Liver Fat Quantification with MRI: Comparison of 2 point-Dixon and 3 point-Dixon methods to T2 corrected multiecho single-voxel spectroscopy

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Introduction: MR sequences including single voxel spectroscopy (SVS) and Dixon based techniques allow for noninvasive quantification of hepatic fat (1). Prior studies have demonstrated excellent correlation between FF (fat fraction) measured with SVS and histopathologic measures of hepatic fat content (2-5). Multiecho SVS methods with T2 correction have been developed for accurate fat quantification by accounting for T2 effects (6). The two point Dixon (2PD) method is widely used clinically. However, this method is highly susceptible to T2* effects seen in the setting of concomitant hepatic iron deposition (7). In order to account for this, Dixon reconstruction methods using 3 echoes (3PD) or more that estimate and correct for T2* have been developed (8). In this study, we compare the diagnostic accuracy of 2PD and 3PD sequences for liver fat quantification using multiecho T2 corrected SVS as the reference standard, and we examined the effect of hepatic iron deposition.

Methods: This is an IRB-approved retrospective single-center study. We included patients who underwent 1.5T MR examinations of the liver on the same system (Avanto, Siemens) that included breath-held 2PD (TE 2.2- 4.4), 3PD (TE 2.4-4.8-9.5) and multi-echo SVS (HISTO, using TEs 12-72) sequences as well as multiecho T2* (TEs 1.96-21) for iron detection. The 3PD sequence estimated a T2* value per pixel from two in-phase echoes (TE 4.8, 9.5) using a linear fit in log space. This was then used to correct the signal intensity (SI) of the out-phase (TE 2.2) and the first in-phase (TE 4.8) echoes to a virtual TE 0 following which a Dixon reconstruction was performed. Using Osirix software, a single observer placed a pair of ROIs of 4-5 cm^2 on each of two slices centered on the portal vein bifurcation on the 2PD and 3PD image sequences. Average SI was used to compute FF measured by 3PD (FF-3PD) and 2PD (FF-2PD), which were compared with FF-SVS using Pearson's correlation and Bland-Altman analysis. Sensitivity and specificity of 2PD and 3PD for detection of FF-SVS > 5% were calculated.

	2PD	3PD
FF (%)	1.0 ± 10.3	6.2 ± 6.1
Correlation with SVS	0.60 p<0.001	0.93 p<0.001
Sensitivity**	47%	81%
Specificity**	100%	82%
Mean ± 1.96 to SVS (Bland Altman)	4.7 ± 16.1	-0.4 ± 4.5

FF observed with 2PD and 2PD, Pearson correlation coefficients and Bland-Altman of 2PD-FF and 3PD-FF compared to SVS-FF used as the reference standard.
**for FF-SVS > 5%

Fig. 2: Limited accuracy of 2PD in a patient with steatosis and iron deposition (T2* 14 msec). 2PD in-phase (A), opposed-phase (B), T2* corrected FF map from 3PD (C), and SVS images (D). FF was underestimated using 2PD (at 7.6%). FF-3PD was 11.3%, and FF-SVS was 11.8%

Results: We identified 211 patients (M/F: 114/97, mean age 55 y, mean BMI 28.0 ± 5.6) with 3 who had repeat imaging, yielding a total of 214 MR studies. The following liver fat distribution on SVS was noted: < 5% (n=133), 5-10% (n=51), 10-20% (n=19), 20-50% (n=8) with a mean SVS-FF of 5.8 ± 5.7% and a maximum of 40.4%. There was a strong significant correlation between 3PD and SVS and a moderate significant correlation between 2PD and SVS **(Table, Fig. 1)**. Bland-Altman analysis revealed strong agreement between 3PD and SVS and weaker agreement between 2PD and SVS **(Table)**. Sensitivity of 3PD for diagnosing FF> 5% was higher than that of 2PD **(Table)**. We identified 32 patients with iron deposition (liver T2* <20 msec) with a mean T2* of 15.0 ± 3.8 msec on multiecho T2* (7) **(Fig. 2)**. When these patients were excluded, the correlation of 2PD with SVS improved significantly (r=0.88, p <0.0001), while 3PD correlation coefficient remained unchanged (r=0.91, p < 0.0001).
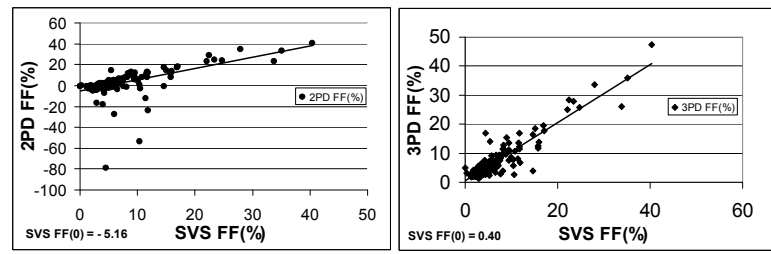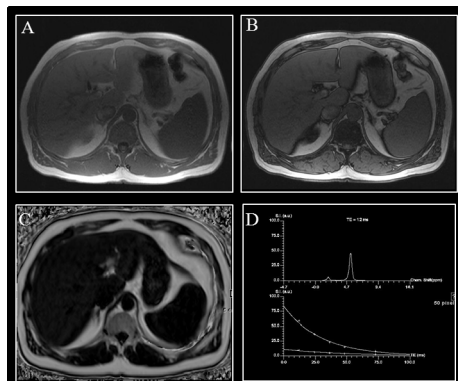
Fig 1: Correlation plots of 2PD-FF vs. SVS-FF (left) and 3PD-FF vs. SVS-FF (right) with y-intercept values are shown.

Discussion: Our large series demonstrates strong correlation and agreement between hepatic fat quantified with 3PD and SVS (used as the reference). Correlation between 2PD and SVS was weaker, particularly in the setting of concomitant iron deposition. This highlights the need to correct for T2* effects with the use of Dixon methods while also showing that the use of two echoes to estimate T2* as done in our 3PD sequence is sufficient for this purpose. Limitations of the study include the lack of histopathologic confirmation of hepatic fat and iron content and absence of spatial co-registration between each of 2PD and 3PD with SVS. **These findings validate the use of the 3PD sequence for accurate quantification of hepatic fat.**

References
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