Sources of Systematic Error in MRI Liver Fat Quantification

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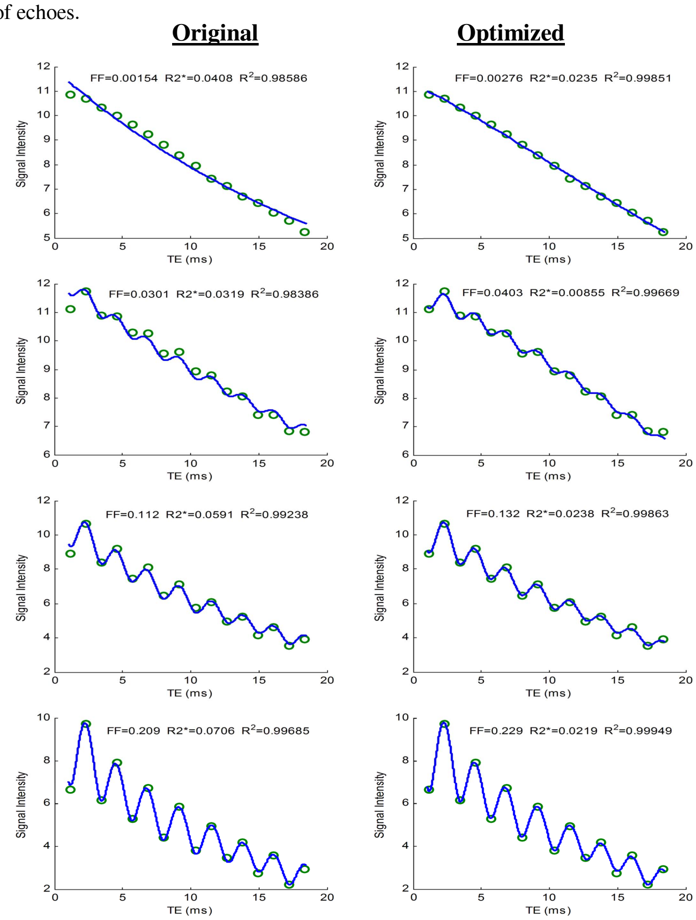
TARGET AUDIENCE: Researchers and clinicians interested in quantitative methods for measuring PDFF and relaxation rates.

PURPOSE: Many fat quantification techniques employ chemical-shift sensitive sequences to estimate the proton density fat fraction (PDFF). The variation of signal with echo time reflects interference between lipid and water protons, which can be modeled to give their relative proportions [1]. Different physical/chemical processes are included in the model to eliminate confounding effects [2], e.g. R2* decay removes a spurious dependence of PDFF on R2* [3]. Establishing the robustness of PDFF quantification to relaxation rates and imaging parameters helps to instill confidence in PDFF as a biomarker of disease progression. One recent study [4] measured PDFF in liver using 3 - 16 echoes and observed that the PDFF decreased in a systematic zig-zag pattern with increasing number of echoes despite correcting for R2* and the fat spectrum. The authors suggested this may indicate remaining errors in the model. The purpose of the present study is to evaluate several physical/chemical processes that may lead to variation in PDFF with number of echoes.

METHODS: This is a retrospective analysis of data from 84 subjects using 2D spoiled gradient echo: 3.0T GE HDx, 8ch body array, 192x192, FOV 40-44cm, 8mm slice, flip 10, TR 125-200, TE[n]=1.15n, n=3-16, magnitude images. Regions of interest were drawn in the right lobe of the liver and the mean signal versus echo time (n=3-16) was fitted using a model that included PDFF and R2* as parameters and a fat spectrum based on the number of double bonds (NDB) = 1.92 [5].

Several additional confounds were considered: non-exponential decay (Gaussian), R2* difference between water and fat, NDB, noise bias and water frequency shift. Signal decay was of the form $\exp(-A \cdot TE - B \cdot TE^2)$, where A represents the exponential (R2*) and B represents the Gaussian. This was applied to fat and water separately and a difference, R2*(water)–R2*(fat) = $C_0 + C_1 \cdot$ PDFF, was introduced. This formulation allows for a constant offset as well as possible dependence on fat (since fat droplets may act as a mild R2* agent). A noise bias term E was included, signal → sqrt($\text{signal}^2 + E^2$), as was the water frequency F (in ppm).

The 5 variables (B, C_0, C_1, E, F) were fitted globally over the 16 echos and 84 subjects (note that the R2* parameter A was fitted individually per subject and NDB was taken from a published value of NDB = 2.436 [6]). The original values were based on Ref [5] and fitting was performed by nonlinear least squares.



RESULTS: Values for the globally fitted parameters are shown in the Table below. The change in the residual norm |r|| due to each parameter is given in the last column and example fits are shown in the Figure to the right. Note the improved quality of fit at all fat levels. The dependence of PDFF on number of echoes was also evaluated. The Figure at the bottom right shows the mean PDFF (over all subjects) estimated using different numbers of echoes with the successive inclusion of different corrections (in order of importance according to Δ||r||). The decreasing zig-zag pattern that is seen with the original model parameters is essentially absent with the optimized parameters.

DISCUSSION: Simplifications in modeling can result in errors in fitting and can create spurious dependences between parameters. In the case of PDFF, employing corrections for Gaussian decay and NDB can account for >95% of the improvement in quality of fit (as determined by Δ||**r**||). However a dependence of PDFF on number of echoes is still observed until a correction for an R2* difference between water and fat is used. While the magnitude of these corrections on PDFF are small, it is useful to recognize the systematic errors and understand their origins.

REFERENCES: [**1**] Ma J. J Magn Reson Imag 2008; 28: 543 [**2**] Hernando D et al. Magn Reson Med 2012; 68: 830 [**3**] Bydder M et al. Magn Reson Imag 2008; 26: 347 [**4**] Levin YS et al. J Magn Reson Imag 2014; 39: 567 [**5**] Hamilton G et al. NMR Biomed 2011; 24: 784 [**6**] Lundbom J et al. NMR Biomed 2011; 24: 23

Parameter	Original ǁrǁ = 7.174	Optimized ǁrǁ = 4.286	Δǁrǁ
B	0	0.97 ± 0.11	2.438
NDB	1.92	2.436	0.301
C_0 C_1	0 0	-0.032 ± 0.017 0.146 ± 0.071	0.119
E	0	0.62 ± 0.32	0.025
F	4.70	4.71 ± 0.02	0.005

PDFF Estimated Using Different No. Echoes With Various Corrections Applied