Accuracy of MR elastography (MRE)-determined liver shear stiffness for the diagnosis of non-alcoholic steatohepatitis (NASH) and advanced fibrosis in adults with known or suspected non-alcoholic fatty liver disease (NAFLD)

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Target Audience: MRI researchers interested in MR elastography technology; medical professionals with interest in liver disease

Purpose: To assess the accuracy of MR elastography (MRE)-determined liver shear stiffness for the diagnosis of non-alcoholic steatohepatitis (NASH) and advanced fibrosis in adults with known or suspected non-alcoholic fatty liver disease (NAFLD), using contemporaneous liver biopsy as reference.

Methods: Seventy-five adult subjects (mean age 50 yrs, mean BMI 32 kg/m^2) with known or suspected NAFLD were prospectively recruited to undergo MRE and percutaneous needle liver biopsy within a 90-day window. MRE was performed at 3T using a General Electric HDxt MRI scanner with wave motion-sensitized gradient-recalled-echo (GRE) and spin-echo echo-planar (SE-EPI) sequences. Data for each sequence were collected over several breath holds. Resoundant Technology Inc. MRE hardware and software were used to generate and image mechanical waves in the liver and, using inversion algorithms, compute liver shear stiffness maps (shown in **Figure 1**). For the GRE sequence, a mechanical frequency of 60 Hz and a 2D inversion algorithm were used. For the SE-EPI sequences, mechanical frequencies of 40, 60, and 80 Hz were used and a 3D inversion algorithm was used. ROIs were drawn on images in portions of the liver with clearly observable wave propagation, avoiding liver edges and large blood vessels. Average shear stiffness was computed from these regions on corresponding stiffness maps for each MRE technique. Liver biopsy specimens were scored by a hepatopathologist using the NASH CRN histologic scoring system. NASH was diagnosed if histologic findings were borderline or definitive for steatohepatitis. Advanced fibrosis was diagnosed if fibrosis stage was ≥ 3 (i.e., bridging fibrosis or cirrhosis). For each MRE technique and each histologic endpoint, the area under the receiver operating characteristic (ROC) curve was computed and the stiffness cutoff that maximized sensitivity at a specificity of ≥ 0.89 was identified. Bootstrap-based 95% confidence intervals were calculated.

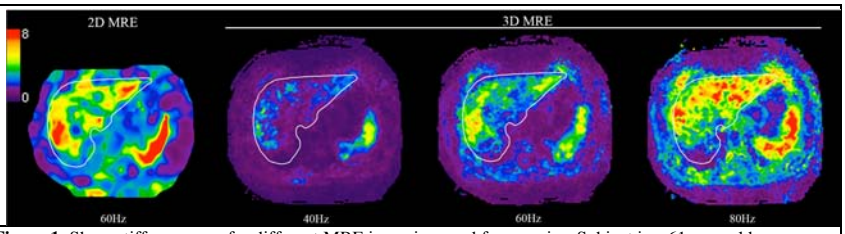

Figure 1. Shear stiffness maps for different MRE inversions and frequencies. Subject is a 61 year-old woman with BMI of 35.5 kg/m^2 and fibrosis stage 3.

Results: Statistical results of the four different MRE acquisition/inversion schemes are shown in **Table 1**. The 2D inversion technique based on GRE images at 60 Hz provided high accuracy for diagnosis of advanced fibrosis (A_z = 0.954; sensitivity 92%, specificity 92%, at cutoff of 3.80 kPa), but had modest performance for diagnosis of NASH (A_z = 0.789; sensitivity 53%, specificity 89%, at cutoff of 2.93 kPa). 3D inversion based on SE-EPI images at 40 Hz provided the highest observed accuracy for diagnosis of both NASH (A_z = 0.926; sensitivity 86%, specificity 89% at a cutoff of 1.50 kPa) and advanced fibrosis (A_z = 0.967; sensitivity 100%, specificity 92%, at cutoff of 2.42 kPa) compared to the other MRE techniques. Computed stiffness values increased with mechanical frequency, requiring correspondingly higher cutoff values for each histologic endpoint.

Table 1. Statistical results of the four acquisition/inversion schemes

MRE inversion	Mechanical frequency	MRI sequence	NASH				Advanced Fibrosis			
			ROC A_z	Cutoff (kPa)	Se (%)	Sp (%)	ROC A_z	Cutoff (kPa)	Se (%)	Sp (%)
2D	60Hz	GRE	0.789 [0.596-0.933]	2.93	53	89	0.954 [0.861-0.987]	3.80	92	92
3D	40Hz	SE-EPI	0.926 [0.778-0.990]	1.50	86	89	0.967 [0.899-0.989]	2.43	100	92
	60Hz	SE-EPI	0.859 [0.692-0.949]	2.30	65	89	0.964 [0.898-0.989]	3.24	92	95
	80Hz	SE-EPI	0.769 [0.608-0.880]	3.20	58	89	0.946 [0.870-0.980]	3.20	83	94

Discussion: This prospective study suggests that, in adults with known or suspected NAFLD, MRE acquired using relatively low-frequency mechanical waves and a 3D inversion algorithm provides high accuracy for the diagnosis of both NASH and advanced fibrosis. Compared to 2D inversion with a mechanical frequency of 60 Hz, potential advantages of 3D inversion with a mechanical frequency of 40 Hz in adults with NAFLD and high BMI may include deeper wave penetration and more complete analysis of complicated wave behavior generated by the multiple tissue interfaces in the abdomen.

Conclusion: MRE shows promise as a non-invasive alternative to liver biopsy for establishing the diagnosis of NASH and advanced fibrosis in patients with known or suspected NAFLD. Larger prospective studies are needed to verify the diagnostic advantages of MRE performed with relatively low-frequency mechanical waves and a 3D inversion algorithm.