Absolute Quantification of Adipose Tissue Fat Mass by MRI Using a Signal Intensity Based Model

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Introduction – MRI is an emerging technique in body composition and obesity research. Its 3D capability is useful in identifying abdominal adipose tissue (AT) depots, as well as fatty infiltration in organs. Abdominal fat (lipid) quantities are important clinical metrics in the risk stratification of diabetes, metabolic disorders, and cardiovascular diseases [1]. Several MRI methods have been proposed to quantify AT. The most common technique utilizes T_1-weighted images, where AT (composed of fat, water, and proteins) is distinguished from lean tissue due to their high signal intensity [1]. Another approach utilizes RF pulses to selectively saturate water spins and isolate lipids within AT [2]. For both of these methods, voxels are subsequently classified by histogram thresholding and summed to give a ***volume*** estimate of AT or lipid quantity. A drawback of thresholding is partial volume, where voxels exhibit fractional fat content. This is typical in organs and near AT boundaries. A third method is based on chemical-shift fat-water separation (IDEAL). Since IDEAL yields co-registered fat (F) and water (W) images, partial volumes are resolved, and a ***fat-signal fraction*** can be computed for each voxel [3]. To minimize T_1-bias in the fat signal, a small flip angle (≤5°) is used to generate proton-density spoiled gradient echo (SPGR) images. In this work, we hypothesize and propose a quantification scheme based on IDEAL-SPGR that computes ***absolute fat mass***, a potentially more relevant metric than volume or signal fraction. Feasibility is demonstrated in swine specimen.

Methods – For low-flip-angles (θ), the steady-state SPGR signal becomes independent of relaxation effects and is approximately a linear function of proton density (P) (Eqn. 1) [3]. The proton-volume density (P_{vol} = number of protons/ml) of pure water can be computed via Eqn. 2, where ρ_{H2O} is the density of water, N_H = number of hydrogens in the molecular formula, N_A = Avogadro's number, and M_W is the molecular mass. However, fat in AT is a heterogeneous mixture of saturated and unsaturated triglycerides. Therefore, $P_{vol,\ fat}$ (number of fat protons/ml of AT) cannot be explicitly determined. Upon low-flip-angle IDEAL separation of fat and water components, $P_{vol,\ fat}$ can be inferred from $P_{vol,\ water}$ by exploiting the relationships in Eqn. 1 and 3 (see also Fig. 1A), where $S_{fat\ (in\ pure\ AT)}$ and $S_{pure\ water}$ are the fat and water signal intensities of voxels containing pure AT and pure water, respectively. The absolute fat mass $M(\vec{r})_{fat}$ can be subsequently calculated on a voxel-by-voxel ($\vec{r}$) basis with Eqn. 4a, where $S(\vec{r})_{fat}$ is the fat signal of any arbitrary voxel in the IDEAL fat image, v is the voxel volume, and $P_{mass,\ fat}$ is the proton-mass density of fat (number of protons/gram of fat). The ratio in brackets in Eqn. 4a is the density of fat in AT, ρ_{fat}. If ρ_{fat} is known, the explicit computation of $P_{vol,\ fat}$ and $P_{mass,\ fat}$ becomes unnecessary, and Eqn. 4a simplifies to Eqn. 4b. For this particular work, we used ρ_{fat} values of 0.72-0.78 (grams of fat)/(ml of AT) obtained from literature [4, 5] to directly compute $M(\vec{r})_{fat}$ after IDEAL fat-water decomposition.

$$\text{Eqn.1}\quad S_{SPGR} \approx P \cdot \theta$$

$$\text{Eqn.2}\quad P_{vol} = \rho_{H2O} N_H N_A / m$$

$$\text{Eqn.3}\quad \frac{S_{fat\ (in\ pure\ AT)}}{S_{pure\ water}} = \frac{P_{vol,\ fat}}{P_{vol,\ water}}$$

$$\text{Eqn.4a}\quad M(\vec{r})_{fat} = \frac{S(\vec{r})_{fat}}{S_{pure\ fat}} \cdot \left\{ \frac{P_{vol,\ fat}}{P_{mass,\ fat}} \right\} \cdot v$$

$$\text{Eqn.4b}\quad M(\vec{r})_{fat} = \frac{S(\vec{r})_{fat}}{S_{pure\ fat}} \cdot \left(\rho_{fat} \right) \cdot v$$

MRI Experiment – To test the hypothesis, three fresh *ex vivo* swine samples (mass: 40.6g, 58.3g, 75.5g) were imaged (Fig. 1B) with IDEAL-SPGR on a 3T GE scanner using the standard transreceive head coil. Samples 2 and 3 contained a mixture of AT and lean tissues. Parameters were: TR = 5 ms, TE = 2.1, 2.8, 3.5 ms, FOV = 20 cm BW = ±62.5 kHz, θ = 3°, and voxel sizes 1.5×1.5×5 mm^3 and 1×1×2.5 mm^3. For illustration purpose, a test tube filled with pure water was placed next to the AT samples during imaging.

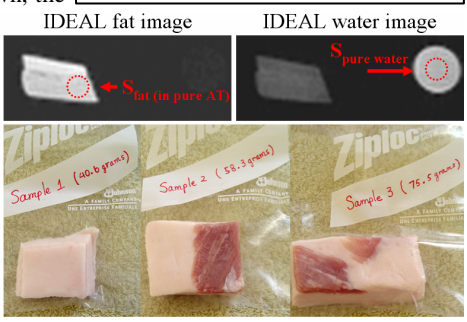

Fig.1 (A) Illustration of Eqn. 3 and (B) swine samples.

Lipid Assay – The samples were sent for lipid analysis after MRI. Samples were weighed, cut into pieces, and placed in cellulose thimbles. Thimbles were reweighed before being placed in a drying oven at 60°C. Samples were dried until constant weight, where water mass was determined. Samples were then placed in a Soxhlet apparatus for fat extraction. Multiple cycles of petroleum ether extraction was performed over a 24-hour period. At the end of the cycles, the petroleum ether in the thimbles was clear, indicating that all fat had been removed. Samples were then reweighed to determine loss in fat mass. Lipid assay were considered the comparison standards.

Table 1

	IDEAL-SPGR		Lipid Assay	
sample	fat mass (g)	fat-signal fraction	fat mass (g)	% fat mass
1	33.2, 33.8	68%	34.5	87%
2	41.6, 44.5	62%	44.5	77%
3	53.3, 54.8	71%	58.2	78%

Results – Table 1 compares fat mass results determined by MRI and lipid assay. Two fat mass values are reported for IDEAL-SPGR, corresponding to θ = 3° data with voxel sizes 1.5×1.5×5 and 1×1×2.5 mm^3, respectively. MRI and lipid assay fat mass values are in excellent agreement, with approximately a 5-8% difference. Lipid assay also yielded a fat mass fraction for each sample. For comparison, we computed the mean fat-signal fraction from IDEAL for each sample. It is evident that the two percentages are noticeably different.

Discussion – We have demonstrated an MRI approach to quantify ***fat mass*** using chemical-shift imaging. Preliminary results show excellent agreement with lipid analysis in *ex vivo* swine samples. Since our proposed quantification technique relies on accurate signal intensities of fat components after IDEAL reconstruction, non-physiological factors that influence signal intensity will need to be addressed in *in vivo* applications. Factors such as non-uniformities within the RF transmit and receive fields, which are expected to be significant in abdominal imaging of obese subjects, are consequences of both high-field imaging systems and multi-receiver coils. In this work, RF non-uniformity was minimized by using a birdcage head coil and small samples. In Table 1, our approach underestimated the fat mass in comparison to lipid assay. This could be due to use of literature values of ρ_{fat}, which were obtained from reports on human cadaver analysis, not swine. Table 1 also suggests more accurate fat mass approximation with smaller and more isotropic voxels. The tradeoff between voxel size and quantitative accuracy is an area of further investigation. Our data also suggests disagreement between the fat-signal fraction and the true percent fat mass. We suspect that the signal fraction will only yield a reasonable measure if fat and water have similar proton and mass densities, which is unlikely *in vivo*. Lastly, explicit knowledge of ρ_{fat} in Eqn. 4b circumvents computation of $P_{vol,\ fat}$ in Eqn. 3 and further obviates the need for a water reference signal. This is beneficial for human studies, as a water marker does not need to be attached to the subject. In conclusion, our approach can potentially provide a more clinically meaningful index of fat mass in body composition and obesity research, and further validation in heterogeneous samples (fatty organs) is needed to evaluate its accuracy.

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