In vivo visceral fat evaluation and IMCL quantification using MRI/MRSI at 3T and their relationship with insulin sensitivity

X. Li[1], B. Hyun[1], J. F. Youngren[2], G. K. Sakkas[3], S. Majumdar[1], I. D. Goldfine[2]

[1]MQIR, Department of Radiology, University of California at San Francisco, San Francisco, CA, United States, [2]Department of Medicine, University of California at San Francisco, Mt. Zion Medical Center, San Francisco, CA, United States, [3]Department of Medicine, University of California at San Francisco, San Francisco General Hospital, San Francisco, CA, United States

INTRODUCTION

Insulin resistance (IR) is known to play an important role in the pathogenesis of human type 2 diabetes. MR technologies have been recently proposed as non-invasive methods to quantify lipids distribution that may correlate insulin sensitivity (IS) in human, among which are intra-myocellular lipid (IMCL) in muscle tissues (1) and abdominal subcutaneous adipose tissue (SAT) and visceral adipose tissue (VAT) contents (2). MR spectroscopy provides unique capability to distinguish IMCL from extra-myocellular lipids (EMCL) non-invasively (3,4). Most previous studies used single voxel (SV) MRS techniques and it is not clear IMCL in which muscle group, solues (SO) vs. tibialis anterior (TA), may be a more reliable indicator of insulin action. In this study, we aimed at using high-field MR technologies at 3T to 1) measure IMCL in both SO and TA muscles; 2) examine the feasibility of using 3D-MRSI in IMCL quantification; 3) to quantify SAT and VAT with MRI; and 4) to examine the correlation between these parameters and IS.

MATERIALS AND METHODS

Subjects: Four healthy volunteers were studied for reproducibility of MR technologies. Ten non-diabetic and sedentary subjects were studied for the whole exam: 7 female and 3 male, median age = 33.5 with a range of 23-50, median BMI = 24 with a range of 18.8 – 27.0.

Euglycemic-hyperinsulinemic Clamps: Subjects were fasted overnight and underwent a primed-continuous infusion (100 mU/m^2·min) for 120 minutes with a variable infusion of 20% glucose. Average glucose infusion rates were calculated for the two twenty-minute periods between 80-120 min of the insulin infusion. Glucose disposal was taken as the mean glucose infusion rate plus endogenous glucose production. Rates of glucose disposal were normalized for body weight (GdB) and lean tissue (GdL) as determined by a whole body Lunar Prodigy^{tm} Dual Energy X-Ray Absorpitometry (DEXA) system.

MR exam: MR data were acquired on a GE 3T Excite scanner. A T1-weighted fast spin-echo breath-held water-suppressed single slice imaging was acquired between L4 and L5 using a body coil (TR/TE=333/12.6 ms, slice thickness = 10 mm, FOV=40 mm). Muscle spectral and image data were acquired from calf using a quadrature knee coil. Single voxel PRESS techniques were used to obtain spectra from both SO and TA muscles: TR/TE=2000/37 ms, 8 average without water suppression, 256 average with water suppression, BW=5000Hz, voxel size=15*15*20mm=4.5cc. 3D water-suppressed PRESS MRSI were acquired with TR/TR=2000/37 ms, phase encoding steps=16*8*1, nominal voxel size=8*8*8mm = 0.51cc. Spectra for the whole PRESS box without water suppression were acquired during prescan.

Data processing: SAT and VAT were segmented automatically on T1-weighted abdominal images using a threshold-based algorithm and their volumes were measured using an in-house developed software based on IDL. VAT/SAT and VAT/total adipose tissue (TAT) were calculated. The spectral data were reconstructed, corrected and fitted with Voigt models using methods developed previously (5,6) to estimate levels of water (4.7 ppm), creatine (Cr2 at 3.95ppm, Cr3 at 3.05ppm), tri-methyl-ammonium (TMA, ~3.2ppm), EMCL (~1.5ppm) and IMCL (1.28 ppm). Ratios of IMCL to unsuppressed water were measured for each patient. In 3D MRSI, voxels with good separation of EMCL and IMCL were selected and average ratios of IMCL to unsuppressed water were calculated. Subjects were divided into insulin resistant (IR) and sensitive (IS) groups based on glucose clamp results. A non-parametric rank test was used to examine differences between IR and IS subjects.

RESULTS

Reproducibility (average coefficient of variation) was 5.2% of VAT/TAT and 14.3% of IMCL/Water with MRS. Fig. 1 shows abdominal images with contours of SAT and VAT (a), calf images (b), single voxel spectra in SO (c) and TA (d) for a IR (upper) and a IS (lower) subject respectively. Fig. 1(e) illustrates the 3D-MRSI for a IS subject. Table 1 presents mean and standard deviation of glucose disposal rate, abdominal fat and IMCL parameters for IR and IS groups respectively. IMCL/water were higher in IR than in IS in both SO and TA muscles, but the difference was only significant in IMCL/Water based on 3D MRSI data (P=0.02). IMCL/water based on 3D MRSI was also significantly inversely correlated with both GdB (R^2=-0.76, P=0.02) and GdL (R^2=-0.77, P=0.04). Volumes of VAT, ratio of VAT/TAT and IMCL measured with single voxel MRS tended to increase as GdB and GdL decreased, but none of these inverse correlations was significant.

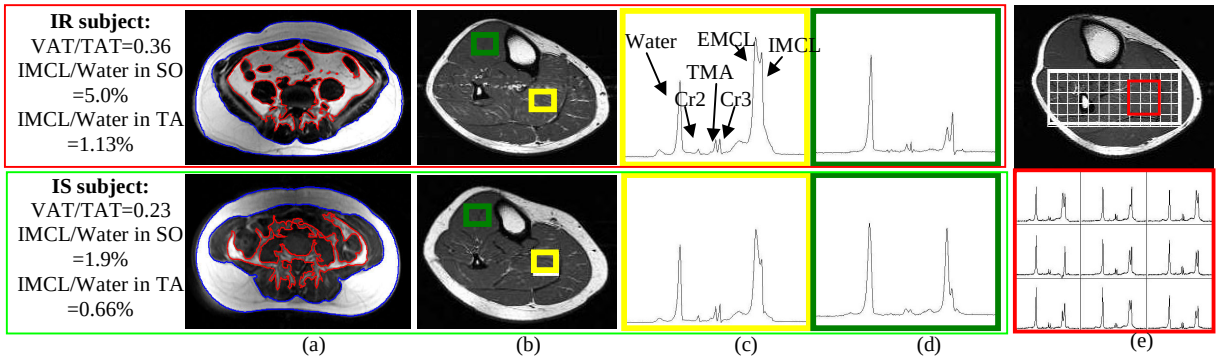

Fig. 1. (a) Abdominal images. Red: visceral fat; Blue: subcutaneous fat; (b) calf images; Single voxel muscle spectra in SO (c) and in TA (d); (e) 3D-MRSI.

DISCUSSION

A robust MR protocol has been developed to evaluate *in vivo* lipids distribution non-invasively. IMCL both in SO and TA muscles tended increased as IS decreased but the significance was only seen in 3D MRSI data with the small sample size in this study. It might be due to better separation of IMCL and EMCL in 3D MRSI. 3D MRSI may also help to study different spectral patterns in different muscle groups. Volumes of visceral fat tended to increase as IS decreased, but a larger cohort of patients is needed to further examine the significance. This is a preliminary report for an ongoing study with a larger population of subjects. Follow-ups for these subjects after exercise training will be also investigated.

Table 1. Mean±STD of GdB and GdL, abdominal fat and IMCL parameters for IR and IS subjects

	Gd (mg/kg/min)		Abdominal Fat			IMCL/Water (%)		
	GdB	GdL	SAT (cm^3)	VAT (cm^3)	VAT /TAT	SO (SV)	TA (SV)	3D MRSI
IR	6.0±1.3	9.7±1.8	246.5±97.1	86.9±28.8	0.27±0.1	3.6±1.5	1.1±0.4	4.5±0.9
IS	10.1±2.3	14.7±1.9	270.4±121.2	71.4±12.7	0.23±0.1	2.4±1.3	0.6±0.2	2.8±0.6
P	0.013	0.004	0.76	0.32	0.48	0.38	**0.07**	**0.02**

REFERENCES

1. Krssak M, et al., Diabetologia (1999) 42: 113-6.
2. Miyazaki Y, et al., Am J Physiol Endocrinol Metab. (2002) 283: E1135-43.
3. Neumann-Haefelin G., et al., Magn Reson Imag (2003) 50: 242-8.
4. Vermathen P., et al, Magn Reson Imag (2004) 51: 253-62.
5. Nelson SJ. Magn Reson Med 2001: 46(2):228-39.
6. Li X, Nelson SJ. Proc IEEE EMBS 2003; Cancun, Mexico.

AKNOWLEDGEMENTS: This research was supported by NIH RO1 DK059358.