Quantification of Absolute Fat Mass: A Validation Study Between Chemical-Shift MRI and Chemical Analysis

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INTRODUCTION: As the prevalence of obesity continues to rise, accurate tools for quantifying abdominal body and organ fat mass are critically needed. Fat accumulation in organs and skeletal muscles are strong biomarkers of diabetes, the metabolic syndrome, and obesity. Rapid fat quantification, particularly in organs and muscles, remains an unmet need in body composition research. Motivated by the fact the chemical analysis (CA) returns an intuitive and direct measure of absolute fat mass in animal body composition experiments, the purpose of this work was to validate an approach based on chemical-shift MRI for computing similar absolute fat mass (grams) from available proton density fat fraction (PDFF) data (%). Since MRI signals fundamentally measure proton density, and not typical SI units of volume or mass, we first describe a simple formulation that relates PDFF to absolute fat mass. Next, the approach was applied to freshly excised samples of adipose tissue, and more importantly, to mixed and heterogeneous fat and lean tissues, organs, and muscle samples from four pigs. The 97 samples were independently analyzed by gold-standard lipid extraction chemical analysis.

METHODS: (Theory) The fat-signal fraction from chemical-shift MRI reflects the ratio of protons in fat and free water in tissues. Assuming that signal confounding factors such as T1 and T2 relaxation, and the multiple spectral peaks of fat [1-3] have been accounted for, the resultant fat-signal fraction is equal to the PDFF. The PDFF is not absolute to equivalent fat mass (volume) or mass (volume) fat fraction. As described previously [4,5], while the proton density and mass fractions are two fundamentally different metrics, they are nonetheless related and that for water and fat, the difference is remarkably small. The pure unconfounded proton-density signals of water and fat, Sw and Sz, for an arbitrary voxel is described by Eq. (1), where ρ is the mass density (g/ml), V is the volume of water or fat in the voxel, λ denotes the number of protons per molecule, Np is Avogadro’s number, and MW represents the molecular weight (g/mol). The numerator of the term in parenthesis has units of # of protons/mole. Dividing this by MW, the resultant unit becomes # of protons/g. Multiplication by ρ and V gives the unit of Sw and Sz as simply the # of protons. Note that the product of ρ and V is mass m. Next, we define PDFF and mass fat fraction in Eq. (2) and substitute for m in Eq. (2b) from Eq. (1). To obtain the 1.02 coefficient, we have substituted the following for water: ρw = 0.993 g/ml, MWw = 18.015 g/mol, and λw = 2; and the following for the average triglyceride in adipose tissue: ρf = 0.92 g/ml, MWf = 845.52 g/mol, and λf = 95.84; and dropped Np entirely for simplicity [6-9]. We note that the expressions for PDFF (2a) and mass fat fractions (2b) are remarkably similar. We now define the approximation of absolute fat mass by PDFF within each imaging voxel v using Eq. (3), where v is voxel volume.

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(1) \quad S_{w,f} = \rho_{w,f} V \left( \frac{\lambda_{w,f} N_p}{M_W} \right) = \rho_{w,f} V \left( \frac{\lambda_{w,f} N_p}{M_W} \right)
\]

\[
(2a) \quad \eta_{PDFF} = S_f - S_w
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(2b) \quad \eta_{mass} = \frac{m_f}{m} = \frac{S_f}{S_w + S_f}
\]

\[
(3) \quad m_f = \eta_{PDFF} \left( \rho_f - \frac{S_w}{S_w + S_f} \right)
\]

RESULTS: FIG.1 illustrates a correlation and a Bland-Altman plot of all 97 samples consolidated across the four pigs. There is excellent agreement between the two fat mass measures as the regression slope is nearly equal to one. The 95% confidence intervals for slope and intercept are (0.98, 1.04) and (1.01, 2.96), respectively. The table summarizes statistics for each pig, showing similar strong agreement between MRI and CA-derived fat mass. The differences between the two techniques were 2.66±4.96g, 1.88±2.89g, 2.73±2.50g, and 1.18±3.90g.

CONCLUSION: The ability to accurately estimate absolute fat mass with MRI from PDFF has been validated. The method allows for the computation of absolute fat mass in any arbitrary specimen, ranging from lipid-rich adipose tissue to heterogeneous organs and muscles. Future work should include a rigorous test of reproducibility and the technique’s ability to non-invasively track longitudinal changes in fat mass in animal and human studies.