ASSESSMENT OF MARROW FAT IN FEMORAL NECK OF OVERWEIGHT AND OBESE VOLUNTEERS USING MRS AT 1.5T

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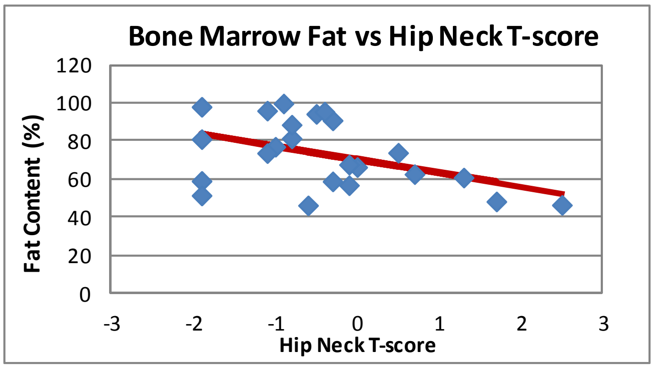
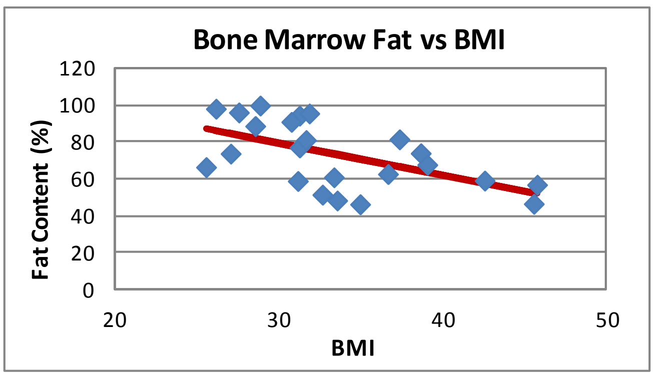
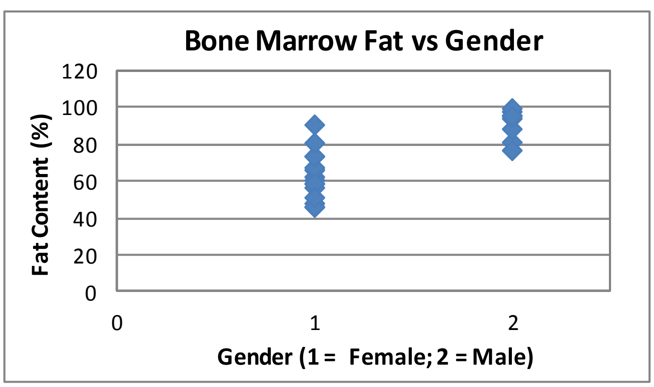
Introduction The skeletal system and adipose tissue have been linked in a large number of studies through a number of factors released systemically by adipocytes ("adipokines", including leptin and adiponectin) (1). More recently, the *local* interaction between these two systems within the bone marrow milieu has also been reported to play a more key role in the pathogenesis of osteoporosis, with increasing mesenchymal stem cell differentiation into adipocytes resulting in lipotoxic effect on bone cells, simultaneously stimulating bone resorption and suppressing bone formation, resulting in osteoporosis (2). An inverse relationship between fat and bone volume has been described in bone obtained from different animal models (2). Few small studies have quantitated bone marrow fat and examined its relationship with bone mineral density (BMD) in humans (3). The goal of this study was to extend prior findings in a cohort of men and women without osteoporosis with a wide range of body weight and body mass index (BMI). Bone marrow fat of proximal femur was measured using ^{1}H magnetic resonance spectroscopy (MRS), and correlated with dual x-ray absorptiometry (DXA).







Methods Twenty-three overweight and obese subjects without prior history of fractures have been consented to participate in this study (15 female & 8 male; Age: 27-68 years, 53.1±10.0; BMI: 25.6-45.8 kg/m^2, 33.6±5.8). DXA examination of the right hip was performed on a Hologic D-4500 instrument. All MR studies were performed on a 1.5 Tesla MR scanner (Achieva, Philips Medical Systems, Cleveland, USA). A SENSE Flex-L coil with two circular elements (loop size = 20 cm) was placed anterior and posterior over the right hip. Three-plane T_2-weighted anatomic images of proximal femur were acquired for voxel placement. Localized single-voxel ^{1}H MRS of femoral neck without water suppression was measured using PRESS (TE/TR = 40/3000 ms, bandwidth = 1000 Hz, sample points = 1024, voxel size = 8x8x8 mm^3, NSA = 64). All spectroscopy data were analyzed using jMRUI software package (4). Zero-order phase correction was manually performed before AMARES quantitation. A total of five peaks were fitted using Gaussian line-shape: methyl (at ~0.9 ppm), methylene (at ~1.3 ppm), methylene (at ~2.03 ppm), water (at ~4.7 ppm), and olefinic (at ~5.35 ppm) (5). The line-width of all peaks was estimated, with ±0.05 ppm constraint on resonance frequencies. Estimated peak amplitudes of fat (1.3 ppm) and water (4.7 ppm) were used to calculate marrow fat content: fat content (%) = 100 x I_{fat} / (I_{fat} + I_{water}). Marrow lipid unsaturation index was calculated according to: Unsaturation index = $I_{olefinic}$ / ($I_{olefinic}$ + $I_{methylene}$ + I_{methyl}) (6). Bone marrow fat measures by in vivo MRS were correlated to BMI, and hip neck and total T-score measured from DXA scans using linear regression. The difference of marrow fat and BMI between genders was compared using t-Test. Statistical significance was declared for p-value < 0.05.

Results Average marrow fat content of femoral neck was 72.96±17.90%. Bone marrow fat was significantly but only moderately correlated with femoral neck T-score (R^2 = 0.20, p-value = 0.03, top figure) and total hip T-score (R^2 = 0.16, p-value = 0.06). An inverse relationship was seen between bone marrow fat content and BMI (R^2 = 0.32, p-value = 0.005, middle figure). Although women and men had similar age (53±11 vs. 54±9 years), body weight (208±39 vs. 208±27 lbs), femoral neck BMD (0.844±0.149 vs. 0.837±0.079 g/cm^2) and total hip BMD (0.979±0.129 vs. 1.004±0.075 g/cm^2) (p > 0.5 for all), bone marrow fat content was significantly higher in men (91.5±8.23%) compared to women (63.08±12.97%) (p-value < 0.001, bottom figure). The unsaturation index of femoral neck was 0.047±0.024 among all subjects. Unsaturation index and BMI had a significant direct correlation (R^2 = 0.17, p-value = 0.048).

Discussion and Conclusion Noninvasive localized ^{1}H MRS has been used to quantify bone marrow fat in men and women with BMI above normal in this ongoing study. Although only weak-to-moderate, there is a significant inverse correlation between bone marrow fat and BMD T-scores confirming results of other smaller studies. In addition, bone marrow fat is found inversely correlated with BMI, which is compatible with known finding that more obese subjects are protected against osteoporosis, likely because of greater weight-bearing leading to bigger/more dense bones. Significant gender difference in bone marrow fat is found in the proximal femur, similar to the finding at the level of the vertebral bodies, where bone marrow fat was also higher in men than in women (7). The significance needs to be further investigated, and this finding should be considered in future studies looking at BMD and bone marrow fat.

References (1) Zhao LJ, et al, *J Bone Miner Res*. 2008;23:17–29. (2) Ng A and Duque G, *IBMS BoneKEy*. 2010;7:108-123. (3) Griffith JF, et al, *Radiology*. 2005;236:945-51. (4) Naressi A, et al, *MAGMA*. 2001;12:141-152. (5) Ren J, et al, *J Lipid Res*. 2008;49:2055-2062. (6) Yeung DKW, et al, *JMRI*. 2005;22:279-285. (7) Kugel H, et al, *JMRI*. 2001;13:263–268.