

Optimization of Flip Angle to Allow Tradeoffs in T1 Bias and SNR Performance for Fat Quantification

C. D. Hines¹, T. Yokoo², M. Bydder², C. B. Sirlin², and S. B. Reeder^{1,3}

¹Biomedical Engineering, University of Wisconsin-Madison, Madison, WI, United States, ²Radiology, University of California-San Diego, San Diego, CA, United States, ³Radiology, University of Wisconsin-Madison, Madison, WI, United States

Introduction: Non-alcoholic fatty liver disease (NAFLD) has become the most common cause of chronic liver disease in the US. The earliest manifestation of NAFLD is intracellular fat (steatosis), and early detection of steatosis is important for treatment. Complex chemical shift based methods such as quantitative IDEAL (Iterative Decomposition of water and fat with Echo Asymmetry and Least-squares Estimation) and magnitude based chemical shift based methods such as LIPOQuant (Liver Imaging of Phase-related Oscillation and quantification), with T₂* correction and accurate spectral modeling of fat^{1,2,3} have shown great promise for accurate quantification of proton density fat-fraction^{3,4,5,6}. Both approaches use a low flip angle approach to minimize bias related to T₁, because the T₁ of water and fat signals are different^{3,7}. However, higher flip angles are preferred to maximize SNR performance - unfortunately higher flip angles lead to greater overestimation of fat; the relationship between tolerable error and the flip angle has not been described in detail, although preliminary work on this topic has been described^{3,7,8,9}. **The purpose of this work** is to describe an algorithm to estimate the highest possible flip angle given a maximum allowable error in fat-fraction, for spoiled gradient echo (SPGR) acquisitions. In this way, tradeoffs between the accuracy of the fat-fraction estimates and maximizing SNR can be established.

Methods: The fat-fraction for an SPGR acquisition depends on the proton densities of fat and water (F,W), the T₁ values of fat and water (T₁^F, T₁^W), flip angle (α), and TR. For the purpose of this work, we assume that all other confounding factors (spectral complexity of fat^{2,3}, T₂* decay^{1,3}, eddy currents¹⁰ and noise bias⁷) have all been addressed. The apparent fat-fraction (η') will be biased by an error (Δη), such that η' = Δη + η, where η is the true fat-fraction. It can be shown that,

$$\eta' = \Delta\eta + \eta = \frac{S_f}{S_f + S_w} = \frac{F(1-E_1^F)\sin\alpha}{1-E_1^F\cos\alpha} \bigg/ \left(\frac{F(1-E_1^F)\sin\alpha}{1-E_1^F\cos\alpha} + \frac{W(1-E_1^W)\sin\alpha}{1-E_1^W\cos\alpha} \right)$$

(1) where E₁^W = exp(-T₁^W/TR) and E₁^F = exp(-T₁^F/TR), for simplicity. Rearranging Equation 1 yields a quadratic equation in cos(α), whose solution has only one real root, with the following solution and substitutions for simplicity:

$$\cos\alpha = \frac{-G + \sqrt{G^2 + 4FE}}{2F} \quad (2) \quad \text{where } \begin{aligned} A &= -E_1^F - E_1^W + (E_1^F)^2 + E_1^F E_1^W & B &= E_1^F E_1^W - (E_1^F)^2 E_1^W & C &= -2E_1^F + 2E_1^F E_1^W \\ D &= (E_1^F)^2 - (E_1^F)^2 E_1^W & E &= \Delta\eta/\eta + E_1^W(-\Delta\eta/\eta + \Delta\eta + \eta - 1) + E_1^F(-\Delta\eta - \eta + 1) \\ F &= B(-\Delta\eta - \eta + 1) + D(-\Delta\eta/\eta + \Delta\eta + \eta - 1) & G &= A(-\Delta\eta - \eta + 1) + C(-\Delta\eta/\eta + \Delta\eta + \eta - 1) \end{aligned}$$

Simulations were performed using Matlab (v.7.0.1, Mathworks, Natick, MA), with user-defined inputs for T₁^F (343ms at 1.5T)⁷, T₁^W (586ms at 1.5T)⁷, at a true fat-fraction (η = 0.5) where the error will be highest. Simulations were performed for short (0-20ms) and long TR (100-200ms) values, and both with maximum error caused by T₁ bias (Δη) ranging from 0.5% to 5%. A phantom with homogeneous fat-fractions was constructed⁵ and scanned at flip angles of 1, 3, 5, 10, 20, and 30° using an investigational version of 3D spoiled gradient echo (SPGR) IDEAL¹¹ using a single channel quadrature head coil at 1.5T (TwinSpeed HDx, GE Healthcare, Waukesha, WI). Imaging parameters included: ETL=6 with minimum echo time of 1.3ms and echo spacing of 2.3ms, TR=14.9ms, BW= ±100kHz, FOV=35x25cm, slice=8mm, and 256x256matrix. Single voxel MR spectroscopy (STEAM) was also performed with increasing TR to measure T₁^W and T₁^F from the 50% vial.

Results: Figures 1 and 2 display the calculated flip angle for T₁ biases of 0.5% to 5% (blue lines) at a fat-fraction of 50% for short TR sequences typically used for 3D acquisitions^{6,7} (Fig.1) and for longer TR sequences typically used for 2D interleaved acquisitions^{3,11} (Fig.2). As expected, higher flip angles yield greater error in fat-fraction from T₁ bias, although this error has not previously been quantified. For comparison, the red lines display the Ernst angle for water for each TR; T₁ bias is calculated to be 5.8% using Equation 1, indicating that the apparent fat-fraction would be 55.8% when the true fat-fraction is 50%.

Using the measured T₁^W and T₁^F values from the phantom as inputs to calculate theoretical apparent fat-fractions (black), Figure 3 compares theoretical results against measured fat-fractions (squares) in the phantom experiment with increasing flip angles for various known fat-fractions. It can be seen from Figure 3 that predicted behavior using Eq. 2 accurately reflects phantom data.

Discussion and Conclusion: Given known values of T₁^F, T₁^W, TR, fat-fraction and maximum allowable error, Equation 2 simplifies the problem of determining the flip angle that maximizes SNR performance while maintaining acceptable maximum error from T₁-related bias. This approach can also be used to quantify the error at various flip angles and fat-fractions. It is our goal that this algorithm may serve as a reference for trying to choose the most appropriate flip angle for 2D or 3D spoiled gradient echo methods aimed at quantifying fat. A Matlab function will be posted online under mathworks.com file exchange.

References: [1] Yu *et al*, MRM 2007 26(4):1153-61 [2] Yu *et al*, MRM 2008 60(5):1122-34 [3] Bydder, *et al*. MRI 2008;26(3):347-59 [4] Yokoo *et al*, Radiology 2009 251(1):67-76 [5] Hines *et al*, JMRI 2009 30(5):1215-22. [6] Reeder *et al*, JMRI 2009 29(6):1332-9 [7] Liu, *et al*. MRM 2007;58(2):354-64 [8] Fishbein *et al*, MRI 1997 15(3):287-93 [9] Hussein *et al*, Radiology 2005 237(3):1048-55. [10] Yu ISMRM 2009 #461 [11] Reeder *et al*, JMRI 2007 25(3):644-52

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