

# Quantitative In Vivo Assessment of Hepatic Lipid Using High-Speed T2-Corrected Multi-Echo Spectroscopy

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**INTRODUCTION.** Hepatic lipid measurements by MR techniques have not fully accounted for variable T2 susceptibility effects within human liver, which may adversely affect accuracy. Proton MR Spectroscopy (<sup>1</sup>H-MRS) offers a means for non-invasively quantifying hepatic lipids (HL) with sufficient spectral resolution for even low amounts of HL. However, in addition to susceptibility effects in the liver, a primary limitation of MRS for clinical use has been motion sensitivity and impractical scan duration. Recently, a rapid, breath-hold, single-voxel MRS technique, termed "HISTO" (High-Speed T2-corrected multi-echo acquisition), was developed to overcome the issues of speed and T2 sensitivity by concatenating 5 MRS acquisitions within one 15 sec scan (1). With T2-correction, HISTO has been shown to provide a highly accurate measurement of HL, and to correct for susceptibility effects that would otherwise produce significant errors, as demonstrated in phantoms(1). In this work, HISTO is applied *in vivo* to quantify the impact of T2-correction, and to measure reproducibility, a critical component for monitoring disease in a practical clinical setting.

**METHODS.** This investigation was approved by our institution's IRB, and all imaging was performed using a 1.5T Siemens Avanto system and phased array body coils. The HISTO MRS pulse sequence has been described previously (1). Briefly, five conventional STEAM sequences, which were each configured with a unique TE, one signal average, and no preparations, were concatenated in time with a TR=3000ms. The adjustable TE set was fixed to {12, 24, 36, 48, 72}ms to encompass the expected T2 range of hepatic water and lipid. Other essential parameters include: mixing time (TM) = 10ms, voxel=3x3x3cm<sup>3</sup>, 1024 points, and 1200 Hz bandwidth. The breath hold duration was 15 sec. HISTO data was exported off-line for processing with LCModel version 6.2-0 (S. Provencher, Oakville, Canada), where spectra at each TE were analyzed automatically assuming presence of lipid and water, possibly choline signals, and signals in the 3.4 - 3.8 ppm region (sometimes attributed to glycogen and other metabolites). The integrated spectrum signals of water and lipid at each TE allowed analysis of exponential T2 decay using Matlab software, whereby the equilibrium signal (M<sub>0</sub>) and the relaxation rate (R2=1/T2) were determined by least-squares approximation. Using M<sub>0</sub> for water and lipid, the T2-corrected HL was calculated from: %HL = M<sub>0lipid</sub> / (M<sub>0lipid</sub> + M<sub>0water</sub>). An "uncorrected" HL measurement was similarly calculated at each TE without first determining R2. A total of 28 human subjects with known or suspected NAFLD were investigated in this study following written informed consent. In 25 subjects, HISTO was applied by prescribing the voxel in the liver, away from large vessels and tissue interfaces, and a final %HL was determined from the average of three separate voxel positions. For each subject, the T2-corrected %HL was compared to the uncorrected measure (TE=24ms) using a Wilcoxon signed-rank test. Three additional subjects were used to evaluate reproducibility of HISTO. Apart from repeating HISTO acquisition *within-session* (x3), the acquisition procedure was repeated 3 times following subject repositioning, re-shimming, and voxel re-positioning. For reproducibility measures of R2<sub>water</sub>, R2<sub>lipid</sub> and %HL, pooled standard deviation (SD) was calculated to estimate the differences in human subjects. In addition, within-subject ANOVA testing was performed with significance set to p=0.05.

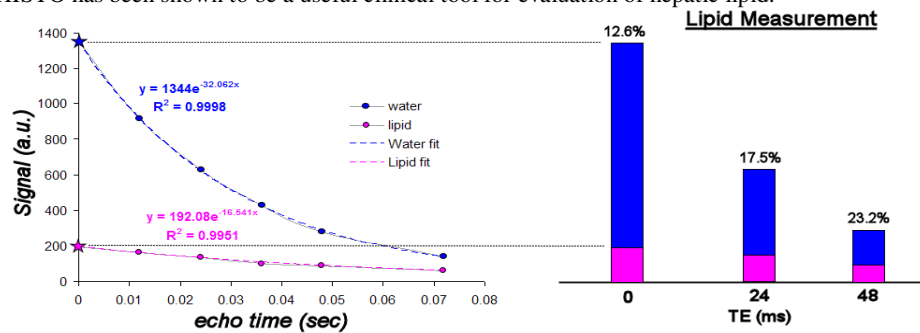
**RESULTS.** HISTO breath hold acquisitions were tolerated by all subjects, while successful curve fitting to spectrums enabled quantification of R2<sub>lipid</sub> (17.6±1.8s<sup>-1</sup>; range: 14.5-21.8s<sup>-1</sup>), R2<sub>water</sub> (28.8±2.8s<sup>-1</sup>; 24.3-35.7s<sup>-1</sup>) and %HL (21.4±8.0%; 6.6-36.5%) (n=25). Figure 1 depicts a plot of relative spectra signals of water and lipid against TE, with subsequent curve fitting allowing determination of R2 and M<sub>0</sub>. As shown, the T2-corrected %HL (TE=0) differs greatly from uncorrected %HL (TE>24ms), due to differences between R2<sub>lipid</sub> and R2<sub>water</sub>. Overall, a comparison revealed a biased overestimation of %HL at TE=24ms of 5.1±2.6% (p=0.0013, n=25), which becomes larger as TE increases (Figure 1). In terms of reproducibility of HISTO, Table 1 shows the results of 3 subjects imaged 3-times within- and between-sessions, along with the SD and pooled SD. A within-subject analysis of variance was found not to be statistically significant between repeated scan sessions (p=0.13), indicating similarity. This finding was also true for R2 measures (p>0.25). These results establish the *in vivo* reproducibility of the HISTO technique.

**Table 1.** Reproducibility of T2-corrected %HL determined from 3 separate scan repetitions

| Subj | %HL        |            |            |
|------|------------|------------|------------|
|      | Scan 1     | Scan 2     | Scan 3     |
| 1    | 14.5 (0.3) | 15.2 (0.5) | 13.2 (0.8) |
| 2    | 6.1 (0.5)  | 5.8 (0.8)  | 4.8 (0.3)  |
| 3    | 11.8 (0.2) | 11.7 (0.5) | 11.7 (0.2) |
| SD*  | 0.69       |            |            |
| p**  | 0.13       |            |            |

Standard deviation of 3 measurements given in parentheses; \*Pooled standard deviation; \*\*within-subject ANOVA for 3 repeated scans

**CONCLUSIONS.** In this study, the HISTO MRS technique was effectively applied *in vivo* within a fast, 15 second breath hold. The inherent ability to quantify T2 using HISTO lends efficiently to T2-corrected %HL measurements, which is shown to be significantly important *in vivo* due to susceptibility effects altering R2 of water and lipid. Clinical utility of HISTO is further established with reproducibility data revealing subject-specific consistency in R2 and %HL measures. Thus, HISTO has been shown to be a useful clinical tool for evaluation of hepatic lipid.



**Figure 1.** T2 decay of spectrum signals acquired in one subject using HISTO (left), with corresponding T2-corrected and uncorrected %HL measures

[1] Pineda, N et al. High-speed multiple echo acquisition (HISTO): a rapid and simultaneous assessment of fat and iron content in liver by <sup>1</sup>HMRS. *ISMRM 2008*