

On The Definition of Fat-Fraction for In Vivo Fat Quantification with Magnetic Resonance Imaging

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Introduction: Several groups are currently focused on the development of MRI methods for accurate, non-invasive quantification of fat. The most commonly used metric for fat quantification with MRI is “fat signal fraction”, ie: $\eta = S_f / (S_f + S_w)$ [1], because it is independent of RF coil sensitivity and provides a direct measure of the relative signal from fat in tissue. Assuming that confounding factors such as T_2^* decay^{1,2}, T_1 bias^{2,3} and the spectral complexity of fat^{2,4} have been addressed, fat signal fraction is equal to the “fat proton density fraction”. Unfortunately, gold standard assays used for validation of MRI methods provide estimates of volume fraction or mass fraction. The purpose of this work is to clarify the various definitions of fat fraction and to describe methods to convert separated fat and water signals to estimates of fat volume fraction and fat mass fraction.

Theory and Methods: The signal from fat (water) within a voxel depends on the mass density of fat (water) and the number of protons per molecule of fat (water), ie:

$$S_f = k \frac{\rho_f \lambda_f v_f}{MW_f} \quad \text{and} \quad S_w = k \frac{\rho_w \lambda_w v_w}{MW_w} \quad [2]$$

where k is a constant, ρ_f and ρ_w are the mass densities of fat and water (g/ml), λ_f and λ_w are the number of protons per molecule of fat and water (unitless), MW_f and MW_w are the molecular weights of fat and water (g/mol), and v_f and v_w are the volumes of fat and water within the voxel (ml). For water, $\rho_w = 0.993$ g/ml (at 37°C), $MW_w = 18.015$ g/mol, and $\lambda_w = 2$. The constants for fat depend on the type of fat. The density of triglycerides in adipose tissue is 0.9196g/ml, average $MW_f = 845.52$ g/mol and average $\lambda_f = 95.84$ ^{5,6}.

Acetone is often used to validate chemical shift separation methods. Acetone has a chemical shift of -155Hz at 1.5T at room temperature (vs -224Hz for the main fat peak). The relevant physical properties of acetone include: density = 0.79g/ml at 22°C, $MW_{\text{acetone}} = 58.08$ g/mol, and $\lambda_{\text{acetone}} = 6$.

Fat volume fraction and fat mass fraction can be estimated with MRI by inverting the expressions in equation 2 and substituting the known definitions of volume fraction = $v_f / (v_f + v_w)$ and mass fraction = $m_f / (m_f + m_w)$, providing MRI estimates of fat volume and fat mass fractions, ie:

$$\eta_v = S_f \frac{MW_f}{\rho_f \lambda_f} \left/ \left(S_f \frac{MW_f}{\rho_f \lambda_f} + S_w \frac{MW_w}{\rho_w \lambda_w} \right) \right. \quad \text{and} \quad \eta_M = S_f \frac{MW_f}{\lambda_f} \left/ \left(S_f \frac{MW_f}{\lambda_f} + S_w \frac{MW_w}{\lambda_w} \right) \right. \quad [3]$$

Phantom: A fat-water phantom was constructed, comprised of nine 20ml vials in varying concentrations of fat: 0, 2.5, 5, 10, 20, 30, 40, 50, and 100% true fat volume fraction, using a revised method of Bernard *et al*⁷. Briefly, 43 mM sodium dodecyl sulfate, 2.0% agar and 43mM sodium chloride were dissolved in distilled, deionized water, creating stable emulsions of water and fat. 3.75mM sodium azide was added to prevent the growth of microbes, and 0.3mM Gd-BOPTA (Multihance, Bracco Inc., Princeton, NJ) was added to shorten the T_1 water to approximately 600ms, to more closely match physiologic values of T_1 . Precise measurement of the volume fraction from contraction during cooling was measured and corrected. An acetone-water phantom was also constructed, with true volume fractions ranging from 0-100% in 10% increments.

Imaging: Imaging was performed on a 1.5T clinical scanner (Signa HDx TwinSpeed, GE Healthcare, Waukesha) using a quadrature knee coil and an investigational version of the multi-echo IDEAL 3D spoiled gradient echo (3D-IDEAL-SPGR) sequence^{8,1}. For the fat-water phantom, imaging parameters were: FOV=35cm, 256x256 matrix, 1 average, 24 slices, slice=8mm, BW=±125kHz. TR=45ms with a 5° flip angle to avoid T_1 related bias^{3,2}. Scan time was 5:23min. 6 echoes / TR were acquired using a flyback readout with $TE_{\text{min}} = 1.3$ ms, $\Delta TE = 2.2$ ms, creating a phase shift just less than 180° between water and the main fat peak. All imaging parameters were the same for the acetone-water phantom, except BW=±62.5kHz, utilizing the increased echo spacing allowed from the reduced chemical shift of acetone (-155Hz vs -224Hz for fat).

Separate water and fat (acetone) images were calculated using an on-line reconstruction algorithm that uses a region growing method to prevent water-fat (acetone) swapping, and a T_2^* correction algorithm that accounts for transverse magnetization decay¹. A pre-calibrated “multi-peak” reconstruction that accounts for the multiple spectral peaks of fat was used for the fat-water phantom⁴, but not for acetone, because acetone has a single NMR peak. Corrected MRI volume and mass fractions were calculated (Eq. 3).

Results: Figure 1a demonstrates large disagreements between the MRI signal fraction for acetone when plotted against true volume fraction. Correction with Eq. 3, improves the agreement between MRI estimates and true acetone volume fraction (fig 1b).

Analogous measurements for the fat-water phantom are plotted in figure 2. Unlike the acetone-water phantom, good agreement exists between the fat signal fraction and true volume fraction, with little improvement after correction with equation 3. This occurs because the relative proton densities of fat ($\rho_f \lambda_f / MW_f$) and water ($\rho_w \lambda_w / MW_w$) are almost equal (fat:water = 0.95). Acetone and water, however, have substantially different relative proton densities (acetone:water = 0.74)

Discussion: Accurate quantification of chemical species such as fat requires precise definition of “fat-fraction” in order to compare measurements made with MRI with gold standard assays. Fortunately, the correction required for fat quantification is very small, often within experimental measurement error, indicating that fat signal fraction, fat volume fraction and fat mass fraction can be used interchangeably. This is not the case, however, for other chemical species such as acetone, and care must be used when comparing MRI results with known species fractions.

References: 1. Yu et al, JMRI, 2007 60(1): 198-209, 2. Bydder et al MRI, 2008 26(3):347-59, 3. Liu et al. MRM, 2007 58(2):354-64, 4. Yu et al. MRM 2008 60(5):1122-34, 5. Eyjolfsson et al, Ann Thorac Surg, 2008 85:975-981, 6. Baker, Am J Clin Nutr, 1969 22:829-835 7. Bernard et al, JMRI 2008, 27(1):192-7. 8. Reeder et al, JMRI, 2007 25(3):644-52.

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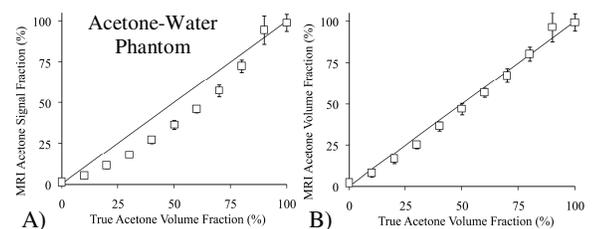


Figure 1: MRI signal fraction shows poor agreement with the true acetone volume fraction. After correction, MRI volume fraction shows substantially improved agreement with the true acetone volume fraction. Mass fraction (not shown) results show similar behavior.

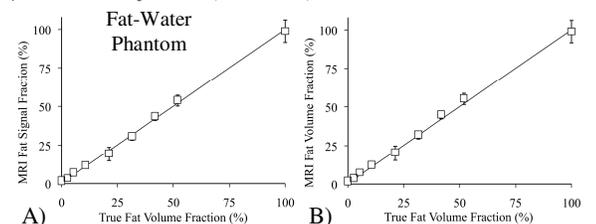


Figure 2: MRI signal fraction and MRI volume fraction both show good agreement with true fat volume fraction. Little correction is needed because the relative proton densities of water and fat are similar. Mass fraction (not shown) results show similar behavior.