Relationship between liver proton density fat fraction and R2* in the absence of iron overload

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

Purpose: Recently developed chemical shift encoded (CSE) techniques have been shown to enable rapid fat[1,2] and iron[3,4] quantification over the entire liver. These techniques measure several parameters, including proton density fat fraction (PDFF) and R2* (=1/T2*), which provide quantitative biomarkers for triglyceride concentration[5] and iron concentration[6], respectively. However, the relationship between liver PDFF and R2* is not yet fully understood[4]. ***The purpose of this study*** was to evaluate the relationship between liver PDFF and R2* in patients with histology-confirmed absence of iron overload.

Methods: After obtaining IRB approval and informed written consent, consecutive severely obese patients in our bariatric clinics were recruited and scanned at 3T (MR750, GE Healthcare, Waukesha, WI), <5 weeks prior to clinically indicated bariatric surgery. Intraoperative biopsies were obtained for research and assessed by an experienced pathologist for steatosis and iron grading. Patients with histologic iron (grade ≥ 1) were excluded from the current analysis. CSE acquisitions were performed using two different whole-liver multi-echo spoiled gradient echo sequences: ***2D CSE***[1] with 6 echoes in a single shot, TR=150ms, TE_{min}=1.1ms, ΔTE=1.15ms, flip angle=10°, BW=±125KHz, FOV=44cm, slice=8mm, 224x160 matrix, 28 slices; and ***3D CSE***[2] with 6 total echoes in two shots, TR=8.6ms, TE_{min}=1.2ms, ΔTE=1.0ms, flip angle=3°, BW=±125kHz, FOV=44cm, slice=8mm, 256x128 matrix, 32 slices. These two CSE acquisitions were reconstructed offline, to obtain PDFF and R2* maps with correction for multi-peak fat[7]. To assess the effects of different reconstructions, three different PDFF and R2* maps were calculated for each subject[8]: 2D CSE with magnitude fitting (no phase data was available for this acquisition), 3D CSE with magnitude fitting, and 3D CSE with complex fitting. For each reconstruction type, liver PDFF and R2* were measured by averaging ROIs from each of the 9 Couinaud liver segments. Linear regression analysis was performed between the resulting PDFF and R2*.

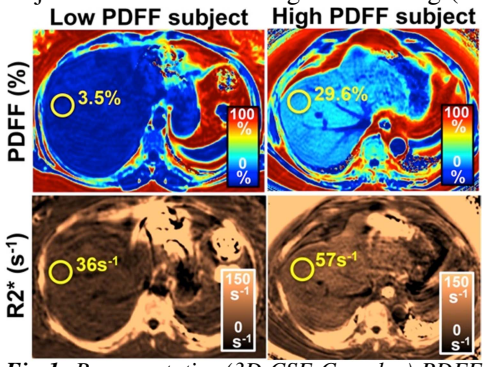

Fig 1: Representative (3D CSE-Complex) PDFF and R2 maps in two subjects with low and high PDFF, respectively, showing higher liver R2* in the subject with high liver PDFF.*

Results: 25 obese patients (49.2±13.1 years, BMI=45.2±4.0 kg/m^2, weight=120.4±16.4 kg) were enrolled. Histologically, all patients had grade 0 iron (none had iron overload), and 19 (76%) had steatosis (grade 0: 6 subjects [24%]; grade 1: 15 subjects [60%]; grade 2: 4 subjects [16%]). Reconstructions were performed successfully from all 25 subjects for 2D CSE, and from 24 subjects for 3D CSE (missing data for one subject). Figure 1 shows representative PDFF and R2* maps from 3D CSE with complex reconstruction, in two subjects with low and high PDFF, respectively. In these examples, the subject with high PDFF also had higher R2*. As shown in Figure 2, a strong positive correlation was observed between PDFF and R2* for all three reconstructions. Correlation coefficients ranged from 0.79 to 0.84 ($p < 10^{-5}$ in all cases), with regression intercepts and slopes as shown.

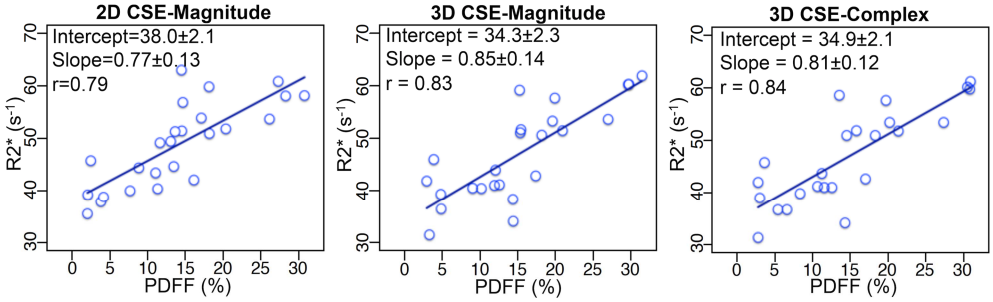

Fig 2: A strong correlation was observed between liver PDFF and R2 using three CSE techniques.*

Discussion & Conclusion: This work demonstrates a strong correlation between PDFF and R2* in subjects with histology-confirmed absence of iron overload. These results contrast those of Kühn et al[4], where no correlation was found between liver steatosis and R2*. This discrepancy may be due to differences in the patient cohorts, MRI platforms or imaging protocols. The presence of strong correlations in all three reconstructions (obtained from two independent acquisitions), however, suggests that this effect is not due to system errors, but rather represents a real effect. We speculate that this correlation may be due to slight mismatches between the true spectral model of fat and that used in the reconstruction algorithm, or due to microscopic susceptibility effects (eg: local B_0 field inhomogeneities induced by intracellular fat vacuoles in cases of steatosis or sub-microscopic iron deposition). The overall impact on R2* (<25s^{-1}) appears small in comparison with the R2* increases observed in the presence of moderate-severe iron overload[3]. Nevertheless, slight elevations in R2* associated with high fat fractions potentially could lead to false-positive diagnoses of mild iron overload. Future work will be needed to fully characterize the source of this effect and to assess its impact on CSE liver fat and iron quantification.

References: [1]Yokoo et al, Radiology 258:749-759, 2011. [2]Meisamy et al, Radiology 258:767-775, 2011. [3]Vasanawala et al, MRM 67:183-190, 2012. [4]Kuhn et al, Radiology 265:133-142, 2012. [5]Reeder et al, MRICNA 18:337-57, 2010. [6]Sirlin et al, MRICNA 18:359-381, 2010. [7]Hamilton et al, NMR Biomed 24:784-90, 2011. [8]Hernando et al, MRM 64:811-822, 2010.

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