High speed multiple echo acquisition (HISTO): a rapid and simultaneous assessment of fat and iron content in liver by ^{1}H-MRS.

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Introduction:

Obesity related fatty liver disease has become the most common cause of hepatitis and fibrosis in the developed nations, affecting young adults and children. We currently depend upon invasive biopsies for detection and monitoring of disease. Liver biopsies may be painful and may cause bleeding that may lead to serious complications and even death in 1% of patients. Various MRI techniques have been introduced for the detection or visualization of fat in the liver. Proton MR Spectroscopy (^{1}H MRS) offers a means for noninvasively determining hepatic lipids (HL) and provides acceptable spectral resolution and high sensitivity even with low amounts of HL. Furthermore, liver iron concentration is considered another important factor that may contribute to hepatitis and cirrhosis. Many studies have demonstrated strong correlation between 1/T2 and liver iron concentration in MRI. MRS has been used to assess T2 values of water signal, using single voxel STEAM sequences at a number of echo times[1] and fitting an exponential decay to the echo amplitude at different TEs. One major difficulty of relaxation time-based MRI studies has been the low signal intensities from the tissue of interest under heavy iron load because of shortened T2. Another limitation of prior reports have included relatively long acquisition times, generally requiring multiple acquisitions of spectra and complicated correction schemes. In this work, we introduce a technique that allows the rapid and simultaneous assessment of fat content and iron content which could be applied for single breath hold liver MRS.

Materials and methods:

Phantoms: We created twelve 200 mL phantoms (2% agarose) with varying concentrations of iron (ferridex) (0, 0.1, 0.3, 0.5 mM) and varying percentage of fat (vegetable oil) (0, 10 and 30%) at a pH of 7.00 +/- 0.2.

Subjects: This investigation was reviewed and approved by our institution's Internal Review Board. Two patients with known fatty liver disease were investigated in this study.

MRS: A new sequence, named HISTO for **hi**gh **s**peed mul**t**iple ech**o** acquisition, as shown in figure 1, was developed. The sequence consists in a concatenation of multiple repeats of a basic sequence (STEAM or PRESS) where each repeat has a different TE. On a 1.5 Tesla MRI system (Avanto, Siemens Medical Solutions, Malvern, PA) with a surface coil, after scout imaging, water spectra of phantoms were obtained with HISTO, based on the STEAM pattern, using a TR of 3 sec, TM = 10 ms and five TE (12, 24, 36, 48 and 72 ms). The bandwidth was 1200 Hz and 1024 points were acquired with one signal accumulation. The voxel size was 30x30x30 mm^3. For the MRS in the patients, we performed the measurement with the standard STEAM sequence with five different acquisitions (five breath holds), each one corresponding to a different echo time, and HISTO (one breath hold). The TR, bandwidth, sampling points, signal accumulations and TE values were the same for both sequences. The shimming was redone for each sequence. The parameters applied were optimized for the clinical application.

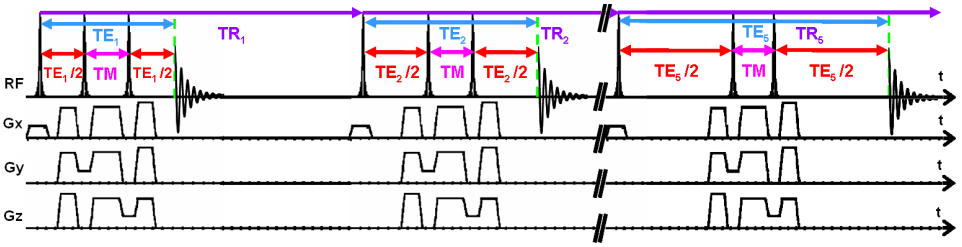

Figure 1: HISTO diagram based on the STEAM sequence. Repetition Time (TR: TR1=TR2 =…=TR5). Echo time (TE1<TE2<…<TE5), TM = Mixing time.

Spectrum post-processing: We exported the spectra from the Siemens console to a personal computer and analyzed them with the software package of jMRUI Version Number: 2.2, with the AMARES quantification. The peak integral in the frequency domain was calculated for water and fat peaks, respectively, for each echo time.

R2 calculation, lipid content estimation and correlation with iron content: With spectral integral obtained at multiple TEs with HISTO, a mono-exponential curve fitting was performed using the equation S = S0*exp(-R2*TE) to estimate both R2 and S0, for water and fat signals. Subsequently, lipid content was calculated as: Lipid% = $S0_{fat}/(S0_{fat}+S0_{water})*100$. In other studies, lipid content was measured by simply looking at fractional fat signal at a given TE. To demonstrate that such an approach is inaccurate, fat content was also calculated using the integrated signal at TE=12msec. To assess the ability to ascertain iron content based on the derived R2, the R2 of water measured by MRS was compared to the iron concentration using linear regression.

Results:

Table 1 lists the results of the estimated lipid content, with and without TE correction, in the phantoms, which were known to be 10% and 30% lipid content. Percent fat calculated with STEAM (TE=12ms) shows strong inaccuracies as iron content increases, while HISTO with T2 correction remains relatively stable. The T2-corrected percentage of fat and R2 of water calculated in the patients are given in Table 2; the values obtained with both techniques are similar, suggesting equivalence between the two techniques for measuring the same unknown variables. In the phantoms we observed that the R2 value of water is correlated to the amount of iron in the sample, independently of the fat percentage (Figure 2). Regression analysis revealed a highly significant linear relationship: R2 = 280.08 × [Fe] +14.599 (r= 0.9796, p = 0.0000), with [Fe] in units of mM Fe and R2 in sec^{-1}. The standard error in R2 is 8.46 sec^{-1}. The intercept is the average R2 of agarose without iron for the 3 different percentage of fat. The lipid content derived with S0 was accurate for all iron concentration levels following but contrasts values obtained without T2 correction. This trend was most significant for high iron concentrations (0.5mM).

Phantom	% fat T2 corrected	% fat TE = 12 ms
10% fat 0 mM iron	8.75	8.14
10% fat 0.1 mM iron	11.61	11.86
10% fat 0.3 mM iron	9.06	17.97
10% fat 0.5 mM iron	9.36	28.81
30% fat 0 mM iron	29.70	29.19
30% fat 0.1 mM iron	27.23	32.15
30% fat 0.3 mM iron	34.35	57.36
30% fat 0.5 mM iron	33.80	64.66

Table 1: Calculation of fat percentage in phantoms.

	Patient 1		Patient 2	
	STEAM	HISTO	STEAM	HISTO
R2 water	27.74	27.54	24.69	25.30
% fat T2 corrected	19.90	20.66	13.81	13.70

Table 2: Comparison between standard STEAM sequence and HISTO sequence. R2 values in patients are given in sec^{-1}.

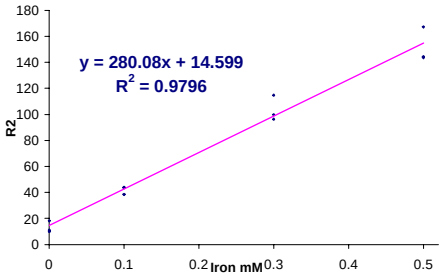

Figure 2: Linear regression of R2 (sec^{-1}) and iron concentration with different percentages of fat in phantoms.

Conclusion:

HISTO is an accurate and fast technique which allows, in 15 seconds, the acquisition of several echoes in order to assess the T2 of water and lipids and determe the corrected lipid concentration. Failure to correct for T2 variations will result in significant errors in lipid measurement. In this study, the feasibility and accuracy for using HISTO to rapidly measure lipid and iron concentrations simultaneously has been demonstrated experimentally in phantoms and applied to patients with fatty liver disease.

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