MR Elastography of the Liver: Observations from a Review of 1,377 Exams

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Introduction:
Multiple studies have reported on developments of hepatic MR Elastography (MRE) to quantitatively assess hepatic fibrosis by measuring the viscoelastic properties of the liver (1-3). Recent studies have shown that other factors, such as dynamic perfusion effects, should be taken into account as potential causes of variability of hepatic stiffness (4,5). The purpose of this study was to perform a retrospective study of patients with MRE-assessed liver stiffness to assess the rates of technical success and to investigate whether there are any other pathophysiological factors that may correlate with the mechanical properties of the liver in select patients with histological and physiological data available.

Methods and Materials:
Our institution has performed over 1,500 hepatic MRE exams on clinical patients since 2007 and we reviewed 1,377 researchable exams in this study which was approved by our institutional review board. The stiffness distribution for this population and causes of technical failures were analyzed, including the impact of body mass index (BMI). Patients with liver biopsies performed less than 1 year from the date of their MRE exam were selected to analyze the effect of varying inflammatory grade on liver stiffness at different stages of fibrosis. A subset of these patients was selected to assess the relation between stiffness and other histologic and physiologic parameters. These patients were selected based on the additional criteria that 1) the patients had chronic liver disease only, 2) were not treated at the time of MRE, and 3) had blood work ≤ 30 days from the date of MRE. Regressions were performed between liver stiffness and fibrosis extent in those patients with NAFLD (nonalcoholic fatty liver disease) and HCV (chronic hepatitis C). Contour profiles were used to investigate the interdependence of stiffness and other parameters including mean blood pressure, ALT (alanine aminotransferase), AST (aspartate aminotransferase), TB (total bilirubin), and Alb (albumin).

Results:

Fig.1
Hepatic Stiffness in 1,377 Patients

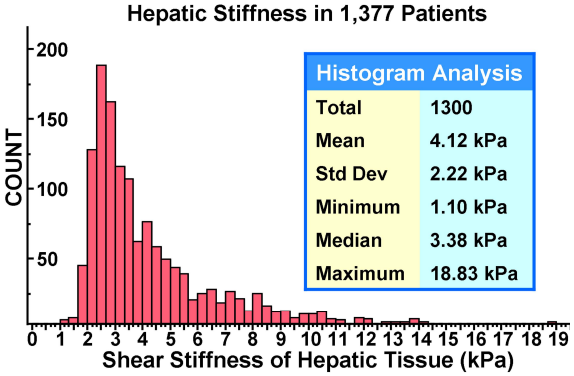


Fig.2
Effect of BMI & Technical Failure Causes

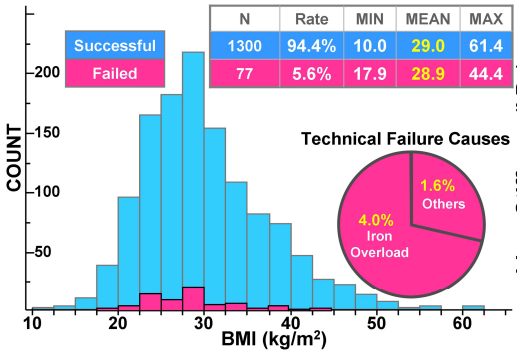
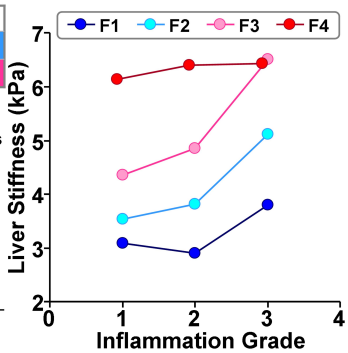


Fig.3
Effect of Inflammation



From the 1,377 patient records examined, Fig.1 shows that the MRE-assessed liver stiffness from 1,300 successful examinations has a broad left-skewed distribution with a mean value of 4.12 ± 2.22 kPa (range: 1.1 to 18.8 kPa). 77 (5.6%) of the 1,377 cases had technical failures with various causes. 55 (4.0%) of these 77 exams suffered from inadequate SNR from iron overload due to hemochromatosis or anemia. The remaining failures were due to causes that can be overcome with operator experience and technical improvements. Patient size, reported using the body mass index (BMI), was not a significant factor in failed MRE exams. Fig.2 shows that the BMI distribution is the same in patients with successful (blue) and unsuccessful (red) MRE exams. From the mean stiffness in 239 patients with biopsies performed within 1 year of the MRE exam, Fig.3 indicates that patients with a higher inflammation grade tended to have a higher liver stiffness than patients with lower inflammation grade, especially for the intermediate fibrosis stages (F1-3: blue, light blue and pink dots). At the end stage of fibrosis (F4: red dots), the inflammation grade seems to not have as significant an effect on the liver stiffness on average.

Fig.4

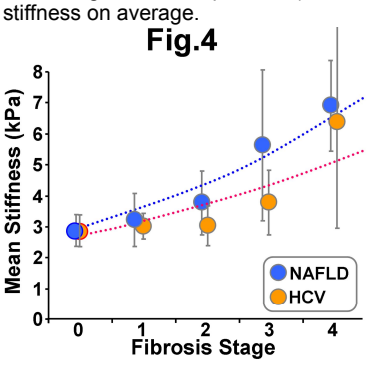


Fig.5

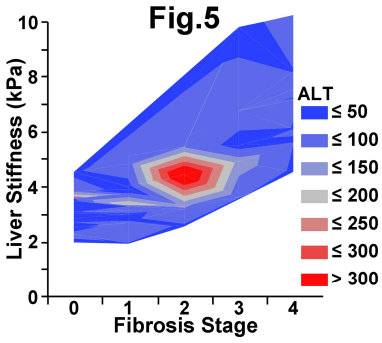


Fig.4 shows the relationship between liver stiffness and fibrosis stage in 72 NAFLD and 18 HCV patients. While the mean stiffness for NAFLD patients was higher than for HCV patients at most fibrosis stages, no statistically significant differences were found for these two different etiologies. BMI did not show a significant correlation with liver stiffness at any stage of fibrosis or inflammation in the NAFLD patients either. This suggest that even the architecture/structure of fibrosis in NAFLD patients may differ from that of HCV patients but it does not lead to significant variation in tissue mechanical properties with similar fibrosis extent. Fig.5 shows one result from the 158 untreated chronic liver disease patients with biopsy and blood analysis performed around the time of the MRE exam. It demonstrates that patients with intermediate fibrosis extent (stage 1-3) and liver stiffness (3.5-5 kPa) had the highest ALT values (AST values behaved similarly), while patients with advanced fibrosis or cirrhosis do not have substantially elevated ALT values (same with AST). This suggests that cirrhosis could be overlooked if liver enzyme tests are used for screening or diagnosis only. We also observed that patients with advanced fibrosis or cirrhosis were prone to have decreased Alb and increased TB values. This suggests that neither Alb nor TB can accurately distinguish patients with early fibrosis. Mean blood pressure was also calculated by averaging systolic and diastolic blood pressures obtained within 30 days of the date of MRE exam. It was found that the most significant amount of inflammation was typically detected in patients with liver stiffness greater than 3.5 kPa and mean blood pressure greater than 92 mmHg. No significant correlations were found between the mean blood pressure, liver stiffness and fibrosis stage.

Discussion and Conclusion:
This review of 1,377 clinical cases illustrates that hepatic MRE is a very robust imaging method for a broad spectrum of patients with a less than 5.6% technical failure rate, which can be decreased further with technical advances to reduce signal loss due to iron overload. The results also demonstrate that liver stiffness is correlated with many factors other than just fibrosis extent, including etiology, inflammation grade, mean blood pressure, hepatic metabolic function (AST, ALT and TB) and hepatic synthetic function (Alb). The use of MRE to assess changes in tissue mechanics associated with these factors could provide new insights into the pathophysiology of hepatic diseases and could have novel applications that should be explored.

References: **1.** Huwart L, NMR Biomed 2006: 19(2):173-9; **2.** Yin M, Clin Gastroenterol Hepatol 2007:5(10):1207-13; **3.** Klatt D, Phys Med Bio 2007:52(24):7281-94; **4.** Mederacke I, Liver Int 2009:29(10):1500-6; **5.** Millonig G, J Hepatology 2010:52(2):206-10.