

In Vivo Application of Breath-hold Single-Voxel ^1H Spectroscopy for T2-Corrected Hepatic Lipid Measurement: Evaluation of Accuracy and Reproducibility

P. Sharma¹, H. D. Kitajima¹, X. Zhong², B. Kalb³, A. B. Farris⁴, M. B. Vos⁵, and D. R. Martin³

¹Radiology, Emory Healthcare, Atlanta, GA, United States, ²MR R&D Collaborations, Siemens Healthcare, Atlanta, GA, United States, ³Radiology, Emory University, Atlanta, GA, United States, ⁴Pathology, Emory University, Atlanta, GA, United States, ⁵Hepatology, Children's Hospital of Atlanta, Atlanta, GA, United States

Introduction. Hepatic lipid (HL) accumulation is the hallmark precursor to the potential development of steatohepatitis, chronic liver disease and cirrhosis. While biopsy has served as a standard for HL detection, a non-invasive more reproducible alternative is preferred. Therapy development for early disease has required accurate and reproducible measurement for the longitudinal monitoring of hepatic lipid. Recently, a breath hold T2-corrected MR spectroscopy technique (HISTO-MRS) has been developed to quantify the percent ratio of lipid metabolites relative to water within a user-defined spectroscopic voxel [1]. Phantom evaluation using this technique has shown the importance of T2-correction for accurate lipid quantification, especially in the presence of susceptibility effects, such as iron [2]. Moreover, phantom results have also demonstrated high measurement repeatability and reproducibility. The purpose of this investigation was to extend the evaluation of accuracy and reproducibility into an in vivo setting, in order to further validate the routine clinical use of HISTO-MRS.

Methods. This study protocol was IRB approved and HIPPA compliant. All MRI and MRS acquisitions were performed on a Siemens 1.5T Avanto system, using phase-array body coils. **Patients** – 25 pediatric patients (17/25 male), who were enrolled in a concurrent NAFLD clinical investigation, underwent repeated MRI and MRS for hepatic lipid quantification. Each subject was imaged on repeated scheduled visits, approximately 12.8 \pm 2.4 days apart (range: 7-15 days), without any designated therapeutic intervention between the exams. 10 additional subjects (6 males) also underwent right lobe percutaneous biopsy, from which hepatic lipid was estimated computationally. The routine liver imaging protocol for each session was less than 15 minutes, and consisted of 3-plane T2 single-shot imaging and T1 opposed-phase gradient echo for localization, in addition to HISTO-MRS. **Lipid Acquisition** - HISTO MRS pulse sequence has been described previously [1]. The adjustable TE set was fixed to {12, 24, 36, 48, 72} ms, with TR=3000ms, voxel=3x3x3cm³, 1024 points, and 1200 Hz bandwidth. The voxel was placed in a homogenous region of the liver, carefully avoiding hepatic vessels and boundaries. The acquisition duration was 15 sec, following automatic shimming, and was repeated three times to assess measurement repeatability. **MRS analysis** - MRS data was exported off-line for processing with Matlab (Mathworks, Natick, MA), where each spectra was analyzed automatically by determining peak area over a user-defined frequency range (water peak: 4.6ppm; lipid peak: 1.3, 2.0ppm). The integrated spectrum signals of water and lipid at each TE allowed analysis of exponential T2 decay, whereby the equilibrium signal (M_0) and the relaxation rate ($R_2=1/T_2$) were determined by least-squares approximation. Using M_0 for water and lipid, the T2-corrected lipid content was calculated from: %lipid = $M_{0\text{lipid}} / (M_{0\text{lipid}} + M_{0\text{water}})$. Linear regression was used to compare the %lipid from the two subjects' visits. Regression analysis was also used to correlate %lipid with biopsy results.

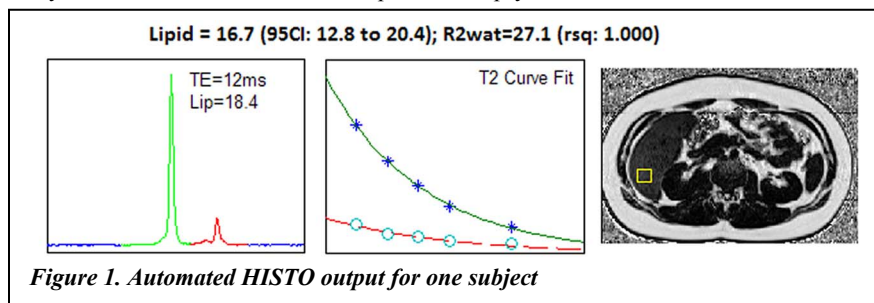


Figure 1. Automated HISTO output for one subject

Results: All 25 subjects completed both imaging sessions without incident. Figure 1 displays the automated output of the HISTO-MRS analysis, consisting of a water-fat spectrum, T2 curve fit, T2-corrected lipid%, and voxel placement. The range of %lipid measures using HISTO-MRS among all subjects was 4.3% to 31.8%. The pooled standard deviation of all repeated intra-subject HISTO-MRS acquisitions (n=50) was 0.93, indicating high measurement repeatability. Figure 2 shows the agreement of %lipid measures between the two visits, along with a line of identity. The average absolute lipid% difference between subject visits was $1.2\% \pm 0.9$, while regression analysis revealed a slope of 0.95 and intercept of 0.57 ($r^2 = 0.96$), indicating strong measurement reproducibility. Figure 3 shows the comparison of HISTO-MRS lipid% and biopsy estimates in 10 subjects. Despite the existence of outliers, the Pearson correlation coefficient was 0.65, which was found to be a significant correlation ($p=0.04$).

Conclusions: In vivo implementation of HISTO-MRS, combined with automated spectrum post-processing steps, was efficient, allowing routine utilization in a clinical setting. From the experimental results, we conclude: 1) High acquisition reproducibility within the same subject allows effective longitudinal monitoring of disease progression and therapies with HISTO-MRS; and 2) Measured hepatic lipid% values significantly correlated with biopsy results, validating the clinical applicability of HISTO-MRS as a biopsy surrogate.

References

- [1] Pineda N, et al. Radiology 2009; 252(2):568-76
- [2] Sharma P, et al JMRI 2009; 29(3):629-35

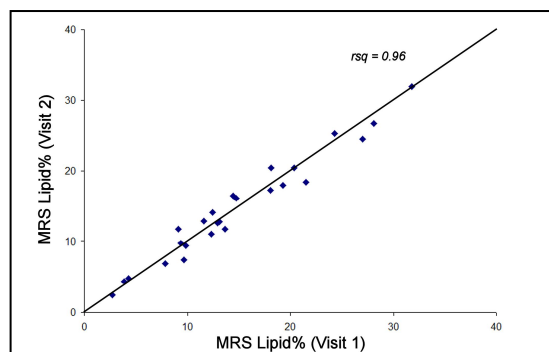


Figure 2. HISTO reproducibility

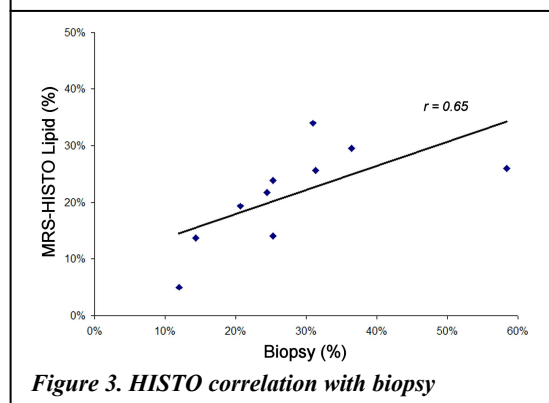


Figure 3. HISTO correlation with biopsy