

Validation of ¹H Magnetic Resonance Spectroscopy (¹H-MRS) for Quantification of Hepatic Triglyceride Content

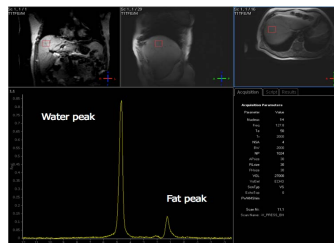
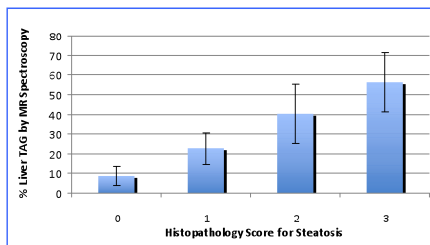
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Introduction: Percutaneous liver biopsy remains the gold standard test to evaluate hepatic fat content, fibrosis and cirrhosis, but there is growing interest in the application of magnetic resonance imaging (MRI) techniques such as ¹H-Magnetic Resonance Spectroscopy (¹H-MRS) as a non-invasive approach to quantify these characteristics. The ability to accurately quantify hepatic metabolites such as intrahepatic lipid has important implications for clinical evaluation and management of patients with liver related diseases and may obviate the need for liver biopsies in a number of clinical settings. The current proposal was designed to develop and validate the quantification of hepatic fat using ¹H-MRS compared to standard histologic ratings at the NIH Clinical Center. Thus far we have completed MRI with ¹H-MRS in 50 adults who also underwent percutaneous liver biopsy. Indications for liver biopsy included viral hepatitis (36%), HIV or HIV/HCV co-infection (48%) and other clinical indications (16%).

Methods: Fifty patients undergoing diagnostic liver biopsy at the NIH Clinical Center were enrolled based on the following inclusion/exclusion criteria: Aged 18+, planned liver biopsy or liver biopsy within the past 30 days with pathology samples available to be read at NIH Clinical Center, no known current pregnancy or pregnancy within 6 months, no contraindications to MRI, subject deemed able to comply with requirements of study participation. A Philips (Best, Netherlands) 3Tesla MR Achieva scanner software level 6.2 was used with medium size flex coils for both spectroscopy and imaging. Spectroscopy was performed with a breath-hold (BH) PRESS based single-voxel technique with a voxel size of 30 x 30 x 30 mm; TR = 2000 ms; TE = 50 ms; imaging time = 12 s; 4 phase cycles; spectral resolution = 1.95 Hz; no water suppression. Hepatic fat content was calculated from integral peak areas using a standardized formula from Longo et al. (1995) for determining lipid volume fraction (Φ_f): $\Phi_f = FTSA / (1.138 - 0.339FTSA)$ FTSA = detectable fat-to-total signal peak area. Phantom experiments were performed to validate acquisition and post-processing methods using serial dilutions of 10, 15, 17.5 and 20%. Intralipid (KabiVitrum Inc. Clayton NC) in 50 ml sample tubes suspended in room temperature water phantom. T₂ relaxation measurements were performed at 30, 40, 50, and 70 msec echo times at a TR of 3 seconds with a single voxel double echo sequence identical to the acquisition technique used for patient data.

Results and Discussion: Phantom serial dilutions of 10%, 15%, 17.5% and 20% intralipid solution in 50 ml tubes correlated with %TAG values by ¹H-MRS (r=0.98, p=0.02). There was a strong positive correlation between %TAG values by ¹H-MRS and histopathology grading of hepatic steatosis on liver biopsy (r=0.88, p<0.0001). Both body mass index (BMI) and AST level were positively associated with hepatic fat content: BMI and %TAG r=0.41, p=0.003; AST and %TAG r=0.46, p=0.0007. We demonstrate that ¹H-MRS has good agreement with histopathologic grading of hepatic steatosis and that it may be a useful non-invasive technique to screen for clinically significant hepatic steatosis. We were also able to validate the current techniques using external phantoms. One strength of the present study is the relatively large cohort of individuals who underwent diagnostic percutaneous liver biopsy for a broad range of indications. In addition, unlike previous validation studies in which labor-intensive morphometric measurements were used to quantify hepatic fat histologically, the present study compared standard histologic grading to MR spectroscopy results. To date, few studies have evaluated the accuracy of ¹H-MRS compared to liver biopsy results using 3T MRI technology. These present findings suggest that ¹H-MRS may be a valid and accurate tool for quantification of clinically significant hepatic steatosis without the need for liver biopsy.



Figures 1 and 2: Hepatic % triacylglycerol by ¹H-MRS vs. histopathology score; Representative Spectra of hepatic triacylglycerol by ¹H-MRS

References:

- 1) Hadigan C, Liebau J, Andersen R, Holalkere NS, Sahani D. Magnetic resonance spectroscopy of hepatic lipid content and associated risk factors in HIV infection. *J AIDS*. 2007; 46(3): 312-7.
- 2) Longo R, Pollesello P, Ricci C, Masutti F, Kvam BJ, Bercich L, Crocè LS, Grigolato P, Paoletti S, de Bernard B, et al. Proton MR spectroscopy in quantitative in vivo determination of fat content in human liver steatosis. *J Magn Reson Imaging*. 1995 May-Jun;5(3):281-5.