1% vs CV=10.7% for peak intensity fit). T_{1f} estimation based on this fit (CV=13.3% vs CV=4.0% for peak intensity fit) may be lower due to different T₁ times present in the fatty acid chain [7].

CONCLUSION

The method described provides rapid and reliable quantification of vertebral marrow fat fraction at multiple spatial locations. Unlike multi-point Dixon methods, the technique presented has the advantage of not requiring any prior assumptions (i.e., main fat and water peaks being the only signal contributing components) for the fat fraction calculation, since all the spectral information is used for its quantification.

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REFERENCES [1] Yeung et al, MRI, 2006 [2] Griffith et al, Radiology, 2005 [3] Rubin et al, PNAS, 2007 [4] Hilaire et al, MRI, 2000 [5] Griffith, Bone, 2009 [6] Rajapakse et al, MRM, 2008 [7] Ren et al, JLR, 2008