BONE MARROW FAT BEHAVES DIFFERENTLY FROM ABDOMINAL FAT, LIVER FAT AND SERUM LIPIDS AFTER A FOUR-WEEK CALORIE RESTRICTION IN OBESE WOMEN

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Target audience: Scientists and clinicians interested in imaging and quantification of fat depots

Purpose: Single-voxel magnetic resonance spectroscopy (MRS) has been shown to non-invasively assess the reduction in liver fat content after dietary interventions [1] and MRI has been shown to monitor changes in subcutaneous adipose tissue (SAT) and visceral adipose tissue (VAT) after lifestyle interventions [2]. Bone marrow is a fat depot that has recently attracted a considerable research interest due to its unique connections to metabolism and bone health [3-4]. Despite the growing interest in measuring properties of bone marrow, bone marrow remains a fat depot that has not been thoroughly studied with regard to the effect of dietary interventions. Therefore, the purpose of the present study was to determine the behavior of vertebral bone marrow fat after a four-week dietary intervention in obese women and relate vertebral bone marrow fat fraction (BMFF) changes with changes in other fat depots (measured using MRI and MRS) and in serum lipids.

Methods: Dietary Intervention: After recruitment, twenty obese women (age range 24-65, BMI 34.9 ± 3.8 kg/m²) underwent a defined dietary intervention using a formula diet (four portions Modifast per day each containing 200 kcal) with a total daily energy intake of 800 kcal and additional 200 g of vegetables (raw or cooked without fat) for 28 days. One day before the start and one day after the end of the dietary intervention (calorie restriction), blood and MRI measurements were performed. MRI/MRS measurements: The abdominal region of the subjects was scanned on a 3.0 T Ingenia scanner (Philips Healthcare, Best, Netherlands) using anterior and posterior coil arrays. A set of axial two-point Dixon images based on a 3D spoiled gradient echo sequence was acquired for the segmentation of SAT/VAT volumes. Single-voxel MRS was performed in the segment VII of the liver to measure the liver fat fraction using a STEAM sequence with: TR/TM = 3500/16 ms, 4 TEs values (for T_2 correction) TE = 10/15/20/25 ms, no water suppression, acquisition time = 17.5 s (single breath-hold). Single-voxel MRS was then performed in the L5 vertebral body to measure the bone marrow fat fraction using a STEAM sequence with: TR/TM = 6000/16 ms, 4 TEs values (for T_2 correction) TE = 11/15/20/25 ms, no water suppression, acquisition time = 3 min and 36 s.

Data analysis: A custom-built post-processing algorithm was used in order to automatically classify the different types of abdominal tissue compartments based on the water-separated and fat-separated images from the two-point Dixon scan: SAT, VAT and non-adipose tissue (NAT). Spectra were fitted using Voigt lineshapes and in-house-built frequency-based methods in MATLAB (Mathworks, Natick, MA). In the processing of the bone marrow spectra, peak fitting was performed by constraining the area of peaks at 4.2 ppm and 5.31 ppm at a given ratio of the sum of the peaks at 0.9, 1.30 and 1.59 ppm, based on the bone marrow triglyceride chemical structure determined previously [5]. The constrained fitting of peaks at 4.2 ppm and 5.31 ppm enabled the more reliable extraction of these two fat peaks and the water peak, which are overlapping due to the relatively broad linewidths in the marrow spectra. In order to increase the robustness of the fitting of the liver spectra, particularly for subjects with low fat content, a priori knowledge about the triglyceride structure [6] was incorporated by constraining the peak area fitting to the triglyceride model and an additional weighting was applied on the region between 1.0 and 1.6 ppm. One sample Student's t-tests and linear regression models were used to perform statistical comparisons and to study relationships between parameters.

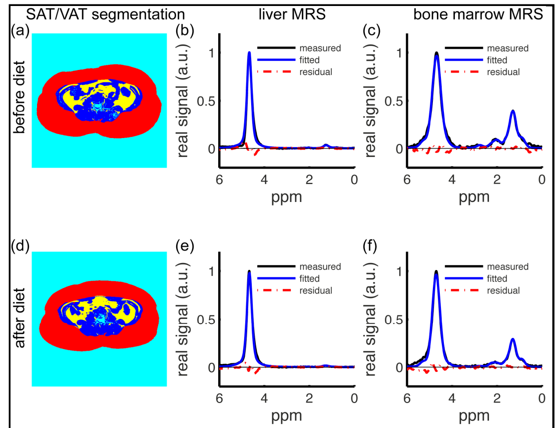

Fig. 1: (a) and (d) abdominal tissue area (SAT in red, VAT in yellow, NAT in blue, air/bone in cyan), (b) and (e) liver spectrum, (c) and (f) bone marrow spectrum in a subject showing decreasing BMFF after diet.

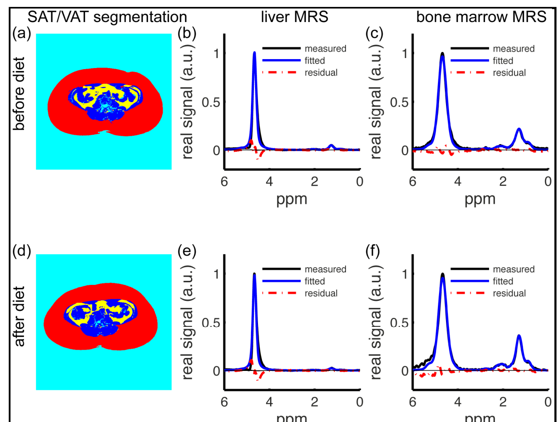

Fig. 2: (a) and (d) abdominal tissue area (SAT in red, VAT in yellow, NAT in blue, air/bone in cyan), (b) and (e) liver spectrum, (c) and (f) bone marrow spectrum in a subject showing increasing BMFF after diet.

Results: After the four-week calorie restriction the mean weight loss of the participants was 7.2 ± 1.6 % ($p < 0.001$) (respectively the BMI decreased by 7.0 ± 1.8%; $p < 0.001$). Serum lipid values (total cholesterol, LDL/HDL cholesterol and triglycerides) showed statistically significant decreases after the intervention ranging between 12.6% and 14.5%. The calorie restriction induced a severe reduction in the liver fat fraction by 40 ± 23.5% ($p < 0.001$). The abdominal fat depots also showed a statistically significant reduction: the SAT volume by 8.5 ± 4.4% ($p < 0.001$) and the VAT volume by 15.1 ± 8.7% ($p < 0.001$). The BMFF showed non-statistically significant changes by – 1.0 ± 8.3% ($p = 0.37$). Specifically, the BMFF decreased in thirteen subjects and increased in seven subjects after diet. Figs. 1 and 2 compare two subjects showing reduction in abdominal fat depots (Figs. 1a, 1d, 2a, 2d) and liver fat fraction (Figs. 1b, 1e, 2b, 2e), but one decreasing BMFF (Fig. 1c, 1f) and one increasing BMFF (Fig. 2c, 2f) after diet. Fig. 3 examines the relationship between BMFF absolute changes and the abdominal tissue volumes before diet. BMFF absolute changes were positively correlating with SAT volume before diet ($r = 0.489$; $p = 0.029$) and negatively correlating with NAT volume before diet ($r = -0.493$; $p = 0.027$).

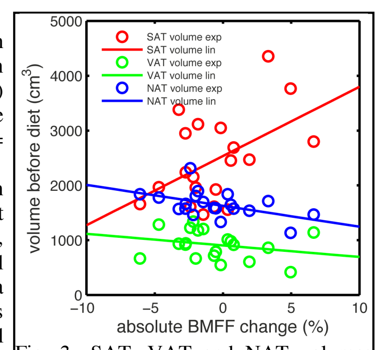

Fig. 3: SAT, VAT and NAT volumes before diet as a function of absolute BMFF changes. The symbols represent experimental points and the solid lines represent the linear regression results.

Discussion & Conclusion: The reported results indicate that bone marrow is a fat depot that shows smaller changes than serum lipids, liver fat, SAT volume and VAT volume after a four-week dietary intervention in obese women. A subsequent analysis showed a dependence of BMFF changes after weight loss on the abdominal tissue distribution before weight loss, highlighting a further connection between bone marrow fat and abdominal fat distribution. If we postulate the general finding that high BMFF is negatively associated with the bone mineral content [7], the present results might suggest that a short-term weight loss might be negatively associated with bone health in subjects with high SAT volume before weight loss and positively associated with bone health in subjects with high NAT volume before weight loss. The suggested abdominal tissue distribution dependence of the effect of weight loss on bone marrow could be also considered consistent with the previously reported reciprocal relations of SAT and VAT to bone strength [8]. In conclusion, bone marrow behaves differently compared to SAT, VAT, liver fat and serum lipids after a four-week dietary intervention in obesity and BMFF changes depend on abdominal tissue distribution before the dietary intervention.

References: [1] Vitola, Obesity 17:1744, 2009, [2] Machann, Radiology 257:353, 2010, [3] Bredella, Obesity 19:49, 2011, [4] Rosen, Nat Clin Pract Rheumatol 2:35, 2006, [5] Karampinos, Magn Reson Med, 71:1158, 2014, [6] Hamilton, NMR Biomed 24:784, 2011, [7] Griffith, Radiology 236:945, 2005, [8] Gilsanz, J Clin Endocrinol Metab 94:3387, 2009

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