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Magnetic resonance elastography of the liver: Preliminary results and estimation of interrater reliability

Utaroh Motosugi¹, Tomoaki Ichikawa¹, Katsuhiko Sano¹, Hironobu Sou¹, Ali Muhi¹, Tsuyota Koshiishi¹, Richard L. Ehman², and Tsutomu Araki¹

¹Department of Radiology, University of Yamanashi, 1110 Shimokato, Chuo 409-3898, Japan

²Department of Radiology, Mayo Clinic, Rochester, MN, USA

Abstract

Purpose—To estimate interrater reliability and validate magnetic resonance elastography (MRE) as a tool to measure liver elasticity.

Materials and methods—The study was approved by the institutional review board. Ten normal volunteers and 110 patients, who provided written informed consent, were enrolled. The pathological fibrosis score was applied as a standard reference of liver fibrosis in 21 patients. MRE was performed with a 1.5-T MR scanner with a cylindric passive longitudinal shear wave driver placed over the right chest wall to deliver vibrations. A gradient-echo MRE sequence was used to acquire axial wave images, which were automatically converted to elastograms representing elasticity in kPa. The region of interest was placed in the right lobe of the liver on elastograms by 2 raters independently. To evaluate interrater reliability, the intraclass correlation coefficient was calculated. The elasticity measurements correlated with the pathological fibrosis score in 21 patients.

Results—The intraclass correlation coefficient was almost perfect (0.993) between the elasticities measured by the 2 raters. The mean elasticity in the case of patients with F4 was 5.7 kPa; F3, 4.4 kPa; F2, 3.1 kPa; F1, 2.2 kPa; and F0, 2.1 kPa.

Conclusion—MRE is a reliable tool to measure liver elasticity.

Keywords

liver; MR imaging; Elastography; fibrosis

Introduction

In the management of patients with chronic liver disease, determining the degree and rate of progression of fibrosis is important for predicting prognosis or cancer development [1-3]. Liver fibrosis is currently assessed by analysis of a liver biopsy specimen with a semiquantitative pathologic scoring system. However, a liver biopsy is an invasive procedure with risks of complications, including hemorrhage and infection. Some noninvasive methods have been proposed to estimate liver fibrosis, such blood tests or liver

elasticity measurements with ultrasounds. Magnetic resonance elastography (MRE) has recently been developed to measure liver elasticity by imaging of propagating shear waves in the tissue [4-6]. Several researchers have already reported that MRE is a promising tool for noninvasive estimation of liver fibrosis [7].

The purpose of this study was to estimate the interrater reliability of MRE measurements and show preliminary results in a Japanese population.

Materials and methods

Subjects

The study was approved after review by the institutional review board. This study included 10 normal volunteers (mean age, 24.9 years; range, 21–32) and 110 patients (mean age, 66.5 years; range, 41–83) who underwent an abdominal MR examination in January and February 2010. Written informed consent was obtained from all the subjects.

The study coordinator referred to the pathological database of our institute and found 21 liver pathology reports of patients included in this study, in which liver specimens were obtained either by biopsy or surgical resection within 3 months of the MRI examination. The pathological liver fibrosis score in the reports was applied as a standard of reference of liver fibrosis in the patients.

MRE

MRE was performed with a 1.5-T MR scanner (Signa, GE Healthcare, Milwaukee, WI). Images were obtained with patients in a supine position by using a cylindric passive longitudinal shear wave driver placed over the right chest wall to deliver vibrations via a transcostal approach [5].

A 2D gradient-echo MRE sequence was used to acquire axial wave images. The scanning position was set above the gallbladder and below the subphrenic region of the liver. To obtain images of the liver at consistent positions at each phase offset, individual subjects were asked to hold their breath after expiration [8]. The imaging parameters of MRE were as follows: TR/TE, 100/27; continuous sinusoidal vibration, 60 Hz; field of view, 30–34 × 40–45 cm; matrix size, 256 × 64; flip angle, 30°; slice thickness, 10 mm; 4 evenly spaced phase offsets; 4 pairs of 60-Hz trapezoidal motion-encoding gradients with zeroth- and first-moment nulling along the through-plane direction. Two spatial presaturation bands were applied on each side of the selected slice to reduce motion artifacts due to blood flow. The total acquisition time was 66 s (four 16 s breath holds).

Analysis of Elasticity

The MR scanner automatically generates elastograms by processing the acquired images of propagating shear waves with a previously described local frequency estimation inversion algorithm [9]. Elastograms represent the shear stiffness of the tissue as a pixel value in kPa [10, 11]. The region of interest (ROI) was placed in the right lobe of the liver on elastograms by 2 raters independently; one was a radiologist and the other was a radiographer. As a rule, the ROIs were at least 1500 mm² and placed with exclusion of blood vessels and the liver

edge. To acquire the ROIs, the radiographer used an MR scanner and the radiologist used a workstation (Advantage Workstation, GE healthcare, Milwaukee, WI).

The difference in the values measured by the radiologist and radiographer was defined as follows: D (kPa) = (elasticity measured by radiologist) – (elasticity measured by radiographer).

Statistical analysis

To evaluate the interrater reliability in MRE analysis, the intraclass correlation coefficient was calculated. The elasticities measured by the 2 raters were also compared with the paired t test.

Results

Interrater reliability

The mean and standard deviation of the elasticity values measured by the 2 raters were 3.8 (2.3) kPa and 3.8 (2.2) kPa, respectively.

The intraclass correlation coefficient was 0.993, which indicated an almost perfect correlation between the elasticities measured by the 2 raters.

The mean and standard error of D was -0.029 (0.035) with a maximum and minimum 95% confidence interval of -0.098 and 0.040 , respectively. Absolute value of D was <0.8 kPa in more than 95% of the patients and <0.3 kPa in more than 70% of the patients (Fig. 1)

Correlation with histopathological fibrosis

The mean elasticity was the highest in patients with F4, i.e., 5.7 kPa (range, 3.7–7.3; $n = 10$), followed by F3 (4.4 kPa; range, 3.2–5.8; $n = 3$), F2 (3.1 kPa; range, 2.1–3.8; $n = 4$), F1 (2.2 kPa; range, 2.0–2.3; $n = 3$), and F0 (2.1 kPa; $n = 1$). (Figs. 2 - 4)

Discussion

Chronic liver diseases can lead to hepatic fibrosis, cirrhosis, portal hypertension, and hepatocellular carcinomas and constitute an important cause of morbidity and mortality. Liver fibrosis is usually diagnosed via analysis of a liver biopsy specimen, for which semiquantitative methods such as the METAVIR classification are used. The fibrosis stage defined via analysis of the liver biopsy sample is believed to be one of the most reliable prognostic factors and biomarkers indicating the development of HCC [1-3]. Many researchers attempted to evaluate liver fibrosis using noninvasive methods, including analysis of serological markers, sonographic elastography, and MRI [12-16]. MRE is a recently developed noninvasive method for estimating liver fibrosis, and this method is reported to have a high validity [7, 17].

To develop a biomarker for a particular disease, estimation of the measurement error of the technique is essential along with standardization and validation. Measurement error is commonly determined in terms of repeatability and reproducibility [18]. The International

Standards Organization (ISO: 5725) defined the 2 terms as follows. Repeatability refers to test conditions that are as constant as possible, where the same operator uses the same equipment within a “short time interval” and obtains independent test results by the same method with identical items in the same laboratory. Reproducibility refers to test conditions under which results are obtained by the same method with identical test items but in different laboratories with different operators. Naturally, non-repeatable methods show no reproducibility. When a new technique is to be used in a clinical setting, the repeatability of the method should always be estimated. Although numerous quantification methods using various imaging modalities have been reported, very few of these have been generally accepted since results from 1 or 2 observers are not indicative of the reliability of the methods.

Measurement errors in most cases occur with manual processes. In terms of MRE, setting up patients by the operator and measurement of elasticity or placement of ROIs by raters are manual processes. Our results proved that MRE has sufficient repeatability on the basis of interrater reliability results with a perfect intraclass correlation coefficient (0.993). However, a 1 kPa difference between the 2 raters was observed in 3 of 120 cases (2.5%). Considering the standard deviation for all subjects was 2.2 or 2.3 kPa, a difference of 1 kPa between the raters must be avoided in any case. A solution for such a problem could be the use of multiple ROIs in an image and averaging the values. However, automatic measurement using software must be the most reliable solution. Further development to improve the reliability of measurement is expected.

The major limitation of our results was the small number of pathologically confirmed liver fibrosis. Further study with a larger cohort is required to confirm the reproducibility of MRE in a Japanese population.

In conclusion, MRE is a reliable tool for measuring liver elasticity as it showed a perfect intraclass correlation coefficient between the 2 raters.

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Histogram of differences of the 2 raters measuring elasticities

Figure 1. Histogram of differences (D) in elasticities measured by the 2 raters. Absolute value of D was <0.8 kPa in more than 95% of the subjects and <0.3 kPa in more than 70% of the subjects.

Figure 2.

(a) Elastograms of cases with a pathological fibrosis score of F4 showed high intensity (red color) for almost the entire liver. (b) T1-weighted image corresponding to the elastogram.

Figure 3.

(a) In case of a patient with F0, the intensity in the elastograms was low (blue color). (b) T1-weighted image corresponding to the elastogram.

Figure 4. Scattered plot of elasticity by magnetic resonance elastography (MRE) correlated with the pathological fibrosis scores for 21 patients.