Bias in liver fat quantification using chemical shift-encoded techniques with short echo times

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Target Audience: Clinicians and scientists interested in liver fat quantification.

Purpose: Chemical Shift Encoded (CSE) techniques for fat quantification, based on multi-echo spoiled gradient-echo (SGRE) acquisitions, have demonstrated great promise for the assessment of non-alcoholic fatty liver disease (NAFLD). By correcting for all known confounding factors (eg: T1 bias, T2* decay, multi-peak fat spectrum, eddy currents, noise bias), these techniques enable rapid and accurate quantification of proton-density fat-fraction (PDFF), a fundamental biomarker of triglyceride concentration in tissue[1-3]. However, these techniques suffer from relatively low signal-to-noise ratio (SNR), largely due to the rapid acquisition with parallel imaging acceleration and the use of very low flip angles to avoid T1 bias[2-3]. In order to improve the SNR, acquisitions with short echo times (eg: initial TE<1ms) and moderate spatial resolution may be performed. In this work, we evaluate the accuracy of short-TE CSE liver fat quantification by comparing it with a standard CSE technique and MR spectroscopy, in healthy volunteers and patients.

Methods: After obtaining IRB approval and informed written consent, eight healthy volunteers and five patients with chronic liver disease were studied prospectively at 1.5T (Signa HDxt and Optima MR450w, GE Healthcare, Waukesha, WI). The imaging protocol included two single-breath-hold CSE acquisitions, based on a 3D multi-echo SGRE pulse sequence[2], with the following acquisition parameters: *Standard CSE:* flip angle=5°, FOV=40×36cm^2, matrix 256×160, 32 slices, 8mm slices, 6 TEs, TE_{init}=1.2ms, ΔTE=2.0ms, bandwidth=±125kHz; *Short-TE CSE:* flip angle=5°, FOV=40×30cm^2, matrix 160×160, 24 slices, 10mm slices, 6 TEs, TE_{init}=0.7ms, ΔTE=1.3ms, bandwidth=±125kHz. Additionally, each subject was scanned using a stimulated echo acquisition mode (STEAM) spectroscopy sequence to provide a T1- and T2-corrected reference PDFF value[4-5]. The spectroscopy voxel had size 20x20x20mm^3 and was placed in the right lobe of the liver. STEAM spectra were quantified offline to obtain a PDFF measurement[6]. The same imaging/spectroscopy protocol was performed on a water bath to rule out pulse sequence-related artifacts in the CSE data.

In order to assess the effects of the short first TE, each CSE dataset was reconstructed twice: including all six echoes (TEs 1-6) and also discarding the first echo (TEs 2-6), for a total of four PDFF maps (2 acquisitions × 2 reconstructions) per subject. In each case, PDFF maps were obtained with correction for all known confounding factors, including T2* decay, multi-peak fat spectrum and eddy currents[1-3]. Co-localized measurements of PDFF were obtained by placing a circular ROI (area~6cm^2) in the right liver lobe, on each of the PDFF maps. PDFF measurements from CSE data as well as STEAM were compared using Bland-Altman analysis.

Results: PDFF measurements in a water bath were accurate for all acquisitions and reconstructions (PDFF between -0.2% and +0.2% in all cases). In liver imaging, short-TE CSE exhibited elevated signal at the first TE (Figure 1). As shown in Figure 2, Standard-TE CSE (TEs 1-6 or 2-6) provides accurate liver PDFF relative to STEAM, but Short-TE CSE using TEs 1-6 results in positive PDFF bias relative to both Standard-TE CSE and STEAM. Importantly, when the first (short) echo is discarded, the bias is eliminated.

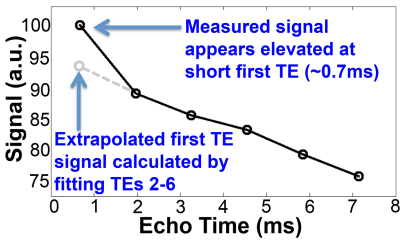

Figure 1: *Short-TE liver CSE acquisitions present elevated signal at the initial short TE. This effect results in bias in fat quantification.*

Discussion & Conclusion: Standard-TE CSE provides accurate PDFF measurements, in agreement with previous studies[2-3]. Short-TE CSE provides high-SNR PDFF maps (due to the moderate spatial resolution and short echo times), but the elevated short-TE signal introduces an additional confounder in liver fat quantification. This effect may complicate the establishment of highly accurate and precise CSE techniques (eg: for assessing subtle differences in PDFF in the low fat range). We speculate that the presence of short T2* species or other patient-dependent factor may be the source of the elevated signal at short TE, leading to this bias in PDFF. Further investigation is needed to fully characterize the source of this effect, as well as its appearance in other scanning platforms.

References: [1]Yokoo et al, Radiology 251:67-76, 2009. [2]Meisamy et al, Radiology 258:767-775, 2011. [3]Hines et al, JMRI 33:873–881, 2011. [4]Hamilton et al, NMR Biomed 2011;24: 784–790. [5]Hamilton et al, ISMRM 2013, p1517. [6]Hernando et al, ISMRM 2014, p2884.

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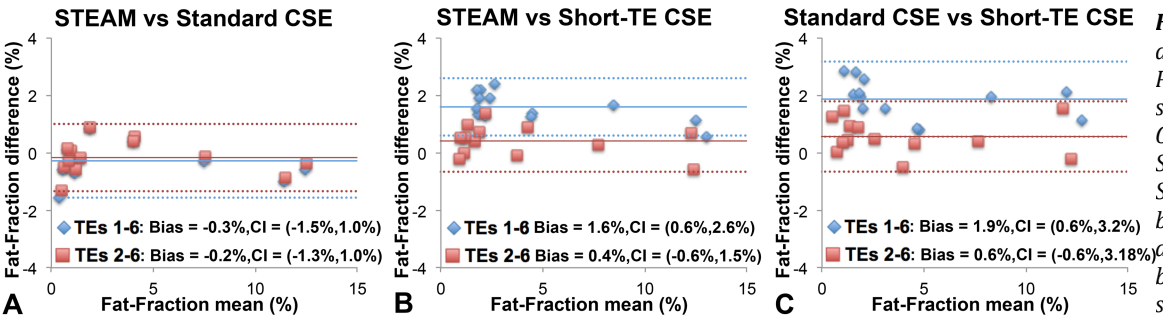

Figure 2: *Bland-Altman analysis shows bias in liver PDFF when using CSE with short TE_{init} ~0.7ms. Standard CSE is unbiased relative to STEAM (A). PDFF from Short-TE CSE has positive bias relative to STEAM (B) and Standard CSE (C). This bias is removed when the short TE is discarded.*