Hepatic Fat Quantification for suspected NAFLD Patients Using 3 Different Methods: HISTO, 3D Multi-Echo GRE DIXON and Invasive Liver Biopsy

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Target Audience: Clinicians and researchers interested in liver fat quantification.

Introduction and Purpose:

Accurate non-invasive detection and quantification of proton density fat fraction (PDFF) as a marker for liver fat in patients with non-alcoholic fatty liver disease (NAFLD) is gaining increasing interest. MR spectroscopy has been proven to be a highly accurate technique. Recently, rapid single breath-hold, multi-echo, T_2 corrected single-voxel spectroscopy (HISTO) has shown its accuracy and feasibility for fat quantification in clinical use [1-4]. Another approach is MR imaging based on multi-echo gradient echo acquisitions[5-9], which have higher efficiency for evaluating the whole liver within one measurement, was also demonstrated to be an accurate alternative. One particular implementation, using a hybrid multi-step fitting approach, and here referred to as advanced Dixon (AD) has been validated using the HISTO technique as reference standard at both 1.5T and 3T[9-10]. The aim of this study was to evaluate both HISTO and AD with conventional, invasive liver biopsy as a reference for hepatic fat quantification in NAFLD patients.

Methods:

This study was approved by our institution review board. Informed consent was obtained from all subjects. From January to October 2014, a total of 10 patients in our hospital were suspected to have NAFLD according to blood tests and biochemical indicators, and liver biopsy was a clinical need for final diagnosis. All MR exams were performed on a 1.5T scanner (MAGNETOM Aera, Siemens Healthcare, Erlangen, Germany) using an 18-channel body matrix coil and 8-12 elements of the integrated spine matrix coil as receiver. Prototype implementations of sequences and inline data processing software were used. The HISTO voxel was positioned in a homogenous area of the right anterior lobe of the liver, avoiding major vessels. The voxel size was 3x3x3cm^3, TR = 3000ms, Five TEs = 12, 24, 35, 48, 72 ms, BW = 1200Hz. A 6-echo AD protocol was run in transversal orientation, with whole liver coverage, including imaging parameters of TR = 9.05ms, TEs = 1.21, 2.48, 3.75, 5.02, 6.29, 7.56 ms; slice thickness = 4mm, FOV = 400x300mm, matrix = 206x256, total scan time = 16s. Both PDFF from HISTO and AD were generated inline. One ROI with an area of 1cm^2 was drawn for every liver lobe (totally five ROIs for five liver lobes) respectively in the fat fraction map; the mean value of the fat fraction within each ROI is computed. The mean value and standard deviation among these 5 ROIs were also calculated for each patient. Ultrasound guided liver biopsy was performed for each patient a day later. The liver tissue sample was taken from the right anterior lobe of the liver. Steatosis grade was evaluated using a method proposed by Brunt et al[11], by calculating the percentage of hepatocytes containing intracellular fat droplets, according to the classification scheme used in [12]: grade 0: < 5% cells affected; grade 1: 5-33% of cells affected; grade 2: 33-66% of cells affected; and grade 3: >66% of cells affected. Afterwards PDFF from HISTO and AD were compared with the steatosis grade.

Results and Discussion:

According to the biopsy result, 7 of 10 patients had steatosis grade 2, 2 patients had steatosis grade 3 and 1 patient had steatosis grade 1. Figure 1 shows good correlation between PDFF measured with HISTO and steatosis grades (A) and between the mean fat fractions of all ROIs measured with AD and steatosis grades (B). Figure 2 shows an overview of all measured data with HISTO and AD (including the mean level within individual ROI, the mean level and the standard deviation of all five ROIs) in 10 patients compared to steatosis grade. It is noted that, for the 2 patients with high steatosis grade (grade 3), results measured with HISTO and AD are closely matching. The standard deviations among different ROIs in DIXON fat fraction map are consistently small for patients with steatosis grade 1 and 3 (1.8%, 2.4% and 2.7% respectively). In 7 cases of steatosis grade 2, the standard deviation varied from 1.3% to 6.7%. Liver biopsy is able to quantify the fat content for the extracted liver sample. However, it is invasive and may suffer from sampling error, and the patients may suffer from serious complications. HISTO is a non-invasive and accurate solution. Although it is a single voxel measurement, applying HISTO in different VOI locations is clinically feasible, due to its fast data acquisition in a single breath hold. AD is able to evaluate the whole liver within one single breath hold, and has high correlation with biopsy results, according to our study. The major limitation for our study is the small number of study objects, especially for steatosis grade 1. A subsequent study with more cases will be conducted to obtain a more statistically significant population.

Conclusion:

Fat fractions evaluated with both HISTO and the recently developed AD, have good correlation with the steatosis grade achieved from liver biopsy. These two non-invasive MR methods might be alternatives for the invasive liver biopsy for liver fat quantification in clinical practice.

Reference:

1. Pineda N, et al. Radiology 2009; 252(2): 568-576; **2**. Sharma P, et al. JMRI 2009; 29:629-635; **3**. Sharma P, et al. Mag. Reson. Med. 19. 2011; **4**. Pineda N, et al. 22th ISMRM 2014; **5**. Yu et al. J Magn Reson Imaging 2007; 26:1153-1161; **6**. Hernando et al. Magn. Reson Med 2010; 63: 79-90; **7**. Bydder et al. Magn Reson Imaging 2008;26:347-349 ; **8**. Yu et al. 17th ISMRM 2009; **9**. Zhong et al. Magn Reson Med 2014;72:1353-1365; **10**. Sanches L, et al. 22th ISMRM 2014; **11**. Brunt EM et al. Am J Gastroenterol 1999; **12**.Kühn J, et al. 20th ISMRM 2012

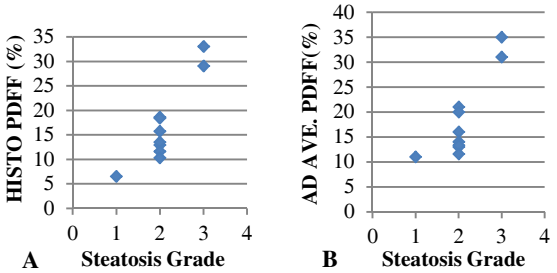

Fig.1 Fat fraction measured with MR Spectroscopy based HISTO (A) and MR imaging based advanced DIXON (B) in all 10 suspected NAFLD patients compared to histological steatosis grade.

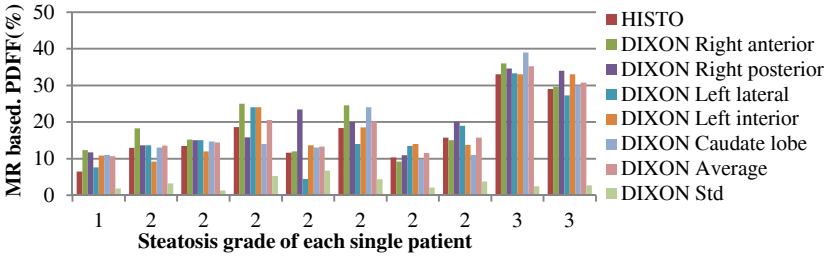

Fig.2 Over view of all measured data with HISTO, advanced DIXON (including the mean level within individual ROI, the mean level and the standard deviation of all five ROIs) in 10 suspected NAFLD patients compared to histological steatosis grade. Patients with steatosis grade 2 are ranked randomly in the chart.