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. Tissue iron deposition can severely increase R2*, resulting in a very rapid signal decay. 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 multiplex fat) was used to measure the noise sensitivity of fat quantification. 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 TEinit 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. The spectroscopy voxel had size 20x20x20-30x30x30 mm3 and was placed in the right lobe of the liver. Each subject was also scanned using two different single breath-hold 3D CSE protocols: 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 using multiplex fat modeling and R2* correction. 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. In addition, for each subject, an estimate of liver iron concentration (LIC) was obtained using a R2-based method (Ferriscan, ResonanceHealth, Claremont, Australia).

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*<200s-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]%). 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*<200s-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]%). 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).