Quantification of Hepatic Steatosis with MRI: Correction for Bias from Noise and T1

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Introduction: Quantification of hepatic steatosis is a significant unmet need for the diagnosis and treatment monitoring of patients with non-alcoholic fatty liver disease (NAFLD)[1]. Using chemical-shift MR imaging methods, water and fat signal can be separated permitting the quantification of fat within the liver. However, fat quantification[2] using MRI is confounded by non-zero mean image noise and relaxation effects such as T_1. The purpose of this work is to describe two approaches "phase-constrained" and "magnitude discrimination" to remove noise bias and two approaches to avoid T_1 bias in fat quantification: "low flip angle" and "dual flip angle" methods. In-vivo and phantom studies were performed for evaluation of spoiled gradient echo (SPGR) imaging in combination with a water-fat separation method known as IDEAL (Iterative Decomposition of water and fat with Echo Asymmetry and Least squares estimation)[3].

Theory: The bias created by noise is demonstrated in Fig. 1, where complex zero mean Gaussian noise was added to signals (SNR=10 in the simulation). For many fat-water separation methods, including IDEAL, calculation of fat fraction is based on magnitude images. In the region of the plot depicting a true fat fraction of zero, the magnitude operation makes the noise non-zero mean, causing a positive bias of nearly 8%. This effect would be clinically significant for low fat-fractions and could lead to false-positive diagnoses of mild steatosis.

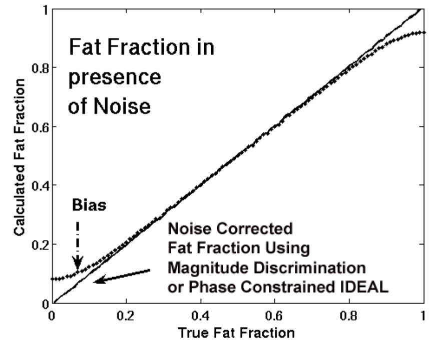

Fig.1 Bias from noise in magnitude images creates bias at low fat-fractions. Simulated noise created bias in fat fraction calculation.

We first propose a "phase constrained" IDEAL[5] model to correct for the noise bias. Using this model, the decomposed fat/water images are real quantities (not complex). We avoid taking the magnitude of a complex signal to estimate the fat fractions and the bias from image noise is reduced as shown in Fig. 1. The "magnitude discrimination" is the second approach, which applies if we can assume that the signal from fat and/or water is sufficiently high that noise remains zero-mean and the sum of the fat fraction and water fraction is one. Estimates of the denominator are also free from noise bias since it is estimated as the in-phase signal directly which always has appreciable amount of signal.

The water signal S_w (S_f for fat) for SPGR depends on the T_1 of water (T_{1w}), flip angle α, TR, TE, and the proton density of water (M_w) as given by Eq 1. This also implies that the fat signal fraction η_s will be different from the true fat fraction, η, when the T_1 values of fat and water are unequal as described by Eq. 2 and Eq. 3. Without T_1 correction, this difference (eg. $\eta_s \neq \eta$) will lead to highly inaccurate estimates of hepatic fat.

$$S_w = \frac{M_w(1-e^{-TR/T_{1w}})\sin\alpha}{(1-e^{-TR/T_{1w}}\cos\alpha)} \quad [1], \quad \eta_s = \frac{S_f}{(S_w+S_f)} \quad [2], \quad \eta = \frac{M_f}{(M_w+M_f)} \quad [3]$$

To reduce the T_1 influence, a low flip angle approach may be used. Using the first order Taylor expansion with respect to small α in Eq. 1, α term cancels in the fat fraction calculation and the two definitions in Eq. 2 and 3 become equal. We refer to this approach as the "low flip angle" method. The second approach to completely remove the effects of T_1 is to perform two consecutive acquisitions with two different flip angles[4]. After IDEAL-SPGR imaging and reconstruction, T_1-corrected water (fat) signal can be calculated using two sets of fat and water images, each at two different flip angles. The optimum flip angles based on T_1 of fat and water were calculated to be 6° and 34°[4].

Materials and Methods: 3D multi-echo SPGR[6] images were acquired on a normal volunteer (with approval from our IRB and after obtaining informed consent) to determine the bias due to image noise. A 2D IDEAL-SPGR sequence (TR=11.3ms, TE=4.4, 6.0, 7.5ms) was applied with flip angles ranging from 5° to 45° using a head coil and an oil/water phantom containing a continuum of fat fractions. To validate the dual flip angle method, the same protocol was used with dual flip angles 6° and 34°. Experiments were performed on 1.5T GE Signa HDx scanners.

Results: Fig. 2 shows the bias created by image noise in fat fraction on a normal volunteer and the correction after phase constrained. Fig. 3 and Fig. 4 demonstrate the effectiveness of small flip angle and dual flip angle methods to reduce the T_1 bias.

Discussions: True fat quantification should be independent of image acquisition parameters and directly reflect the amount of fat in the tissue. Naive calculation of the signal fraction will be confounded by the effects of image noise and T_1. We describe two approaches that effectively reduce the noise bias in estimates of fat fraction using separated water and fat images. We also demonstrate two approaches for the correction of T_1 bias including small flip angle and dual flip angle methods. The correction of this bias is clinically important for detection of early disease with mild steatosis. Future work will validate these methods in a clinical setting for the detection and quantification of hepatic steatosis.

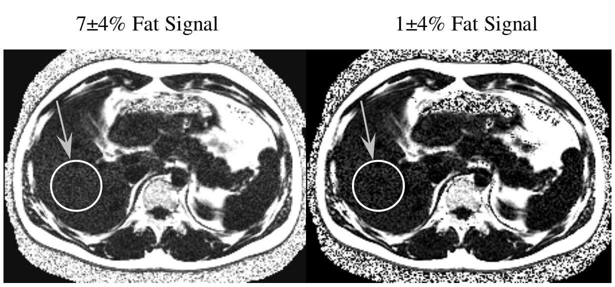

Fig. 2 Fat-signal fraction images from a normal volunteer (no steatosis) calculated using magnitude images (left), and phase constrained images (right, magnitude discrimination gave very similar results). A bias occurs at low fat fractions using magnitude images that would lead to over-estimation of the apparent fat-fraction, even when no fat is present.

Ref [1] Harrison SA. et al, Clin Liver Dis 2004;8:861-879, ix. [2] Liu et al, MRM.2007;58:354-364 [3] Reeder SB. et al, MRM.2004;51:35-45 [4] Deoni et al, MRM.2003;49:515-526. [5] Yu H. et al, MRM. 2005;55:413-422. [6] Reeder SB. et al, ISMRM 2006, p2444.

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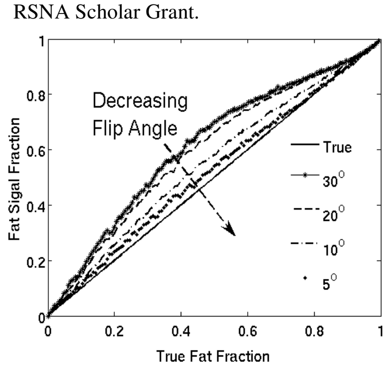

Fig. 3 Fat signal fractions of different flip angles due to confounding T_1 effects. A maximum error of 40.5% (relative to 0.5 of true fat fraction) was observed with 30° flip and 7.5% of error with 5° flip.

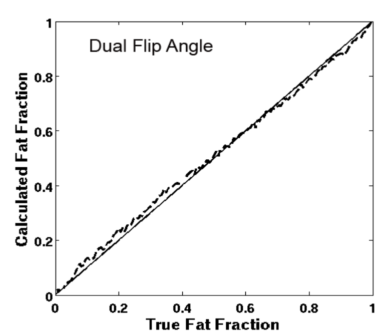

Fig. 4 Fat fraction estimated with dual flip angle. The estimated fat fraction (dashed line) agrees well with the expected values (solid line).