Efficient measurement of liver T1, T2 and PDFF by multi-TR, multi-TE single breath-hold ^{1}H MR spectroscopy.

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

Introduction: We have developed a rapid multi-TR, multi-TE ^{1}H MRS sequence for *in vivo* hepatic fat quantification and characterization that acquires 32 single-average spectra in a single breath-hold (**Table 1**), allowing collection of liver proton density fat fraction (PDFF), and water and fat T1 and T2 values as part of a standard clinical MR exam. We present here mean values of these measurements, and examine the relationship between liver water and fat T1 and T2, and PDFF in adult subjects without contrast.

Methods: Acquisition**:** *In vivo* ^{1}H MR spectra were acquired without contrast at 3 Tesla (GE Signa EXCITE HDxt, GE Healthcare, Waukesha, WI) using an 8-channel torso array coil in 252 adult subjects between January 2012 and October 2013. A 20 x 20 x 20 mm voxel was selected within the liver, avoiding liver edges and major blood vessels. Thirty-two spectra (including four preparatory acquisitions) were acquired in a 21 s breath-hold using a modified Stimulated Echo Acquisition Mode (STEAM) sequence (timings in **Table 1**). A minimum mixing time (5 ms) was used to reduce j-coupling effects. Bandwidth was 5000 Hz, and 256 data points per spectrum were acquired with no water or spatial saturation. The selected voxel was shimmed during free breathing.

Table 1: Sequence timing of the multi TR-TE 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

Analysis**:** Spectra from the individual channels were combined using singular value decomposition (**1**). A single experienced observer analyzed the spectra using the AMARES algorithm (**2**) included in the MRUI software package (**3**). The results were analyzed with a custom Matlab routine that non linearly fitted the measured peaks area to 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) as well as the individual fat spectral peaks; PDFF was corrected for fat included in the 'water' peak from a previously-established standard liver spectrum (**4**). Correlation analyses were performed.

Parameter	Mean (SD)
Water T1	906 (149) ms
CH_2 (2.1 ppm) T1	271 (43) ms
CH_2 (1.3 ppm) T1	342 (46) ms
CH_3 (0.9 ppm) T1	730 (168) ms
Fat (0-3 ppm) T1	349 (48) ms
Water T2	24.6 (4.8) ms
CH_2 (1.3 ppm) T2	64.1 (6.4) ms
Fat (0-3 ppm) T2	59.8 (5.7) ms
PDFF (%)	10.1 (8.6)

Table 1: Mean and SD of measured liver values. For fat values subjects with PDFF > 10% (n = 104).

Results: Mean and standard deviation (SD) of liver water and fat T1, T2 and PDFF are shown in **Table 2.** For fat T1 and T2, only values from subjects with PDFF > 10% (n = 104) were used to compute mean values and to calculate correlation between parameters. The sequence could determine mean T1, but not mean T2 of the CH_2 (2.1 ppm) and CH_3 (0.9 ppm) peaks. Fat and water T1 values showed the strongest correlation (**Figure 1**: slope 0.282, intercept 99.3, R = 0.767, $p < 0.001$), There were weaker correlations between water T2 and T1 (**Figure 2**: slope 0.0179, intercept 8.43, R = 0.556, $p < 0.001$), fat T2 and T1 (slope -0.0327 intercept 70.8, R = -0.266, p = 0.006), water T2 and PDFF (**Figure 3**: slope -0.181 intercept 26.4, R = -0.324, $p < 0.001$), and fat T2 and PDFF (slope 0.201 intercept 56.0, R = 0.220, p = 0.025). There was no significant correlation between water and fat T2 (R = 0.190), PDFF and water T1 (R = -0.112) or PDFF and fat T1 (R = -0.058).

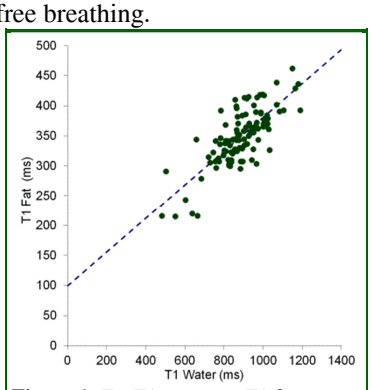

Figure 1: Fat T1 vs. water T1 for subjects with PDFF > 10% (n = 104)

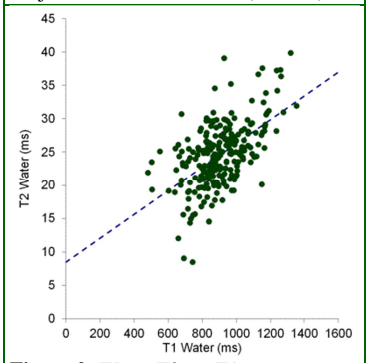

Figure 2: Water T2 vs. T1

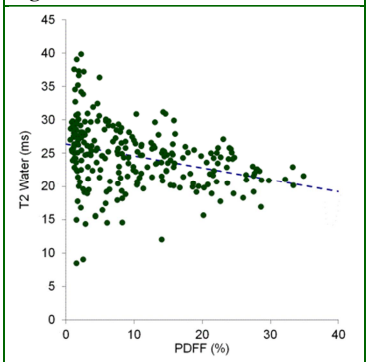

Figure 3: Water T2 vs. PDFF

Discussion: We successfully implemented the multi-TR, multi-TE sequence as part of a clinical exam, allowing routine measurement of T1, T2 of water and fat and PDFF. The ability to estimate all these parameters in a single breath-hold represents a technical advance although further research is needed to determine the clinical relevance. Water and fat T1 were strongly correlated, whereas water and fat T2 were uncorrelated. For water, T2 increased with increasing T1, whereas for fat, T2 decreased with increasing T1. For increasing PDFF, water T2 decreased and fat T2 increased.

Refs: 1) Bydder M, Magn Reson Imaging 2008; 26: 847-850. **2)** Vanhamme L, J Magn Reson 1997; 129: 35-43. **3)** Naressi A. MAGMA 2001; 12: 168-76. **4)** Hamilton G, NMR Biomed 2011; 24: 784-790.