Real-time MR-guided Biopsies to Target Focal Hepatic Fibrosis Detected with Magnetic Resonance Elastography

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INTRODUCTION

Hepatic fibrosis is a dynamic and reversible process (1); hence early diagnosis is critical. To this end, magnetic resonance elastography (MRE) emerged as a non-invasive technique to quantify liver stiffness by generating tissue viscoelasticity maps (MR elastograms) (2). Although MRE has to-date proven effective in distinguishing mild from severe fibrosis (3), sub-classification within the early stages of hepatic fibrosis has remained elusive (2, 4). The heterogeneous nature of liver fibrosis, particularly in the early stages of disease, may contribute to this limitation (4, 5). There is a need for a technique to enable the targeted sampling of focally fibrotic areas of liver. Real-time MR guidance has been used to biopsy liver lesions with exceptional technical success (6). However, real-time MR-guided biopsy technique has not previously been used to target focal segments of liver for correlation with MR elastography. We tested the hypothesis that real-time MR-guided biopsies could be used to target focal segments of liver for histopathologic correlation with MRE stiffness measurements.

METHODS

Clinical Setting and Patients This HIPPA-compliant study was approved by our local IRB. Between Feb. and Sept. 2009, 11 consecutive patients with suspected hepatic fibrosis (age range, 42-65 years), 9 of whom were post-liver transplant patients with suspected recurrent hepatitis C infection, underwent conventional MRI with additional MRE sequences. The inclusion criterion was referral by Hepatology for liver biopsy. Exclusion criteria were (i) age younger than 18 years, (ii) inability to provide informed consent, (iii) PLT<50,000/μL, (iv) INR>1.5, (v) contraindications to MRI. Patients provided written consent to add MRE to their conventional MRI and to undergo MR-guided biopsy.

MR Unit Diagnostic MRI (including MRE) and MR-guided biopsy were both performed using a 1.5-T MR scanner (Siemens Espree).

MRE Following conventional liver MRI, patients underwent MRE of their livers. We used a 30-cm diameter cylindrical acoustic driver to apply 60-Hz mechanical vibrations to the skin above the liver (2). MRE wave images were collected with a modified phase-contrast GRE sequence (TR=100ms; TE=24.2ms; FA=15°; 390mm FOV; 288x512 matrix; ST=5.0 mm; imaging frequency=63.5 MHz; bandwidth=390.0 Hz/pixel; scan time=29 s/image). We generated quantitative images of shear stiffness (MR elastograms) by processing the acquired propagating shear waves (wave images) with a previously described local frequency estimation inversion algorithm (3, 7).

MRE Analysis Using MRE scans, the same radiologist first identified one Couinaud segment of higher stiffness and one segment of lower stiffness as targets for MR-guided biopsy for each patient and then measured MRE stiffness values for each of these focal areas using a 200 mm^2 region of interest (ROI). The overall MRE stiffness for each liver was also measured by selecting and averaging the stiffness values for two to three 200 mm^2 ROIs in four distinct axial slices of the liver.

Real-time MR-guided Biopsies Patients underwent MR-guided biopsies within one month of diagnostic MRI. Patients were placed supine on the gantry table of the MR scanner and prepped with a sterile field above the liver span. We placed three fish oil tablets along each patient's liver span as surface markers on localizer sequences to determine the insertion point of the biopsy needle. During patient breath-hold, axial and coronal T2-w HASTE images were acquired for localization. Patients were given lidocaine as a local anesthetic and IV sedation with midazolam and fentanyl if needed. All patients were biopsied using MR-compatible 18-gauge core needle devices (EZ-M, Inc, NY, USA). Real-time intraprocedural imaging involved axial T2-w IRT HASTE imaging (TR=2000-2500ms; TE=64.0ms; 400mm FOV; 205x256 matrix; ST=5.0mm; bandwidth=390.0 Hz/pixel). The interventional radiologist communicated image plane selection orally to the technologist in the control room via a two-way audio system. Free-hand image-guided biopsy technique involved slow advancement and adjustment of the needle toward the desired liver segment while simultaneously observing needle position on the monitor. Needle advancement was stopped once the needle tip was within the liver segment targeted on MRE and acquired a tissue sample.

Surgical Pathology Reports Liver tissue specimens were fixed in formalin and paraffin-embedded. After staining with hematoxylin and eosin, periodic-acid Schiff, and/or Masson's trichrome, the specimens were assessed for METAVIR fibrosis stage (F0-F4) by a surgical pathologist blinded to imaging findings (8).

Data Analysis Technical success was assessed by measuring the number of biopsies that resulted in specimens that could be effectively graded for fibrosis by the pathologist. Our secondary outcome measure involved visualization of needle tip position at the end of the MR-guided biopsy procedure in the Couinaud segment targeted on MRE. The frequency of patients experiencing major post-procedural complications was also measured. We measured the association between segmental fibrosis stage and MR elastography stiffness for the overall liver using Spearman's rank correlation coefficient. Statistical analysis was performed with SPSS (Chicago, IL). A p-value of <0.05 was judged statistically significant.

Fig. 1a-c Final needle tip position for a patient's liver biopsy of segment 8 **(a)** targets an area of elevated stiffness detected on MRE **(b)**. Histology reveals mild fibrosis (stage F1) **(c)**.

Fig. 1d-f Final needle tip position for a post-transplant patient's liver biopsy of segment 4 **(d)** corresponds with MR elastogram **(e)**. Histology reveals no fibrosis (stage F0) **(f)**.

RESULTS

22/22 (100%) biopsy specimens were of sufficient quality to assess METAVIR fibrosis stage (**Fig 1c and f**). Needle tips for all targeted liver biopsies could be visualized with MRI (**Fig 1a and d**) and corresponded with segments targeted on MRE (**Fig 1b and e**). There were no major complications. Mean MRE stiffness measurements were: for overall livers-3.42 kPa; higher stiffness biopsied segment-5.20 kPa; lower stiffness biopsied segment-3.40 kPa. There was a significant positive correlation between hepatic fibrosis stage and overall liver MRE stiffness values (ρ=0.527; p<0.05).

CONCLUSION

Real-time MRI can be used to biopsy focal segments of liver for histopathologic correlation of fibrosis using MRE scans as targets. Early-stage hepatic fibrosis can present as focal lesions that may be missed by conventional US-guided biopsies. As the under-staging of patients may delay initiation of interferon therapy, the impact of our proposed technique on patient outcomes awaits verification in future studies.

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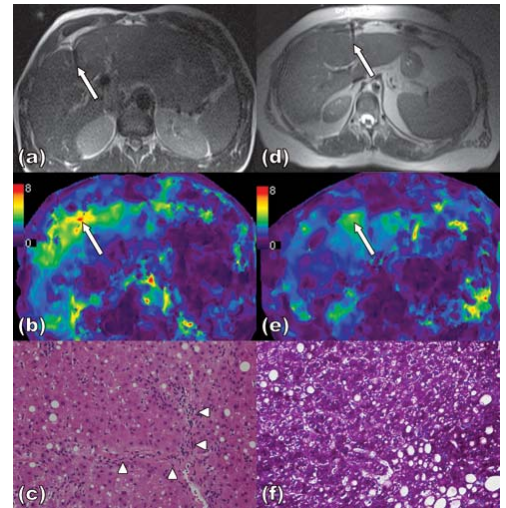[8] The French METAVIR Cooperative Study Group. 1994; 20:15-20.