Linkage of vertebral bone marrow fat content with biomechanical strength and trabecular bone structure parameters

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Target audience: Basic scientists interested in bone imaging and clinicians working in osteoporosis research.

Purpose: A property of bone marrow, which has recently gained significant attention due to its potential association with bone loss pathophysiology, is the bone marrow fat content [1,2]. It has been long known that bone marrow fat content increases with age [3]. MR investigations employing single-voxel Magnetic Resonance Spectroscopy (MRS) have recently shown the increase of vertebral bone marrow fat content with age in large-scale studies [4]. Above any physiological connection of bone marrow fat content with age, recent studies have also shown that an increase in bone marrow fat content is associated with a decrease in bone mineral density (BMD) [5-8]. However, there has been no previous groundwork on directly investigating the relationship between bone marrow fat content and biomechanical strength and the relationship between bone marrow fat content and trabecular bone structure parameters. Therefore, the purpose of the present pilot study is to investigate the effect of MRS-based proton density fat fraction on the trabecular bone structure parameters from CT measurements and on the biomechanical strength from biomechanical testing, ex vivo using human vertebral bone specimens.

Methods: Ten vertebrae between thoracic vertebra 5 and 10 (T5-T10) were harvested from four fresh human cadavers (1 woman and 3 men; age of of 58 ± 12 years). Each vertebra was embedded in resin at the vertebral endplates for the purpose of biomechanical testing and was placed in vacuum plastic boxes, filled with sodium chloride solution during imaging.

MDCT imaging: Multi-detector computed tomography (MDCT) images of the vertebrae were acquired by using a whole-body CT scanner. Mean BMD (in ROIs drawn in the ventral half of the vertebra) were determined using the calibration phantom (Fig. 1a). Four morphometric parameters were calculated in the ROIs in analogy to standard histomorphometry using the mean intercept length method [9]; bone volume divided by total volume (BV/TV), trabecular number (TbN [mm−1]), trabecular thickness (TbTh [mm]), and trabecular separation (TbSp [mm]). Parameters were labeled as apparent (app.) values, since they cannot depict the true trabecular structure due to the limited spatial resolution.

MR imaging: The vertebrae were scanned on a 3 T Philips MRI scanner using an 8-channel extremity coil. Based on the specimen geometry outlined in PD-weighted sequences (Fig. 1b), a voxel was selected in the center of the vertebral body to perform single-voxel (12×12×12 mm) MR investigations using a stimulated echo acquisition mode (STEAM) sequence with parameters: TR=6 s (long TR to remove any T1 effects), TE=15/20/25/30 ms (STEAM with short TE to reduce J-coupling effects), 10 averages per TE, 2 phase cycles, 4096 data points, 5 kHz acquisition bandwidth, no water suppression and no regional saturation bands. Representative MR spectra at different TEs are shown in Fig. 1c.

Spectra were fitted using Gaussian line shapes and frequency-based methods based on in-house-built routines written in MATLAB. Fig. 1d shows a typical bone marrow fat spectrum with peaks A-F observed at typical spectral locations. Two water peaks were employed accounting for short and long T2* components [10]. Peak fitting was performed by constraining the area of peaks E and F at a given ratio of peak A+B, based on the bone marrow triglyceride chemical structure determined previously [10]. Peak fitting was performed for the spectra at individual TEs. T2* correction was then performed using non-linear least squares fitting, assuming the same T2 relaxation time for all fat peaks and a different T2 relaxation time for the water peak. The derived proton density fat fraction was determined as the water peak area (A-F) area with the sum of all the fat peaks and the narrow (long T2*) water peak area (i.e. excluding the broad water peak area) [10].

Biomechanical testing: The resin embedded vertebrae were fixed in a mechanical testing system. The load–displacement curve was recorded and vertebral failure load (FL) was defined as the first peak of the load-displacement curve with a subsequent drop of >10%.

Results: Fig. 1c shows the spectra acquired at different TEs on a vertebra, confirming a faster T2* relaxation for the water peak than for the fat peaks and verifying the need for T2* correction to derive a proton density fat fraction. Fig. 1d shows the experimentally measured spectrum and the fitted spectrum. There is a strong overlap between fat peaks E and F and the water peak, verifying the need for a constrained fitting of peaks E and F to achieve a reliable estimation of the water peak.

Fig. 2 shows the relationship of proton density fat fraction with BMD and failure load. Fig. 2a shows a negative correlation of proton density fat fraction with BMD (r = −0.75, p = 0.013). Fig. 2b shows a negative correlation of proton density fat fraction with failure load (r = −0.73, p = 0.017). Proton density fat fraction also correlated with trabecular bone structure parameters, showing statistically significant correlations with app.TbN and a trend close to statistical significance (p < 0.1) for app.BV/TV, app.TbSp and app.TbTh. Negative correlations were found between proton density fat fraction and app.BV/TV (r = −0.63), app.TbN (r = −0.64) and app.TbTh (r = −0.57) and a positive correlation was found between proton density fat fraction and app.TbSp (r = 0.58).

Discussion & Conclusion: The present work shows a negative association between marrow fat content and biomechanical strength. Despite the fact that the observed relationship in the present small size sample cannot be corrected for the effect of bone density and cannot provide further insight on which exact mechanism is responsible for the linkage between bone marrow adiposity and bone health, the present results provide to the best of our knowledge the first direct validation of the association between bone marrow fat content and biomechanical strength. Therefore, the present results complement the existing knowledge about the importance of bone marrow adiposity in understanding the pathophysiology of bone weakening and about the value of the MRS-based proton density fat fraction of bone marrow as an additional useful parameter in monitoring osteoporosis diagnosis, progression and therapy. However, future larger scale ex vivo specimen studies would be necessary to understand whether marrow fat content could become a predictor of bone strength after correcting for BMD effects.


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