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A Bayesian Method for Accelerated Magnetic Resonance Elastography of the Liver

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Abstract

Purpose—Magnetic resonance elastography (MRE) is a noninvasive tool for quantifying soft tissue stiffness. MRE has been adopted as a clinical method for staging liver fibrosis. The application of liver MRE, however, requires multiple lengthy breath holds. We propose a new data acquisition and processing method to reduce MRE scan time.

Theory and Methods—A Bayesian image reconstruction method that utilizes transform sparsity and magnitude consistency across different phase offsets to recover images from highly undersampled data is proposed. The method is validated using retrospectively downsampled phantom data and prospectively downsampled in vivo data (n=86).

Results—The proposed technique allows accurate quantification of mean liver stiffness up to an acceleration factor of R=6, enabling acquisition of a slice in 4.3 seconds. Bland Altman analysis indicates that the proposed technique (R=6) has a bias of −0.04 kPa and limits of agreement of −0.36 to +0.28 kPa when compared to traditional GRAPPA reconstruction (R=1.4).

Conclusion—By exploiting transform sparsity and magnitude consistency, accurate quantification of mean stiffness in the liver can be obtained at acceleration rate of up to R=6. This potentially enables collection of three to four liver slices, as per clinical protocol, within a single breath hold.

Keywords

Bayesian model; compressive sensing; elastography; factor graph; MRI; Liver MRE

Introduction

Tissue stiffness serves as an established biomarker in the detection of a variety of diseases. Magnetic resonance elastography (MRE) has emerged as a non-invasive, quantitative method of measuring the stiffness of soft tissue (1–4). MRE has found clinical application in

the diagnosis of hepatic fibrosis and cirrhosis (5–7) and demonstrates potential in diagnosing various other hepatic, cardiac, brain, breast, aorta and skeletal muscle diseases (8–12).

In MRE, an acoustic transducer generates mechanical waves, which are then routed to an MR safe passive driver placed above the anatomy of interest. The resulting oscillatory motion in the region of interest is encoded into the phase of the complex MR images through application of a motion encoding gradient (MEG). A series of motion-encoded images are acquired with different polarities of the MEG and with various phase offsets between the MEG and the mechanical motion, characterizing the wave propagation through the region of interest. After the complex-valued images are reconstructed for each offset, an MRE inversion algorithm is applied to produce a spatial map of the shear modulus, known as an elastogram.

MRE can be performed in two or three spatial dimensions and with multiple motion encoding directions. In practice, however, volumetric acquisitions or multi-directional encodings are not utilized due to prohibitively long acquisition times. Even low-resolution imaging with a single encoding direction, when used in conjunction with parallel MRI (pMRI), typically requires a long breath-hold (> 15 s) to image each slice. To improve clinical utility of MRE, techniques to further accelerate the acquisition process are thus required.

Recently, several acquisition and processing methods have been proposed to accelerate MRE. Johnson et al. achieved an acceleration rate of four by utilizing correlation between offsets with a low rank model (13). Similarly, Grimm et al. demonstrated an acceleration rate of three by utilizing a generalization of the calibration-free parallel imaging using locally low-rank encouraging reconstruction (CLEAR) method, which promotes low-rankedness across the coil, motion encoding, and phase offset dimensions (14). Klatt et al. proposed a method known as sample interval modulation – magnetic resonance elastography (SLIM-MRE), which permits multidirectional motion encoding with a single acquisition through MEG shifting and spectral analysis (15).

Outside the MRE literature, several compressive sensing (CS) methods have been successfully employed to recover images at high acceleration rates for different MRI applications (16–18). CS enables recovery from highly undersampled data by exploiting the underlying compressibility of the image, which manifests as sparsity in a transform domain. More recently, Rich et al. (19,20) proposed a Bayesian method, called ReVEAL, to highly accelerate phase-contrast MRI. ReVEAL goes beyond the concept of utilizing transform sparsity and additionally exploits magnitude structure unique to phase-contrast MRI. In this work, we propose a new method, called **B**ayesian method for magnetic resonance **E**lastography using **A**pproximate **M**essage passing (BEAM). BEAM can be considered an adaptation of ReVEAL. BEAM, like traditional CS methods, employs pseudorandom sampling and exploits spatial transform sparsity in the image at each offset. In contrast to traditional CS methods, the proposed approach also exploits structure unique to MRE. To that end, BEAM enforces magnitude consistency across different offsets through implementation of a mixture density and a hidden indicator variable that automatically controls the strength of magnitude consistency for a given pixel. Therefore, BEAM is

equipped to handle spatial variation – invariably present in the MRE data – in the magnitude consistency. In that aspect, BEAM is different from other magnitude regularization techniques where the enforcement of magnitude consistency is spatially invariant (21). The aim of this study is to develop and validate BEAM using data from an MRE phantom and using liver data from healthy volunteers.

Theory

In this section, we describe a Bayesian approach to MRE recovery. First, we describe the signal model for MRE. Second, we discuss enforcing a magnitude constraint across different offsets using a mixture density with a hidden indicator variable. Third, we briefly describe the exploitation of sparsity in the wavelet domain. Finally, we describe belief propagation on a factor graph as a method to reconstruct MRE images while imposing magnitude and wavelet regularization.

Notation

We adopt the following notation. Vectors and matrices are represented in bold, with matrices represented by capital letters. Elements of matrices are denoted a_{ij} for the i^{th} row and j^{th} column of A , while x_j indicates the j^{th} element of vector $\mathbf{x}$. For vectors identified by subscripts, vector elements are designated by a second subscript, such as $\mathbf{x}_{01}$ representing the 1st element of vector $\mathbf{x}_0$. Elementwise multiplication of vectors is denoted $\mathbf{a} \times \mathbf{b}$. The n -by- n identity matrix is expressed as $\mathbf{I}_n$. Finally, $\mathcal{CN}(x; \mu, \sigma^2)$ represents a circularly symmetric complex Gaussian distribution on random variable x with mean μ and variance σ^2 .

MRE Signal Model

The raw MRI signal acquired by the c^{th} coil of a receiver array for the j^{th} offset between the mechanical oscillation and the motion encoding gradient can be expressed as

$$\mathbf{y}_j^c = \mathbf{D}_j \mathcal{F} \mathbf{S}^c \mathbf{x}_j + \boldsymbol{\eta}_j^c, \quad (2)$$

where $\mathbf{S}^c$ is the coil sensitivity encoding matrix for coil $c = 0, 1, \dots, C-1$, $\mathcal{F}$ is the Fourier transform, $j = 0, 1, \dots, J-1$ represent J different offsets, $\mathbf{D}_j$ is the sample selection operator for the j^{th} offset, $\mathbf{x}_j \in \mathbb{C}^N$ is the complex-valued image to be recovered for the j^{th} offset, $\boldsymbol{\eta}_j^c \in \mathbb{C}^M$ is complex-valued, zero-mean Gaussian noise with variance ω^2 for the j^{th} offset, and $\mathbf{y}_j^c \in \mathbb{C}^M$ is the measured complex-valued data for the j^{th} offset. In this work, the term offset refers to any combination of the MEG polarity and phase offset between the MEG and the mechanical motion. For example, data collected with both positive and negative MEG polarities and with four phase offsets will have total eight offsets ($J = 8$).

The measurements for a multi-coil acquisition with C total coils can therefore be represented as

$$\begin{bmatrix} y_j^0 \\ y_j^1 \\ \vdots \\ y_j^{C-1} \end{bmatrix} = \begin{bmatrix} D_j \mathcal{F} S^0 \\ D_j \mathcal{F} S^1 \\ \vdots \\ D_j \mathcal{F} S^{C-1} \end{bmatrix} x_j + \begin{bmatrix} \eta_j^0 \\ \eta_j^1 \\ \vdots \\ \eta_j^{C-1} \end{bmatrix}, \quad (3)$$

Thus, by defining A_j as the encoding matrix above, the signal acquired for the j^{th} offset can be written as

$$y_j = A_j x_j + \eta_j, \quad (4)$$

where $y_j \in \mathbb{C}^{MC}$ and $\eta_j \in \mathbb{C}^{MC}$ are obtained by concatenating y_j^c and η_j^c , respectively, from all coils.

To promote incoherent aliasing, a variable density pseudorandom sampling pattern called variable density incoherent spatiotemporal acquisition (VISTA) was employed (22). Since VISTA operates in the offset-ky domain, it implicitly discourages repeated sampling of the same k-space location across different offsets, increasing the information content of the sampled data. A typical VISTA pattern is shown in Figure 1, where the offset on the x-axis represents positive and negative encoding with four equally spaced samplings of the external motion required for MRE.

For MRE, we model images at different offsets according to

$$\begin{aligned} x_0 &= m_0 \times e^{i(\phi + \theta_0)} \\ x_1 &= m_1 \times e^{i(\phi + \theta_1)} \\ &\vdots \\ x_{J-1} &= m_{J-1} \times e^{i(\phi + \theta_{J-1})}, \end{aligned} \quad (5)$$

where θ_j is the spatially varying phase accumulated due to motion encoding for the j^{th} offset, and ϕ is the spatially varying reference phase incurred by, for example, magnetic field inhomogeneity and off-resonance effects. Without loss of generality, we can redefine ϕ such that $\theta_0 = 0$, yielding $x_0 = m_0 e^{i\phi}$.

In the absence of any non-ideal behavior, one expects $m_0 = m_1 = \dots = m_{J-1}$. However, due to intravoxel dephasing and other potential sources of model mismatch, the magnitudes across different offsets can vary. Since it is unknown in advance which pixel (voxel) will exhibit

dephasing, we introduce a pixel-wise Bernoulli indicator random variable, $\mathbf{v} \in \{0,1\}^N$, to denote the presence (or absence) of potential magnitude discrepancy among offsets.

Magnitude Constraint via Mixture Density

Now, we write the posterior probability distribution of the unknown parameters, $\mathbf{x}_0, \mathbf{x}_1, \mathbf{x}_2, \boldsymbol{\theta}_1, \boldsymbol{\theta}_2, \mathbf{v}$. For notational simplification, we assume $J=3$, i.e., the measurements are made at three offsets. The model, however, is amenable to any arbitrary number of offsets, J . Using Bayes' rule, the posterior distribution can be expanded as

$$p(\mathbf{x}_0, \mathbf{x}_1, \mathbf{x}_2, \boldsymbol{\theta}_1, \boldsymbol{\theta}_2, \mathbf{v} \mid y_0, y_1, y_2) \propto p(\mathbf{x}_0, \mathbf{x}_1, \mathbf{x}_2, \boldsymbol{\theta}_1, \boldsymbol{\theta}_2, \mathbf{v}) p(y_0 \mid \mathbf{x}_0) p(y_1 \mid \mathbf{x}_1) p(y_2 \mid \mathbf{x}_2), \quad (6)$$

where $p(y_j \mid \mathbf{x}_j)$ is the likelihood function for offset j . By invoking the chain rule, the prior in Equation 6 can be further factorized as follows.

$$p(\mathbf{x}_0, \mathbf{x}_1, \mathbf{x}_2, \boldsymbol{\theta}_1, \boldsymbol{\theta}_2, \mathbf{v}) = p(\mathbf{x}_2 \mid \mathbf{x}_0, \mathbf{x}_1, \boldsymbol{\theta}_1, \boldsymbol{\theta}_2, \mathbf{v}) p(\mathbf{x}_1 \mid \mathbf{x}_0, \boldsymbol{\theta}_1, \boldsymbol{\theta}_2, \mathbf{v}) p(\boldsymbol{\theta}_1 \mid \mathbf{x}_0, \boldsymbol{\theta}_2, \mathbf{v}) p(\boldsymbol{\theta}_2 \mid \mathbf{x}_0, \mathbf{v}) p(\mathbf{v} \mid \mathbf{x}_0) p(\mathbf{x}_0),$$

(7)

This model is greatly simplified by adopting several independence assumptions. First, it is assumed that magnitude discrepancy map $\mathbf{v}$ is independent of the reference offset, $\mathbf{x}_0$, such that $p(\mathbf{v} \mid \mathbf{x}_0) = p(\mathbf{v})$. Next, it is assumed that the motion-encoded phase of each offset is independent of the magnitude and phase of each other offset and $\mathbf{v}$. Thus, $p(\boldsymbol{\theta}_j \mid \mathbf{x}_0, \boldsymbol{\theta}_k, \mathbf{v}) = p(\boldsymbol{\theta}_j)$ for all $k \neq j$. Finally, it is assumed that all offset images are independent when conditioned on the reference image. Therefore, $p(\mathbf{x}_j \mid \mathbf{x}_0, \mathbf{x}_k, \boldsymbol{\theta}_j, \boldsymbol{\theta}_k, \mathbf{v}) = p(\mathbf{x}_j \mid \mathbf{x}_0, \boldsymbol{\theta}_j, \mathbf{v})$ for all $k \neq j$. Consequently, the simplified prior yields

$$p(\mathbf{x}_0, \mathbf{x}_1, \mathbf{x}_2, \boldsymbol{\theta}_1, \boldsymbol{\theta}_2, \mathbf{v}) \approx p(\mathbf{x}_2 \mid \mathbf{x}_0, \boldsymbol{\theta}_2, \mathbf{v}) p(\mathbf{x}_1 \mid \mathbf{x}_0, \boldsymbol{\theta}_1, \mathbf{v}) p(\boldsymbol{\theta}_1) p(\boldsymbol{\theta}_2) p(\mathbf{v}) p(\mathbf{x}_0), \quad (8)$$

The resulting posterior distribution, consisting of the likelihood functions and simplified prior, benefits from drastic reduction in computational complexity while retaining the fundamental structure relating offset images. The data model is fully characterized through selection of each of the posterior factors.

For zero-mean circularly-symmetric additive Gaussian noise, with variance ω^2 , the likelihood distributions are given by the following expression.

$$p(y_j \mid \mathbf{x}_j) = \mathcal{CN}(y_j; \mathbf{A}_j \mathbf{x}_j, \omega^2 \mathbf{I}), \quad (9)$$

The factor, $p(\mathbf{y}_j|\mathbf{x}_j)$, represents the noise uncertainty in the MRE acquisition and provides a traditional sum-of-squares data fidelity term in the reconstruction. The magnitude consistency across offsets is enforced through selection of the conditional prior distribution relating each offset to the reference offset, $\mathbf{x}_0$. For example, the conditional prior for offset image $\mathbf{x}_j$ is given by the following mixture density conditioned on the magnitude discrepancy indicator, $\mathbf{v}$.

$$p(\mathbf{x}_j|\mathbf{x}_0, \boldsymbol{\theta}_j, \mathbf{v}) = \mathbf{v} \mathcal{CN}(\mathbf{x}_j; \mathbf{x}_0 e^{i\boldsymbol{\theta}_j}, \sigma_1^2 \mathbf{I}) + (1 - \mathbf{v}) \mathcal{CN}(\mathbf{x}_j; \mathbf{x}_0 e^{i\boldsymbol{\theta}_j}, \sigma_2^2 \mathbf{I}), \quad (10)$$

The two components of this mixture are shown in Figure 2. Each term of the mixture constrains the magnitude of $\mathbf{x}_j$ to resemble that of reference image $\mathbf{x}_0$, while leaving the encoded phase $\boldsymbol{\theta}_j$ unconstrained with respect to the reference image. The variance of each component represents the strength of the magnitude consistency, with zero variance enforcing strict magnitude equality and infinite variance enforcing no magnitude constraint across offsets. By selecting two different variances for the mixture components, i.e. $\sigma_1^2 < \sigma_2^2$, both a strong and a weak magnitude constraints can be applied throughout the image. The prior probability of strong magnitude consistency at each pixel n is uniformly assigned as $p(v_n = 1) = \gamma$. The appropriate magnitude constraint is then automatically applied pixel-wise throughout the image based on the learned posterior value of $\mathbf{v}$. Therefore, the modeling parameter $\mathbf{v}$ provides, at each pixel, an automated tuning of the intra-offset regularization. For the prior on the motion-encoded phase, $p(\boldsymbol{\theta}_j)$, an uninformative uniform distribution is selected on the interval $[0, 2\pi)$.

Wavelet Compression

Selection of the prior, $p(\mathbf{x}_j)$, on each complex-valued offset is the final remaining modelling decision to be addressed. Here, a prior is selected such that sparsity is promoted in each offset under a two-dimensional undecimated wavelet transform. To this end, we assume an analysis compressed sensing formulation, where the wavelet synthesis operator Ψ is appended as additional rows to forward operator $\mathbf{A}_j$, as in (23). The image prior is defined as a zero-mean Laplace distribution on the complex-valued wavelet coefficients with shape parameter λ .

$$p(\mathbf{x}_j) \propto \prod_{n=0}^{N-1} \frac{\lambda^2}{2\pi} e^{-\lambda |\Psi \mathbf{x}_j|_n}, \quad (11)$$

Belief Propagation

The posterior distribution of the Bayesian MRE model can be represented visually via factor graph, as shown in Figure 3. Circular nodes represent random variables, while square nodes represent distributions. Edges between these nodes represent dependence of distributions on variables. By analogy, just as the gradient of a cost function can specify an iterative

algorithm, such as conjugate gradients, the factor graph can specify an iterative algorithm for determining the posterior mean image using a Bayesian model. Specifically, application of the sum-product algorithm on the factor graph provides a computationally efficient method of estimating the marginal posterior distributions of $\mathbf{x}_j$, $\boldsymbol{\theta}_j$, and $\mathbf{v}$ (24,25). The algorithm passes messages between nodes containing beliefs about the values of surrounding variables. The marginal posterior distributions of variables in the loop free region of the graph are exactly determined after a message is passed in each direction across each edge. In the densely interconnected regions introduced by the Fourier measurement operator the generalized approximate message passing (GAMP) algorithm is utilized to significantly reduce computational complexity through application of the central limit theorem and Taylor series approximations; GAMP leverages the large number of pixels in each offset to approximate messages as simply Gaussian (26). Once marginal posterior distributions are obtained, the maximum a posteriori (MAP) estimate of each unknown variable is obtained by finding the maximum value of the distribution.

In summary, each offset image is first reconstructed from noisy measurements via GAMP. The resulting approximated messages are then passed between offset images. The messages received by each offset image are then used to update the prior distribution for the subsequent GAMP iterations. This algorithm alternates between loopy GAMP iterations and standard message passing to update the GAMP prior until convergence.

Methods

The study protocol involving human subjects was approved by the Institutional Review Board. Written, informed consent was obtained from each volunteer. All imaging was performed on a 3T clinical MRI scanner (Tim Trio, Siemens Healthineers, Erlangen, Germany), using a gradient echo MRE pulse sequence. Offline reconstruction was performed in MATLAB (Mathworks, Natick, MA). For phantom imaging, we compared BEAM to spatial CS (SCS) as well as SENSE with uniform undersampling (27), SENSE with randomized VISTA undersampling (SENSE-R), and reconstruction with spatial L2 regularization (SL2). Here, SCS enforces transform sparsity, but does not apply magnitude regularization. In other words, when performing BEAM and SCS reconstructions, the same VISTA sampling patterns (22), wavelet compression (single-level undecimated Haar), and GAMP solver were used. However, the SCS reconstructions were performed independently on each offset image without application of any magnitude constraint across offsets. The implementation of SL2 was similar to SCS but employed a more traditional L2-norm penalty. For in vivo results, BEAM was compared to GRAPPA reconstruction (28).

Retrospectively Accelerated Phantom MRE Acquisition and Reconstruction

BEAM was first validated using a cylindrical phantom with known stiffness (5.6 kPa). Mechanical waves were applied to the phantom at a frequency of 60 Hz with an MEG frequency of 60 Hz. Fully sampled data were acquired on a 256×256 matrix with four phase offsets with positive and negative motion encoding ($J=8$). The field of view was 280×280 mm², with 5 mm slice thickness, TE = 21.9 ms, and TR = 50 ms. The data were retrospectively downsampled using a VISTA sampling pattern to allow SENSE-R, SCS,

SL2, and BEAM reconstructions and a uniform sampling pattern for SENSE reconstruction at $R = 1, 2, \dots, 15$. The coil sensitivity maps were estimated using the technique proposed by Walsh et al. (29); the center 128 lines of k-space from a single offset were used for estimation. This study was also used to optimize parameters for SCS, SL2, and BEAM.

Prospectively Accelerated In Vivo Liver MRE Acquisition and Reconstruction

Liver MRE was performed on 23 healthy individuals (14 men, 9 women, mean age 26 years, age range 21 to 38 years) using an 18-channel coil array. Three or four axial slices were sequentially collected for each volunteer, yielding a total of 86 axial slices. In each scan, the field of view was 320×320 mm, with 5 mm slice thickness. Data were collected on a 128×64 matrix with $TE = 21.16$ ms and $TR = 50$ ms. Mechanical waves were applied to the abdominal region at a frequency of 60 Hz while an MEG of 60 Hz was applied.

For each slice, a low resolution pre-scan (48 lines of k-space) was acquired under a separate breath hold (4 s) to generate coil sensitivity maps. Next, prospectively downsampled MRE data were acquired using a VISTA sampling pattern for $R = 1, 4, 6$, and 8 with four MRE phase offsets with positive and negative motion encoding ($J = 8$), requiring breath holds of 25.6, 6.4, 4.3, and 3.2 seconds, respectively. For comparison, each slice was also acquired at $R = 1.4$ with 24 reference lines (18 s breath hold) and reconstructed online with GRAPPA. Additionally, repeated GRAPPA scans were acquired from 5 volunteers (19 slices) to determine the variance among GRAPPA measurements collected under similar settings but different breath holds. BEAM reconstruction was performed offline in MATLAB on a 128×128 grid. A Gaussian window was applied to the k-space of each reconstructed image to reduce Gibbs ringing before interpolation to a 256×256 grid by zero padding k-space. The $R = 1.4$ GRAPPA acquisitions were reconstructed online on a 256×256 grid.

Parameter Selection

Noise variance, ω^2 , was estimated from the periphery of measured k-space. The prior probability of strong magnitude consistency, γ , was set at 0.9 for all datasets, and moderate changes (range: 0.8—0.95) in γ resulted in no appreciable difference in the image quality. For phantom study, the values of the Laplace shape parameter controlling the strength of the wavelet compression, λ , and the mixture density variances controlling the degree of magnitude regularization, σ_1^2 and σ_2^2 , were manually adjusted using an additional phantom dataset (not shown). For in vivo study, the values of λ , σ_1^2 , and σ_2^2 were manually adjusted using separate retrospectively downsampled datasets (not shown) from three volunteers.

MRE Inversion

The phase from reconstructed complex-valued offsets was then used to generate elastograms in MRELab (Mayo Clinic, Rochester, MN). After applying a phase unwrapping algorithm, directional filtering was applied in four directions with passbands spanning 2 to 128 waves per field of view to mitigate interference from longitudinal and reflected mechanical waves (30). Elastograms were created for each dataset via multimodel direct inversion (MMDI) (31). Manual regions of interest (ROI) were drawn avoiding large vessels and poor wave amplitudes within the liver to report mean stiffness.

Reconstruction Quality Metrics

For the retrospectively accelerated phantom data, reconstruction quality was quantified through calculation of the normalized mean squared error (NMSE), defined as

$$NMSE\{\hat{\mathbf{x}}\} = 10 \log_{10} \frac{\|\hat{\mathbf{x}} - \mathbf{x}_{ref}\|_2^2}{\|\mathbf{x}_{ref}\|_2^2}, \quad (12)$$

where $\hat{\mathbf{x}}$ is the reconstructed image and $\mathbf{x}_{ref}$ is the fully sampled SENSE-based reference image with high signal-to-noise ratio (SNR). For $\mathbf{x}_{ref}$, the SNR calculated by the ratio of the mean magnitude value in the region of interest and the standard deviation of the background noise was 63. We believe this value of SNR is high enough that NMSE values beyond $R > 2$ are indicative of image quality. This metric provides a global measure of reconstruction quality by considering the entire complex reconstruction across all offsets.

For all studies, mean stiffness of accelerated techniques within a user defined ROI was compared with that of SENSE (phantom) or GRAPPA (in vivo). For phantom data, SENSE ($R=1$) was used to compute NMSE for SENSE ($R>1$), SENSE-R, SCS, SL2, and BEAM, which are also based on a SENSE formulation. For in vivo data, GRAPPA was used as reference to emulate the existing clinical protocol. For the phantom, the ROI was selected based on magnitude threshold and consisted of the entire circular cross section. For in vivo data, the ROI was localized inside the liver near the driver and was manually selected. The mean stiffness within the ROI was then compared across reconstructions and accelerations to determine the effectiveness of each reconstruction at preserving estimated stiffness.

In the prospectively accelerated in vivo study, Bland Altman analysis was performed to assess the agreement between GRAPPA and BEAM derived stiffness estimates (32). In this analysis, the mean difference across estimates yields the overall bias of BEAM compared to GRAPPA, and the 95% limits of agreement capture the overall variance between BEAM and GRAPPA. Additionally, examination of the Bland Altman plot provides insight into the possibility of proportional bias, where the agreement between methods varies based on the average value of the measurements. Additionally, the Pearson correlation coefficient, r , was assessed between GRAPPA and BEAM derived stiffness estimates.

Results

Retrospectively Accelerated Phantom MRE Results

Reconstructed magnitude images, wave images, and elastograms for the phantom data are shown in Figure 4; SENSE, SENSE-R, SCS, SL2, and BEAM are compared at various acceleration factors. Phantom reconstructions at additional accelerations are shown in Supporting Figure S1. The NMSE (in dB) of each reconstruction for $R = 1, 2, \dots, 15$ was calculated and is shown in Figure 5; Figure 5 also depicts the mean stiffness of the phantom, as calculated from each reconstruction using MMDI.

Prospectively Accelerated In Vivo Liver MRE Results

Figure 6 depicts GRAPPA and BEAM magnitude images, wave images, and elastograms for one of the volunteers. Supporting Figure S2 displays reconstructions for an additional in vivo volunteer. Figure 7 shows Bland Altman analyses of stiffness estimates between GRAPPA and BEAM with different acceleration rates. Compared to the stiffness values derived from GRAPPA $R = 1.4$, the BEAM derived values at $R = 1, 4, 6$, and 8 yield biases of $-0.06, -0.07, -0.04$, and -0.06 , respectively. The 95% limits of agreement between GRAPPA and BEAM derived stiffness values at $R = 1, 4, 6$, and 8 are $-0.35 - 0.23, -0.36 - 0.21, -0.36 - 0.28$, and $-0.46 - 0.33$, respectively. Pearson correlation coefficients between BEAM and GRAPPA-derived stiffness values at $R = 1, 4, 6$, and 8 were $0.831, 0.821, 0.800$, and 0.637 for $R=1, 4, 6$, and 8 , respectively.

Additionally, Bland Altman analysis (Figure 8) provided insight into the relationship between stiffness measurements derived from two subsequent GRAPPA acquisitions with identical parameters but collected under separate breath holds. The difference between the measurements demonstrated a bias of -0.04 and limits of agreement of $-0.32 - 0.23$. The correlation between the subsequent GRAPPA-derived stiffness measurements was 0.86 .

Discussion

The proposed acquisition and reconstruction strategy for MRE utilizes parallel MRI, transform sparsity, and magnitude regularization across MRE offsets to enable image reconstruction at high acceleration rates without significant impact to NMSE or stiffness quantification. In the phantom data, BEAM demonstrated significant improvement over SENSE reconstruction in NMSE, and produced very high quality reconstructions for acceleration rates as high as $R = 10$. In the liver data, BEAM at $R = 6$ exhibited high levels of agreement with standard clinical protocol (GRAPPA at $R = 1.4$). Additionally, BEAM at $R = 6$ demonstrated similar variation in performance compared to repeated GRAPPA scans.

BEAM exploits both spatial sparsity (in the wavelet domain) and magnitude consistency to enable image recovery from undersampled data. A distinguishing feature of BEAM is its ability to enforce spatially varying magnitude constraint to account for spatially varying intravoxel dephasing. We observed that enforcing strict magnitude equality across all pixels led to significant image artifacts, as shown in Supporting Figure S3 for phantom data and in Supporting Figure S4 for in vivo data. These figures were produced using a gradient descent based reconstruction with an ℓ_1 norm penalty enforced, independently on each offset, on undecimated Haar wavelet coefficients (33). This indicates that the artifacts are a consequence of enforcing strict magnitude equality and not a product of GAMP-based reconstruction. In the phantom data, the artifacts are subtle, appearing in the vicinity of maximal magnitude mismatch. In the in vivo images, magnitude deviation across offsets is far more pronounced, yielding more extensive artifacts in the reconstructed images. Also, the magnitude deviation across offsets demonstrates a high degree of spatial variation. BEAM utilizes a mixture density with a hidden indicator variable to automatically adjust the extent of magnitude regularization applied on a per-pixel basis. Also, with a computationally efficient approximate message passing algorithm, BEAM enabled image recovery in less than 8 minutes using ordinary CPU-based computation. Reconstruction in less than 30

seconds is feasible by employing parallel computing, which has demonstrated over 20-fold improvement in computation time for MRI reconstruction (16,34).

In reconstruction of the retrospectively accelerated phantom data, BEAM achieved the lowest NMSE of all accelerated reconstructions considered, enabling acceleration rates as high as $R = 10$ without substantially impacting results. At acceleration rates exceeding $R = 4$, BEAM provides an improvement over SCS (second best) of approximately 1 dB, which increases to more than 5 dB beyond $R = 10$. Both SCS and BEAM produce stiffness errors of less than 0.25 kPa (4%) for accelerations up to $R = 9$. At $R = 10$ and beyond, BEAM demonstrated significant improvement over SCS in stiffness measurements. While BEAM explicitly improves the quality of image magnitude, the recovery of accompanying phase also implicitly benefits from this constraint as evident by the wave images at $R = 6$ and $R = 12$ (Figure 4). Compared to BEAM and SCS, SENSE and SENSE-R reconstructions exhibit excessive noise amplification even at lower acceleration rates and SL2 fails to suppress undersampling artifacts.

For the in vivo data, at low acceleration rates, BEAM effectively reduced the noise seen in smooth regions of the liver without sacrificing detail in vessels. These details are mostly preserved through $R = 6$, while images at $R = 8$ demonstrate visible reduction in fine detail. On average, across all in vivo datasets, the BEAM reconstruction at $R = 6$ yielded a stiffness estimate which differs from the GRAPPA derived stiffness by 6.5%. From Bland Altman analysis, stiffness measurements resulting from all four tested BEAM acceleration rates demonstrated no appreciable bias. A strong agreement ($r = 0.8$) between BEAM and GRAPPA at $R = 1.4$ is observed for $R = 6$. At $R = 8$, however, the correlation degrades to $r = 0.68$.

We conjecture that some of the variation between BEAM and GRAPPA was due to small differences between the subsequent breath holds. Since each scan was performed under a separate breath hold, slight variation was introduced in the slice location of each scan, leading to small discrepancies in the resulting stiffness estimates. This conjecture is supported by the fact that Bland Altman for repeated GRAPPA measurements demonstrated very similar bias and limits of agreement as GRAPPA-BEAM analysis up to $R = 6$. Although BEAM demonstrates potential in reconstructing highly accelerated MRE data, the method has several inherent limitations. As with other CS reconstruction methods, BEAM enables reconstruction of undersampled MRE data through the assumption of sparsity in wavelet domain. At higher accelerations, the dependence of the reconstruction on the assumption of transform sparsity increases, introducing bias to the image estimate. Additionally, the combination of magnitude and wavelet regularization yields a non-convex reconstruction. Thus, it is possible for BEAM to produce reconstructions that originate from local minima.

As implemented, BEAM reconstruction requires manual tuning of several parameters. Of principal importance are the Laplace shape parameter λ , controlling the tradeoff between data fidelity and wavelet compression, and the variance of the components of the mixture density σ_1^2 and σ_2^2 , controlling the strength of the two magnitude constraints across offsets. The values of these parameters were manually tuned using separate training datasets that were not included in the subsequent validation. For all phantom and in vivo datasets, we

used $\lambda = 20$ and observed that the recovery process was relatively robust to the choice of λ . For example, in the in vivo training data, less than 1 dB change in NMSE was observed for 50% variation in λ . For σ_1^2 and σ_2^2 , selecting small values generated lower NMSE but provided inconsistent performance across different training datasets. To favor robustness over optimality, we selected relatively large values σ_1^2 and σ_2^2 (0.01 and 0.05, respectively, for phantom and 0.1 and 0.3, respectively, for the in vivo data). Being a Bayesian approach, BEAM is amenable to auto-tuning using expectation maximization (35) or similar algorithms. Such extensions of BEAM are beyond the scope of current work and will be considered separately.

Several simplifications are made in the derivation of BEAM to ensure the algorithm is tractable and computationally efficient, including the assumption of independence between each offset when conditioned on the reference offset. This assumption enforces a non-informative prior and yields a factor graph without loops, enabling rapid convergence of the message passing algorithm used to compute the posterior distribution of the model. However, this assumption forfeits the potential regularizing benefits of the motion-induced harmonic phase structure between offsets and generates non-harmonic solutions, which would be physically infeasible. Future implementations of BEAM may find additional benefit by choosing to model these relationships.

The performance of BEAM can be further improved by enforcing additional or different constraints. For example, further compression could be achieved through leveraging the smooth boundaries of the abdominal organs with alternative sparsifying transforms such as curvelets or contourlets (36,37). Furthermore, the mixture density could be modified to additionally enforce structure in the encoded phase, e.g., by constraining the phase accumulation from one offset to the next. Alternatively, the magnitude discrepancy indicator variable can be further regularized in space via Markov Random Field. BEAM is also amenable to multidimensional motion encoding, which provides a more complete depiction of the mechanical wave propagation through the region of interest by application of an MEG in multiple orientations. BEAM can also be extended to volumetric imaging.

All participants in this study were healthy volunteers with no history of liver disease. Future testing of BEAM in clinical patients could investigate the possibility of proportional bias at higher liver stiffness and validate the method against biopsy. After demonstrating success in staging liver fibrosis, BEAM could be assessed for detection and staging of a variety of other diseases. The preliminary data strongly suggest that BEAM is a viable option to accelerate clinical application of liver MRE. Acceleration due to BEAM may also potentially permit acquisition of volumetric MRE within a single breath hold.

Conclusion

An acquisition and reconstruction strategy was presented for magnetic resonance elastography which enabled high rates of acceleration by utilizing spatially varying magnitude regularization across offsets, transform compression, and accelerated computation via generalized approximate message passing. The algorithm, BEAM, was

validated through reconstruction of retrospectively accelerated phantom data as well as prospectively accelerated in vivo liver data. Stiffness measurements derived from prospectively accelerated BEAM R = 6 reconstructions demonstrated strong consistency with stiffness measurements derived from GRAPPA R = 1.4 reconstructions.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.
Example VISTA sampling pattern for 128 phase encodes and $R = 11.6$. The pattern is generated in the integrated offset-ky domain.

Figure 2.

Mixture density relating offset $\mathbf{x}_j$ to the reference offset $\mathbf{x}_0$. (a) The conditional distribution that enforces weak magnitude consistency, accommodating large magnitude variations across offsets, for example, due to dephasing. (b) The conditional distribution that enforces strong magnitude constraint, permitting little variation in magnitude. BEAM automatically assigns the probability that a given pixel belongs to $\nu = 0$ or $\nu = 1$ and enforces appropriate contributions from the two components of the mixture density.

Figure 3.

Factor graph representation of the joint posterior distribution of an MRE dataset with three offsets. This structure is expandable to an arbitrary number of offsets, retaining this structure which relates each offset to the reference offset x_0 . Application of an iterative message passing algorithm provides a computationally efficient method of estimating the posterior marginal distribution of variables of interest. GAMP permits rapid estimation of messages passed in the densely interconnected loopy regions of the graph, which represent each offset.

Figure 4. Comparison of SENSE, SENSE-R, SCS, SL2, and BEAM phantom reconstructions at $R = 6$ and $R = 12$. Magnitude images, wave images, and elastograms are shown for each reconstruction.

Figure 5.

Quantitative reconstruction metrics of SENSE, SENSE-R, SCS, SL2, and BEAM phantom reconstructions. (a) NMSE of reconstructed images, providing a measure of the error between each complex reconstruction and the fully sampled SENSE reconstruction. (b) Mean stiffness from ROI.

Figure 6. Comparison of GRAPPA at R = 1.4 and BEAM at R = 1, 4, 6, and 8 reconstructions of a prospectively accelerated in vivo dataset.

Figure 7.

Bland Altman analysis of BEAM-derived stiffness measurements to GRAPPA-derived stiffness measurements. (a) Comparison of GRAPPA, R = 1.4, and BEAM, R = 1. (b) Comparison of GRAPPA, R = 1.4, and BEAM, R = 4. (c) Comparison of GRAPPA, R = 1.4, and BEAM, R = 6. (d) Comparison of GRAPPA, R = 1.4, and BEAM, R = 8.

Figure 8.

Bland Altman analysis of stiffness measurements derived from two separate GRAPPA scans. The two GRAPPA scans were collected from the same volunteer using identical parameters but under separate breath holds.