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ORIGINAL ARTICLE

Reliability of Quantitative Assessment of Hepatic Steatosis on Breath-hold Dual Echo In-phase and Opposed-phase Gradient-echo MRI

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ABSTRACT

Objective: *To assess the reliability of quantitative measurement of signal intensity change in the liver on breath-hold gradient echo in-phase and opposed-phase imaging in hepatic steatosis.*

Patients and Methods: *The study population comprised 19 subjects with previous sonographic diagnosis of hepatic steatosis, who had repeat magnetic resonance imaging examinations for the quantification of the degree of liver fat content by signal intensity change in liver on breath-hold gradient echo in-phase and opposed-phase imaging.*

Results: *In the first examination, the range of percentage signal loss was from -3.6% (signal gain) to 84.8%, with a mean of 27% and a standard deviation of 25.6%. In the repeat examination, the range of percentage signal loss was from -8.9% to 85.9%, with a mean of 25.7% and a standard deviation of 26.1%. The standard error of measurement was 2.9%. Correlation of measurements in signal change between the two examinations was high (r = 0.99).*

Conclusions: *The quantitative assessment of hepatic steatosis on gradient echo in-phase and opposed-phase magnetic resonance imaging showed high reliability on repeat examinations.*

Key Words: *Fatty liver, Magnetic resonance imaging*

INTRODUCTION

Hepatic steatosis is a condition in which lipids accumulate in hepatocytes. It can occur in alcohol-induced liver disease, and in association with obesity, diabetes mellitus, hyperlipidaemia and with corticosteroid use. Non-alcoholic fatty liver disease (NAFLD) is increasing in prevalence in association with the epidemic of obesity and type 2 diabetes. Obesity as a cause or predisposing factor of hepatic steatosis has assumed increasing importance due to changes in dietary habit. In an autopsy study in 1990, hepatic steatosis with lipid present in greater than 25% of hepatocytes was found in 29% of obese patients, and 7% of non-obese patients.[1] In a patient-based study conducted in the same period, it was shown that 7% of patients undergoing abdominal computed tomography examinations had diffuse hepatic steatosis.[2] More recent epidemiological studies have witnessed a worldwide rise in the prevalence of NAFLD to between 17-33% of the adult population.[3] In Japan, the prevalence of NAFLD among adults has been reported as 22%,[4] while a Chinese population study conducted in Taiwan gave a prevalence rate of 36.9%.[5]

Although hepatic steatosis is a benign process, in the presence of excessive oxidative stress there is hepatocyte injury, inflammation and the development of fibrosis. The high prevalence rates and the associated health risks thus call for a non-invasive technique, not only for qualitative diagnosis but also for quantitative measurement. Chemical shift magnetic resonance imaging (MRI) is a proven technique for confirming

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the presence of fat in tissues.[6] Chemical shift MRI using in-phase (IP) and opposed-phase (OP) gradient-recalled echo (GRE) sequences has been shown to be very useful in the detection of fatty components of focal liver lesions.[7-9] Using the GRE sequence, Fishbein et al[10] recently have shown a high correlation between the signal intensity change measured on OP and IP images and biochemical fat quantification in prepared fatty liver specimens. Different methods of calculation to estimate liver fat have been employed for the IP and OP MRI but all depended on the measurement of the signal intensity of the liver parenchyma in the OP and IP images.[7,10-12] The reliability of IP and OP MRI to assess hepatic steatosis has not been evaluated.

The objective of the present study was to evaluate the reliability of quantitative assessment of hepatic steatosis on GRE IP and OP MRI in a group of subjects previously diagnosed with hepatic steatosis.

PATIENTS AND METHODS

The study population comprised 19 Chinese subjects (14 men, 5 women) aged 24 to 74 years (mean, 51.7 years), who had a previous ultrasound diagnosis of hepatic steatosis within the past two years. The inclusion criterion was a positive diagnosis of hepatic steatosis on ultrasound, irrespective of the degree. None of the subjects had cirrhosis according to clinical or sonographic criteria. All subjects underwent abdominal MRI examination, which was performed in a 1.5 Tesla unit (Gyroscan ACS NT; Phillips Medical Systems, Best, the Netherlands), using a body coil. A single breath-hold dual echo sequence covering the whole liver was employed, with the following parameters: repetition time (TR) 132 ms, echo time (TE) 2.3 ms (OP) and 4.6 ms (IP), flip angle 80°, 10 mm slice thickness with 1 mm gap, field of view 40 cm, matrix 256 x 256. The typical dual echo sequence typically provides an 18-slice coverage, with an acquisition time of 14 s. In the same breath-hold held in end-inspiration, both IP and OP images of the whole liver were obtained in the dual echo-sequence, in which the receiver gain and scale factor were kept constant at both the IP and OP images.

All subjects underwent the two MRI examinations, using the same sequence protocol, within the same day. After the first MRI examination, each subject was asked to leave the MRI scanner suite, which was then used to examine other patients. After waiting for 15 to 60 minutes, the subject underwent a repeat MRI, with fresh positioning in the scanner and planning of the MRI sequences. In the machine-equipped Viewforum workstation, a region of interest (ROI) of 50-100 mm^2 was drawn in segment VI of the right lobe of the liver on the IP image, to include liver parenchyma without contamination with blood vessels or motion artifacts. The same ROI was copied and transposed on to the same location on out-of-phase image. An example of an ROI drawn for a subject is shown in Figure 1.

Measurements of the first and repeat MRI were performed in random order, with the operator blinded to the name of the subject and any previous clinical and sonographic results, and whether the MRI was the first or the repeat examination. All measurements were performed by a single operator. The assessment of the liver fat content was based on the percentage of signal intensity reduction (SIR%) in the OP as compared to the IP GRE T1-weighted images, which was calculated as follows:

(signal intensity at IP – signal intensity at OP)/signal intensity at IP x 100%.

A higher fatty content therefore would be associated with a higher SIR%.

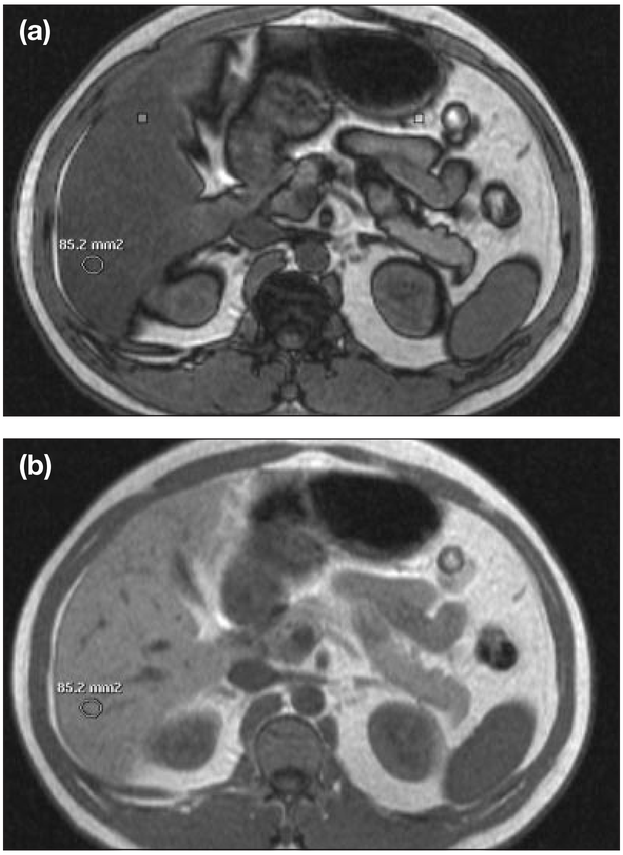

Figure 1. Example of a region of interest (oval) drawn in segment VI of the right lobe of the liver. (a) Opposed-phase image; and (b) in-phase image.

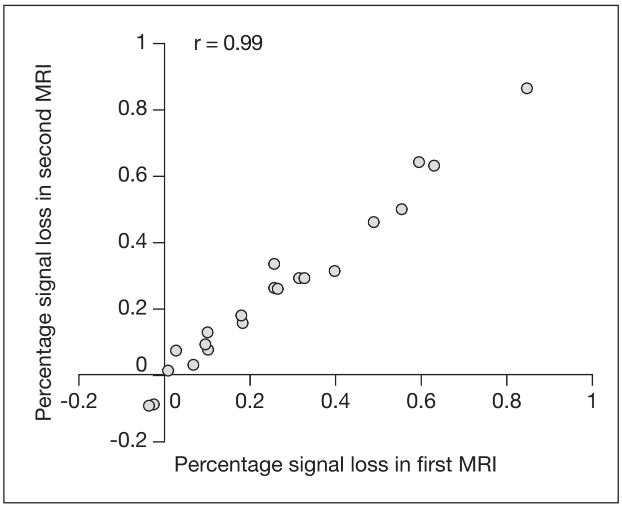

Figure 2. Scatterplot of percentage signal loss in the liver between the first and repeat magnetic resonance imaging (MRI) examinations.

With in- and out-phase images being taken in the same single breath-hold, and the consequential relatively constant receiver gain and scale factor at both the IP and OP images, no additional correction or reference with signal intensity of muscle or spleen was instituted for these factors.

Statistical Analysis

The standard error of measurement was calculated by dividing the standard deviation of the differences in percentage signal change in the two MRIs by root 2. The test-retest correlation was calculated by Pearson correlation of the percentage signal change between the two MRI examinations.

RESULTS

All subjects successfully underwent both MRI examinations and image qualities obtained in all subjects were satisfactory. In the first MRI examination, the range of SIR% was from -3.6% (signal gain) to 84.8%, with a mean of 27% and a standard deviation of 25.6%. In the repeat MRI examination the range of SIR% was from -8.9% to 85.9%, with a mean of 25.7% and a standard deviation of 26.1%. The standard error of measurement was 2.9%. Figure 2 is a scatterplot of the SIR% between the first and the repeat MRI examinations. Correlation of measurements in signal change in the two MRI examinations was high (r = 0.99).

DISCUSSION

Quantification of fatty liver is important because hepatic steatosis is known to be associated with alcoholic liver disease, diabetes, obesity, hyperlipidaemia and the use of corticosteroids. Steatohepatitis may ensue, with the known manifestations of lobular hepatitis, focal necrosis and liver inflammation.[1] The association of hepatic steatosis with visceral obesity is well documented. Various treatments to combat the general effect of obesity have been recommended or are presently under evaluation. It is thus important to have a non-invasive tool allowing reliable quantification of hepatic steatosis, so that serial changes in hepatic steatosis on various treatment regimes can be monitored. MRI is a noninvasive technique with no ionising radiation hazard, unlike computed tomography scanning. It also allows numeric quantification, which is more precise than can be achieved with ultrasonography. With advances in the technique, the whole liver can now be imaged in a single breath-hold, to obtain both the IP and OP images.

On a GRE sequence, the phases of water and fat protons vary with the TE. When the water and fat protons are in phase, the signal intensity of the water protons and fat protons adds up to give the final signal intensity of the voxel. However, cancellation of signal will result if the phases of water protons and fat protons in the same voxel are in the opposite phase with each other when the echo is formed.[13] In hepatic steatosis, the fat protons in fatty hepatocytes cancel out the water proton signals in the same voxel on OP GRE imaging, resulting in a dark appearance. Short TR/TE OP images, with a higher signal of fat and a greater chemical-shift phase cancellation, are more sensitive to fatty infiltration than long TR/TE OP images.[14] The magnitude of signal loss will depend on the proportion of water and fat.[15] The heavier the fatty change, the darker the liver will become. This chemical-shift related signal change constitutes the basis for quantitative measurement of signal change in livers with different fat content on IP and OP images.

Technical factors that may affect signal intensities of a structure in an MRI include TR, TE, and number of excitations, which are thus kept constant as sequence parameters. The receiver gain and scale factors are also kept constant in the OP and IP images in the same breath-hold sequence. However, these may show some variation with the body build and shape of the patient. The present study was not affected by these factors as the body build and shape of subjects was constant over the short period of time between examinations. At the same time, the study did not address this issue of change in body build and shape, which would occur in some patients, especially those receiving treatment for obesity.

There are also other subject factors that may potentially affect the reliability of repeat examinations. The subject may demonstrate variation in the depth of inspiration so that the slice location along the long axis (z-axis) in the two examinations may not exactly align. Positioning of the subjects in the two positions may also not exactly align. Due to the manual and subjective drawing of the ROI, the anatomical location of the ROI between two MRI examinations at different times may also show some variation with regard to its depth and relation to intrahepatic vessels. The ability to hold breaths may vary in the two examinations and subtle deviation from breath-holding may lead to signal intensity-to-noise changes not evident to the naked eye. Although these possibilities exist, the current study suggests these are probably minor, given the similarity of the mean and standard deviations of the SIR% and the excellent correlation of SIR% obtained from the two MRI examinations. The 2.9% standard error of measurement would indicate that percentage signal changes greater than this are probably due to changes in steatosis in the liver and not due to random error.

The range of SIR% in the subjects studied was wide (from around 0% to 85.9%), which supports the reliability of the method across a wide spectrum of hepatic steatosis. Two subjects had a negative SIR%, suggesting that steatosis was not present. This could reflect change occurring during the interval between the ultrasound and MRI examinations. The inclusion of such data does not necessarily decrease the value of the study, as conversion to non-steatotic status is definitely a possible and desirable end point in the serial monitoring of liver fat status.

A recent study has shown that quantitation of hepatic steatosis on out-of-phase GRE MRI is not as accurate as fat-saturated fast spin-echo MRI, especially in patients with cirrhosis.[16] None of the subjects in the current study had cirrhosis, and the high reliability obtained in the current group would justify the use of the much faster, and therefore more economical, in- and out-phase GRE technique in monitoring patients affected by hepatic steatosis without cirrhosis. For patients with cirrhosis, the use of other methods, such as fat-saturated fast spin-echo MRI, chemical shift imaging or spectroscopy may be necessary.

CONCLUSION

The present study has shown that quantitative assessment of hepatic steatosis on GRE IP and OP MRI has high reliability. This technique has potential value as a monitoring tool for long-term changes in hepatic steatosis.

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