Limits of liver fat quantification in the presence of severe iron overload

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Target Audience: Researchers and clinicians interested in liver fat quantification in the presence of iron overload.

Purpose: Chemical shift encoded (CSE) fat quantification requires the acquisition of images at multiple (often six or more) echo times (TEs) to enable simultaneous fat quantification and R2* (=1/T2*) estimation[1]. Tissue iron deposition can severely increase R2*, resulting in a very rapid signal decay[2]. The loss of signal, especially at later echoes, complicates fat quantification. The ***purpose of this work*** is to assess the feasibility and limits of CSE fat quantification in the presence of liver iron using theoretical analysis and in vivo patient data.

Methods: The Cramer-Rao bound (CRB, accounting for R2* and multipeak fat) was used to measure the noise sensitivity of fat quantification[3]. In order to assess the maximum R2* that enables stable fat quantification for a given TE combination, the effective number of signal averages (NSA) for fat estimation was calculated over a wide range of R2* values, between 0 and 1000 /s at 1.5T. The maximum R2* such that fat estimation had NSA > 0.25 was recorded for each TE combination. This threshold was chosen to provide acceptable fat-water separation under typical imaging conditions. This process was repeated for a range of TE combinations consisting of 6 echoes by varying initial echo TE_{init} and echo spacing ΔTE.

After obtaining IRB approval and informed consent, a total of 37 subjects (9 healthy controls and 28 patients with known or suspected iron overload) were scanned at 1.5T (GE HDxt, GE Healthcare). Each subject was scanned using a stimulated echo acquisition mode (STEAM) spectroscopy sequence including multiple TEs (10, 15, 20, 25, and 30ms) to provide a T2-corrected reference fat-fraction (FF) value[5]. The spectroscopy voxel had size 20x20x20-30x30x30 mm^3 and was placed in the right lobe of the liver. Each subject was also scanned using two different single breath-hold 3D CSE protocols[6]: 1) a standard 6-echo clinical protocol (TE_{init}=1.2ms, ΔTE=2ms in a single echo train), and 2) a protocol with 12 short TEs (TE_{init}=0.7ms, ΔTE=0.8ms in two interleaved echo trains). Other parameters included: 8mm slices, 28 slices, flip = 5°, FOV=40x36cm, TR=14.1ms (standard protocol) or 11.0ms (short-TE), acquisition matrix=256×160 (standard) or 144×128 (short-TE). FF maps were estimated including multi-peak fat modeling and R2* correction[1]. An ROI was placed in the right liver lobe (segment 6) in each fat-fraction map. CSE-FF was compared to the STEAM-FF reference in each subject[6]. In addition, for each subject, an estimate of liver iron concentration (LIC) was obtained using a R2-based method (Ferriscan, ResonanceHealth, Claremont, Australia)[4].

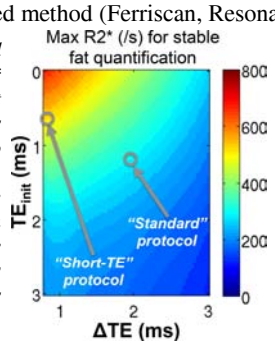

Figure 1: *CRB-based theoretical maximum R2* that would enable stable fat quantification. CRB was calculated for various echo combinations. For each (6-TE) echo combination, the plot shows the maximum R2* such that the effective number of signal averages (NSA) of fat estimation is >0.25.*

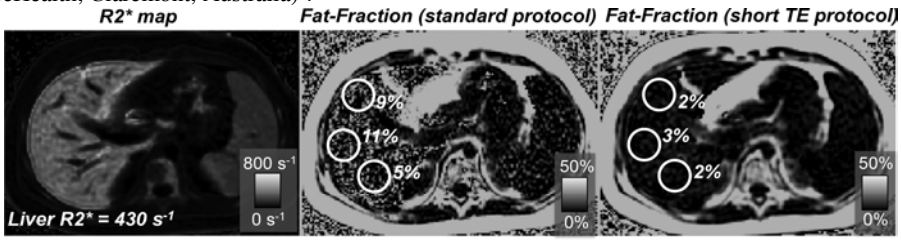

Figure 2: *Fat fraction maps in a patient with high liver iron (LIC = 19.2 mg/g dry), resulting in high R2* (left). Spectroscopy-based fat quantification measured FF=1.4%. A standard CSE protocol results in unstable FF whereas a short TE protocol enables more accurate fat quantification with low bias.*

Results: Figure 1 shows CRB results as a function of the TE combination. Figure 2 shows representative results from a patient with high liver iron. The standard protocol results in very noisy fat-fraction maps in organs with iron accumulation (spleen and liver). The short TE protocol provides stable fat-fraction maps with low bias (1-2%). Over all subjects, STEAM-FF ranged from 0% to 23.6% (4.5±6.4%). Ferriscan-LIC ranged from 0.3 to 19.2 mg/g (4.3±4.4 mg/g). Figure 3 shows the results for all subjects. For LIC<7 mg/g ($R2^*<200 s^{-1}$), there was good agreement with STEAM-FF for both protocols (95% CI for FF error: standard: [-2.7,2.4]%, short-TE: [-1.9,3.2]%). For LIC>7mg/g, there was good agreement only for short-TE (95% CI standard: [-25.6,6.2]%, short-TE: [-5.4,4.8]%). The short-TE protocol provided accurate fat quantification up to an LIC of 19.2mg/g dry. This improvement in accuracy is likely due to three factors: 1) shorter TEs (as predicted by Figure 1), 2) higher SNR (due to lower spatial resolution), and 3) more echoes, although later echoes are expected to contribute little in the presence of rapid R2* decay.

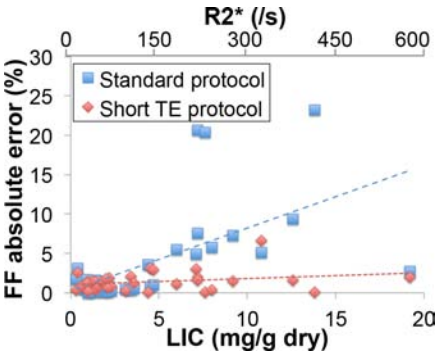

Figure 3: *Fat quantification results in patients with liver iron overload. A standard protocol fails at high iron levels (LIC>7mg/g dry). A short TE protocol performs well up to LIC=19.2mg/g dry.*

Discussion and conclusion: Fat quantification in the presence of moderately elevated R2* has been demonstrated in previous works[7,8]. In the presence of higher R2* (eg: liver iron overload), fat quantification becomes unstable due to severe noise amplification. Theoretically, at least three echoes are needed for R2*-corrected fat quantification; hence, FF is unstable if the signal has decayed away by the third TE. Short-TE protocols enable stable and accurate fat quantification over an extended range of R2*. However, fat quantification may be limited in cases of extreme iron overload (eg: R2*>1000) even when using short echoes, because the transverse signal decays before the water and fat components can achieve sufficient dephasing to enable fat-water separation.

References: [1]Yu, MRM 2008;60:1122–1134. [2]Wood, Blood 2005:106:1460-1465. [3]Hernando, MRM 2010;64:811–822. [4]St Pierre, Blood 2005;105:855-861. [5]Hamilton, NMR Biomed 2011;24:784. [6]Meisamy, Radiology 2011;258:767-775. [7]Bydder, MRI 2010;28:767-776. [8]Hines, JMRI 2012;35:844-851.

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