## Fully automated processing of multi-echo spectroscopy data for liver fat quantification

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Target Audience: Researchers interested in spectroscopy-based fat quantification.

**Purpose:** MR spectroscopy enables rapid and robust liver fat quantification. Specifically, stimulated-echo acquisition mode (STEAM) spectra obtained with multiple echo times (TEs) can provide T2-corrected fat-fraction (FF) measurements in a single breath-hold<sup>1</sup>. Unfortunately, processing of spectroscopy data can be cumbersome. Current jMRUI-based<sup>2</sup> quantification requires: 1) conversion of the multi-coil spectroscopy raw data files to a single-coil text file compatible with jMRUI (converted using an SVD approach in a custom Matlab script), 2) semi-automatic quantification in jMRUI using AMARES<sup>3</sup> with pre-determined constraints, and 3) analysis of the AMARES results for T2-corrected FF measurement (performed using Microsoft Excel). In this work, we develop and validate a fully automated algorithm for fat quantification from multi-echo spectroscopy data.

## **Methods:**

Spectroscopy quantification algorithm: An algorithm for fully automated processing of multi-echo spectroscopy datasets was developed (Figure 1). This algorithm includes the following key parameters: a) Signal model: Voigt line shapes<sup>4</sup> were used to fit each of the peaks, including a single water peak and multiple fat peaks. T2 decay was included to capture the relationship between spectra at multiple TEs. b) Constraints: six fat peaks were used, which were allowed to shift in frequency relative to the water peak, but the frequency separation between fat peaks was kept constant<sup>5</sup>. The relative amplitudes of the smaller fat peaks were allowed to change in the range  $\pm 1\%$  of the total fat signal, and the main fat peak was automatically re-scaled to maintain the normalization of the fat relative amplitudes. Line-widths were estimated for water and fat peaks. For stability, the line-width of all fat peaks was constrained to be the same, and within 5 Hz of that of the water peak.

*Validation:* A total of 425 multi-echo STEAM liver datasets (1.5T: 152 datasets, 3T: 273 datasets) were retrospectively analyzed for this study. Datasets had been originally acquired with IRB approval and informed consent as part of several studies, on two platforms (GE HDxt at 1.5T, GE MR750 at 3T) using a cardiac or body phased array coil. In each case, a breath-held, single voxel STEAM acquisition was performed in the right liver lobe (Couinaud segment 6 or 7) with the following typical acquisition parameters<sup>1</sup>: voxel size  $20 \times 20 \times 20 \text{mm}^3$ , five echoes with TEs (10,15,20,25,30)ms or (10,20,30,40,50)ms, repetition time 3500-3800ms, spectral width ±2.5kHz, 2048 points. Reference FF values were obtained using the jMRUI-based technique<sup>1</sup>. Automated FF values were obtained by batch processing all datasets (with the same constraints in all cases)

Signal model: Constraints on: Single water peak Frequency shifts Multiple fat peaks Relative amplitude T2 decay T2s Inititialization of parameters Fitting routine: Joint for all TFs Least-squares Fat-Fraction < 3%3 No Yes Output: Fit with strong Fat-fraction constraints on fat Water T2 T2 (≥100ms)

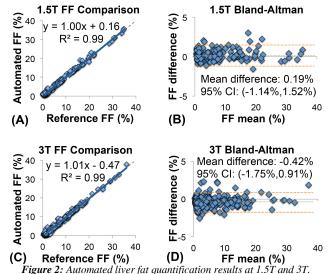
Figure 1: Outline of proposed method

using the algorithm described above. Automated FF values were compared to the reference FF using correlation as well as Bland-Altman analysis, separately for 1.5T and 3T data.

**Results:** A broad distribution of FF values were observed (reference FF range at 1.5T: 0.1-34.9%, mean FF= $8.0\pm8.1$ ; range at 3T: 0.5-36.1%, mean FF= $6.0\pm6.5$ ). Fat-fraction quantification results are shown in Figure 2. Linear regression showed excellent correlation and agreement between automated and reference FF values at both field strengths (1.5T: slope= $1.00\pm0.01$ , intercept= $0.16\pm0.08\%$ ,  $r^2$ =0.99; 1.5T: slope= $1.01\pm0.01$ , intercept= $-0.47\pm0.06\%$ ,  $r^2$ =0.99). Further, Bland-Altman analysis demonstrated close agreement (1.5T: mean difference=0.19%, 95% CI=[-1.14,1.52]%; 3T: mean difference=-0.42%, 95% CI=[-1.75,0.91]%).

**Discussion and Conclusion:** Excellent correlation and agreement between automated FF measurements and reference FF measurements was observed, demonstrating that the proposed algorithm may be able to provide fully automated processing of fat quantification spectroscopy data.

In addition to fat quantification, T2 relaxation times of both fat and water can be measured from multi-echo STEAM datasets, and are also provided by the automated quantification algorithm, although validation of T2 values has not yet been performed. Further, recently developed multi-TR, multi-echo STEAM acquisitions enable additional measurement of T1 relaxation times of water and fat<sup>6</sup>. The proposed algorithm can account for multiple TRs and, upon appropriate optimization and validation, may also be applicable to these data.



The majority of datasets used in this study were themselves used for optimization of the automated fat quantification constraints (eg: ranges of frequency shifts, relaxation parameters, etc). Hence, although these constraints were kept constant for the entire validation study, further validation on separate datasets is needed. Once additional validation has been completed, we will submit this algorithm to the ISMRM Fat-Water Toolbox (http://ismrm.org/workshops/FatWater12/data.htm), in order to help enable widespread dissemination of spectroscopy-based fat quantification.

**References:** <sup>1</sup>Hamilton, NMR Biomed 2011;24:784. <sup>2</sup>Stefan, Meas Sci Technol 2009; 20:104035. <sup>3</sup>Vanhamme, JMR 1997;129:35. 4Marshall, MRM 1997;5:651-657. <sup>5</sup>Hamilton, NMR Biomed 2011;24: 784–790. <sup>6</sup>Hamilton, ISMRM 2013, p1517.

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