Hitachi Real-time Tissue Elastography:

Publications & International Communications

Clinical Abstracts
Hitachi Real-time Tissue Elastography for Liver Disease
EVALUATION OF LIVER FIBROSIS IN DIFFUSE LIVER DISEASE USING REAL-TIME TISSUE ELASTOGRAPHY

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[Objective] Real-time Tissue Elastography (RTE) is developed for visualizing the tissue hardness/softness by using ultrasound. We have been investigating its ability of evaluating fibrosis in diffuse liver disease. Recently, newly developed low frequency probe (EUP-L52) has been applied to RTE, and a patient who had difficulty of visualizing RTE image for the reason of low penetration such as obesity has been improved. In this study, multiple linear regression analysis was performed using several features of RTE image to estimate the RTE fibrosis value, and compared with the fibrosis stage to evaluate the clinical usefulness of RTE.

[Material and Method] 26 patients with chronic hepatitis C or liver cirrhosis diagnosed by liver biopsy, and 6 healthy volunteers were examined in this study. The indicated stages of fibrosis were F0 in 2 patients, F1 in 6 patients, F2 in 8 patients, F3 in 6 patients, and F4 in 4 patients. RTE were performed with HITACHI HI VISION 900 and EUP-L52 linear probe (3-7MHz). Scan was performed through the right intercostal space to observe right lobe. Probe was slightly held to detect the strain by heartbeat. All RTE images were transferred to an external PC, and analyzed with prototype image analysis software. Color data inside the ROI were converted to relative strain value, and features of RTE image such as mean of relative strain value (MEAN), standard deviation of relative strain value (STD), area of blue region (AREA), and complexity of blue region (COM) were calculated. Then, multiple regression analysis was performed with features of RTE image and fibrosis stage.

[Results] Features of RTE image were highly correlated with fibrosis stage. Correlation coefficient of MEAN, STD, AREA, and COM were r=-0.604, 0.593, 0.592, and 0.578. With these 4 parameters, multiple regression analysis was performed and derived the regression equation, which significantly fit with the data. RTE fibrosis value was calculated from this equation and had high correlation with fibrosis stage(r=0.729).

[Conclusion] As a result of having analyzed RTE quantitatively, the quantity of characteristic reflected staging well. RTE is particularly useful as the modality that can grasp improvement of the fibrosis by a hepatitis diagnosis and the treatment non-invasively.

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Digestive Disease Week, May 30th – June 4th, 2009, Chicago, USA, M1774

REAL-TIME SONOELASTOGRAPHY - A NEW APPLICATION IN THE FIELD OF LIVER DISEASE

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Ultrasound elastography is a new imaging technique that allows a noninvasive estimation and imaging of tissue elasticity distribution within biological tissues using conventional real-time ultrasound equipment with modified software. Elastography has been reported to be useful for differentiation and characterization of various malignant tumors, such as breast, prostate, thyroid, pancreas, lymph nodes, gastrointestinal stromal tumors, hepatocellular carcinoma and liver metastasis. Transient and, more recently, real-time elastography has been proved to be useful for noninvasive assessment of liver fibrosis in patients with diffuse liver diseases. Elasticity imaging promises to make an important contribution to ultrasound practice.

J Gastrointestin Liver Dis, December 2008 Vol.17 No 4, 469-474
REAL-TIME ELASTOGRAPHY - A PILOT STUDY FOR NON-INVASIVE DETECTION OF SMALL HEPATOCELLULAR CARCINOMA IN CIRRHOTIC PATIENTS
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BACKGROUND: Ultrasound (US) screening for hepatocellular carcinoma (HCC) is worthwhile because early detection is the only approach to improve outcome. Small nodules (<3 cm) detected on US in cirrhotics represent the most challenging category for noninvasive diagnosis of HCC. By assessing tissue elasticity distribution, real-time sonoelastography may represent a reliable method for differentiating between benign and malignant lesions in this setting.

AIM: To evaluate real-time sonoelastography as a noninvasive tool for the detection of small HCC nodules in cirrhotic patients.

METHODS: Nineteen cirrhotic patients with small nodules (1-3 cm) were evaluated with real-time elastography (SonoElastography mode, HITACHI EUB-6500); the mean intensity of colors red, blue, green were measured using a semi-quantitative method. Analysis of histograms for each color of the sonoelastography images was performed for quantifying the elasticity of nodule tissue comparative with cirrhotic liver tissue. In order to investigate the predictive role of sonoelastography for diagnosis of HCC, the c-statistic parameter was used. The final diagnosis of HCC was obtained by liver biopsy within the nodule, surgical pathology or at least 6 months follow-up.

RESULTS: There were analyzed 213 sonoelastography images from 19 patients (12 men; 7 women) who underwent transabdominal ultrasound. The mean age was 58±12.9 years and 73.5% patients were in Child-Pugh class A, 10.5% class B and 16% class C. The histologic diagnosis found trabecular and microglandular aspects of moderate differentiated carcinoma in 8 patients and well differentiated carcinoma in 2 patients. The c-statistic for green color is 0.8, a cut-off value of <106.5 being diagnostic for HCC with a specificity of 84%, sensitivity 58%, positive predictive value 81% and negative predictive value 62%. Blue color proved to be an excellent diagnostic tool for HCC (c-statistic=0.95); for a cut-off value >121.4, the specificity was 86%, sensitivity 91%, positive predictive value 89% and negative predictive value 89.7%. The kappa reliability test was 0.8 for concordance between blue criteria of HCC and histologic diagnosis. Combined criteria for green and blue color have a diagnostic accuracy for HCC of 82.3%.

CONCLUSION: US real-time elastography is a promising method for screening and non-invasive diagnosis of HCC. It allows to distinguish between HCC nodules and regenerative cirrhotic macronodules, being an useful tool for early referral of Child-Pugh class A cirrhotic patients for liver transplantation or curative resection.

Digestive Disease Week, May 17th – 22nd, 2008, San Diego, USA T1947
American Association for the Study of Liver Disease, 2008, A-827

REAL-TIME ELASTOGRAPHY FOR NONINVASIVE DIAGNOSIS OF LIVER FIBROSIS
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INTRODUCTION Accurate evaluation of liver fibrosis has significant importance in following up patients with viral or nonviral chronic hepatitis. Although percutaneous needle liver biopsy is still the gold standard for such assessments, it is an invasive procedure with possible undesirable complications including serious bleeding events. In the current study, we have focused on a new mode of sonogram “Real-time Elastography”, which can show tissue elasticity up on the image, and express the elasticity numerically. The aim of this study was to evaluate the usefulness of “Real-time Elastography” in the assessment of liver fibrosis.

MATERIALS AND METHODS Twenty six patients, who had been underwent intra-operative liver biopsy or hepatectomy between August in 2005 and November in 2007, were included in this study. Hepatic elasticity was measured using Real-time Elastography (EUB-8500, Hitachi Medical Systems). In evaluation of liver fibrosis, we calculated elastic ratio of the liver for the subcutaneous tissue. We examined correlation of the elastic ratio with histological fibrosis staging. In addition, hyaluronic acid and type IV collagen levels were included in the analysis.
RESULTS As liver fibrosis staging advanced, elastic ratio was lower. There was correlation between the elastic ratio and the histological fibrosis stages (F0: F1: F2: F3: F4= 1.53: 1.08: 0.46: 0.54: 0.48; p<0.001). The elastic ratio of F3 was lower than that of F0 and F1. And the elastic ratio of F4 was especially lower than that of F0 and F1. Moreover, there was correlation between the histological fibrosis stages and hyaluronic acid levels (F0: F1: F2: F3: F4= 38: 80: 89: 134: 228; p<0.001). On the other hand, there was no correlation between the fibrosis stages and type IV collagen levels.

CONCLUSION Real-time elastography is a new and promising sonography-based noninvasive methods for the assessment of liver fibrosis.

Digestive Disease Week, May 17th – 22nd, 2008, San Diego, USA T1951

INTRA-OPERATIVE APPLICATION OF REAL-TIME TISSUE ELASTOGRAPHY FOR THE DIAGNOSIS OF LIVER TUMOURS

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Objective: Real-time tissue elastography (RTE) has made it possible to visualize tissue elasticity. The aim of this study was to evaluate the usefulness of RTE for the differential diagnosis of liver tumours during surgical exploration.

Methods: Fifty-five liver tumours in 44 patients were examined with RTE, concomitant with routine intra-operative ultrasonography. Elasticity images were classified into four types, from type A (even strain) to type D (no strain), according to the distribution and the degree of the strain contrasted with that of the surrounding liver [elasticity type of liver tumour (ETLT)]. We evaluated the consistency of the findings of RTE with the pathological diagnosis as a reference standard.

Results: All malignant lesions showed various degrees of strain reduction in the tumour tissue. Twenty-one of 22 hepatocellular carcinomas (HCCs) were classified as type B with a sensitivity of 95.5%, a specificity of 90.9% and an accuracy of 92.7%, while all 24 metastatic adenocarcinomas were classified as either type C or type D with a sensitivity of 100%, a specificity of 80.6% and an accuracy of 89.1%.

Conclusion: Application of RTE in surgical exploration provided significant information about the elasticity of liver tumours. RTE, using a new criterion, ETLT, enabled us to distinguish rather accurately between two common malignancies: HCC and metastatic adenocarcinoma.

Liver International ISSN 1478-3223

EARLY AND NON-INVASIVE DIAGNOSIS OF SMALL HEPATOCELLULAR CARCINOMA USING REAL-TIME ELASTOGRAPHY

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Background and aim: Small nodules (< 3 cm) detected on ultrasound (US) in cirrhotics represent the most challenging category for noninvasive diagnosis of hepatocellular carcinoma (HCC). The study aim was to evaluate real-time sonoelastography as a noninvasive tool for the detection of small HCC nodules in cirrhotic patients.
Methods: Twenty eight cirrhotic patients with small nodules (1-3 cm) were evaluated with real-time elastography (SonoElastography mode. HITACHI EUB-6500); the mean intensity of colors red, blue, green were measured using a semi-quantitative method. Analysis of histograms for each color of the sonoelastography images was performed for quantifying the elasticity of nodule tissue comparative with cirrhotic liver tissue. In order to investigate the predictive role of sonoelastography for diagnosis of HCC. the c-statistic parameter was used. The final diagnosis of HCC was obtained by liver biopsy within the nodule, surgical pathology or at least 6 months follow-up.

Results: There were analyzed 303 sonoelastography images from 28 patients (17 men; 11 women) who underwent transabdominal ultrasound. The mean age was 57.2 ± 11.1 years and 75% patients were in Child-Pugh class A, 14.2 % class B and 10.8 % class C. The c-statistic for green color is 0.76, a cut-off value of < 129.3 being diagnostic for HCC with a specificity of 82.5%, sensitivity 58.3%, positive predictive value 80.6 % and negative predictive value 61.4 %. Blue color proved to be an excellent diagnostic tool for HCC (c-statistic = 0.97); for a cut-off value > 121.4, the specificity was 86.6%, sensitivity 96%, positive predictive value 93.8% and negative predictive value 91.2%.

Conclusion: US realtime elastography is a promising method for screening and non-invasive diagnosis of HCC. It allows, to distinguish between HCC nodules and regenerative cirrhotic macronodules. being an useful tool for referral of Child-Pugh class A cirrhotic patients for liver transplantation or curative resection.

Ultraschall in Med, 2008, suppl 1, PP1.16

THE ROLE OF REAL-TIME ELASTOGRAPHY IN THE NON-INVASIVE ASSESSMENT OF FIBROSIS IN DIFFUSE HEPATOPATHIES
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Aim: Ultrasound elastography was recently reported to offer supplemental information that appears to yield a better characterization of liver tissue. The principle of real-time elastography (RTE) is that tissue compression produces displacement within the tissue and that the strain is smaller in harder tissue as compared to softer tissue. The aim of the study was to analyze whether computer-enhanced dynamic analysis of RTE movies is able to better characterize the degree of fibrosis in chronic hepatic diseases.

Material and methods: We included in this prospective study 97 consecutive patients examined in the Research Centre of Gastroenterology and Hepatology Craiova by RTE, with a Hitachi 8500 US system with an embedded SonoElastography module. Patients with alcoholic fatty liver disease (n = 21), viral B, C or B+D hepatitis (n = 26), cirrhosis (n = 29) and healthy volunteers (n = 21) were examined. RTE was performed through the right intercostal space, during breath holding at end-expiration phase. Two examinations consisting in three distinct ten seconds elastography movies were consecutively recorded by two different operators, blinded to each other and to the liver biopsy information. Each acquired elastography movie was subject to computer-enhanced dynamic analysis using a public domain Java-based image processing tool (ImageJ). The final diagnosis was based on the results of liver biopsy, with liver fibrosis quantified according to the Metavir scoring system.

Results: Using dynamic hue histogram analysis we were able to quantify the degree of liver elasticity inside a defined region of interest located at the periphery of the right liver lobe. The correlation between the mean elasticity values calculated by hue histogram analysis on average images and the degree of histologic fibrosis stage was statistically significant. Furthermore, we have obtained good intra- and inter-observer variability values, with kappa values between 0.41 - 0.60, indicating moderate agreement. The use of neural networks has also increased the discriminative ability of the method in order to accurately differentiate between liver fibrosis degrees.

Conclusion: Real time elastography is a new and promising method for the characterization of liver fibrosis in chronic hepatic diseases but it should be compared with other non-invasive markers,
transient elastography and liver biopsy results in large multicentric studies with improved methodology.

Young Investigators Award
Ultrasschall in Med, 2008, suppl 1, OP17.1

DYNAMIC HUE HISTOGRAM ANALYSIS OF REAL-TIME ELASTOGRAPHY FOR NON-INVASIVE ASSESSMENT OF LIVER FIBROSIS

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INTRODUCTION: Sono-elastography is a recent imaging method used for the realtime visualization of tissue elasticity. The method reveals the physical properties of the tissue, by characterizing the difference of hardness between diseased tissue and normal tissue. The principle of elastography is that tissue compression produces strain (displacement) within the tissue and that the strain is smaller in harder tissue as compared to softer tissue.

AIMS & METHODS: The study design was prospective. A total of 45 consecutive patients with alcoholic fatty liver disease (n = 7), viral B or C hepatitis (n = 18), cirrhosis (n = 20) and 20 healthy volunteers were examined by real time elastography with a Hitachi 8500 US system with an embedded SonoElastography module. Realtime sonoeastography was performed through the right intercostal space, during breath holding at end-expiration phase. Two examinations consisting in three distinct elastography movies were consecutively recorded by two different operators, blinded to each other and to the liver biopsy information. Each acquired elastography movie was subject to computer-enhanced dynamic analysis using a public domain Java-based image processing tool (ImageJ). The final diagnosis was based on the results of liver biopsy, with liver fibrosis quantified according to the METAVIR scoring system. RESULTS: Patients diagnosed with alcoholic fatty liver disease, chronic viral hepatitis and liver cirrhosis were prospectively included, with a total number of 65 cases examined by real-time sonoelastography. By using dynamic hue histogram analysis we were able to quantify the degree of liver elasticity inside a defined region of interest located at the periphery of the right liver lobe. The correlation between the mean elasticity values calculated by hue histogram analysis on average images and the degree of histologic fibrosis stage was statistically significant (p < 0.05). Moreover, the diagnostic accuracy of real-time sono-elastography was also estimated by using receiver operating characteristic (ROC) analysis.

CONCLUSION: Real time elastography is a new and promising method for the characterization of liver fibrosis in chronic hepatic diseases. Prospective studies, with blinded comparisons and multicentric design should aim to compare sonoelastography with other non-invasive methods for the assessment of liver fibrosis (including Fibroscan and magnetic resonance imaging). The methodology of real-time sono-elastography should be also carefully assessed, with studies that should also aim to test the intra- and interobserver variability of the method.

Gut 2007; 56 (Suppl III) A275
15th United European Gastroenterology Week, October 29th – 31st, 2007, Paris, France
REAL-TIME ELASTOGRAPHY FOR NONINVASIVE ASSESSMENT OF LIVER FIBROSIS IN CHRONIC VIRAL HEPATITIS.
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OBJECTIVE: Recently, transient elastography (FibroScan) has been introduced for noninvasive staging of liver fibrosis. Here, we investigated a novel approach for noninvasive assessment of liver fibrosis using sonography-based real-time elastography, which can be performed with conventional ultrasound probes during a routine sonography examination.

MATERIALS AND METHODS: Real-time elastography was performed in 79 patients with chronic viral hepatitis and known fibrosis stage and in 20 healthy volunteers. A specially developed program was used for quantification of tissue elasticity. Stepwise logistic regression analysis was performed to define an elasticity score using variables with high reproducibility in a preceding analysis of data from 16 different patients. In addition, aspartate transaminase-to-platelet ratio index (APRI) and routine laboratory values were included in the analysis.

RESULTS: The Spearman’s correlation coefficient between the elasticity scores obtained using real-time elastography and the histologic fibrosis stage was 0.48, which is highly significant (p < 0.001). The diagnostic accuracy expressed as areas under receiver operating characteristic (ROC) curves were 0.75 for the diagnosis of significant fibrosis (fibrosis stage according to METAVIR scoring system [F] > or = F2), 0.73 for severe fibrosis (F > or = F3), and 0.69 for cirrhosis. For a combined elasticity-laboratory score, the areas under the ROC curves were 0.93, 0.95, and 0.91, respectively.

DISCUSSION: Real-time elastography is a new and promising sonography-based noninvasive method for the assessment of liver fibrosis in patients with chronic viral hepatitis.

AJR 2007; 188:758–764

ASSESSMENT OF THE STAGE OF HEPATIC FIBROSIS WITH REALTIME ELASTOGRAPHY
(Translated)
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Background: Realtime Elastography (SonoElastography mode, HITACHI EUB-8500) is a method for calculating the displacement of the ultrasound signals returned from the examined structures before and after compression. Calculation of the reconstructed strain field is encoded in colour from red to blue (red = high-elasticity / soft tissues; blue = low elasticity / hard tissues) and overlaid on the B-mode image allowing the tissue elasticity pertaining to the examined area to be evaluated quantitatively. It is not been shown previously whether Realtime Elastography can be used as a non-invasive assessment of the stage of hepatic fibrosis.

Methods: Seventeen patients suffering from chronic viral hepatitis with a METAVIR score F0 – F4 determined by histology from liver biopsy performed during the previous 14 days; 12 patients with liver cirrhosis confirmed histologically; and as controls, 20 healthy patients, have been examined with Realtime Elastography (HITACHI EUB-8500, probe frequency 13 MHz, offering penetration of 2-5 cm. The average scan area was 350-500 mm², and examination time 5-10 min.). In each case, 10 intercostal elasticity values have been acquired and displayed in colour. For the analysis, only images acquired with standardised compression were retrieved (Compression 3-4 on a scale 1-6). Using a specific computer program, a re-quantification of the encoded colour could be made on a scale from 0 to 1 (0= max. elasticity; 1 = min. elasticity), and various calculations of the elasticity were processed and correlated with the stage of fibrosis on histology.
Results: The results showed optimal correlation allowing the elasticity to be described by the median of all values for each candidate. The mean elasticity values correlated to the stage of fibrosis determined histologically were: for the healthy candidates, 0.66 ± 0.07; patients with fibrosis score F0-F1, 0.74 ± 0.09; and patients with fibrosis score F2-F4, 0.80 ± 0.07 (Kruskal-Wallis-Test p < 0.001). The Pearson’s correlation coefficient between these parameters and the APRI score (AST to platelet ratio index) was 0.61 (p < 0.001).

Discussion: Realtime-Elastography is a simple, non-invasive method for the assessment of liver fibrosis which can be performed during a normal liver ultrasound examination without the need for any additional equipment. By differentiating between patients with fibrosis score ≤ F1 and those with fibrosis score ≥ F2 up to F6 (cirrhosis), it could be used as a method to select the therapy for patients suffering from chronic hepatitis avoiding an invasive liver biopsy for many patients.

XVIII th Congress of European Federation of Societies for Ultrasound in Medicine and Biology, 25th – 27th September, 2005, Geneva, Switzerland