^{1}H Spectroscopic Imaging Measurement of Intramyocellular Lipids in Response to Exercise in Obese and Control Adolescents: A Feasibility Report

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Introduction

The incidence of obesity and type 2 diabetes in children has increased several fold during the past two decades. Obesity results in insulin resistance, which in turn increases the risk of type 2 diabetes. Insulin resistance has been associated with increased intra-myocellular lipid (IMCL) content (1). Proton MRS has been used to measure the IMCL level, in most cases with single voxel techniques (2) and a voxel volume greater than 1 cm^3. In studying obese subjects, the selected voxel location may not yield spectra with good IMCL and EMCL separation for reliable quantification. To overcome this difficulty, we have implemented a chemical shift imaging protocol with a relatively high spatial resolution. We are applying this protocol to study the effects of exercise on IMCL in a group of obese and control adolescents. This is a preliminary report on an ongoing study.

Materials and Methods.

Subjects and Exercise: Four control and 3 obese subjects have been studied (Table 1). The obese subjects have either more than 35% total body fat or a body mass index (BMI) greater than 30 kg/m^2. All of them have a Tanner stage 4 or 5 and sedentary lifestyle. The exercise protocol consists of 12 weeks of aerobic exercise at 70-80% of VO_2 max, 30 minutes per session, and 4 sessions per week. The period of replenishment between the last exercise session and the MRS scan is 72 hours.

MRS acquisition: The IMCL level in the middle of the soleus of the right leg is measured in a transverse slice. Vitamin-E pills are taped to the leg at the transverse location of measurement to facilitate the positioning of the region of interest (ROI). The height of the pills from the heel is recorded for each study so the same location can be examined in follow-up studies. All data are acquired on a 1.5T Gyroscan Intera whole-body clinical scanner using a knee coil. Multi-slice T1 weighted turbo-spin echo images are first acquired to guide the positioning of the MRS ROI. The proton MRS data are obtained by using a 2D PRESS CSI technique without water suppression. The data acquisition parameters are: field of view = 140 mm (in most cases), 28 phase encoding steps in one direction with a 2D reduction factor of 0.75, a slice thickness of 10 mm, TR/TE = 1500/31 ms, and NSA = 1. Eight outer volume saturation pulses (MREST) are applied to suppress the subcutaneous lipid signals. This protocol requires a data acquisition time of approximately 17 minutes, which results in a nominal voxel size of 0.25 cc. For subjects with a large leg size, a field of view of 160 mm is used with 32 encoding steps along one direction. The reproducibility of the measurement was tested in one normal adult subject.

MRS data processing: Data is first reviewed using the Philips SpecTool software, which displays the lipid map generated from the CSI data as well as a spectral map. Spectra showing good EMCL and IMCL separation are selected for quantification using the AMARES feature in the jMRUI software (beta version v.95) (3) using prior knowledge (4) and a lorentzian line shape. The IMCL/water peak area ratio is obtained. Spectra with an excessive EMCL or IMCL linewidth are then excluded. The mean value and the standard error of the mean obtained from each CSI measurement are listed in Table 1.

Results

In the reproducibility study of one adult (Table 2), 4 out of the 5 measurements agreed very well in terms of the IMCL/water ratio, but the 4th of the 5 scans showed deviation from the rest. The subject noted that the positioning of the leg was uncomfortable during that scan. This underscores the importance of comfortable positioning in obtaining a motion-free study and hence more reliable results.

Spectra showing good IMCL and EMCL separation have been obtained during each session for both control and obese adolescents. At the baseline study, control subjects have lower IMCL/water ratios then the obese subjects (Table 1). Two control and 2 obese subjects have completed the 12-week exercise protocol and all MRS scans (Table 1). The IMCL/water ratio has been relatively stable for the two control subjects. The two obese subjects showed decreased IMCL/water ratios. We have observed that there are alterations of the total lipid distribution pattern shown by the lipid map. Consequently, voxel locations with good spectral quality also changed with time. Furthermore, regions showing low total fat signal may not have good spectral separation between the IMCL and EMCL signals.

Discussion and Conclusions

The use of CSI to study IMCL has been validated by others against a single voxel technique (5). CSI offers the possibility to study different muscle groups and the variation of lipids within one muscle (6). Furthermore, the smaller voxel size used in the CSI measurement reduces the variation of the fiber orientation across the voxel, resulting in improved spectra separation between the EMCL and IMCL peaks. In this study, the use of CSI has been very helpful for obtaining quantifiable spectra from obese subjects in a serial study. Our preliminary result suggests that the exercise protocol may have the effect of lowering IMCL in obese subjects.

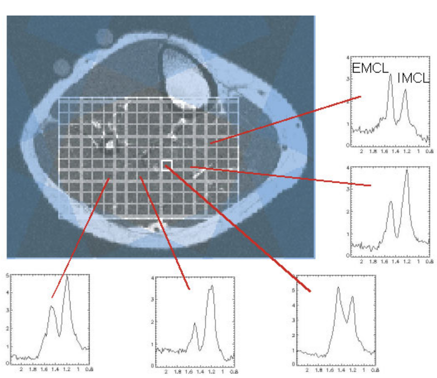

Figure. CSI study of the soleus in a control subject. The nominal voxel dimension is 0.5x0.5x1 cm^3. The blue region is saturated by MREST pulses.

Table. 1. Subject information and MRS results.

	Age*/ gender	BMI kg/m^2	%fat	IMCL/water(10^{-2}), mean$\pm$s.e.m.	
				baseline	12 week
C1	16y/m	17.1	13.7	2.6$\pm$0.2	1.9$\pm$0.2
C2	17y/f	25.8	28.5	3.3$\pm$0.7	4.0$\pm$0.6
C3	15y/f	20.0	25.2	1.9$\pm$0.5	
C4	14y/f	19.9	26.9	2.2$\pm$0.5	
S1	15y/f	26.3	36.2	4.1$\pm$0.7	2.7$\pm$0.5
S2	13y/f	31.0	33.4	3.5$\pm$1.0	2.0$\pm$0.4
S3	16y/f	37.6	39.6	5.4$\pm$1.6	

*at the time of the baseline study.

Table 2. Reproducibility test on one adult subject.

Scan	IMCL/water(10^{-2}), mean$\pm$s.e.m.
1	4.1$\pm$0.6
2	3.6$\pm$0.5
3	3.9$\pm$0.4
4*	6.0$\pm$1.1
5	3.8$\pm$0.8

* the subject reported stressful

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