Published in final edited form as:

Magn Reson Med. 2021 October ; 86(4): 2011–2024. doi:10.1002/mrm.28855.

Fast 3D MR elastography of the whole brain using spiral staircase: Data acquisition, image reconstruction, and joint deblurring

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Abstract

Purpose: To address the need for a method to acquire 3D data for MR elastography (MRE) of the whole brain with substantially improved spatial resolution, high SNR, and reduced acquisition time compared with conventional methods.

Methods: We combined a novel 3D spiral staircase data-acquisition method with a spoiled gradient-echo pulse sequence and MRE motion-encoding gradients (MEGs). The spiral-out acquisition permitted use of longer-duration motion-encoding gradients (ie, over two full oscillatory cycles) to enhance displacement SNR, while still maintaining a reasonably short TE for good phase-SNR. Through-plane parallel imaging with low noise penalties was implemented to accelerate acquisition along the slice direction. Shared anatomical information was exploited in the deblurring procedure to further boost SNR for stiffness inversion.

Results: In vivo and phantom experiments demonstrated the feasibility of the proposed method in producing brain MRE results comparable to the spin-echo-based approaches, both qualitatively and quantitatively. High-resolution (2-mm isotropic) brain MRE data were acquired in 5 minutes using our method with good SNR. Joint deblurring with shared anatomical information produced SNR-enhanced images, leading to upward stiffness estimation.

Conclusion: A novel 3D gradient-echo-based approach has been designed and implemented, and shown to have promising potential for fast and high-resolution in vivo MRE of the whole brain.

Keywords

deblurring; joint anatomical constraint; magnetic resonance elastography; off-resonance; spiral staircase imaging

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CONFLICT OF INTEREST

Our group received research support from Philips Healthcare.

SUPPORTING INFORMATION

Additional Supporting Information may be found online in the Supporting Information section.

1 | INTRODUCTION

Magnetic resonance elastography (MRE)¹ has been recognized as a unique noninvasive technique for in vivo mapping of tissue mechanical properties. Magnetic resonance elastography is now a reliable noninvasive technology for assessing liver fibrosis,² and has shown considerable scientific and diagnostic potential for assessing diseases in the brain such as multiple sclerosis,^{3,4} hydrocephalus,^{5,6} Alzheimer's disease,⁷ and tumors.^{8,9}

Resolving accurate mechanical property of tissues in the brain from in vivo MRE scans requires high SNR, high spatial resolution, and full vector field and multiple MRE phase encodings, which makes achieving short scan times a challenging problem. Additionally, the power of the mechanical vibration that reaches in vivo brain tissue is dampened by the skull, further limiting the displacement SNR.

Most brain MRE studies were performed with spin-echo (SE)-based sequences¹⁰ for SNR consideration. Recent studies have used faster techniques such as SE EPI^{7,11,12} and spiral imaging.^{13,14} However, one factor limiting the scan time of SE-based MRE is the intrinsically long TR required by longitudinal magnetism recovery in the brain (eg, over 2 seconds). Although the use of 3D imaging would be of great value due to better continuity, motion consistency, resolution in all directions and potential SNR gains, the long TR requirement and the many required MRE encodings make 3D acquisitions impractical for SE-based MRE. Therefore, multislice¹³ or multislabs¹⁴ approaches are exploited to fully make use of the long magnetism recovery time and thus improve SNR efficiency, obtaining some, but not all, of the benefits of 3D acquisition methods.

An attractive solution for 3D MRE uses spoiled gradient echo (GRE) acquisitions,¹⁵ using a much shorter TR (eg, about 50–200 ms). A major challenge of GRE-based MRE is signal dephasing in the presence of off-resonance, which creates areas of reduced SNR as well as signal dropout. Moreover, the standard phase encoding for 3D Cartesian GRE-based MRE is very time-consuming¹⁵ (eg, over 20 minutes for 3-mm isotropic resolution with four MRE phases and six motion-encoding directions). Recently, another 3D-MRE method was proposed using hybrid radial-Cartesian EPI acquisition and significantly reduce the scan time to under 4 minutes in brain.¹⁶ However the EPI trajectory used in this method may introduce image distortions due to B₀ inhomogeneity.

In this work, we designed and implemented a multishot, variable-density spiral staircase (SSC) acquisition to enable fast and high-quality MRE of the whole brain using a 3D GRE-based sequence. Because spiral-out trajectory begins at the k-space center, it facilitates the use of a relatively longer motion-encoding gradient (MEG) to enhance motion-encoding efficiency, while still maintaining a reasonably short TE for brain imaging at 3 T. The duration of the spiral readout was chosen to balance increased SNR efficiency (longer duration), while still allowing robust off-resonance deblurring¹⁷ for high-quality images. The SSC acquisition produces incoherent aliasing with through-plane undersampling, which allowed application of acquisition speed-up and parallel-imaging reconstruction with negligible SNR penalty (ie, “g-factor” close to 1). A method for joint deblurring of the spiral images from different MRE phases and MEG encodings was proposed to take advantage

of the shared anatomical information, to further enhance the SNR for subsequent stiffness inversion.

2 | METHODS

2.1 | Data acquisition

The multishot, variable-density 3D SSC trajectory used in this work is illustrated in Figure 1A. The SSC trajectory uniformly distributes N_z groups of N_a spiral arms along the k_z axis,¹⁸ where N_z and N_a were defined in the framework of stack of spiral (SOS) acquisitions (ie, N_a is the number of spiral arms needed to cover the k_x - k_y plane, and N_z is the encoding dimension length in k_z). Within this uniform distribution along the k_z axis, each of the N_a arms in each group is rotated about the k_z axis by $(n_a/N_a)*360^\circ$. As a consequence of this ordering, each set of N_z spiral arms with a particular index n_a (all with the same rotation about k_z) is shifted along k_z , relative to SOS, by $(n_a/N_a)*k_z$, where k_z is the Nyquist distance. This in turn introduces a linear phase variation in z along image slices. If the encoding in k_z is undersampled by some factor R (changing the pitch of the arm rotation around k_z by R), this arm-to-arm phase variation creates incoherence in the aliasing between slices that are N_z/R apart from each other. This allows separation of these slices with very low SNR penalty (g -factors near 1 with small R) compared with that incurred by a standard SOS acquisition. More details of the SSC acquisition with improved through-plane parallel-imaging performance can be found in previous work.¹⁸

The 3D GRE-based pulse sequence for MRE data acquisition is illustrated in Figure 1B. Given the spiral-out trajectory, a MEG of 2 T was adopted to double the motion-encoding efficiency while keeping a reasonably short TE. For example, with a vibration frequency of 60 Hz in this study (ie, $TR = 4$ T), a MEG duration of 33.33 ms and a TE of approximately 35 ms can be achieved, both of which are within the range of T_2^* values of the brain at 3 T that give the optimal phase-SNR in the MRE data¹⁹ and GRE images.²⁰ Putting these methods together, we improved the SNR of GRE-based MRE by improving through-plane parallel imaging, doubling the MEG sensitivity, and achieving an reasonably short TE.

The acquisition scheme provides flexibility in trade-off among resolution, SNR, spatial blurring (ie, duration of spiral readout), and scan time. Given a desired resolution, acquisition parameters such as through-plane acceleration factor, number of spiral arms/shots (ie, in-plane acceleration), readout duration, and variable density pattern can be adjusted accordingly to achieve an acceptable scan time with good image quality.

2.2 | Spiral staircase image reconstruction

For simplicity, we consider a discrete image model throughout this paper, in which $\rho_{ssc} \in \mathbb{C}^{N \times 1}$ is a $N \times 1$ (ie, $N = N_x \times N_y \times N_z$) vector denoting an SSC image for each MRE phase and MEG encoding, and $s_c \in \mathbb{C}^{N \times 1}$ is the c th coil sensitivity function. For each image, a finite number of measurements (ie, total $N_a \times N_z/R_z$ spiral arms with M sampling points per arm), denoted as $d_{c,n_a} \in \mathbb{C}^{(M \times N_z/R_z) \times 1}$ for the n_a th spiral arm, were collected.

The value of R_z is the uniform undersampling factor along the slice direction. In this setting, the imaging equation of the proposed SSC acquisition can be written as

$$\mathbf{d}_{c, n_a} = \mathbf{G}_{n_a}^H \mathbf{F}_u \mathbf{P}_{n_a} (s_c \odot \rho_{ssc}) + \epsilon_{c, n_a}, \quad (1)$$

where $\mathbf{P}_{n_a}$ is a matrix operator introducing the linear phase variation (ie, $e^{i2\pi \frac{R_z n_z n_a}{N_z N_a}}$) at the n_z th slice location (ie, $n_z = 0, 1, 2, \dots, N_z$) for the n_a th set of spiral arms (ie, $n_a = 0, 1, 2, \dots, N_a$). Operator $\odot$ denotes element-wise multiplication; $\mathbf{F}_u$ denotes the 3D Fourier encoding matrix with uniform undersampling along slice; $\mathbf{G}_{n_a}$ is the 2D in-plane gridding operator; H denotes Hermitian conjugation; and ϵ_{c, n_a} represents the measurement noise that is assumed to be complex white Gaussian.

Each set of spiral arms represent a uniquely shifted, uniform (Cartesian) sampling along k_z , such that image reconstruction can be parsed into N_z/R_z sets of R_z overlapping slices. Each of these sets contains coherent aliasing in Z (along each spiral arm) and incoherent in-plane aliasing (from arm-to-arm phase variations as well as in-plane undersampling, if applied). Specifically, for uniform k_z undersampling, an (N_z/R_z) -point inverse discrete Fourier transform was performed along k_z to generate N_a sets of aliased data $\mathbf{d}_{c, n_a}^{aliased} \in \mathbb{C}^{(M \times N_z/R_z) \times 1}$ with reduced FOV along z :

$$\mathbf{d}_{c, n_a}^{aliased} = \mathbf{F}_z^{-1} \mathbf{d}_{c, n_a} = \mathbf{G}_{n_a}^H \mathbf{F}_{xy} \mathbf{U}_{R_z} \mathbf{P}_{n_a} (s_c \odot \rho_{ssc}) + \epsilon_{c, n_a}^{aliased}, \quad (2)$$

where $\mathbf{F}_z^{-1}$ denotes the one-dimensional inverse discrete Fourier transform operator along k_z ; $\mathbf{F}_{xy}$ is the 2D in-plane DFT operator; and $\mathbf{U}_{R_z} \in \mathbb{C}^{(N/R_z) \times N}$ performs a superposition of slices to generate an aliased image according to the uniform undersampling. To this end, one may reconstruct the entire 3D SSC volume, set by set, by solving the following optimization problem:

$$\hat{\rho}_{ssc} = \underset{\rho_{ssc}}{\operatorname{argmin}} \sum_{c=1}^L \sum_{n_a=1}^{N_a} \left\| \mathbf{G}_{n_a}^H \mathbf{F}_{xy} \mathbf{U}_{R_z} \mathbf{P}_{n_a} (s_c \odot \rho_{ssc}) - \mathbf{d}_{c, n_a}^{aliased} \right\|_2^2 + \|\lambda_T \rho_{ssc}\|_2^2, \quad (3)$$

where Tikhonov regularization was used to improve the conditioning of the inverse problem. In this study, a linear conjugate gradient algorithm was adopted to solve the reconstruction in Equation 3, and SSC images for each MRE phase and MEG encoding were reconstructed separately.

2.3 | Joint deblurring with shared anatomical constraints

Given the reconstructed SSC images, the remaining artifacts due to off-resonance need to be corrected before subsequent MRE processing. Taking into account the off-resonance effect, the k -space data measured in spiral imaging can generally be expressed as

$$d(\mathbf{k}) = \int \rho(\mathbf{r}) e^{i2\pi \Delta f(\mathbf{r})[TE + t(\mathbf{k})]} e^{-i2\pi \mathbf{k} \cdot \mathbf{r}} d\mathbf{r} + \varepsilon(\mathbf{k}), \quad (4)$$

where $\rho(\mathbf{r})$ is the desired spin density function at $TE = 0$; $f(\mathbf{r})$ the static field inhomogeneity (ie, B_0 map); $t(\mathbf{k})$ is the relative sampling time at every $\mathbf{k}$ -space location along the spiral readout; and $\varepsilon(\mathbf{k})$ is the complex white Gaussian noise. The values of $\mathbf{r}$ and $\mathbf{k}$ are coordinates in the image domain and $\mathbf{k}$ -space, respectively. Similarly, we discretize $\rho(\mathbf{r})$ and $f(\mathbf{r})$ using ideal delta function and rectangular function, respectively, which assumes that the spin density function and field inhomogeneity can be represented completely by the values on a grid at N spatial locations. Therefore, Equation 4 can be rewritten in discrete form as

$$d[m] = \sum_{n=-N/2}^{n=\frac{N}{2}-1} \rho[n] e^{i2\pi \Delta f[n]TE} e^{i2\pi \Delta f[n]t[m]} e^{-i2\pi nm/N} + \varepsilon[m], \quad (5)$$

where n and m denote the discrete coordinates in image and $\mathbf{k}$ -space, respectively (ie, $n, m = 1, 2, \dots, N$). By applying an inverse discrete Fourier transform on both sides of Equation 5, the blurred spiral image ρ_{ssc} can then be expressed as

$$\rho_{ssc}[n] = \{\rho[n] e^{i2\pi \Delta f[n]TE}\} \otimes h[n] + \varepsilon'[n], \quad (6)$$

where $h[n] = \sum_{m=-N/2}^{m=\frac{N}{2}-1} e^{i2\pi \Delta f[n]t[m]} e^{i2\pi nm/N}$ is a spatial-dependent blurring kernel; $\otimes$ is the discrete convolution operator; and ε' is the noise term in the image domain. With a known B_0 map, the image function ρ can be recovered using a deblurring procedure²¹ by solving the following least-squares reconstruction problem:

$$\hat{\rho} = \underset{\hat{\rho}}{\operatorname{argmin}} \|H\rho - \rho_{ssc}\|_2^2, \quad (7)$$

where matrix operator H performs the off-resonance compensation and discrete convolution defined in Equation 6. In this work, we tailored the deblurring method in Equation 7 (named as standard deblurring hereafter) for MRE image reconstruction, to take advantage of the highly correlated anatomical structures between different MRE phases and MEG encodings. Additionally, brain MRE images may contain many locally smooth regions that can be leveraged to improve SNR if averaged properly. Based on these premises, we exploited this shared structure information^{22–24} in a joint deblurring formulation to further boost SNR. The deblurred MRE SSC images were reconstructed jointly by solving the penalized least-squares problem:

$$\begin{aligned} \{\hat{\rho}_1, \hat{\rho}_2, \dots, \hat{\rho}_J\} = \underset{\{\hat{\rho}_1, \hat{\rho}_2, \dots, \hat{\rho}_J\}}{\operatorname{argmin}} & \sum_{j=1}^L \|H\rho_j - \rho_{j,ssc}\|_2^2 \\ & + \lambda \sum_{n=1}^N \sum_{m \in \Omega_n} \left[w_{mn}(\rho_1, \rho_2, \dots, \rho_J) \sum_{j=1}^J |\rho_{j,m} - \rho_{j,n}|_2^2 \right] \end{aligned} \quad (8)$$

where index j indicates images with different MRE phase or MEG encodings (ie, $J = 24$ in this study); m or n denotes the m th or n th pixel of an image; Ω_n defines a four-pixel neighborhood of pixel n adjacent both horizontally and vertically; and w_{mn} is a function of all the images, defining the edge structure and controlling the strength of spatial smoothness. By penalizing $\sum_{j=1}^J |\rho_{j,m} - \rho_{j,n}|_2^2$, we impose the same anatomical structures across all J images jointly. Specifically, in homogeneous regions, a large w_{mn} is derived to significantly enforce similarity between adjacent pixels to enhance SNR. In regions that possibly contain edge structures, a small w_{mn} is used to allow the preservation of edges. In this study, we chose to compute w_{mn} ($0 < w_{mn} \leq 1$) using²³

$$w_{mn}(\rho_1, \rho_2, \dots, \rho_J) = \begin{cases} 1, & \sqrt{\sum_{j=1}^J |\rho_{j,m} - \rho_{j,n}|_2^2} \leq \epsilon \\ \frac{\epsilon}{\sqrt{\sum_{j=1}^J |\rho_{j,m} - \rho_{j,n}|_2^2}}, & \sqrt{\sum_{j=1}^J |\rho_{j,m} - \rho_{j,n}|_2^2} > \epsilon \end{cases}. \quad (9)$$

By substituting Equation 9 into Equation 8, the overall cost function becomes

$$\{\hat{\rho}_1, \hat{\rho}_2, \dots, \hat{\rho}_J\} = \underset{\{\hat{\rho}_1, \hat{\rho}_2, \dots, \hat{\rho}_J\}}{\operatorname{argmin}} \sum_{j=1}^L \|\mathbf{H}\rho_j - \rho_{j,ssc}\|_2^2 + \lambda \sum_{n=1}^N \sum_{m \in \Omega_n} \Phi \left(\sqrt{\sum_{j=1}^J |\rho_{j,m} - \rho_{j,n}|_2^2} \right), \quad (10)$$

where Φ is known as the Huber function

$$\Phi(x) = \begin{cases} x^2, & x \leq \epsilon \\ 2\epsilon x - \epsilon^2, & x > \epsilon \end{cases}, \quad (11)$$

and ϵ is a predetermined threshold controlling the sensitivity of the edge structures in an image. Note that the penalized least-squares problem in Equation 10 is convex with a guaranteed global minimum, and was solved iteratively using a half-quadratic optimization procedure (ie, the outer loop). The quadratic problem (ie, with fixed w_{mn}) in Equation 8 was solved efficiently using a linear conjugate-gradient algorithm (ie, the inner loop).

2.4 | Magnetic resonance elastography inversion

The deblurred SSC images are used subsequently to extract tissue-stiffness information. First, phase-difference maps with MEG-encoded motion along each axis were calculated through conjugate multiplication of MRE images with positive and negative MEG polarities; then, curl of the motion-induced phase was determined using a technique that does not require unwrapping the phase information,²⁵ and the shear stiffness was reconstructed using the 3D direct inversion of the Helmholtz equation.²⁶

2.5 | Experiments

2.5.1 | In vivo—To validate the proposed technique, in vivo experiments were performed on a 3T Philips system (Ingenia Elition X; Best, the Netherlands) using a 14-channel receive-only head coil on 4 healthy subjects (28–56 years old) with written informed consent. All experiments were carried out with the approval of institutional review board. Mechanical vibrations at 60 Hz were introduced into the subject's head, primarily along the anterior–posterior direction, using a commercial pneumatic active driver (Resoundant, Rochester, MN) and a pillow-like passive driver placed under the subject's head. Four wave-propagation phases evenly spaced over a single vibration period were sampled by adjusting the delay between the trigger and the sequence. Six motion directions (ie, positive and negative x, y, and z) were encoded repeatedly with MEG applied to each gradient axis, sequentially, to acquire the full displacement field. All MRE experiments were carried out with the same brain coverage (FOV = 240 × 240 × 120 mm³), vibration strength, and MEG amplitude (37 mT/m).

Whole-brain MRE data were acquired using the proposed 3D GRE-SSC acquisition (TR/TE = 66.67/35 ms, FA = 23°, 1.2× slice oversampling, 2× through-plane uniform undersampling, and 13.6-ms spiral readout with mixed-arm ordering). Variable density acquisition was implemented for 3-mm isotropic resolution with two spiral arms (fully sampled in the center with a 30% of radius and undersampled by a factor of 2 in the outer region of k-space). Nyquist density acquisition was also implemented for 3-mm isotropic resolution with three spiral arms, and 2-mm isotropic resolution with five spiral arms. The total scan times were 1:20, 2, and 5 minutes, respectively. To compare with conventional SE-based approaches, multislice SE-based scans with spiral and single-shot EPI acquisition were also performed at 3 × 3 × 3 mm³ resolution (SE spiral: 13.5 ms spiral readout, three spiral shots, TR/TE = 3333/50 ms, flip angle = 90°, scan time = 4 minutes; SE-SS-EPI: TR/TE = 4000/67 ms, flip angles = 90°, scan time = 1:36 minutes). Two MEGs of a single vibration period duration were placed on both sides of the refocusing pulse, producing the same displacement-encoding sensitivity (ie, the same maximum phase induced by vibration) as the GRE-SSC sequence. To this end, we relate the comparison of phase-SNR of the MRE data to the SNR of the magnitude images generated by the 3D-GRE and 2D-SE methods. Theoretical SNR efficiency can be computed to compare the two methods (ie, assuming the same spiral arms and durations) purely from the data-acquisition standpoint. Specifically, the SNR efficiency of the proposed 3D-GRE acquisition was calculated by²⁷

$$\eta_{GRE} = S_{GRE} \sqrt{\frac{N_{AV}}{T_{GRE}}} = M_0 \sqrt{\frac{1 - e^{-TR/T1}}{1 + e^{-TR/T1}}} \cdot e^{-TE/T2^*} \sqrt{\frac{N_a N_z}{T_{GRE}}}, \quad (12)$$

where N_{AV} is the effective number of averages, including encoding steps; S_{GRE} is the maximum signal obtained with Ernst angle; and T_{GRE} denotes the total scan time. Similarly, the SNR efficiency of the 2D-SE method was calculated by²⁸

$$\eta_{SE} = S_{SE} \sqrt{\frac{N_{AV-SE}}{T_{SE}}} = M_0 (1 - e^{-TR/T1}) \cdot e^{-TE/T2} \sqrt{\frac{N_a}{T_{SE}}}. \quad (13)$$

Using 2D SE-Spiral as a reference, the relative SNR efficiency is defined as $\eta = \eta_{GRE}/\eta_{SE}$.

The SSC image reconstruction and joint deblurring were implemented in an open-source software (ie, graphical programming interface²⁹) using python and C++ libraries. Empirically selected regularization parameters (eg, $\lambda_T = 0.1$ and $\lambda = 0.09$) were adopted for all of the data sets and exhibited stable performance. For SSC image reconstruction and the inner loop of joint deblurring, the conjugate-gradient iteration was stopped when the normalized conjugate-gradient residual was smaller than 10^{-5} . For the outer loop of joint deblurring, the algorithm was stopped when the relative l_2 distance between two adjacent iterations (ie, $\|\rho^{k+1} - \rho^k\|_2 / \|\rho^k\|_2$) was smaller than 10^{-3} . The value of ε was chosen as one-fifth of the maximum finite difference (ie, $\sqrt{\sum_{j=1}^J |\rho_{j,m} - \rho_{j,n}|_2^2}$), to balance edge identification and noise rejection. The computational time of the 2-mm isotropic data set was 3:30 minutes for the SSC image reconstruction of a single 3D volume, and 22 minutes for joint deblurring of 24 MRE images on a portable workstation (MacOS Mojave, CPU 2.9 GHz Intel Core i9, RAM 32 GB 2400 MHz DDR4).

To quantitatively access the stiffness values estimated from different methods, an anatomical scan (MPRAGE sequence with 1-mm isotropic resolution) was also collected. Masks of white matter, gray matter, cerebellum, and brainstem were generated using the brain extraction (BET), segmentation (FAST), registration (FLIRT) tools, and atlas in FSL 6.0 (<https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/>).³⁰ The coil-sensitivity functions required in Equation 3 and field-inhomogeneity maps required in Equation 8 were obtained separately using vendor-provided low-resolution prescans.

2.5.2 | Phantom—A homogeneous head-shaped MRE phantom (ie, made of bovine gel) was also used to demonstrate the feasibility of our method in producing shear stiffness estimates compared with the state-of-the-art methods (eg, 2D SE-EPI and 2D SE-Spiral). The MRE settings and sequence parameters were the same as those in the in vivo experiments.

2.5.3 | Simulations—To demonstrate the feasibility of the proposed anatomical constrained joint-deblurring method in reducing reconstruction error, enhancing image SNR, and improving the subsequent stiffness mapping, simulations with synthesized complex Gaussian noise were performed using another fully sampled SE spiral data set (2-mm isotropic resolution, 10-minute scan time) as ground truth. For comparison, the standard deblurring with Tikhonov regularization was conducted, as follows:

$$\{\hat{\rho}_1, \hat{\rho}_2, \dots, \hat{\rho}_J\} = \operatorname{argmin}_{\{\hat{\rho}_1, \hat{\rho}_2, \dots, \hat{\rho}_J\}} \sum_{j=1}^L \|\mathbf{H}\rho_j - \rho_{j,ssc}\|_2^2 + \lambda \sum_{j=1}^J \|\rho_j\|_2^2$$

Regularization parameters were adjusted empirically to provide the minimum L2-norm image-reconstruction error.

3 | RESULTS

Phantom MRE results from 2D SE-EPI, 2D SE-Spiral, and 3D GRE-SSC methods are shown in Supporting Information Figure S1. Both the curl wave images and shear stiffness maps are comparable among these methods. The median stiffness measured from the two regions of interest were 3.34 kPa and 3.42 kPa for SE-EPI, 3.31 kPa and 3.42 kPa for SE-Spiral, and 3.34 kPa and 3.45 kPa for GRE-SSC, respectively. Note that our method produced comparable stiffness estimates in half the scan time (2 minutes) of the SE-Spiral method (4 minutes).

We computed η using the 3-mm isotropic resolution case as an example to demonstrate the SNR performance of our 3D-GRE spiral method using reported T_1 and T_2 values in the literature.^{31,32} With an average T_1 , T_2 , and T_2^* of 1331 ms, 80 ms, and 51.8 ms and 832 ms, 110 ms, and 44.7 ms for the gray and white matter,³¹ respectively, η was 1.16 and 1.04 for the gray and white matter, respectively. With an average T_1 and T_2 of 1820 ms and 99 ms, and 1084 ms and 69 ms for the gray and white matter³² (using the same T_2^* as in Wansapura et al³¹), respectively, η was 0.96 and 1.23 for the gray and white matter, respectively. Note that Ernst angle was chosen for the gray and white matter, respectively. The estimated scan time was 240 seconds for the SE-Spiral method and 192 seconds for the GRE-SSC method with no parallel imaging and slice oversampling applied. Therefore, taking into account the SNR improvement that our new data-processing methods provide, we believe that our method achieves comparable or even better SNR performance than the SE-based counterpart. Example images from our 3D GRE-SSC and the standard multi-slice SE spiral implementations are displayed in Figure 2. Again, the 3D GRE-SSC data were acquired in 2 minutes with through-plane parallel imaging compared with the 4-minute scan time of the SE method. Although the magnitude images from the proposed acquisition exhibited noticeable signal dropout in regions with large field inhomogeneities, the proposed acquisition scheme still provided high-quality shear stiffness maps with clearly identified brain structures. The magnitude SNR (ie, magnitude mean divided by noise SD) of two representative regions of interest in the white matter were also measured and reported in Figure 2. Noise SD was estimated from image background.

Results from the proposed technique and the state-of-the-art multislice SE-SS-EPI method are illustrated in Figure 3. Only two spiral shots were performed in our method to match the scan time of SE-SS-EPI. The stiffness maps produced by our method exhibited well-delineated brain structures and higher stiffness values, particularly in the white matter. Quantitative comparisons of stiffness values in white matter and gray matter from different methods are summarized in Figure 4. In this study, the SE-spiral data produced higher stiffness values (consistent with higher SNR) than the SE-SS-EPI acquisition, possibly due to the longer scan time. Although 3D GRE-SSC acquisition and the associated parallel-imaging reconstruction produced slightly lower SNR (ie, with half of the scan time due to acceleration along kz) than the SE-based spiral acquisition, it was further boosted by the proposed anatomical constrained joint deblurring to the level provided by the SE-based approaches, especially in the white matter. Quantitative assessments of stiffness values across 4 subjects using our method are summarized in Supporting Information Table S1.

Data from all subjects produced reasonable stiffness values as compared with those in the literature.^{13,34} Anecdotally, the measurements indicated reduced brain stiffness in the older subjects (ie, 44 and 54 years old) in this preliminary result, which was consistent with known changes of tissue mechanical properties with age.³⁵

Simulation results of the anatomical constrained joint deblurring method are shown in Figures 5 and 6. The residual noise from Tikhonov regularization is apparently higher and uniformly distributed as compared with those from anatomical constraint, which were further suppressed within the homogeneous regions. The anatomical weights were set to capture major edge structures while free of noise visually, which primarily depicted the boundary of the brain and CSF in this case. Given the lower reconstruction error, the displacement and stiffness maps from the proposed method also exhibited higher quality in terms of SNR and stiffness estimation. The stiffness estimates were also compared at different SNR levels at 3-mm isotropic resolution. As SNR decreases, the stiffness maps generated from both methods degraded accordingly. Quantitatively, the median stiffness values in both white matter and gray matter went downward as noise level increased, which was consistent with previous findings.³³ In this regard, the proposed method led to increased stiffness values by approximately 0.2 kPa, consistent with enhanced SNR in the MRE images. More specifically, in the presence of synthesized noise with a SD of 50 (ie, corresponding to a peak SNR of 28, where peak SNR is defined as the ratio of maximum signal amplitude over noise SD), the proposed method produced stiffness maps comparable to that from the standard deblurring method with no synthesized noise.

Finally, two representative high-resolution (2-mm isotropic) brain MRE results obtained using the proposed technique and one obtained with the 2D SE-Spiral sequence are presented in Figures 7 and 8, respectively. Our method produced stiffness maps exhibiting detailed brain structures, such as the ventricles, with good SNR (Figure 7) and comparable to that from the 2D-SE method using less scan time (Figure 8), demonstrating the promising potential of our method for high-resolution brain MRE.

4 | DISCUSSION

This work introduced a novel GRE-based 3D data-acquisition and processing method using SSC for fast MRE of the whole brain while simultaneously achieving high SNR. This method included steps to improve the SNR of MRE data through the entire acquisition and processing. In data acquisition, it leveraged the short TE available with spiral-out imaging to use a long MEG (two vibration periods), such that enhanced displacement information and optimal phase-SNR can be achieved. An undersampled SSC acquisition with iterative SENSE³⁶ were used to reconstruct spiral images with reduced SNR penalty. Finally, in the deblurring procedure, the shared anatomical information of all MRE images was exploited in a joint-deblurring formulation to further boost the SNR for stiffness inversion. One limitation of the current sequence implementation is that the TR time is restricted to be an integer multiple of the vibration period for synchronization, whereas the per-slice TR in SE-based approaches can be arbitrary but at the cost of a possible phase shift between slices. To increase the acquisition efficiency, an interleaved phase-offsets acquisition scheme³⁷ (eg, TR is set to be an odd integer multiple of $T/2$) can be adopted to further reduce scan time.

Although other 3D spiral trajectories (eg, SOS, Distributed Spirals^{38,39}) can be used, SSC was designed to improve SNR performance in reconstruction while retaining computational efficiency. Specifically, unlike spherically distributed spirals,³⁹ SSC allows reconstruction in k_z along a Cartesian grid such that a fast inverse discrete Fourier transform can be used directly to decouple the entire 3D reconstruction into multiple sets (ie, R_z slices per set) of reconstructions, to reduce computational time. Moreover, in SSC, each arm resides on a unique position along k_z , which introduces more incoherence and leads to alleviated noise amplification for through-plane parallel imaging compared with SOS methods.

In this study, given the assumption that coil-sensitivity functions vary smoothly within local regions, parallel imaging and deblurring were treated as two sequential steps to reduce computational complexity. Ideally, they should be considered jointly. We used an image-based deconvolution method to correct the off-resonance effect in spiral imaging, while other iterative approaches can also be adopted^{40,41} in the presence of a known B_0 map. Moreover, to account for possible long-term variations of B_0 during the scan, dynamic field estimation can also be incorporated by introducing a TE variation into the sequence, such as using a spiral-in and spiral-out trajectory,⁴² which will be explored in future research.

The joint anatomical constraint was exploited within the deblurring framework, to further improve the SNR based on the observation that MRE images have highly correlated edge structures. Other approaches, such as those using joint sparsity⁴³ or low rank,⁴⁴ could also be adopted. In our method, there were different options to calculate the anatomical weight governing the edge structures. Once the weights were determined, the solution from the final quadratic problem can be easily characterized. Please note that we estimate the weights from the MRE volumes jointly, and apply the same spatial regularization governed by such weights to each complex-valued MRE data set, so there is no across talk between different MRE volumes. In this study, we chose to calculate the weight in a way such that the underlying cost function stayed convex. Mathematically, this was similar to enforcing the joint sparsity of the MRE images in the finite-difference domain. Therefore, one should be aware that certain reconstruction bias would be introduced, depending on the anatomical weights and regularization parameter. As shown in Supporting Information Figure S2, with proper anatomical weights derived from the actual data, our method smooths the homogeneous region as regularization increases and does not introduce false edge information in neither the magnitude nor displacement field. However, an overly strong regularization would cause large reconstruction bias, resulting in unreliable stiffness estimates in spite of enhanced SNR. A complete study of how reconstruction bias would influence the subsequent MRE inversion is out of the scope of this study and will be reported in future research.

Motion-related phase errors due to mechanical actuation or physiological motion can lead to signal loss and artifacts in multishot acquisitions. Multislice SE-based approaches suffer from such artifacts, known as interslice phase jitters, resulting in false wavelength and inaccurate stiffness estimation. To reduce this artifact, low-pass filtering⁴⁵ can be applied along the slice direction, or more sophisticated approaches⁴⁶ are needed to determine and correct the phase jitters. One of the benefits of 3D acquisition for MRE, such as that used in this work, is that this motion variability is expressed in k -space, and the resulting artifacts

are dispersed incoherently in the reconstructed volume. In this aspect, the proposed 3D acquisition can provide higher spatial resolution and greater continuity along slice direction than the 2D SE-based method. One must be aware that these motion-induced phase errors between different spiral shots still exist in the data, and thus in the volume as artifacts. This work focused primarily on addressing the speed and SNR challenges of the conventional 3D GRE-based MRE method and demonstrated the feasibility of the proposed approach for whole-brain MRE. Correction of motion-induced phase errors among spiral shots will be investigated in future research.

Finally, higher spatial resolution (eg, 1.6-mm isotropic) has been achieved in brain MRE,⁴⁷ which is valuable to study subcortical structures but cannot be done in clinical feasible time (ie, 5 minutes). The proposed method is able to acquire whole-brain MRE data at 1.6-mm resolution within 5 minutes by performing in-plane undersampling at a factor of 1.8, but at the cost of noticeable SNR loss, as reported in a preliminary study.⁴⁸ A more comprehensive and quantitative evaluation of the proposed method at higher spatial resolution will be done in future research.

5 | CONCLUSIONS

A novel 3D GRE-based data-acquisition and processing scheme was demonstrated for whole-brain MRE using spiral staircase, with supporting in vivo and phantom results. This technique integrates a new acquisition scheme, image reconstruction, and joint deblurring to enable fast and high-quality in vivo MRE of the brain. The proposed method provides a promising potential for high resolution or dynamic brain MRE applications.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGMENT

The authors thank Dr. Sandeep Ganji and Dr. Guruprasad Krishnamoorthy from Philips Healthcare for the useful discussion and help with the sequence programming and scanner configurations.

Funding information

Philips Healthcare and National Institutes of Health (R37 EB001981)

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FIGURE 1.

The proposed 3D gradient-echo (GRE)-based data-acquisition scheme for MR elastography (MRE) of the whole brain. A, The 3D stack-of-spiral (SOS) and spiral staircase (SSC) trajectories (ie, for simplicity, linear arm ordering is displayed here) are shown for comparison, with each set of spiral arms shown in a different color. B, The MRE pulse sequence illustrates how motion-encoding gradients were combined with the spiral trajectory. Abbreviation: MEG, motion-encoding gradient

FIGURE 2.

Qualitative comparison of brain MRE results from a 2D multislice spin-echo (SE)-Spiral method and the proposed SSC acquisition and processing at 3-mm isotropic resolution with scan time of 4 minutes and 2 minutes, respectively. A uniform undersampling of 2 was conducted for SSC along k_z with $1.2\times$ slice oversampling. Both scans used three spiral shots to cover the k_x - k_y space. Our acquisition and processing scheme provided comparable SNR and shear stiffness maps compared with the SE sequence. The measured magnitude SNRs in the region of interest (ROI) of the axial slice are 84.2 for the SE method and 77.3/109.0 for the SSC method, with/without anatomical constrained deblurring. The measured magnitude SNRs in the ROI of the coronal slice are 63.3 for the SE method, and 78.9/114.9 for the SSC method with/without anatomical constrained deblurring.

FIGURE 3.

Qualitative comparison of in vivo brain MRE results from a standard 2D multislice SE single-shot (SS) EPI and the proposed 3D GRE-SSC (two spiral shots) acquisition at 3-mm isotropic resolution with scan time of 1:36 minutes and 1:20 minutes, respectively. Although signal dropout can be observed in the magnitude images from the GRE-based acquisition, the curl wave images and stiffness maps of our method are comparable to that of the standard SE-SS-EPI method

FIGURE 4.

Quantitative comparison of the stiffness values obtained from different methods at 3-mm isotropic resolution: SE-EPI, SS EPI (scan time = 1:36 minutes); SE-Spiral, three spiral shots (scan time = 4 minutes); GRE-SSC3, three spiral shots (scan time = 2 minutes); and GRE-SSC2, two spiral shots (scan time = 1:20 minutes). Abbreviations: Std-deblur, standard deblurring (each image is deblurred separately without anatomical constraint); AC-deblur, anatomical constrained deblurring

FIGURE 5.

Simulation results of joint deblurring with Tikhonov regularization and our anatomical constraint using another fully sampled SE-Spiral data set acquired at 2-mm isotropic resolution. Complexed Gaussian noise (a noise SD of 50, a peak SNR [pSNR] of 28) were synthesized to generate a moderate noisy image. Regularization parameters were adjusted empirically to provide the minimum L2-norm reconstruction error (the percentage number). The estimated weights from our method are also displayed (white indicates 1 and dark is close to zero). Our method provides lower reconstruction error and suppressed noise especially within the homogeneous regions. The resulting displacement and stiffness maps also exhibit higher quality in terms of SNR and stiffness prediction

FIGURE 6.

Simulation results of the deblurring algorithms at 3-mm isotropic resolution with various synthesized noise levels. A, Qualitative comparison of the stiffness maps generated using the standard and our joint deblurring methods. B, Quantitative comparison of the stiffness values in white matter and gray matter. As noise increased, the quality of the stiffness maps degraded and the mean stiffness value decreased. The proposed anatomical constrained method consistently provided higher shear stiffness than the standard method, which was consistent with enhanced SNR of the MRE images and subsequent improvement of the MRE inversion

FIGURE 7.
High-resolution (2-mm isotropic) brain MRE results from the proposed 3D GRE-SSC technique performed on a 35-year-old male subject within 5 minutes

FIGURE 8.

Comparison of in vivo brain MRE results from a standard 2D multislice SE-Spiral scan (6 minutes with an in-plane acceleration factor of 1.67) and the proposed 3D GRE-SSC acquisition (5 minutes) at 2-mm isotropic resolution performed on a 50-year-old male subject. The mean stiffness values of cerebral white matter (blue), cerebellum (green), and brainstem (red) are 1.35, 1.01, and 0.98 for SE-Spiral and 1.48, 1.27, and 0.80 for GRE-SSC, respectively