Fatty acid composition of subcutaneous fat and bone marrow in human calf is affected by diet and exercise: An ^{1}H-MRSI study at 4T

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Introduction. Lipid fatty acid (FA) composition may influence diseases such as cardiovascular disease and diabetes. Noninvasive *in vivo* analysis of lipid composition has been reported using proton magnetic resonance spectroscopy (^{1}H-MRS) in subcutaneous fat (SAT) and bone marrow (BM) of human calf (1) and mouse adipose tissue (2) at 7T, or by ^{13}C-MRS in human calf (3) and abdomen (4) at 1.5T. ^{13}C-MRS data have shown that a fat-reduced diet (4) or a fish oil supplemented diet (3) can introduce significant differences in the degree of saturation and mono- or poly- unsaturation of adipose tissue. However, the availability of ^{13}C-MRS is still limited in clinical and research facilities. Though the recent availability of ^{1}H-MRS at higher magnetic field strength (1, 2) provides a robust tool to quantify fatty acid composition of human and mice adipose tissues, no data has been reported of its application in monitoring FA composition changes during different diets or life style changes. Therefore, this study applied proton magnetic resonance spectroscopic imaging (^{1}H-MRSI) at 4T to examine the effect of obesity, exercise and weight-loss diet on the degree of FA saturation vs. mono- and di-unsaturation of adipose tissue and bone marrow in the human calf.

Methods. Subjects: In Protocol 1, 9 non-obese healthy subjects (NOB: 9M. BMI = 25.8±0.7 kg/m^2, age = 36.3±3.4 yr), 10 moderately trained athletic subjects (ATH: 7M/3F. BMI = 24.2±0.8 kg/m^2, age = 33.0±2.5 yr, VO_{2max} = 37.9±2.2 ml/min/kg), 7 obese (OB: 4M/3F. BMI = 31.6±0.7 kg/m^2, age = 34.6±4.0 yr) and 7 type 2 diabetic mellitus subjects (DM: 4M/3F. BMI = 31.4±2.1 kg/m^2, age = 44.7±3.3 yr) were studied. No subjects were on high polyunsaturated FA diets. In Protocol 2, 19 obese subjects (18F/1M) (BMI = 33.9±0.8 kg/m^2, age = 54.5±1.2 yr) randomized to low carbohydrate (LC: 5%CHO) vs. low fat (LF: 20%Fat) moderately hypocaloric diets for 6 weeks, crossover, and 6 more weeks on the other diet (LF or LC diet). ^{1}H-MRSI (5, 6): Water-suppressed ^{1}H-MRSI were carried out using a 4T Varian Inova whole body MR system with a TEM ^{1}H resonator. Experiments were performed with the following parameters: phase encoding = 32 × 32, FOV = 16 × 16 cm^2, slice thickness = 1 cm, TR = 1 s, TE = 24 ms. Spectra from two or three voxels were selected and analyzed in SAT and BM to give an averaged value in each region. Calculation of lipid composition: The percentage of diunsaturated (FD), monounsaturated (FM) and saturated (FS) FAs were calculated as previously described (1, 2): FD (%) = peak area (F/E)*100%; FM (%) = (0.5*peak area (D/E))*100% - FD (%); FS (%) = (1-FD-FM)*100%. We assume that tissue triglycerides contain only saturated, monounsaturated and diunsaturated FA since higher unsaturated FAs are scarce in humans on ordinary Western diets. Corrections for relaxation effects were applied.

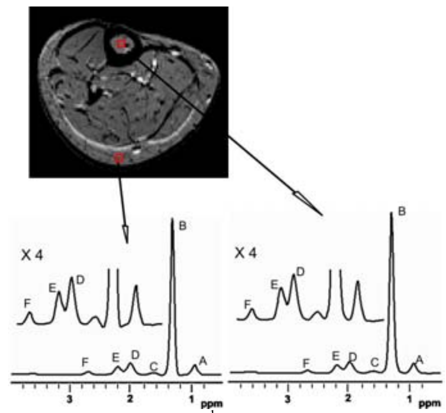

Fig. 1. Representative ^{1}H-NMR spectra from voxels in SAT (bottom left) and BM (bottom right) in a human calf.

Table 1. Assignment of six peaks shown in Fig.1

Peak	Chemical Shift	Triglyceride-associated ^{1}H of the spectra
A	0.90 ppm	$C\mathbf{H}_3$-$(CH_2)_n$-
B	1.30 ppm	-$(C\mathbf{H}_2)_n$-
C	1.58 ppm	-CH_2-O-CO-CH_2-$C\mathbf{H}_2$-
D	2.03 ppm	-CH_2-$C\mathbf{H}_2$-CH=CH-
E	2.26 ppm	-CH_2-O-CO-$C\mathbf{H}_2$-CH_2-
F	2.75 ppm	-CH=CH-$C\mathbf{H}_2$-CH=CH-

Results. Table 1 lists the positions of the six different peaks from human calf SAT and BM (Fig.1) ranging from 0 to 4 ppm. The six peaks were generally well-resolved at 4T except for peak E which partially overlaps with peak D. The spectral quality from current study was similar to that obtained in human calf at 7T (1) and mouse adipose tissue at 7T (2). In Table 2, fat composition in SAT and BM of four groups of subjects are listed. The athletic subjects have significantly higher FM and lower FS in SAT than the rest of three groups. In Table 3, fat composition in SAT and BM of subjects before and after weight-loss diets is listed. After LF diet, FD in SAT increased significantly compared to that before diet (29.1±0.8 vs. BL: 26.8±1.0. p=0.006) and FS decreased (22.5±1.4 vs. BL: 25.8±1.5. p=0.011). After 12-week weight loss (-9.1±0.6 kg), FD in SAT increased and FS in SAT decreased significantly (Table 3).

Table 2. Fat composition in SAT and BM of four groups of subjects.

	SAT			BM		
	FD (%)	FM (%)	FS (%)	FD (%)	FM (%)	FS (%)
NOB	27.4±1.5	42.3±1.8	30.3±1.6	25.0±1.8	42.1±2.5	33.0±1.9
OB	29.9±1.5	42.0±2.1	28.5±2.6	24.9±1.8	40.6±2.0	34.5±1.9
ATH	29.4±1.6	48.9±1.9*	21.7±1.6*	27.8±1.4	44.5±2.5	27.7±2.1¶
DM	29.5±1.5	41.7±2.0	28.8±0.9	29.1±1.1	40.0±1.6	30.9±1.4

*p<0.05 vs. NOB, OB and DM; ¶ p<0.05 vs. OB.

Table 3. Fat composition in SAT and BM of subjects before and after weight-loss diets.

	SAT			BM		
	FD (%)	FM (%)	FS (%)	FD (%)	FM (%)	FS (%)
BL	26.8±1.0	47.3±1.1	25.8±1.5	24.0±0.9	48.2±1.3	27.8±1.3
LF	29.1±0.8*	48.4±1.2	22.5±1.4*	25.1±0.8	47.3±1.5	27.6±1.1
LC	28.6±0.6	48.3±1.2	23.1±1.2	24.8±0.9	47.1±1.0	28.1±0.9
12-wk	28.6±0.7*	48.6±1.2	22.8±1.3*	24.8±0.7	46.9±1.1	28.2±0.9

*p<0.05 vs. BL.

Discussion and Conclusion. High-quality ^{1}H NMR spectra from human calf adipose tissue and bone marrow were obtained *in vivo* by using ^{1}H-MRSI at 4T. The spectral quality is similar to those acquired from human (1) and mouse (2) adipose tissue at 7T. This technique can effectively detect a difference in degree of FA saturation between sedentary and athletic subjects. It can also monitor changes in the degree of FA saturation with a weight-loss diet. Interestingly, athletic subjects have the highest fraction of monounsaturated FA and lowest of saturated FA. However, obesity doesn't seem to affect FA composition. On the other hand, the diet and weigh loss both affect the FA composition. The fraction of diunsaturated FA improved, and that of saturated FA decreased after low fat diet as well as after moderate weight loss.

In conclusion, ^{1}H-MRSI at 4T allows the determination of lipid composition in adipose tissue and bone marrow in human subjects. Using this methodology, we find that exercise, low fat diet and weight loss can lower the degree of FA saturation and increase the degree of FA unsaturation in adipose tissue.

References. 1. Ren J et al. J Lipid Res 49: 2055-2062, 2008. 2. Strobel K et al. J Lipid Res 49: 473-480, 2008. 3. Hwang J-H et al. NMR Biomed 16: 160-167, 2003. 4. Beckmann N et al. MRM 27: 97-106, 1992. 5. Hwang J-H et al. J Appl Physiol 90: 1267-1274, 2001. 6. Cui M-H et al. J Appl Physiol 103: 1290-1298, 2007.