Ultra-short T_E STEAM improves hepatic lipid quantification and profiling at 7T

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TARGET AUDIENCE: In vivo MR spectroscopy, Human lipid metabolism

PURPOSE: Previous ^{1}H MRS measurements in the brain have demonstrated advantages of ultra-short T_E (USTE) at ultra-high fields[1]. Besides higher SNR, T_2 relaxation and J-modulation effects in the spectra can be minimized. This is of particular importance in the liver tissue, where both effects along with iron deposition have to be taken into account for correct calculation of hepatocellular content of lipids (HCL). The trade-off for short T_E are larger spurious peaks (sidebands), arising from gradient vibrations[2] and oscillation of the magnetic field[3]. The sidebands occur in the neighborhood of the most prominent signal, e.g. water. A simple and robust solution has been proposed via alternative switching of the spoiler gradients orientations[4,5]. The aim of this study was to optimize the conventional STEAM sequence for an ultra-short echo time and to test its performance in *in vivo* measurements of hepatic lipids. Therefore we: (i) implemented Hermite pulses and alternative gradient switching scheme into the STEAM sequence, (ii) compared the performance of T_E optimized STEAM acquisition with the standard STEAM sequence at 7 and 3T and (iii) tested the repeatability of HCL measurements by ^{1}H MRS using USTE STEAM at 7T. The assessment of HCL using ^{1}H MRS at 3T has been shown to be accurate[6] and was taken as a reference in this study.

METHODS: USTE STEAM sequence design: The sequence programming was done in Siemens API IDEA (ver. 1.86) with 7T_SC72CD gradient system. The default 7-lobe sinc pulses (2600µs, standard STEAM) were replaced with 3-lobe Hermite pulses (1200µs). The spoiler gradients were shortened from 4000µs to 1200µs with a ramptime of 800µs. The unwanted stimulated echoes were destroyed by increasing strength of the spoiler gradients from 11.5mT/m to 35mT/m. To overcome the occurrence of the disturbing water sidebands caused by stronger gradients, the gradient orientation cycling method was implemented[4]. These modifications in the sequence resulted in a minimum T_E of 6ms. *In vivo* measurements: Ten healthy volunteers (age 31±6years, BMI 26±3kg.m^{-2}, m/f=8/2) were studied for HCL, T_2 relaxation and repeatability (test-retest within 1 hour) measurements at 7T and for HCL (20 min.) at 3T. MRS measurements were performed on a whole body 7T scanner (Magnetom, Siemens Healthcare, Erlangen, Germany) with nominal maximum gradient amplitude of 40mT/m using double tuned ^{1}H/^{31}P circular surface coil (10cm in diameter, Rapid Biomedical GmBH, Rimpar, Germany) and on a whole body 3T MR system (Trio TIM, Siemens Healthcare, Erlangen, Germany) with nominal maximum gradient amplitude of 26mT/m using a spine and body-matrix coil (Siemens Healthcare) for signal detection. The sequence parameters for 7T: T_E=6ms (USTE STEAM) and T_E=20ms (standard STEAM), T_M=10ms, T_R=5s, BW=3000Hz, NA=8, free flat breathing. All measurements at 7T were done at both frequency offsets of 0 (on water) and -3.4ppm (on lipids) to eliminate effects from chemical shift displacement. The sequence parameters for 3T: T_E=20ms, T_M=10ms, T_R=2s, NA=7, BW=1500Hz, frequency offset -2.3ppm, during several breath-holds. All spectra were acquired without water suppression with 1024 complex data points. Size of VOI was set to 3×3×3cm^3. The 7T data were corrected with published T_1[7] and individually measured T_2 relaxation times (T_E range: from 6 to 90ms), the data from 3T measurements were corrected for relaxation times from literature for T_2[8] and T_1[9]. The HCL was calculated according to formula: F/(W+F), where W represents the water signal and F represents the fat signal consisting of lipid resonances at: 2.8, 2.2, 2.0, 1.3 and 0.9 ppm. Data processing: All spectra were processed using the jMRUI software package with the AMARES fitting algorithm[10]. For each subject every single spectral transient for a specific T_E was automatically frequency shifted, manually phased and summed before fitting. For correct calculations, the last 100 points were truncated from the end of the FID in case of offset of 0.0ppm and the last 400 points in case of offset of -3.4ppm. No filter was applied before fitting. Cramér-Rao lower bound (CRLB, lower limit of a parameter error estimate) and coefficients of variation (CV) were calculated. As a measure of linear correlation, the Pearson product-moment correlation coefficient was used.

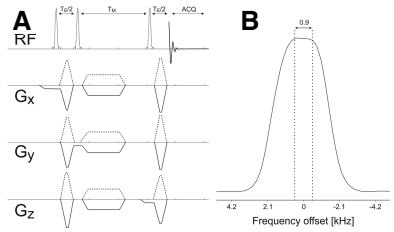

Figure 1: *A – the scheme of USTE STEAM sequence. B – the profile of the Hermite pulse (abs. freq. domain)..*

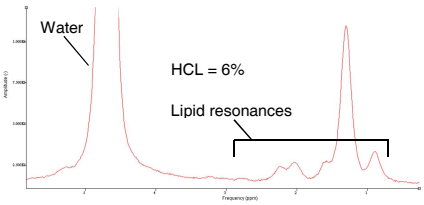

Figure 2: *Liver ^{1}H MRS at 7T with USTE STEAM.*

RESULTS/DISCUSSION: The USTE STEAM sequence scheme and profile of applied Hermite pulse are depicted in Figure 1. Example of the liver spectra measured with T_E=6ms without detectable water satellites and with high spectral resolution and SNR is depicted in Figure. 2. CRLB's of all lipid resonances included in the spectral fitting and CV's of two different HCL measurements at 7T are given in Table 1. The USTE STEAM showed acceptable repeatability also for subjects with HCL≤5%. The results for the reproducibility assessment of the HCL measurements with different T_E and at different B_0 field are depicted in Bland-Altman plots in Figure 3 A,B. The correlations between standard STEAM, USTE STEAM at 7T and STEAM at 3T are depicted in Figure 3 C,D. The processing of 7T data minimized the effect of breathing on the quality of the spectra and the scan with two offsets reduced the chemical shift displacement error.

CONCLUSION: The USTE STEAM with T_E=6ms provided higher SNR and reproducibility for precise estimation of HCL. This resulted in excellent correlation with standard STEAM at 3T. Furthermore the high spectral resolution at 7T with sufficient CRLB's of single lipid resonances highlights the potential of this sequence to be used in advanced studies of hepatic lipid profiles *in vivo*.

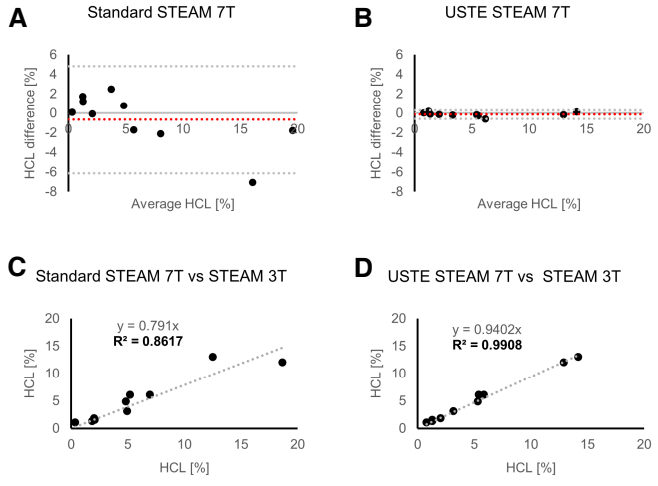

Figure 3: *A,B – Bland-Altman plots of HCL repeatability at 7T. C,D – reproducibility assessment of HCL measurements - correlations of HCL fractions between 7 and 3T.*

CRLB [%] *

Chemical group	Standard STEAM 7T		USTE STEAM 7T		Standard STEAM 3 T	
Methyl (0.90 ppm)	**23±26**	(n=17)	**5±5**	(n=20)	**11±11**	(n=10)
Methylene (1.30 ppm)	**6±8**	(n=20)	**2±2**	(n=20)	**3±5**	(n=10)
a-Olefinic (2.02 ppm)	**13±19**	(n=12)	**12±12**	(n=20)	**34±55**	(n=10)
a-Carboxyl (2.24 ppm)	**13±07**	(n=12)	**17±16**	(n=20)	**42±29**	(n=10)
Diacyl (2.77 ppm)	**45±16**	(n=11)	**60±48**	(n=14)	**35±25**	(n=9)

HCL - CV [%]	Standard STEAM 7T		USTE STEAM 7T	
All volunteers	**33±30**	(n=10)	**4±3**	(n=10)
HCL ≤ 5%	**47±38**	(n=5)	**6±3**	(n=5)
HCL > 5%	**18±9**	(n=5)	**3±3**	(n=5)

Table 1: *CRLB values for five lipid resonances measured at 7 and 3T and results of HCL repeatability with standard and USTE STEAM. The n denotes the cases when calculation was feasible.*

REFERENCES:

1. Tkáč et al. Appl. Magn. Reson. 2005. **2.** Clayton et al. J. Magn. Reson. 2001 **3.** Ryner et al. Proc.ISMRM.1998. p. 1903. **4.** Clayton et al. Proc. ISMRM.; 1998. **5.** Dong et al. MRM. 2004. **6.** Krššák et al. Eur. J. Radiol. 2010 **7.** Gajdošík et al. JMRI 2013. **8.** Hamilton et al. 2011. **9.** De Bazelaire et al. Radiology 2004. **10.** Vanhamme et al. J. Magn. Reson. 1997

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