Noninvasive Assessment of Hepatic Stiffness in Nonalcoholic Fatty Liver Disease Using Magnetic Resonance Elastography at Multiple Frequencies

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Purpose: To compare measurements of liver stiffness in patients with nonalcoholic fatty liver disease (NAFLD) by 1 axis and 3 axes motion-sensitized magnetic resonance elastography (MRE) at 3.0 T performed at different frequencies. To compare MRE-derived liver stiffness with histology-determined fibrosis, steatosis, lobular inflammation, hepatocellular ballooning, NAFLD activity score (NAS) and nonalcoholic steatohepatitis (NASH) diagnosis.

Materials and Methods: Twenty-five patients with clinical suspicion of NASH and liver biopsy were evaluated. This study was approved by our institutional review board. All subjects gave written informed consent. All studies were perfomed on a 3.0 T MRI (Signa HDxt, GE Healthcare, Milwaukee, WS) with MRE hardware (Resoundant Technology, Rochester, MN) and a 8-channel phased-array torso coil. MRE was performed with a 1 axis motion-sensitized gradient recalled echo (GRE) phase-contrast sequence and 3 axes motion-sensitized spin echo echo-planar imaging (SE-EPI) phase-contrast sequences at multiple frequencies (Table 1). Wave images were processed with an inversion algorithm. Stiffness measurements were performed in the liver parenchyma excluding major blood vessels and reported in kilopascals (kPa). Histologic grading and staging for NASH were based on the NASH-CRN histologic staging system [1]. The image analyst and pathologist were blinded to each other's results and clinical data. Spearman's correlation coefficient or Wilcoxon's test were used to compare stiffness measurements and liver histology. In case of biopsy measures with few ordinal categories, Kruskal-Wallis test was also used. Since all measurements were obtained on the same group of patients, a bootstrap-based test was used to compare the strongest and weakest correlations between MRE methods and fibrosis, adjusting for within-sample correlations between the test statistics.

Table 1. MRE acquisition parameters.

Sequence	PSD	TR (msec)	TE (msec)	FA (°)	ST (mm)	Matrix	Slices	BW (kHz)	Parallel imaging	Breath-holds	Phase offsets	Acq. time	Mechanical Frequency
MRE 2D 60 Hz	GRE	50	20	30	10	256 x 64	15	30	2x	4	90°	< 1 min	60 Hz
MRE 3D 40 Hz	SE EPI	1333	Min (51.2)	90	3.5	72 x 72	32	90	3x	3	120°	< 1 min	40 Hz
MRE 3D 60 Hz	SE EPI	1400	Min (63.9)	90	3.5	72 x 72	32	90	3x	3	120°	< 2 min	60 Hz
MRE 3D 80 Hz	SE EPI	1200	Min (45.2)	90	3.5	72 x 72	32	90	3x	3	120°	< 2 min	80 Hz

Results: Strong and statistically significant correlations were found between liver stiffness measurements and NASH fibrosis stages (rho = 0.79, $p < 0.0001$; rho = 0.76, $p < 0.0001$; rho = 0.75, $p < 0.0001$; rho = 0.69, $p < 0.0001$) with 2D 60 Hz, 3D 40 Hz, 3D 60 Hz, and 3D 80 Hz respectively. There was no statistically significant difference in the correlation between liver stiffness determined by any of the four MRE techniques and fibrosis stage ($p \geq 0.15$ for all pairwise comparisons). Weaker correlations were found between stiffness measurements and histology-determined steatosis grade, and NAS (Fig. 1). There was a trend toward higher stiffness with increasing lobular inflammation grades and diagnosis of NASH, although not significant with our sample size. Kruskal-Wallis test *p*-values confirmed the correlation *p*-values for the three and four category biopsy measures.

Conclusion: MRE performed at 3.0 T with 1 axis and 3 axes motion sensitization at multiple frequencies showed strong correlations with fibrosis stage and a trend toward higher stiffness with increasing lobular inflammation grades in adults with NAFLD. These results confirm that MRE is useful for noninvasive assessment of fibrosis not only in a variety of chronic liver disease [2-4] but also in a population of NAFLD patients [5-6].

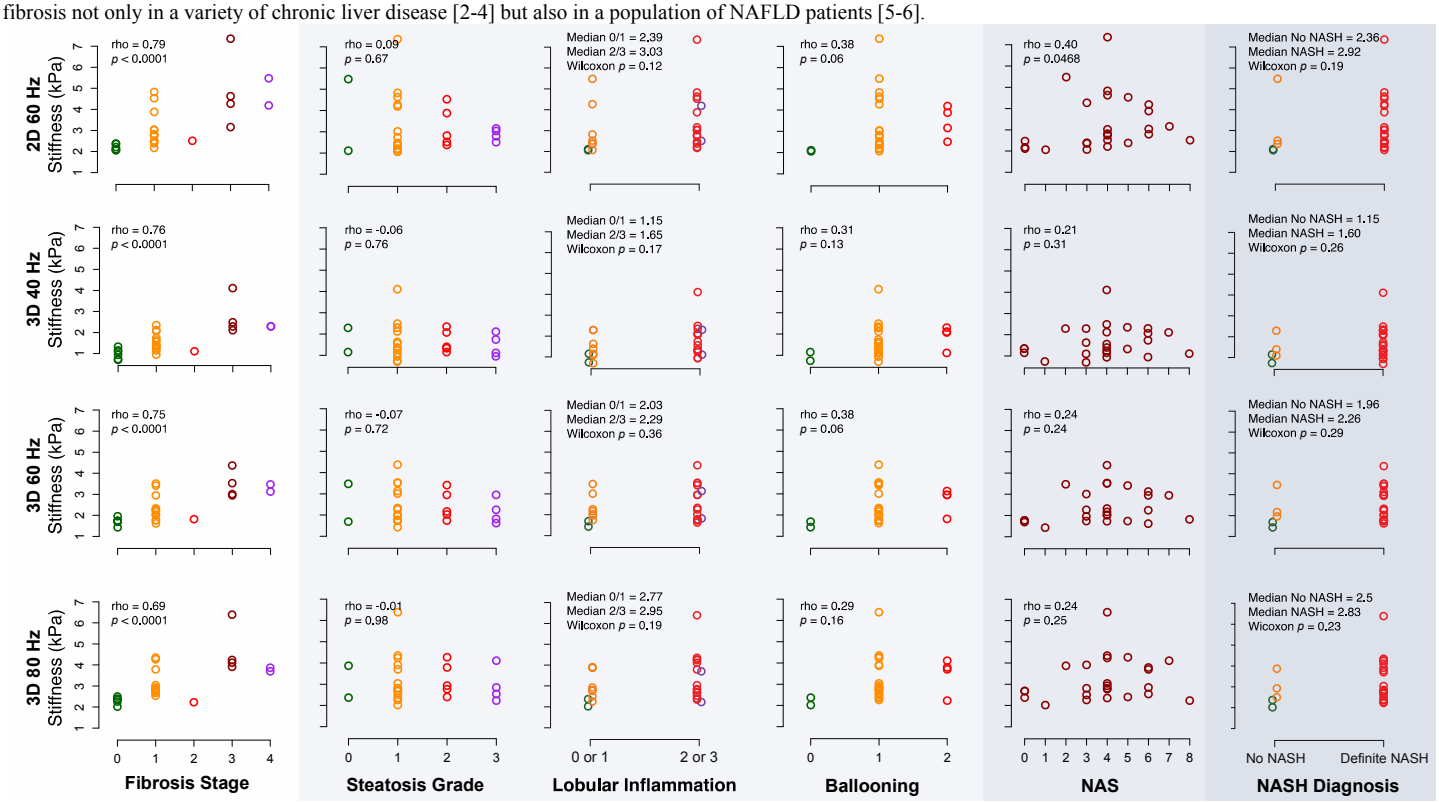

Fig 1. Scatterplots of liver stiffness (kPa) as determined by 2D MRE at 60 Hz, 3D MRE at 40 Hz, 60 Hz and 80 Hz as a function of histologically determined fibrosis stage, steatosis grade, lobular inflammation, ballooning, NAFLD activity score (NAS) and NASH diagnosis.

References: 1) Kleiner, Hepatology 2005. 2) Rouviere O, Radiology 2006. 3) Yin M, Clin Gastroenterol Hepatol 2007. 4) Huwart L, Gastroenterology 2008. 5) Salameh N, Radiology 2009. 6) Chen J, Radiology 2011.