Published in final edited form as:

Abdom Imaging. 2015 April ; 40(4): 803–809. doi:10.1007/s00261-014-0255-1.

Simultaneous Measurement of Hepatic and Splenic Stiffness Using MR Elastography: Preliminary Experience

Hadrien A. Dyvorne, PhD, Guido H. Jajamovich, PhD, Cecilia Besa, MD, Nancy Cooper, MD, and Bachir Taouli, MD

Department of Radiology /Translational and Molecular Imaging Institute Icahn School of Medicine at Mount Sinai One Gustave Levy Place New York, NY 10029 USA

Abstract

Purpose—To compare MR elastography (MRE) using a single and a dual driver excitation for the quantification of hepatic and splenic stiffness (HS and SS), and to investigate the performance of HS and SS measured with single or dual driver excitation for the detection of liver cirrhosis in subjects with liver disease.

Patients and Methods—This prospective HIPAA compliant and IRB approved study involved 49 subjects who underwent MRE at 3.0T, comparing 3 different acquisition methods (single driver on the liver, single driver on the spleen and dual driver acoustic excitation). A Mann-Whitney test was used to assess changes in stiffness values. Bland-Altman analysis was used to compare single and dual driver configurations for each organ. Performance for detection of liver cirrhosis was assessed using ROC analysis. Pearson correlation was used to estimate the dependence of HS and SS on spleen size.

Results—There were 40 noncirrhotic and 9 cirrhotic patients. There was good agreement between stiffness values measured with a single or a dual driver (Bland-Altman limits of agreement -14.3%–18.9 % and -18.1%–29.7 %, CV 6.4 % and 9.4 %, for HS and SS respectively). HS and SS were higher in subjects with liver cirrhosis ($p < 0.001$), with excellent detection performance (AUROC range 0.87–0.93). SS correlated strongly with spleen size ($r = 0.69$, $p < 0.001$) while HS showed weak correlation ($r = 0.38$, $p = 0.006$).

Conclusion—Using a dual acoustic driver configuration, hepatic and splenic stiffness can be simultaneously estimated with good concordance with single driver measurement.

Keywords

Portal hypertension; liver stiffness; spleen stiffness; MR elastography

INTRODUCTION

Ultrasound-based transient elastography and MR elastography (MRE) provide information on stiffness properties in vivo and reflect changes in tissue stiffness related to pathological

conditions. In addition to tissue structure [1], vascular pressure is another driver of tissue stiffness – higher vascular pressure leading to stiffer, congested organs [2]. Portal hypertension is a complication that develops in patients with advanced liver disease, leading to the formation of collaterals associated with variceal bleeding [3], which can be diagnosed using the hepatic venous pressure gradient (HVPG) measurement [4–6], which is an invasive test. It has been shown that the occurrence of varices, ascites and splenomegaly correlate with elevated HVPG [7] and that a gradient higher than 12 mm Hg indicates significant risk of variceal bleeding [8]. While portal venous blood pressure may be difficult to assess noninvasively, observing the effect of an elevated portal pressure on hepatic and splenic stiffness (HS and SS) may lead to a quantitative method to diagnose portal hypertension noninvasively [9, 10].

Transient elastography has been proposed to assess portal hypertension by measuring HS and SS. Recently, Colecchia et al [11] reported a significant positive correlation between HS ($r=0.836$) or SS ($r=0.885$) and pressure gradient. HS and SS measured with transient elastography have also been shown to predict the presence of varices and the risk of hepatic decompensation [12, 13]. However, transient elastography is limited by sampling errors because of the reduced acoustic window provided, with failure rates as high as 20 % in the liver (mostly in subjects with ascites and overweight) [14]. The success rate of transient elastography may be further decreased in the spleen due to the variable location and size of the spleen and difficulty of the intercostal approach [15]. MR elastography (MRE) is an imaging technique that provides full organ coverage [16] and low variability for stiffness measurement evidenced by excellent inter-scan reproducibility [17–19] and inter-reader agreement [20]. For liver fibrosis detection, MRE was shown to be superior to other noninvasive modalities, including transient elastography [19, 21–24]. Using MRE, it is possible to measure HS and SS and provide a comprehensive assessment of liver fibrosis and portal hypertension. Talwalkar et al performed MRE-based SS measurement in 38 patients with chronic liver disease and found that patients with esophageal varices demonstrated higher SS [25]. Morisaka et al [26] compared multiple noninvasive techniques and found that SS best correlated with the presence of gastroesophageal varices observed at endoscopy in 93 patients. A recent retrospective study confirmed that HS and SS measured with MRE are strongly associated with the presence of esophageal varices [27]. In addition, strong correlation was reported ($r > 0.80$) between SS measured with MRE and HVPG in animal models [28, 29].

Currently, most MRE experiments apply an acoustic excitation by placing a vibrating pad (or passive driver) close to the organ or region of interest. Typically for HS or SS measurement, two different acquisitions should be performed with the driver placed proximal to the liver or spleen respectively. However, by propagating acoustic waves to both organs simultaneously using a dual driver configuration, HS and SS may be measured in a single acquisition, thus enabling the acquisition of SS maps with no increase in scan time.

The purpose of this study is to compare MRE using a single and a dual driver excitation for the quantification of HS and SS, and to investigate the performance of HS and SS measured with single or dual driver excitation for the detection of liver cirrhosis in subjects with liver disease.

SUBJECTS AND METHODS

Patients

This was a prospective single center study, HIPAA compliant, IRB approved, and funded by ----. All subjects gave signed informed consent prior to the exam. Between April 2012 and February 2013, 49 subjects (M/F 26/23, mean age 48 y, range 19–70 y), including 8 healthy volunteers (M/F 3/5, age 29 y, range 19–39 y) and 41 subjects with liver disease (M/F 23/18, age 53 y, range 21–70 y) were enrolled. All subjects underwent MRE to assess liver and spleen stiffness. Diagnostic of liver cirrhosis was based on clinical history and imaging findings. Among the subjects with liver disease, nine had liver cirrhosis. Among cirrhotic patients, 7 had hepatitis C virus (HCV) infection, 1 had NASH and 1 had primary biliary cirrhosis. The patient group with no cirrhosis (n=32) included 28 with chronic liver disease [HCV (n=18), HBV (n=5), NASH (n=3), autoimmune hepatitis (n=1), Wilson disease (n=1)], 4 with suspected benign or metastatic liver lesions and no history of chronic liver disease.

MRI/MRE acquisition

All examinations were performed on a 3T scanner (GE 750, GE-Healthcare, USA) using a phased array 32 channel body coil. The routine part of the exam consisted of turbo spin echo anatomical sequences, T2* imaging for iron quantification (not reported in this work), 3D in- and opposed-phase for fat quantification diffusion-weighted imaging (b-values 0, 50, 500, 1000 s/mm²) (not reported in this work), and contrast-enhanced T1 weighted multiphase acquisition used for detection of hepatic lesions and abdominal varices. For MRE wave generation, two 19 cm-diameter passive acoustic drivers were placed on either side of the chest, with their center at the level of the xiphoid process. 4 slices including mid liver and spleen were prescribed in axial orientation, using turbo spin echo coronal and axial localizer images. To compare different acoustic excitation methods, two acquisitions were performed with each driver connected (driver amplitude 50% of maximum amplitude), followed by a third acquisition with both drivers connected using a PVC Y-shaped connector (driver amplitude 70%) (Fig. 1). The driver amplitude for the latter configuration was chosen to compensate for the decrease in wave intensity when connecting two drivers in parallel (70% = $\sqrt{2} \times 50\%$). Wave imaging was performed using a modified phase contrast gradient echo sequence with motion encoding gradients along 3 orthogonal axis, with TR/TE 50/22 ms, resolution 1.4 × 2.8 mm², slice thickness 10 mm, ASSET 2. The frequency of acoustic excitation was set to 60 Hz. A 2 dimensional inversion algorithm generated stiffness maps from wave images during the exam, assuming in-plane wave propagation. The elastogram was calculated using wave images from all three encoded motion directions. For each driver configuration, all 4 slices were acquired in 4 consecutive breath holds at end expiration. The same slice locations were reproduced for the 3 different configurations. An example of MRE acquisition is shown in Fig. 1.

Image analysis

MRE analysis was performed by a physicist with 3 years of postdoctoral experience using MRE Quant software (Mayo Clinic, Rochester, USA). ROIs were drawn on stiffness maps of 4 slices in the liver (mean liver ROI size 23 cm²) and spleen (mean spleen ROI size 10

cm²) parenchyma. Voxel wise stiffness values were extracted for the liver and spleen, and an average organ stiffness value was computed from all measured voxels in all 4 slices. A confidence index (ranging from 0–100%) for stiffness measurement was estimated using an algorithm reflecting signal to noise ratio, wave amplitude, multi path wave interference and inversion algorithm performance. Voxels with less than 95% confidence were discarded from the ROI analysis. In order to compare single and dual driver acquisitions, the ROI locations were copied between the 3 different driver configurations.

Two radiologists in consensus (--, --, with 3 and 1 years' experience) assessed spleen dimension, measured in craniocaudal direction using anatomical images (HASTE).

Statistical analysis

Agreement in HS and SS between single and dual driver acquisitions was analyzed in terms of the Bland-Altman limits of agreement (LA, in %) and coefficient of variation (CV, in %). We defined excellent, good, moderate and poor agreement as CV <10%, 10 <CV <20%, 20 <CV <30% and CV >30% respectively. HS and SS differences were compared using Mann Whitney test. Pearson correlation was used to assess the relation between single and dual driver measurements of the stiffness, as well as between HS/SS and spleen size. Performance for detection of liver cirrhosis was assessed using receiver operating characteristic (ROC) analysis. Differences in area under the ROC curve between single and dual driver configurations were estimated using the DeLong test [30]. P values lower than 0.05 were deemed significant. Matlab Statistical Toolbox (R2014a, Mathworks, Natick, USA) was used for statistical analysis.

RESULTS

Comparison of single and dual driver excitation

There were no cases of MRE failure. When comparing stiffness values between a single and a dual driver excitation, we found excellent agreement for HS (Table 1, CV 6.4 %, LA -14.7 / 19.3 %) and SS (CV 9.4 %, LA -18.6 / 30.2 %). Similar agreement between single and dual driver acquisitions was observed in subjects with cirrhosis or without cirrhosis (Table 1). Bland Altman plots are shown in Fig. 2. Correlation between single and dual driver stiffness values was high ($r = 0.98$ for HS, 0.94 for SS, $p < 0.001$ for both). There was no significant difference between single and dual driver for HS ($p = 0.744$) or SS ($p = 0.290$). There was a weak correlation between HS and SS values in all subjects ($r = 0.35$, $p = 0.013$).

Detection of liver cirrhosis using liver or spleen stiffness

Subjects with liver cirrhosis had significantly higher HS and SS compared to subjects without ($p < 0.001$, Table 2) for single as well as for dual driver configurations. Performance for the detection of liver cirrhosis was excellent, with area under the ROC curve (AUROC) of 0.92 (single driver) and 0.93 (dual driver) using HS and 0.87 (single driver) and 0.92 (dual driver) using SS (Table 2). Detection performance was similar between single and dual driver configurations ($p > 0.16$). ROC curves are shown in Fig. 3.

Variation of stiffness with spleen size

A strong significant correlation was observed between SS and spleen size ($r=0.69$, $p<0.001$), while HS correlated weakly with spleen size ($r=0.38$, $p=0.006$). Scatter plots are shown in Fig. 4.

DISCUSSION

We have investigated the potential for simultaneous measurement of hepatic and splenic stiffness within one acquisition using a dual acoustic driver configuration, compared to repeated acquisitions with a single driver on each organ of interest. We found that HS and SS values were in good to excellent agreement between a single and a dual driver configuration, and that the performance for detection of liver cirrhosis using HS or SS was similar with either configuration. Moreover, we observed strong correlation between SS and spleen size, while HS showed only weak correlation.

The comparison between single and dual driver acquisitions suggest similar values for HS and SS. Given that each acoustic driver efficiently excites a region about the size of its diameter (19 cm), it may be anticipated that placing one driver on either side of the chest would cause minimal wave interference and thus the quality of stiffness determination should not be affected by a dual driver configuration. In addition, the inversion algorithm used in our study includes correction of interference patterns [31]. In the liver, the agreement between single and dual driver configurations lies within previously reported reproducibility of the technique [limits of agreement ranging from 18–35% as reported by Lee et al [19]]. There is no data available for variability of spleen stiffness measurement using MR elastography. Preliminary data comparing test and retest SS measurement in 14 subjects in our group yielded CV of 10.1%. Thus, HS and SS may be measured in a single acquisition, which reduces MRE scan time by 50% for the simultaneous assessment of hepatic and splenic stiffness.

MRE is currently amongst the most accurate techniques for noninvasive diagnosis of liver fibrosis, with reports indicating AUROC as high as 0.99 for detection of moderate (METAVIR stage F2 and higher) and advanced (stage F3 and higher) fibrosis [21, 23, 24, 32]. Changes in HS that occur in fibrosis likely reflect changes in tissue structure due to collagen deposition, capillarization of sinusoids, tissue degeneration and scarring. However, blood flow/pressure in the hepatic vascular system also affects HS [2], which leads to confounding effects between liver fibrosis and an elevated portal pressure. Alternatively, SS may reflect exclusively the occurrence of portal hypertension. In our experience, we found that SS correlated strongly with spleen size, which may reflect splenomegaly that occurs in portal hypertension. Furthermore, excellent performance was observed for liver cirrhosis detection using HS or SS in a single or dual driver configuration.

Using transient elastography, previous studies have reported correlation between hepatic vein pressure gradient and both HS and SS, with higher performance for SS [11–13, 33–35]. Although feasibility of splenic stiffness measurement with transient elastography has been demonstrated, it should be mentioned that the measurement procedure involves placing the tip of the probe in a region previously targeted using ultrasound imaging as spleen

parenchyma, thus might be prone to localization errors [15]. Splenic stiffness measurement using MRE has been investigated in fewer studies. The feasibility of SS measurement using MRE was demonstrated with either a passive [25] or an active piezoelectric driver [36]. Talwalkar et al [25] evaluated hepatic and splenic stiffness in 12 healthy volunteers and 38 patients with liver disease, and found that in patients with esophageal varices the SS was above 10.5 kPa. Similarly, Morisaka et al [26] found that SS had highest correlation with gastroesophageal varices observed at endoscopy, and found 93% sensitivity for diagnosing severe varices when using a SS threshold value of 7.1 kPa. A recent retrospective study using 3D EPI sequence also demonstrated that HS-MRE and SS-MRE are strongly associated with the presence of esophageal varices [27], and may be a better marker than spleen size for assessing the presence of esophageal varices. In a canine model of portal hypertension, Nedredal et al [28] observed a strong correlation between SS and HVPG ($r^2=0.86$). In a porcine model, Yin et al [37] observed also a strong correlation between HS and SS and direct portal pressure measurement. In a recent study, Ronot et al [38] evaluated multifrequency MRE vs. HVPG measurements in patients with portal hypertension and found that the spleen loss modulus has highest performance for severe portal hypertension and high risk varices.

Although our experience suggests that MRE is a promising tool to assess advanced liver disease using SS and HS in the same acquisition, there are some limitations to this study. First, the sample size of patients with liver cirrhosis was small. Second, we have used a 2 dimensional stiffness inversion algorithm that assumes in-plane wave propagation. Using a 3 dimensional algorithm may lead to improved precision for HS and SS and further increase the agreement between stiffness values measured with single and dual driver configurations.

In conclusion, MRE of the liver and spleen can be performed simultaneously using a dual acoustic driver configuration. Hepatic and splenic stiffness showed high performance for liver cirrhosis detection using either a single or dual driver acquisition, and splenic stiffness correlated strongly with spleen size. Spleen MRE is a promising method to assess portal hypertension and may complement liver MRE for assessment of the severity of liver disease.

Acknowledgments

Grant support: NIDDK Grant 1R01DK087877, GE Healthcare

Abbreviations

LS	liver stiffness
MR elastography	magnetic resonance elastography
PH	portal hypertension
SS	splenic stiffness

REFERENCES

1. Salameh N, Peeters F, Sinkus R, et al. Hepatic viscoelastic parameters measured with MR elastography: correlations with quantitative analysis of liver fibrosis in the rat. *J Magn Reson Imaging*. 2007; 26:956–962. [PubMed: 17896384]
2. Millonig G, Friedrich S, Adolf S, et al. Liver stiffness is directly influenced by central venous pressure. *J Hepatol*. 2010; 52:206–210. [PubMed: 20022130]
3. Garcia-Tsao G, Groszmann RJ, Fisher RL, Conn HO, Atterbury CE, Glickman M. Portal pressure, presence of gastroesophageal varices and variceal bleeding. *Hepatology*. 1985; 5:419–424. [PubMed: 3873388]
4. Escorsell A, Garcia-Pagan JC, Bosch J. Assessment of portal hypertension in humans. *Clin Liver Dis*. 2001; 5:575–589. [PubMed: 11565131]
5. Moitinho E, Escorsell A, Bandi JC, et al. Prognostic value of early measurements of portal pressure in acute variceal bleeding. *Gastroenterology*. 1999; 117:626–631. [PubMed: 10464138]
6. Ripoll C, Groszmann R, Garcia-Tsao G, et al. Hepatic venous pressure gradient predicts clinical decompensation in patients with compensated cirrhosis. *Gastroenterology*. 2007; 133:481–488. [PubMed: 17681169]
7. Wadhawan M, Dubey S, Sharma BC, Sarin SK, Sarin SK. Hepatic venous pressure gradient in cirrhosis: correlation with the size of varices, bleeding, ascites, and child's status. *Dig Dis Sci*. 2006; 51:2264–2269. [PubMed: 17080245]
8. Groszmann RJ, Bosch J, Grace ND, et al. Hemodynamic events in a prospective randomized trial of propranolol versus placebo in the prevention of a first variceal hemorrhage. *Gastroenterology*. 1990; 99:1401–1407. [PubMed: 2210246]
9. Chin JL, Chan G, McCormick PA. Spleen stiffness: the new kid on the block for diagnosing portal hypertension? *Gastroenterology*. 2013; 144:1152–1153. [PubMed: 23523840]
10. Takuma Y, Nouse K, Morimoto Y, et al. Measurement of spleen stiffness by acoustic radiation force impulse imaging identifies cirrhotic patients with esophageal varices. *Gastroenterology*. 2013; 144:92–101. e102. [PubMed: 23022955]
11. Colecchia A, Montrone L, Scaiola E, et al. Measurement of spleen stiffness to evaluate portal hypertension and the presence of esophageal varices in patients with HCV-related cirrhosis. *Gastroenterology*. 2012; 143:646–654. [PubMed: 22643348]
12. Robic MA, Procopet B, Metivier S, et al. Liver stiffness accurately predicts portal hypertension related complications in patients with chronic liver disease: a prospective study. *J Hepatol*. 2011; 55:1017–1024. [PubMed: 21354450]
13. Vizzutti F, Arena U, Romanelli RG, et al. Liver stiffness measurement predicts severe portal hypertension in patients with HCV-related cirrhosis. *Hepatology*. 2007; 45:1290–1297. [PubMed: 17464971]
14. Castera L, Foucher J, Bernard PH, et al. Pitfalls of liver stiffness measurement: a 5-year prospective study of 13,369 examinations. *Hepatology*. 2010; 51:828–835. [PubMed: 20063276]
15. Fraquelli M, Giunta M, Pozzi R, et al. Feasibility and reproducibility of spleen transient elastography and its role in combination with liver transient elastography for predicting the severity of chronic viral hepatitis. *J Viral Hepat*. 2014; 21:90–98. [PubMed: 24383922]
16. Bensamoun SF, Wang L, Robert L, Charleux F, Latrive JP, Ho Ba Tho MC. Measurement of liver stiffness with two imaging techniques: magnetic resonance elastography and ultrasound elastometry. *J Magn Reson Imaging*. 2008; 28:1287–1292. [PubMed: 18972339]
17. Hines CD, Bley TA, Lindstrom MJ, Reeder SB. Repeatability of magnetic resonance elastography for quantification of hepatic stiffness. *J Magn Reson Imaging*. 2010; 31:725–731. [PubMed: 20187219]
18. Lee DH, Lee JM, Han JK, Choi BI. MR elastography of healthy liver parenchyma: Normal value and reliability of the liver stiffness value measurement. *J Magn Reson Imaging*. 2013; 38:1215–1223. [PubMed: 23281116]
19. Lee YJ, Lee JM, Lee JE, et al. MR elastography for noninvasive assessment of hepatic fibrosis: Reproducibility of the examination and reproducibility and repeatability of the liver stiffness value measurement. *J Magn Reson Imaging*. 2013

20. Runge JH, Bohte AE, Verheij J, et al. Comparison of interobserver agreement of magnetic resonance elastography with histopathological staging of liver fibrosis. *Abdom Imaging*. 2013
21. Huwart L, Sempoux C, Vicaux E, et al. Magnetic resonance elastography for the noninvasive staging of liver fibrosis. *Gastroenterology*. 2008; 135:32–40. [PubMed: 18471441]
22. Ichikawa S, Motosugi U, Ichikawa T, et al. Magnetic resonance elastography for staging liver fibrosis in chronic hepatitis C. *Magn Reson Med Sci*. 2012; 11:291–297. [PubMed: 23269016]
23. Wang Y, Ganger DR, Levitsky J, et al. Assessment of chronic hepatitis and fibrosis: comparison of MR elastography and diffusion-weighted imaging. *AJR Am J Roentgenol*. 2011; 196:553–561. [PubMed: 21343496]
24. Yin M, Talwalkar JA, Glaser KJ, et al. Assessment of hepatic fibrosis with magnetic resonance elastography. *Clin Gastroenterol Hepatol*. 2007; 5:1207–1213. e1202. [PubMed: 17916548]
25. Talwalkar JA, Yin M, Venkatesh S, et al. Feasibility of in vivo MR elastographic splenic stiffness measurements in the assessment of portal hypertension. *AJR Am J Roentgenol*. 2009; 193:122–127. [PubMed: 19542403]
26. Morisaka H, Motosugi U, Ichikawa S, Sano K, Ichikawa T, Enomoto N. Association of splenic MR elastographic findings with gastroesophageal varices in patients with chronic liver disease. *J Magn Reson Imaging*. 2013
27. Shin SU, Lee JM, Yu MH, et al. Prediction of Esophageal Varices in Patients with Cirrhosis: Usefulness of Three-dimensional MR Elastography with Echo-planar Imaging Technique. *Radiology*. 2014; 272:143–153. [PubMed: 24620910]
28. Nedredal GI, Yin M, McKenzie T, et al. Portal hypertension correlates with splenic stiffness as measured with MR elastography. *J Magn Reson Imaging*. 2011; 34:79–87. [PubMed: 21608066]
29. Yin M, Kolipaka A, Woodrum DA, et al. Hepatic and splenic stiffness augmentation assessed with MR elastography in an in vivo porcine portal hypertension model. *J Magn Reson Imaging*. 2013
30. DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. *Biometrics*. 1988; 44:837–845. [PubMed: 3203132]
31. Manduca A, Lake DS, Kruse SA, Ehman RL. Spatio-temporal directional filtering for improved inversion of MR elastography images. *Med Image Anal*. 2003; 7:465–473. [PubMed: 14561551]
32. Huwart L, Sempoux C, Salameh N, et al. Liver Fibrosis: Noninvasive Assessment with MR Elastography versus Aspartate Aminotransferase to-Platelet Ratio Index. *Radiology*. 2007; 245:458–466. [PubMed: 17940304]
33. Castera L, Garcia-Tsao G. When the spleen gets tough, the varices get going. *Gastroenterology*. 2013; 144:19–22. [PubMed: 23164570]
34. Castera L, Pinzani M, Bosch J. Non invasive evaluation of portal hypertension using transient elastography. *J Hepatol*. 2012; 56:696–703. [PubMed: 21767510]
35. Fraquelli M, Rigamonti C, Colombo M. Spleen stiffness measured by transient elastography accurately predicts esophageal varices in liver cirrhosis. *Gastroenterology*. 2012; 143:e23. author reply e23–24. [PubMed: 22921672]
36. Hirsch S, Guo J, Reiter R, et al. MR Elastography of the Liver and the Spleen Using a Piezoelectric Driver, Single-Shot Wave-Field Acquisition, and Multifrequency Dual Parameter Reconstruction. *Magn Reson Med*. 2014; 71:267–277. [PubMed: 23413115]
37. Yin M, Kolipaka A, Woodrum DA, et al. Hepatic and splenic stiffness augmentation assessed with MR elastography in an in vivo porcine portal hypertension model. *J Magn Reson Imaging*. 2013; 38:809–815. [PubMed: 23418135]
38. Ronot M, Lambert S, Elkrif L, et al. Assessment of portal hypertension and high-risk oesophageal varices with liver and spleen three-dimensional multifrequency MR elastography in liver cirrhosis. *Eur Radiol*. 2014; 24:1394–1402. [PubMed: 24626745]

Fig. 1.

63 year old male with advanced liver fibrosis secondary to chronic hepatitis C. Example of wave patterns (top, with acoustic drivers shown as grayed rectangles) and stiffness maps (bottom) in a single driver excitation in the liver (left) and spleen (middle); and a dual driver exciting the liver and spleen simultaneously (right). Using a dual driver in a single acquisition, high wave amplitudes are observed in both organs simultaneously. Average stiffness values were HS (hepatic stiffness, single driver): 4.99 kPa, SS (splenic stiffness, single driver): 6.68 kPa, HS (dual driver): 5.33 kPa, SS (dual driver): 6.86 kPa. When using a single liver driver, the low wave amplitude at the location of the spleen did not provide sufficient confidence for stiffness measurement (confidence 50–80%). Similarly, a single driver placed proximal to the spleen generated low wave amplitude, low measurement confidence resulting in underestimated stiffness in the liver right lobe. Only using two drivers allowed for high wave amplitude and good measurement confidence in both organs.

Fig. 2.

Bland Altman analysis comparing stiffness values obtained using dual vs. single driver excitation in the liver (left) and spleen (right). Solid lines represent Bland Altman limits of agreement (2 SD) and mean deviation. Limits of agreement were -14.7 and 19.3 % for HS and -18.6 and 30.2 % for SS.

Fig. 3.

ROC curves for the detection of liver cirrhosis using hepatic stiffness (left) or splenic stiffness (right). Similar performance was measured between a single driver (solid line) and dual driver excitation (dashed line). AUCs are given in **Table 2**.

Fig. 4.

Hepatic stiffness (left) and splenic stiffness (right) as a function of spleen size. Splenic stiffness correlated strongly with splenic size ($r=0.69$, $p<0.001$) while liver stiffness correlated weakly with splenic size ($r=0.38$, $p=0.006$).

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 1

Hepatic stiffness (HS) and splenic stiffness (SS) measurements with MR elastography using single and dual driver excitations. Differences and variability expressed by means of coefficient of variation (CV, range in parenthesis) and Bland-Altman limits of agreement (BALA). Dual driver acquisition provided significantly higher SS values, and equivalent HS values.

	Single driver	Dual driver	P *	r **	CV (%)	BALA (%)
HS (kPa)	2.91 ± 1.46	2.97 ± 1.43	0.744	0.98 (p<0.001)	6.4 (0.3–29.8)	–14.7/19.3
HS (kPa) No cirrhosis	2.55 ± 1.27	2.59 ± 1.21	0.726	0.98 (p<0.001)	6.5 (0.3–29.8)	–15.5/19.8
HS (kPa) Cirrhosis	4.53 ± 1.13	4.64 ± 1.09	0.796	0.94 (p<0.001)	5.8 (0.7–14.5)	–12.2–17.6
SS (kPa)	5.44 ± 1.89	5.74 ± 1.84	0.290	0.94 (p<0.001)	9.4 (0.9–45.2)	–18.6/30.2
SS (kPa) No cirrhosis	4.94 ± 1.35	5.19 ± 1.30	0.328	0.91 (p<0.001)	9.1 (0.9–36.1)	–17.9/28.4
SS (kPa) Cirrhosis	7.66 ± 2.40	8.18 ± 1.99	0.387	0.91 (p<0.001)	10.9 (3.2–45.2)	–22.4/39.2

* Mann Whitney non-parametric test, bolded when significant (p<0.05)

** Pearson correlation (p-value in parenthesis)

Table 2

Hepatic stiffness (HS) and splenic stiffness (SS) measurements with MR elastography using single and dual driver excitations obtained in subjects without or with liver cirrhosis. Performance for detection of liver cirrhosis was assessed by the area under the ROC curve (AUC, with 95% confidence interval in parentheses).

	No cirrhosis (n=40)	Cirrhosis (n=9)	p*	AUC
HS single driver (kPa)	2.55 ± 1.27	4.53 ± 1.13	<0.001	0.92 (0.79–1)
HS dual driver (kPa)	2.59 ± 1.21	4.64 ± 1.09	<0.001	0.93 (0.82–1)
SS single driver (kPa)	4.94 ± 1.35	7.66 ± 2.40	<0.001	0.87 (0.71–1)
SS dual driver (kPa)	5.19 ± 1.30	8.18 ± 1.99	<0.001	0.92 (0.80–1)

HS: hepatic stiffness, SS: spleen stiffness

* Mann Whitney non parametric test, bolded when significant (p<0.05).