Effect of gadolinium-based contrast agent on the relaxation properties of water and fat in human liver as measured *in vivo* by ^{1}H MRS.

Gavin Hamilton[1], Michael S Middleton[1], Guilherme M Cunha[1], and Claude B Sirlin[1]
[1]*Department of Radiology, University of California, San Diego, San Diego, California, United States*

Target Audience: The abstract is aimed at radiologists and physicists with an interest in liver fat quantification and characterization.

Purpose. Gadolinium-based contrast agents may affect water and fat differently in liver MR imaging. Fat is stored as droplets within hepatocytes which may limit interaction of the contrast agent and fat even if the contrast agent is taken up by the cell. In this study we evaluate the effect of a hepatocyte-specific MR gadolinium-based contrast agent, gadoxetate (Gd-EOB-DTPA, Bayer Healthcare), on T1 and T2 of fat and water in human subjects using a ^{1}H MRS pulse sequence designed to measure T1, T2, and proton density fat fraction (PDFF) simultaneously in a single 21 s breath-hold.

Methods. This study was IRB approved and HIPAA compliant with subjects signing informed consent. *In vivo* ^{1}H MR spectra were acquired at 3 Tesla (GE Signa EXCITE HD, GE Healthcare, Waukesha, WI) using an 8-channel torso array coil in 59 subjects who were undergoing a gadoxetate-enhanced MR examination of the liver as part of clinical care. After conventional imaging, a 20 x 20 x 20 mm voxel was selected within the liver that avoided liver edges and major blood vessels. A version of a Stimulated Echo Acquisition Mode (STEAM) sequence was used which acquired spectra at multiple TRs and TEs to measure the T1 and T2 of fat and water, and PDFF, in single 21 s breath-hold. The minimum mixing time (TM 5 ms) was used to reduce j-coupling effects, the bandwidth was 5000 Hz, and 256 data points were acquired per spectrum and no water or spatial saturation was used. The MRS voxel was shimmed during free breathing. Sequence timing is detailed in **Table 1**. The sequence was acquired pre-contrast and then again post-contrast, with the typical time between injection and post-contrast MRS being 20 min. The spectra from the individual channels were combined using a singular value decomposition based approach (**1**). A single experienced observer analyzed the spectra using the AMARES algorithm (**2**) included in the MRUI software package (available from www.mrui.uab.es). Results were saved in a text file and analyzed in a custom Matlab routine that non-linearly minimizes the difference between peak area and the peak given by the standard equation $S = S_0\left(1 - \exp\left(-\frac{TR}{T1}\right)\right).\exp\left(-\frac{TE}{T2}\right)$. T1 and T2 were calculated for water (4-6 ppm) and fat (0-3 ppm). PDFF was corrected for the fat included 'in' the water peak from a previously established standard liver spectrum (**3**).

Table 1: The sequence timing of the proposed sequence. P1-P4 are pre-pulse excitations. Scan time 20.95 s.

Spect No.	**P1**	**P2**	**P3**	**P4**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
TR (ms)	150	150	150	150	150	225	300	400	600	900	2000	1500	700	450	325	250
TE (ms)	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
Spect No.	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**24**	**25**	**26**	**27**	**28**
TR (ms)	175	200	275	350	500	800	1250	1000	1000	1000	1000	1000	1000	1000	1000	1000
TE (ms)	10	10	10	10	10	10	10	10	15	20	25	30	50	70	90	110

Results. Typical T1 recovery curves for water pre- and post-contrast are shown in **Figure 1**. T1 and T2 of water and fat are shown in **Figure 2** and **Figure 3**. In these figures, only subjects with PDFF > 5% (n = 20) have fat T1 and T2 displayed, as at low fat levels there is insufficient fat signal to measure fat T1 and T2. Comparison of the PDFF pre- and post-contrast is shown in **Figure 4**. The dotted line indicates unity. There is no evidence of change in fat T1 (pre 361 ms, post 359 ms, p = n.s.) or fat T2 (pre 53.6 ms, post 54.3 ms, p = n.s.); for water there is a significant difference in T1 (pre 933 ms, post 358 ms, p < 0.0001) and T2 (pre 25.9 ms, post 23.4 ms, p < 0.0001). There is no significant difference in the PDFF estimate pre- and post-contrast.

Conclusion and Discussion. While gadolinium-based contrast agents significantly reduced T1 and T2 of water, there was no change in fat T1 and T2. Post-contrast water and fat both showed similar T1 values. This suggests that hepatic PDFF MRI measurement methods could benefit from being carried out post-contrast administration to reduce T1 bias.

Refs: 1) Bydder M, Magn Reson Imaging 2008; 26: 847-850. **2)** Vanhamme L, J Magn Reson 1997; 129: 35-43. **3)** Hamilton G, NMR Biomed 2011; 24: 784-790.

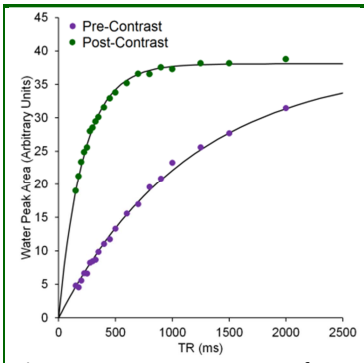

Figure 1: T1 recovery curves for water pre- and post-contrast

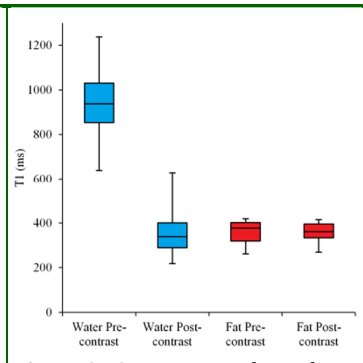

Figure 2: Comparison of T1 of water and fat pre- and post-contrast

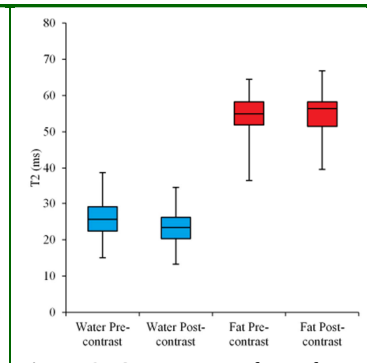

Figure 3: Comparison of T2 of water and fat pre- and post-contrast

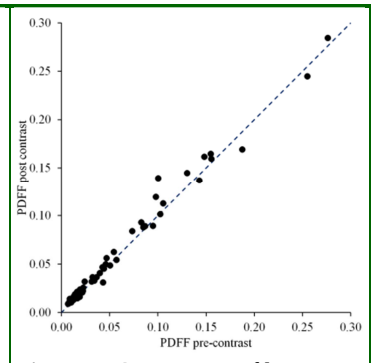

Figure 4: Comparison of liver PDFF pre- and post-contrast