R2* of water and fat in hepatic iron overload: implications for R2*-corrected fat quantification

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Target audience: Researchers and clinicians interested in liver fat quantification.

Purpose: Accurate fat-fraction (FF) quantification using chemical shift-encoded techniques necessitates correction for R_2^* ($=1/T_2^*$) decay[1,2]. Estimation of a common R_2^* for both fat and water ("single-R_2^*") has been shown to be more accurate and stable than independent estimation ("dual-R_2^*") in a clinical study[3]. However, that study was performed on a patient population without iron overload. The presence of iron in liver leads to elevated R_2^* (***Fig. 1***), and the relative increase of R_2^* of water and fat components is unknown. If these values are significantly different, this may compromise the accuracy of single-R_2^* correction methods. The ***purpose of this work*** is to characterize the R_2^* behavior of water and fat in the presence of liver iron, and to determine whether single-R_2^* correction is accurate for measurement of fat fraction (FF).

Methods: After obtaining IRB approval and informed consent, we performed liver scans on 42 subjects: 32 patients with known or suspected iron overload and 10 healthy controls. Chemical shift-encoded imaging and MRS was performed at 1.5T (SignaHDx, GE Healthcare, Waukesha, WI) and at 3.0T (MR750, GE Healthcare, Waukesha, WI) using 8-channel and 32-channel phased array coils, respectively.

At both field strengths, single-voxel MRS was performed with STEAM (STimulated Echo Acquisition Mode) in a single breath-hold, with TE_1=10ms, ΔTE=5ms, 5 echoes. At 1.5T a multi-echo 3D SPGR acquisition was performed, with TE_1=0.9 ms, ΔTE=0.7ms, TR=11 ms, 6 echoes/TR, 2 interleaves, flip angle=5°, and matrix=144×128. At 3.0T a multi-echo 3D SPGR acquisition was performed, with TE_1=0.6 ms, ΔTE=0.6ms, TR=5.9 ms, 4 echoes/TR, 2 interleaves, flip angle=3°, and matrix=128×128.

FF was measured from MRS by AMARES fitting with jMRUI (Universitat Autònoma de Barcelona, Barcelona, Spain) and Matlab (Mathworks, Natick, MA). FF was also measured from the imaging data with a multi-peak, confounder-corrected[4,5], single-R_2^* model, performed with magnitude fitting to avoid the effects of eddy currents[6]. We compared the accuracy of FF measurement at 1.5T and 3.0T, using MRS as the reference. To evaluate the need for dual-R_2^* correction we measured the relative difference in R_2^* values of fat and water measured with MRS. R_2^* estimates were obtained from Lorentzian fits of the water and main methylene peaks, from the MRS data. Although the MRS R_2^* values are not necessarily the same as the imaging R_2^* values due to macroscopic B0 variations across the larger spectroscopy voxel, the *difference* between $R_2^*{}_f$ and $R_2^*{}_w$ in both spectroscopy and imaging should be the same since the water and fat signals are co-localized in the same voxel[3].

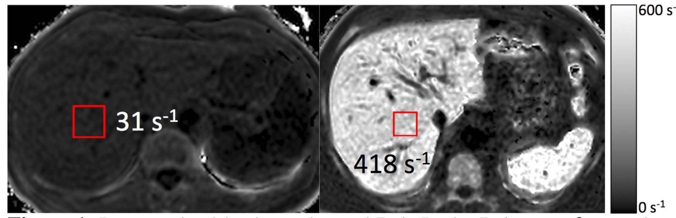

Figure 1. Iron overload leads to elevated R_2^*. In the R_2^* map of normal liver (left), the mean R_2^* in the ROI depicted is **31 s^{-1}**; in an iron-overloaded liver (right), the mean R_2^* in the ROI depicted is **418 s^{-1}.** The ROIs are the same size.

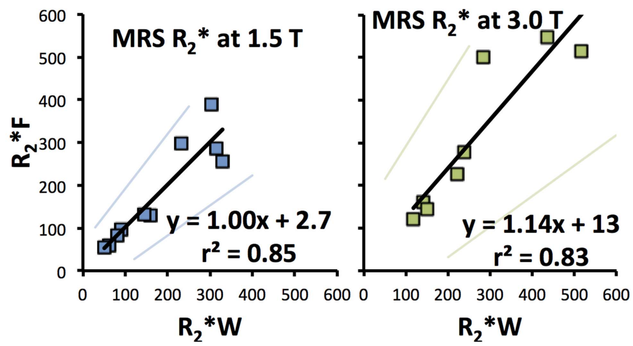

Figure 2. The R_2^* of fat is close in value to the R_2^* of water, even at the elevated values that are observed in the iron-overloaded liver. The 95% confidence intervals are shown in light blue and light green lines.

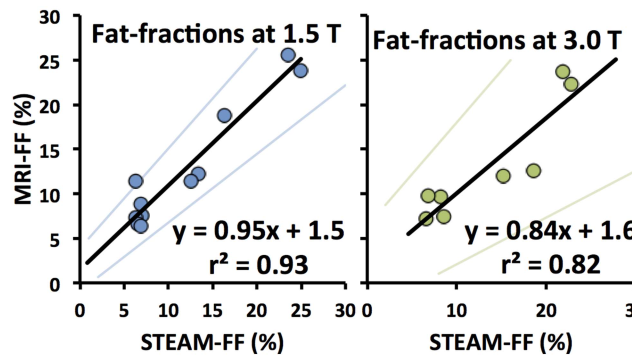

Figure 3. Fat-fraction quantification is accurate over a wide range of fat and iron levels, at 1.5 T (left) and 3.0 T (right). The 95% confidence intervals are shown in light blue and light green lines.

Results: Out of the 42 exams, we identified 10 subjects with fatty liver at 1.5T and 8 at 3.0T (FF>5.6%, based on MRS). The 2 cases that had fatty liver at 1.5T, but not at 3.0T, had FF just below 5.6% at 3.0T. The linear correlation of $R_2^*{}_f$ and $R_2^*{}_w$ (measured from MRS) shows good overall agreement (***Fig. 2***): at 1.5T the fit is slope=1.00 [95% CI 0.70, 1.3], intercept=2.7 [CI -57, 63], r2=0.85, and at 3.0T slope=1.14 [CI 0.72, 1.6], intercept=13 [CI -112, 137], r2=0.83. Since the R_2^* of water and fat are very similar, we expect FF estimated using a single-R_2^* model to be accurate, even at high R_2^*. FF measured from imaging vs. FF measured from spectroscopy at two field strengths is plotted in ***Fig. 3***. Linear regression demonstrates good correlation and agreement between imaging and spectroscopy at both 1.5T: **slope=0.95 [95% CI 0.77, 1.1], intercept=1.5% [CI -0.93%, 3.9%], r^2=0.93,** and at 3.0T: **slope=0.84 [CI 0.53, 1.2], intercept=1.6 [CI -3.2%, 6.4%], r^2=0.82**.

Discussion and Conclusion: ***Single-R_2^* correction is an accurate and acceptable model for R_2^* correction for fat quantification in the liver, even in the presence of iron overload***, due to the minimal difference between $R_2^*{}_f$ and $R_2^*{}_w$. Single-R2* correction had previously been shown to be accurate, but only at normal iron levels (low R_2^*). The estimation of FF at high R_2^* using a single-R_2^* model already suffers from poor noise performance, particularly at 3.0T (note the increased CI). Dual-R_2^* correction introduces additional degrees of freedom that significantly degrade the noise performance of FF estimates[7]. Therefore it is fortuitous that a single-R_2^* model is accurate in the presence of iron overload.

References: **1.** Yu H et al. JMRI. 2007;26(4):1153-61. **2.** Bydder M et al. MRI. 2008;26(3):347-59. **3.** Horng DE et al. JMRI. 2013;37(2):414-22. **4.** Meisamy S et al. Radiology. 2011;258(3):767-75. **5.** Hines CD et al. JMRI. 2011;33(4):873-81. **6.** Yu H et al. MRM. 2011;66(1):199-206. **7.** Chebrolu VV et al. MRM. 2010;63(4):849-57.

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