Published in final edited form as:

J Magn Reson Imaging. 2016 May ; 43(5): 1055–1063. doi:10.1002/jmri.25072.

Automated Liver Elasticity Calculation for Magnetic Resonance Elastography

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Abstract

Purpose—Magnetic Resonance Elastography (MRE) is a phase-contrast MRI technique that is used to quantitatively assess liver stiffness for staging hepatic fibrosis. The current approach requires manual selection of an ROI with good wave quality from which to measure stiffness. The purpose of this work was to develop and evaluate a fully automated approach for measuring hepatic stiffness from MRE images to further reduce measurement variability.

Methods—An automated liver elasticity calculation (ALEC) algorithm was developed to address reader stiffness measurement variability. ALEC has three stages: initial tissue estimation, segmentation, and ROI cleanup. Stiffnesses measured by the algorithm were compared to technicians and an expert radiologist in a set of 121 clinical cases acquired at 1.5T. Intra-class correlation, Bland-Altman analysis, and a non-inferiority test were performed to evaluate whether the algorithm can be used in place of manual analysis by technicians.

Results—The stiffness measurement difference with the expert was $1.42\% \pm 11.17\%$ (mean $\pm$ standard deviation) for the algorithm and $1.82\% \pm 13.65\%$ for the technicians. The ICC's were 0.981 and 0.984, respectively. Both the algorithm and technicians were equivalent to the expert within a 5% significance margin ($p < 0.01$). The algorithm had no failures in the 119 cases that were considered analyzable by the human readers.

Conclusions—The results of this study show that the newly developed automated algorithm is able to measure stiffness in clinical liver MRE exams with an accuracy that is equivalent to that of an expert radiologist. Therefore, ALEC may be useful for analysis of archived data and suitable for performing multi-center studies.

Keywords

automated measurement; image processing; MRE; elastography; liver; hepatic; stiffness; fibrosis

Introduction

Chronic liver disease is a significant health problem worldwide and associated with over 150,000 acute hospitalizations annually [1]. Liver fibrosis, a manifestation of many chronic

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liver diseases, can be treated at early stages if correctly diagnosed [2–6], but more often develops into cirrhosis, leading to complications and an increased risk of hepatocellular carcinoma, esophageal varices, and death.

The invasiveness and reading variability associated with small sample size and manual interpretation [7, 8] of biopsy have led to the emergence of alternatives in the form of imaging techniques, such as Ultrasound Elastography [9, 10], and Magnetic Resonance Elastography (MRE)[11]. While being fully non-invasive, these alternatives have been shown to have high reliability and are thus gaining in clinical acceptance.

MRE is a phase-contrast MRI technique which images propagating acoustic waves to calculate tissue stiffness [12]. In a typical implementation, an acoustic speaker generates waves which are delivered to a drum strapped to the chest wall through a series of tubes [13–15]. The low-amplitude waves are then imaged at multiple offsets between the driver vibration and the motion encoding gradient to generate images of shear wave propagation. The phase or “wave” images, containing wave-propagation information, are then inverted to calculate quantitative stiffness maps (elastograms) [16, 17].

Skilled interpretation of the magnitude and wave images is currently required to select an ROI from which the average hepatic stiffness can be calculated from the elastogram. Areas with wave interference and noise, as well as partial volume effects and hepatic blood vessels, can bias the stiffness calculation and need to be avoided when selecting this ROI [18, 19]. The procedure needs to be repeated for every slice, with magnitude, phase, and elasticity images all needing to be analyzed, which takes approximately 15 minutes for a four-slice exam. Despite the confidence map calculated during the stiffness inversion, as the fit of a smooth polynomial to the phase images [20], being available to guide manual ROI selection, reader variability is the biggest limitation for MRE reproducibility. Prior studies using experienced MRE readers observed a within-subject coefficient of variation of 6–11% [21] and an inter-reader stiffness discrepancy of $6.7 \pm 11\%$ [22].

An automated tool capable of deriving ROIs from MRE images and accurately calculating hepatic stiffness would be instrumental in reducing measurement variability. There are two major challenges for automated MRE analysis. First, reliable segmentation of magnitude images is very difficult due to poor tissue contrast, intensity inhomogeneity, and motion artifact. Second, areas of the liver with low wave SNR, blood vessels that are not conspicuous on magnitude images, and areas with partial volume effects need to be excluded from the ROI. The proposed automated method addresses these issues while providing 100% reproducible ROIs, due to all processing steps being deterministic, while also potentially simplifying the workflow, as the processing can be done in the off-hours.

An algorithm for automatic liver elasticity calculation (ALEC) that addresses these issues was developed in this study and evaluated. Our hypothesis was that ALEC can accurately reproduce the expert measurement of hepatic stiffnesses from clinical images, while decreasing the stiffness measurement variability associated with the manual approach.

Methods

I. MRE Data

The algorithm described below was tested in a retrospective study designed in compliance with our institutional review board. The imaging parameters were the same as those described in [22]. All MRE exams were performed on a 1.5T GE Signa Excite HDx scanner with a gradient-echo MRE sequence, an 8-channel receive-only torso coil array, and 60-Hz mechanical vibrations. The passive driver was placed on the chest wall of the patient and connected through a series of tubes to an active driver located outside of the scanner room [13]. The typical imaging parameters were: 44-cm FOV; 256×64 acquisition matrix, with a parallel imaging factor of 2 (reconstructed to 256×256); TR/TE/flip angle/bandwidth = 50 ms/20 ms/30°/32 kHz; 4 sequentially acquired contiguous axial 10-mm-thick slices; 4 time offsets; superior and inferior spatial saturation bands; right-left frequency-encoding direction; and 1 16.7-ms, 3.2 G/cm, 1st-moment-nulled motion-encoding gradient in the through-plane direction. Imaging was performed using four 14-second breath holds. Examples of the acquired magnitude image, the wave image (processed phase information) and the calculated stiffness MRE images are shown in Figure 1. At our institution, all interpretation of clinical images is done by image analysis technicians. A 10 hour training session is given for the analysis of MRE images and a typical reader has a year of experience analyzing several MRE cases a day (15 minutes each). The ROIs drawn by the technicians need to be approved by a radiologist, typically with several years of MRE experience, before the calculated average hepatic stiffness can be used diagnostically. All of the data used for the analysis, including magnitude, phase, and elasticity images, as well as the generated ROI masks, are archived.

For this retrospective IRB-approved consent-waived study, 121 consecutive cases of patients who had an MRE performed for liver fibrosis assessment from 2013 and 2014 were taken from the clinical archive. The archive contained ROIs drawn by trained, experienced technicians at the time of acquisition and stiffnesses calculated from them for diagnostic purposes, as well as raw MRE data. Since human analysts are known to have measurement discrepancy on the order of 11% [21, 22], a radiologist with 7 years of hepatic MRE experience was asked to independently analyze the data to provide a reference standard. ALEC, which is available as a set of MATLAB functions or a standalone executable, was provided with a set of patient ID's and exam dates. The data were retrieved from a server and processed overnight without user interactions using a standard desktop (i5 processor, 8GB 1666MHz ram). The automated ROIs used to calculate stiffnesses were screened for failures the following day. Cases with automated ROIs of <2000 pixels, when a larger ROI was possible, and ROIs containing approximately >10% non-liver tissue, based on visual examination, were marked as failed. These limits were selected empirically to help ensure adequate sampling and are based on the 11×11-pixel spatial extent of the inversion. Due to this large spatial extent, inclusion of up to 10% of voxels which appear outside of the liver based on the magnitude images mostly includes partial-volume voxels for the purpose of elasticity calculation and leads to a minor effect on the average stiffness. The stiffnesses calculated by the technicians and by ALEC were compared to those from the expert reader. In addition, a previously published automated MRE analysis method [22] was used to

process the cases and calculate hepatic stiffnesses to compare to ALEC. This earlier algorithm yielded accurate stiffnesses but required a training set to optimize parameters which limited the scope of its application. The failure rates and stiffness differences from the expert were compared between the two automated methods.

II. Automated Liver Elasticity Calculation (ALEC)

The types of image artifacts, common in MRE magnitude images, which present major challenges for any automated technique, are shown in Figure 2. The automated liver elasticity calculation (ALEC) algorithm has three stages: initial tissue estimation, segmentation, and elasticity artifact removal. In order to deal with variable tissue intensities and edge contrast, a combination of spatial and intensity information was used for the initial estimation and segmentation of tissues in the magnitude images. Subsequently, an artifact-free ROI within the liver was derived by analyzing both wave and stiffness images. The histogram portions of the initialization and ROI selection were performed for the entire volume, while the segmentation and spatial analysis was done in 2D, as a full 3D analysis gives an insignificant improvement at a large time expense. A flowchart of the entire process is presented in Figure 3.

i. Initial tissue estimation—Initial masks for the three major classes of interest (background, fat and liver – bg, F, L) were calculated based on the magnitude images as follows:

1. Background

- a. Calculate a background level as $u_{bg} = \text{mean} + \text{standard deviation}$ from the corners of the image to be used as an estimate of the background present in parallel MRI accelerated images.
- b. Threshold out the pixels below u_{bg} , morphologically close with a size-5 disk kernel and fill holes to generate the mask of the whole body (M_B).
- c. Assign all areas outside of the body mask to the background mask (M_{bg}) and recalculate u_{bg} from this mask.

2. Abdominal fat

- a. Perform a series of erosions on M_B with a 5-pixel disk kernel and calculate the differences in mean intensity between consecutively eroded bands.
- b. Find the step with maximum difference in mean intensity and keep the part of M_B distal to this point as an abdominal fat mask estimate, M_F . The maximum (outer - inner) difference occurs at the interface of abdominal fat (bright) and internal organs (lungs = dark, liver = intermediate).
- c. Calculate the mean, u_f , of the image within M_F .
- d. Calculate the thickness of the abdominal fat as the difference in average distance of the outer and inner contours of M_F from the image center.

- e. If the fat layer cannot be found due to a very thin abdominal wall or signal void from the driver, define the fat layer as a 10-pixel wide ring from the outside of the body.

3. Liver

- a. Assign the area which is part of the body but is not abdominal fat to the initial liver mask ($M_L = M_B \& \neg M_F$).
- b. Find the centroid of M_L . Mask out all M_L which is to the bottom-right of a diagonal line passing through the center of M_L to exclude areas more likely to contain spleen, kidneys, and stomach, than liver, from the initial estimate.
- c. Calculate u_L from the area covered by M_L .
- d. If $u_f < u_L$ due to the signal void and low inter-tissue contrast, set u_f to the maximum intensity in the image.

The liver and background masks were eroded by the thickness of the fat layer and distance transforms between the adjacent masks were calculated and normalized to 1 to generate spatial membership functions illustrated in Figure 4 b.

In the next step, intensity membership functions were calculated to indicate the likelihood of a pixel belonging to a major tissue type (background, liver, and fat) based on intensity (Figure 4 a). Using the liver membership as an example, the intensity membership functions were generated as follows:

- a. Set function to 1 at the mean intensity of that class (u_L), as calculated above.
- b. Set membership to 0 at the means of adjacent classes (u_{bg} and u_F) or the maximum/minimum of the image, if the means of other classes cannot be calculated or appear to overlap with u_L .
- c. Linearly interpolate the membership function between these points.

The membership functions were then combined to produce class membership functions via a product, as follows:

$$U_k(j) = I_k\{j\} * D_k\{d\{M_k\{j\}\}\} \quad (1)$$

where j is the image, k is the class index, M are the initial tissue masks, d is the distance transform to each mask, I and D are the normalized membership functions for the intensity and spatial position, and U is a combined membership function. Every pixel with at least one combined membership value >0.3 was then assigned to the highest membership class yielding masks for the background, liver, and abdominal fat. Pixels in which all memberships were low ($\max(U) < 0.3$) were assigned to internal background (lung tissue or cavities), if their intensity was below u_{bg} , or “other tissues,” otherwise (Figure 4 c).

ii. Segmentation—Magnitude images were corrected for intensity inhomogeneity using the Local Entropy Minimization with Bicubic Spline (LEMS) technique, using the parameter settings suggested in [23] to improve edge-contrast and intra-tissue homogeneity. Then, three hundred homogeneously-spaced pixels randomly selected from each of the

background, liver, fat, internal background, and “other tissues” masks were used to initialize the Random Walker Segmentation, with input parameters suggested in [24], to segment the image into the liver and other classes. Finally, the liver mask was cleaned by opening with a size-5 disk, removing objects (groups of contiguous 4-connected pixels) smaller than 50 pixels, closing with the same disk, and filling holes smaller than 50 pixels. Examples of seed points selected from the initial estimate masks are shown in Figure 4 d. The segmentation is not constrained by the prior assumptions (e.g., about the abdominal wall thickness or liver location in the anterior-right side of the body) used in the initialization step and is allowed to expand into these areas.

iii. Elasticity artifact removal—Wave interference, partial volume, and low SNR result in stiffness reconstruction artifacts and can significantly bias the calculation of average stiffness, so it is necessary to exclude such areas from the ROI [18]. The proposed algorithm first uses wavelet analysis to detect sharp perturbations in the wave images as well as areas with low SNR, and then evaluates the elasticity of these areas to exclude artifacts with a higher degree of specificity.

The wave images were processed using the phase congruency algorithm, described in [25]. The calculation applies a set of wavelet filters at different scales to the image and calculates the degree to which the terms are in-phase at every point. This approach is sensitive to sharp features, allowing small vessels to be detected, while being insensitive to smooth MRE waves with wavelengths commonly >20 pixels. Furthermore, since phase congruency is a normalized metric (0 to 1 range) independent of the wave amplitude, low SNR areas result in generally high congruency values. The input parameters were set to 3 scales (between 5 and 20 pixels) and 6 orientations to optimize detection of small vessels and areas with low SNR (high-frequency noise). Phase congruency images were calculated based on each of the 4 MRE phase-offset images. The maximum projection across the phase offsets was taken and thresholded at 0.1 to derive a mask of areas in the liver suspected for vessels or low SNR.

The histogram of stiffnesses within the high congruency regions (h_c) and the histogram of liver stiffnesses (h_L) were calculated and normalized, and their difference was taken:

$$H = \left(\frac{h_c}{\sum h_c} - \frac{h_L}{\sum h_L} \right) \quad (2)$$

Let H_+ and H_- indicate the positive and negative portions of H . To encourage a cleaner ROI the values of H_- were set to zero if they belonged to a contiguous histogram segment at least 0.5 kPa wide, and to the value of the nearest H_+ maximum otherwise. The values of H were then used as a global membership function for indicating outliers.

To account for the partial volume around areas with artifact, a local stiffness heterogeneity metric was calculated, as follows:

$$L = \frac{(L \circ G) \circ e}{G \circ e} \quad (3)$$

where L is the membership function for local stiffness change (assumed to be due to partial volume), e is the elastogram, $(L \circ G)$ is the Laplacian-of-Gaussian operator, G is a Gaussian of size 22 (based on the size of the processing kernel that had been used in the calculation of stiffness images), and $\circ$ is the convolution operation. Finally, the confidence map generated by the stiffness inversion algorithm, the multimodel direct inversion (MMDI), by calculating the quality of fit of low order polynomials to the wave data in 11×11 -pixel processing windows and commonly used in manual ROI drawing, was used to threshold out low wave SNR areas. The final ROI for the stiffness calculation was obtained by taking the intersection of the liver mask, eroded from the edges by 7 pixels to account for the elastogram partial volume, with the thresholded local and global membership functions and the confidence map, as follows:

$$ROI = \text{Eroded Liver Mask} \cap ((H * L) < 0.2) \cap (conf > 0.9) \quad (4)$$

III. Statistical Analysis

The diagnostic product of the ROI drawing process that is used to stage fibrosis is average hepatic stiffness. To evaluate the performance of the algorithm, it was used to calculate stiffnesses in a set of 121 consecutive retrospective clinical cases and compared to the manual analysis done by clinical technicians and an expert radiologist. The MRE experience of the radiologist (7 years) was much greater than the level of experience of the majority of technicians (1 year or less) who perform routine analysis of MRE for clinical purposes.

First, the intra-class correlation coefficient (ICC) was calculated. Second, the Bland-Altman confidence interval for percent differences with the expert was calculated. Finally, to determine if the algorithm could be used instead of manual analysis a paired equivalence t-test [26] was performed with the following hypotheses:

$$\begin{aligned} H_0: \left| \hat{\mu}_{\frac{A-E}{E}} \right| &\geq \varepsilon \\ H_A: \left| \hat{\mu}_{\frac{A-E}{E}} \right| &< \varepsilon \end{aligned} \quad (5)$$

where $\hat{\mu}_{\frac{A-E}{E}}$ was the normalized mean algorithm-expert difference in the stiffness measurement, and ε was the equivalence margin. Based on the previous study that found an 11.4% standard deviation in stiffnesses differences between two experienced readers, the equivalence margin, representing the smallest practically significant difference, was chosen to be 5% of the stiffness value. Note that the equivalence-test formulation has the opposite hypothesis of a typical t-test for the difference in the means, which cannot be used to evaluate similarity of distributions due to both small sample size and true lack of difference producing large p-values. The two one-sided test (TOST) procedure was used, as implemented in JMP (JMP9.0, Cary, NC), with a significance value (α) set to 0.02. Since the

TOST procedure uses two one-sided t-tests, using critical t-score at an α -level of 0.02 corresponds to showing significance at the level of 0.01.

Results

The test set contained cases ranging from healthy to severe fibrosis (1.37 to 14.17 kPa), with 60 of the exams having a stiffness greater than 2.93 kPa which is indicative of fibrosis. The patient population was 59.5% male (72/119) with an age of 41 ± 13.68 years and a BMI of 28 ± 6.41 (mean $\pm$ standard deviation). Of the 121 cases analyzed, two MRE acquisitions failed due to iron overload. In the remaining 119 cases with successful acquisition, the analysis of a 4-slice, 4-offset MRE exam took 5 minutes on average and was done in a batch-process mode. Examples of segmentations, including segmentations of challenging cases, are shown in Figure 5. A representative final ROI from which stiffness was calculated is shown in Figure 6.

Bland-Altman confidence intervals and ICC coefficients between ALEC and the expert, the technicians and the expert, and the old method and the expert are presented in Table 1. The corresponding ICC and percent difference plots are shown in Figure 7 and Figure 8. Both stiffnesses calculated by the algorithm and those calculated by technicians were equivalent to the expert at a 5% equivalence margin ($p = 0.0003$ and $p = 0.0059$, respectively). Automatically-calculated stiffnesses exhibited a smaller bias (mean difference) and discrepancy (standard deviation of difference) with the expert, as shown in Table 1. Figure 9 shows typical ROIs drawn by the algorithm, the technicians, and the expert radiologist.

The data in this study were also processed with a previously published automated algorithm. The older method also had a good correspondence with the expert (difference of $-2.61\% \pm 12.75\%$; ICC = 0.979), however, it had 10 failures in the 119 analyzable cases based on the criteria described in the Methods section (3 with failure to initialize leading to no ROIs in any slices, 3 cases with initialization failure in some slices, and 4 cases with segmentation or artifact removal areas leading to very small combined ROI area).

Discussion

The automated algorithm was shown to be statistically equivalent to the expert reader and yielded stiffnesses that had a smaller discrepancy with the expert than those calculated by technicians. The correlations with both the expert and technicians, which are the standard of analysis at our institutions, were at least as high as the inter-expert agreement (ICC 0.9) in previous studies [21, 27]. The only cases where stiffness could not be calculated were due to iron-overload-associated acquisition failure, rather than algorithm failure, suggesting that the algorithm has very high stability.

ALEC is the only method, other than our previous approach, which has been demonstrated to segment low-quality MRE magnitude images with motion artifact, low contrast, and intensity inhomogeneity, in a fully automated manner. The fit-free initialization approach which constructs spatial and intensity membership functions similar to those used in fuzzy logic emphasizes reliance on areas where information is available and avoids overfitting to regions with artifacts. The random walker segmentation complements this by allowing high-

artifact and low-contrast areas to be separated along intuitive boundaries when provided with a sufficient number of carefully placed seeds. As demonstrated in the examples, this combination allows high-quality segmentation of difficult cases, although the goal is simply to select a large region of hepatic tissue. With modifications, the initialization/segmentation scheme may be useful for other applications, such as DWI or iron quantification, which calculate global non-morphometric properties and acquire images with low anatomic quality. The segmentation may be improved by acquiring additional images with better quality, however, their registration to high artifact images may not be accurate and the added acquisition time may not be an acceptable solution for all MRE studies. The comparison with our previous method demonstrated that ALEC has better stability, although the stiffness correspondence with the expert was similar for the two approaches. Further, ALEC's assumptions are more general which made a dedicated training set unnecessary and suggests broader applicability.

Objective exclusion of areas with wave-propagation artifacts in MRE has historically been a challenge. The confidence map that is calculated in the MRE inversion measures wave smoothness. It is commonly employed to assist in the drawing of manual ROIs and can be used to remove low SNR areas or localized strong features, such as blood vessels. However, since wave SNR varies across the liver, a single threshold does not ensure accurate exclusion of both, which is an issue for all metrics purely reliant on wave-SNR. Further, features such as hepatic fissures may have sufficient tissue content within the voxel and high SNR, making intensity or stiffness information necessary to exclude this region which has a stiffness different from real hepatic tissue. ALEC's approach relies on a combination of quantities which take into account wave and stiffness information to exclude areas with artifact-like properties, and is currently the most complete objective framework for selecting an ROI for reliable stiffness measurement from liver tissue. As no assumptions are made about the stiffness distribution within the liver, heterogeneous livers, having either broad Gaussian or multi-modal stiffness histograms, can be analyzed with this method. A degree of local homogeneity in space will be enforced by the approach but local homogeneity is already assumed in the inversion. The proposed elasticity artifact exclusion can be used in combination with other segmentation methods, including manual and semi-automated techniques, in the liver and other organs.

The accuracy of fibrosis detection and staging with MRE has been validated extensively against biopsy and other imaging techniques in the past [21, 27–31]. ALEC was designed to automate the manual image analysis and thus validated against stiffness measurements obtained via expert and standard analysis. Hepatic stiffness can be calculated from ROIs of varying sizes and placements. Due to the subjectivity of wave analysis, non-expert ROIs can often overlap by <50%, and even 0%, while still yielding similar mean stiffnesses leading to a correct diagnosis. For this reason, MRE validation studies have not reported measures of ROI overlap and rarely report ROI size comparisons [21, 27–31]. ALEC was designed to reliably provide a large ROI of hepatic tissue, while excluding partial volume and low wave SNR areas rather than match an expert's ROI, so the overlap of ROIs with the expert was not evaluated directly. Furthermore, the segmentation is an intermediate step which is only required to provide an appropriate tissue sample. While segmentation quality even in the challenging cases presented was good, it is not necessary and was also not evaluated directly.

A limitation of the automated algorithm is that some modes of failure are difficult or impossible to detect automatically. Unusual anatomy, including a displaced liver or a large tumor, as well as very poor magnitude image quality can cause non-liver tissue to be selected. As the stiffnesses of other tissues overlap with the range of healthy through cirrhotic liver tissue, and due to the greatly variable intensity in the magnitude images, such failures can only be detected visually, often based on patient history or other additional information. Although no manual input is used during the ALEC processing, it is beneficial for a reader with MRE training to screen the final ROIs. An interface is available which allows the final contour to be replaced with a manual drawing, if needed. Compared to a semi-automated workflow, full automation with post-processing screening allows a more convenient workflow, especially for large datasets, and has higher reproducibility as few cases (none in this study) need to be modified.

The primary limitation of this study is the comparison of automatically calculated stiffnesses to only one expert, with experts having an inter-reader variability of approximately 10% based on a previous study [22]. The variability between the technicians was also not evaluated because no record is kept of which technician analyzed a particular case. Another limitation of the study was that the final ROI's, and liver segmentations, were not evaluated directly. Finally, ALEC was only tested on the product version of hepatic MRE, which is a GRE-based acquisition with an MMDI inversion, and only in images acquired at 1.5 T. While this is the most common clinical setup, spin-echo and EPI sequences also exist and exams may be performed on 3T scanners. ALEC has general assumptions (mainly about relative intensities and locations of major organs) and a low failure rate in challenging images with artifact, variable intensity, and low contrast. Its adaptation to other acquisitions with comparable image quality should be straightforward, with preliminary tests supporting this supposition. For exams which used alternative inversions to generate elastograms, the MMDI inversion can be included with ALEC and used to re-generate the elastograms. Alternatively, the exams may be analyzable directly by changing the spatial extent of the artifact exclusion based on the known inversion kernel size.

Future work includes the extension of the algorithm to process data from other acquisitions and 3D MRE data. The same artifact-exclusion approach can be modified to incorporate information from all three motion directions. Due to the highly-accelerated nature of 3D MRE acquisition, however, alternative initialization methods, such as the one presented in [32], may need to be used. Additionally, with an objective artifact-exclusion framework and a convenient method for data mining now available, the value of measuring the elastogram spatial information will be explored.

In conclusion, the fully automated algorithm presented in this study demonstrated better agreement with the expert than did clinical technicians and yielded results statistically equivalent to the expert. The method can be used to process all new MRE exams for clinical diagnosis or for analysis of large data volumes in longitudinal and multi-center studies. ALEC has the potential to greatly improve the reproducibility of MRE by removing the intra-reader and reducing the inter-reader variability as well as decreasing the cost of analysis.

Acknowledgments

Grant: NIH EB01981

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Figure 1.

Images from an MRE exam including the acquired magnitude image (a), a wave image (processed phase-data) (b), and the calculated elasticity image (c). Typically, 4 sets of magnitude/phase images are acquired with different offsets between the driver motion and the motion-encoding gradient.

Figure 2.

Issues frequent in MRE magnitude images include (a) intensity inhomogeneity, (b) motion artifact and partial volume, and (c) low SNR and low inter tissue contrast. Absolute intensities for tissue types are highly variable.

Figure 3.

Flowchart of ALEC processing. The anatomic processing steps obtain a liver segmentation using the MRE magnitude images. The stiffness quantification steps analyze the wave and elasticity images to select an artifact-free ROI within the liver.

Figure 4.

Membership functions used to initialize the segmentation. Intensity (a) and spatial (b) membership functions are combined via multiplication (c). Initialization seeds (d) for background, liver, and abdominal fat are points subsampled from the thresholded combined membership function. Seeds for the intra-body background (purple) and the “other tissues” (blue) classes are derived by intensity-thresholding the area where all memberships are low.

Figure 5.
Segmentations of normal (a) and challenging exams (b, c, and d) yield excellent results.

Figure 6.

Illustration of the final ROI derived by the automated algorithm. Red arrows indicate the blood vessels visible on the magnitude image (a) which are avoided by the ROI in the elastogram (c). The green arrow in (b) indicates a vessel visible in only one of the phase offset images, and not detectable on the magnitude image, which can cause an artifact and is avoided by the automated ROI in (c).

Figure 7. Correlations between ALEC and the expert, and technicians and the expert. The automated method has very high ICC.

Figure 8. Mean differences from the expert. The box plot indicates the 95% confidence interval for the mean (mean $\pm$ standard error) while the whiskers indicate the 95% confidence interval for the population ($\pm$ standard deviation). The confidence interval for the mean of stiffnesses measured by the algorithm lies fully within the $\pm 5\%$ margin, supporting equivalence with the expert.

Figure 9.

Comparison of representative ROIs drawn by the expert radiologist (a, d), the automated algorithm (b, e), and a clinical technician (c, f). The stiffnesses for the exam are, respectively, 7.37 kPa, 6.6 kPa, and 5.3 kPa, with the technician having the lower expert-agreement. The checker boarded areas have confidence <0.95 , as calculated by MMDI and are masked out from the averaging in manual analysis. ALEC uses a more lenient confidence threshold of 0.9, as part of its artifact removal process.

Table 1

Comparison of automated measurements to expert and standard manual measurements

	Bland-Altman	ICC
<i>Algorithm – Expert</i>	1.42% ± 11.17%	0.981
<i>Technicians – Expert</i>	1.82% ± 13.65%	0.984
<i>Algorithm - Technicians</i>	−0.12% ± 16.55%	0.965
<i>Old Algorithm - Expert</i>	−2.61% ± 12.75%	0.979