Quantification of Liver Fat Content Using Selective Saturation at 3.0 T

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INTRODUCTION. Non-alcoholic fatty liver disease (NAFLD) affects up to 30% of population in the United States (1). Currently, the diagnosis of NAFLD is based on estimation of the percent of hepatocytes containing macrovesicular steatosis on a liver biopsy specimen. Such estimates are based on the pathologist's gestalt in reviewing a histologic section and are somewhat subjective. The risk, discomfort, and invasive nature of liver biopsy make it difficult to justify repeated biopsies to study the natural history of hepatic steatosis or the response to therapeutic interventions for NAFLD. MRI is an attractive noninvasive technique that can provide a quantitative measure of liver fat content (2). Recent studies have used MRI with Dixon techniques to assess for changes in hepatic steatosis in response to therapeutic interventions (3-6). However, the accuracy of the MRI techniques used for measuring liver fat was not rigorously assessed. In this paper, we report a technique, which relies on chemically selective saturation and requires a calibration scan of a liver phantom, for quantitatively measuring liver fat content at 3T. We have also evaluated the performance of this technique by comparing MRI measurements in human subjects with estimates of liver fat content made by optical image analysis and pathologists' assessment.

METHODS. Participants of the study included ten adult patients who underwent a liver biopsy to evaluate for evidence of NAFLD. To develop a calibration standard for fat quantification, a liver phantom consisting of calf liver homogenized with 0%, 5%, 10%, 20%, 30%, and 100% (by weight) corn oil (2) was constructed using ping-pong balls. For each patient, the MRI examination began with scanning a standard 18cm spherical water phantom with a fixed acquisition protocol (a gradient echo sequence) and fixed receiver gain on a 3T GE Excite scanner (GE Health Care, Milwaukee, WI). This allowed us to monitor for scanner instability and to normalize the measured signal intensity to reduce the adverse effect of signal variations. Following the water phantom scan, the liver phantom was scanned to generate a calibration curve that relates the measured fat signal percentage to the known fat percentage. The phantom MRI protocol consisted of two series: (a) fat imaging using an RF pulse to saturate the water signal, and (b) water and fat imaging without using any saturation pulses. In both series, a fast gradient echo pulse sequence was used with the following parameters: flip angle = 30º and TR/TE = 12/2ms. Patients were scanned immediately after the phantom series using the same protocol, except that the FOV was increased to 36-40 cm depending on the patient size. The acquisition time for each scan was approximately 25 seconds, allowing for completion within a single breath hold, thereby minimizing respiratory motion.

Based on the signal intensity ratio between series (a) and (b) of the liver phantom images, a calibration curve was generated and fitted to a quadratic function using a least-squares method. On the human liver images, two ROIs were selected in the right liver lobe, corresponding to the area where percutaneous biopsies were obtained. For each ROI, the signal intensity ratio between series (a) and (b) was evaluated and entered into the quadratic equation representing the calibration curve. The equation was then solved to obtain an MRI-based measurement of liver fat content.

The liver biopsy specimens were sectioned and stained for histophathologic analyses. A computer program was developed to fit ellipses to macrovesicular fat globules on digitized sections of liver biopsy specimens and to calculate the area fraction representing fat. Liver fat content was also estimated independently by two experienced liver pathologists, based on the percent of hepatocytes containing macrovesicular steatosis.

RESULTS. MRI measurements of the phantoms were highly reproducible with standard deviations of 0.41% (0% fat), 0.82% (5% fat), 2.20% (10% fat), 3.1.% (20% fat), 5.56% (30% fat) and 0.32% (100% fat) among the ten examinations. Figure 1 shows a representative calibration curve from one of the ten patients, along with a water-suppressed liver phantom image (inset; with the fat percentage labeled on the image). This curve was well fitted to a quadratic equation $y=-0.0068x^2+1.56x + 3.03$ ($r^2=0.9995$). Liver fat content measurements based on the calibration curves were strongly correlated with estimates of liver fat content made by optical image analysis (r=0.96, p<0.001) and with estimates made by the pathologists (r=0.93, p<0.001) (Figure 2). There was a linear relationship between optical image analysis and MRI measurements with a slope of 0.91. In other words, image analysis provided slightly lower measures of liver fat content than MRI. In contrast, the linear relationship between the pathologists' estimates of liver fat and MRI measurements had a slope of 2.67. That is, the liver pathologists provided much higher estimates of liver fat content than MRI (or optional image analysis), and the differences were greatest in specimens in which more fat was present.

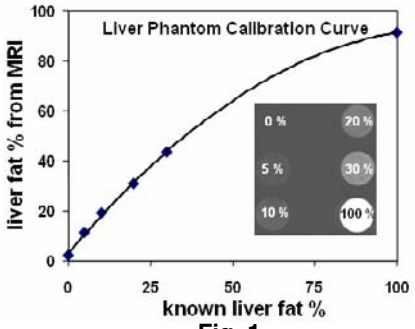

Fig. 1

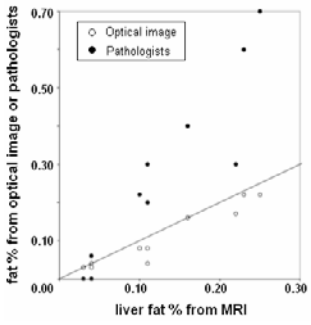

Fig. 2

DISCUSSION. Although a gold standard is yet to be established, our results suggest that pathologic assessment, which represents the current standard for measuring liver fat, appears to overestimate fat content and this tendency is accentuated with higher degrees of liver fat. It is likely that visual evaluation of hepatic steatosis performed by estimating the percent of fat laden hepatocytes provides an inflated measure of liver fat content because hepatocytes that contain fat are not actually replaced by fat. In comparison to the Dixon techniques, a major advantage of the proposed technique is that it does not require specialized pulse sequences and can be readily performed in most clinical scanners. The current study has several limitations, including sensitivity to B0-field inhomogeneity and B1-field non-uniformity, lack of a true gold-standard, and possible misregistration between the ROIs in MRI and the biopsy sites. Nonetheless, the findings of this study suggest that a readily available MRI technique can provide a reliable, non-invasive means to quantify liver fat content. This noninvasive technique can be potentially applied to evaluate the presence of NAFLD and to measure changes in liver fat content over time.

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