Validation of Fat Volume Quantification with IDEAL MRI

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Introduction: The increasing prevalence of obesity has led to the recognition of new clinical entities, including the metabolic syndrome (MetS). MetS is defined as a combination of phenotypes that increase the risk of developing type 2 diabetes, cardiovascular endpoints and death from all causes. Amongst other things, MetS is characterized by dysglycemia, dyslipidemia, increased blood pressure, central obesity, and liver steatosis. The core molecular defect of the MetS is insulin resistance [1]. To better understand MetS, we are studying patients with Familial Partial Lipodystrophy (FPLD), which is an extreme monogenic form of insulin resistance that demonstrates most of the clinical and biochemical manifestations of the common MetS [2]. FPLD is characterized by the loss of subcutaneous fat in the extremities and the gluteal region, resulting in well-defined musculature. Excess intra-abdominal (visceral) fat deposition is also seen. Characterizing the distribution of adipose tissue is important since visceral adipose tissue and hepatic lipid content are associated with the development of type 2 diabetes and cardiovascular disease. Specifically, the visceral fat component is most intimately associated with cardiometabolic disease and adverse outcomes. However, it is difficult to quantify fat volume using most imaging modalities. MR Imaging is a sensitive, replicable, non-invasive, and safe method to determine the distribution of adipose tissue [3]. Nonetheless, existing MRI methods for evaluating fat volume cannot simultaneously evaluate lipid content (fat mass fraction). Therefore we will be validating an MRI technique known as Iterative Decomposition of water and fat with Echo Asymmetry and Least-squares estimation (IDEAL) that allows MR images to be produced only from fat containing tissues [4]. IDEAL has already been validated for measuring hepatic lipid content [5]. Because IDEAL images show only adipose tissues, quantifying fat volume should be simpler and more accurate than with current methods. We hypothesize that IDEAL will offer a reliable and non-invasive option for adipose tissue volume quantification both in patients with MetS and in those at high risk for developing MetS. Our aim is to first validate IDEAL for fat volume measurements.

Methods: Four healthy normal-weight controls were recruited; ethics approval was obtained from the University of Western Ontario Research Ethics Board. All subjects were imaged at both 1.5T and 3.0T (GE Healthcare, Waukeshau, WI, USA). 1.5T images were acquired using a T1-weighted Spin Echo Pulse sequence used in a previous study that validated MRI measurements of fat volume [6]. 3.0T images were acquired using T1-weighted Spoiled Gradient Echo (SPGR) and IDEAL-SPGR (using an investigational version of IDEAL). A previously validated fat quantification protocol was used for all the MR images (Figure 1) [6, 7]. Subcutaneous adipose tissue volume was quantified using ImageJ image analysis software (version 1.34 n). Subcutaneous adipose tissue was defined as the adipose tissue that circulated the circumference of the anatomical region of interest, adjacent to the skin. Visceral adipose tissue volume was quantified for the abdominal region using a similar approach. Abdominal (at L4 level), gluteal (at the level of the femoral heads), mid-thigh (at the mid-point of the femur), and mid-calf (at the mid-point of the tibia) fat volumes were calculated for all imaging measurements by two independent readers for a single slice in each anatomic region.

Results: Mean fat volumes as a percent of total slice volume are shown in Figure 2. We used a 2-factor ANOVA with replication to determine if there is a significant difference in fat volume measurements between observers or between the 3 modalities (1.5T, 3T and IDEAL). No significant differences ($P>0.05$) were found between readers or between the gold standard (1.5T) and the other two modalities (3T and IDEAL) for subcutaneous fat volume measurements in the abdominal, gluteal, mid-thigh and mid-calf regions. However, when the three modalities were compared for visceral fat volume measurements in the abdominal region we found the null hypothesis of no difference was rejected with $P=0.16$. This led us to perform post hoc paired sample 2-tailed t-test between the three possible pairs of 1.5T SE, 3.0T SPGR and 3.0T IDEAL-SPGR. We found that there is a significant difference ($P<0.0001$) between 1.5T and IDEAL; there was also a significant difference ($P<0.01$) between 3T and IDEAL. At the same time there was no significant difference ($P>0.05$) between 1.5T and 3T measurements. The inter-observer correlation coefficients were: abdominal-visceral (0.78), abdominal-subcutaneous (0.87), gluteus (0.97), mid-thigh (0.90), mid-calf (0.91).

Discussion: We have determined that IDEAL correlates strongly with our gold standard (1.5T imaging) except for visceral abdominal fat measurements. The lower value of visceral fat volume given by IDEAL may reflect an improved ability to differentiate between true visceral fat and bright structures like blood vessels or bowel contents that could be mistaken for fat in the non-fat suppressed T1 weighted images. However, we need to increase the number of study subjects before we can make more definite conclusions. We are in the process of recruiting more normal controls with a range of visceral fat mass to strengthen our results.

Conclusion: IDEAL MRI allows simultaneous quantification of adipose tissue volumes (subcutaneous adipose tissue, visceral adipose tissue) and organ lipid content (liver). IDEAL is a reliable and non-invasive method for the determination of quantitative differences in fat distribution between normal controls.

References: **1.**Reaven GM, Ohysiol Rev, 1995, 75(3):473-486. **2.**Hegele RA, Trends Cardiovasc Med, 2004, 14(4):133-137. **3.**Abate et al, J Lipid Res. 1994, 35(8):1490-1496. **4.**Reeder et al, J Magn Reson Imaging. 2007, 25(3):644-652. **5.**Reeder et al, Quantification of Hepatic Steatosis with MRI, J Magn Reson Imaging (In Press). **6.**Al-Attar et al, BMC Med Imaging. 2007, 7:3. **7.**Al-Attar et al, BMC Med Imaging. 2006, 6:11.

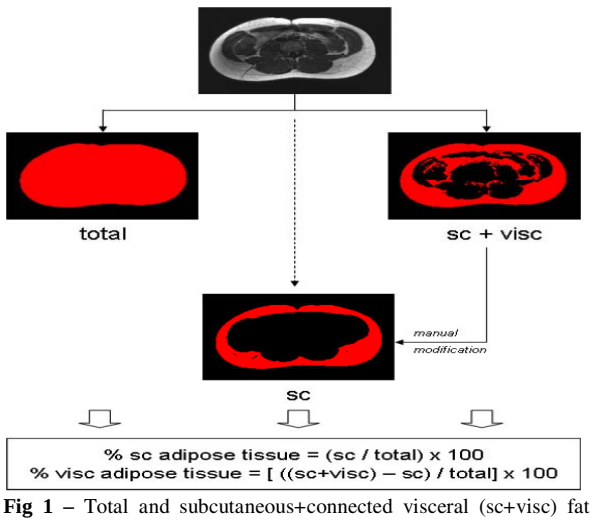

Fig 1 – Total and subcutaneous+connected visceral (sc+visc) fat volumes were selected. Subcutaneous adipose was selected by manually eliminating visceral signals present in the (sc+visc) image. %sc adipose tissue was calculated by dividing the voxel count for the sc fat by total voxels for the slice. %visc adipose tissue was calculated by subtracting sc fat voxel count from sc+visc and then dividing by the total voxels for the slice. [6]

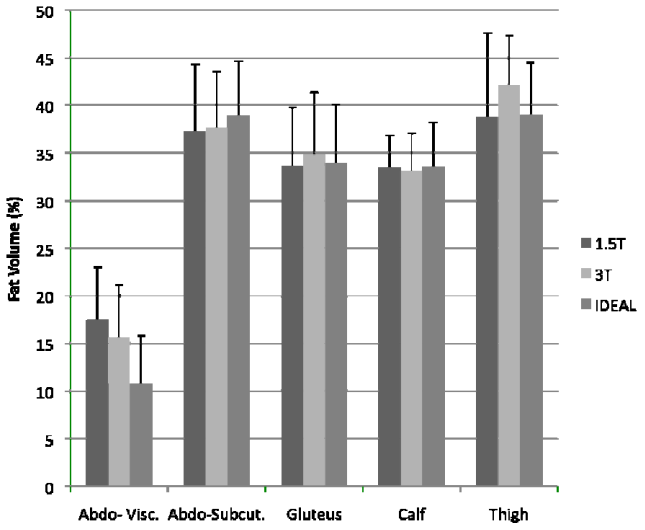

Fig 2 - Average fat volume measurements for the following regions: abdominal viscera (abdo visc.), abdominal subcutaneous (abdo subcut.), gluteus, thigh and calf. Average volumes are being compared between the three modalities (1.5T, 3T and IDEAL).