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80 x 80, GRAPPA R=3. Total scan time was 3 minutes and 15 seconds. Additional images were acquired to capture noise according to the experiments described in the following sections. All participants provided written, informed consent for this study approved by our Institutional Review Board.

Experiment 1: Quantification of Noise from Physiomechanical Sources

Three subjects (2F/1M, 23-25 years old) were scanned with a protocol that included the MRE scan described above along with three additional scans to quantify noise under different conditions. Each noise scan had the same FOV, matrix size, and resolution as the full MRE scan, but with only a single phase offset and 20 repetitions. Average phase across the repeated images was subtracted from individual repetitions and the remaining signal was considered as noise. Each noise scan was 7 minutes and 17 seconds.

The first noise scan had both MEG and applied vibration off. The noise from this scan was considered to contain primarily noise contributions from image acquisition (Im noise). The second noise scan had MEGs of 70 mT/m, while the applied vibration remained off. The noise from this scan (ImPhys noise) is considered to include signal from physiological motion captured with the MEGs, including from cardiac pulsation, respiration, or small subject motions or table vibrations, in addition to image noise. Finally, the third noise scan had both MEGs of 70 mT/m and applied vibrations at 50 Hz delivered to the head. This last scan captures noise contributions from the vibration, in addition to the image and physiological noise sources (ImPhysVib noise). These noise contributions are evaluated on an additive basis as the random distribution of noise in each scan prevents isolation of a single type of noise.

Noise was quantified separately for each of the three subjects by averaging the absolute value of noise observations, with group averages and standard deviations computed and reported across the three subjects. The full width at half maximum (FWHM) of the noise distribution was then calculated for each subject and mean and standard deviation of FWHM were reported. Differences between Im, ImPhys, and ImPhysVib noise were assessed via paired, one-sided t-tests for both individual average absolute noise and FWHM.

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We repeated this experiment in three agarose phantoms. Each phantom was created using 1% agar as specified in (30) in a case of approximately 1000 mL volume. All imaging parameters were the same except the phantom had 40 slices and used an MEG strength of 10 mT/m to limit phase wrapping in the images as the phantom is easier to actuate and thus exhibits more displacement. All noise metrics were computed as described for the in vivo experiment.

The correlation length for each type of noise in every imaging direction was computed, which is indicative of how spatially correlated noise observations are. Short range correlations for a voxel at position r_0 can be approximated by $|C(\Delta r)| \sim k \exp(-\Delta r/r_c)$ where $|C|$ is Pearson's Linear correlation coefficient for noise between two points, Δr is the distance between two voxels, $\Delta r = |r - r_0|$, r_c is the correlation length, and k is the constant of proportionality, which is equal to 1 in this scenario. Correlation lengths were calculated for each image point by sequentially correlating noise at that point with all other points. The log of short-range correlations can be expressed as $f(\Delta r) = \log(|C(\Delta r)|) \sim -\Delta r/r_c$. We observed that correlations between two points decreased with distance until they reached a point where they were generally uncorrelated. Thus, we used a piecewise function to fit the log of the short-range correlations to determine r_c:

$$f(\Delta r) = \begin{cases} -\Delta r/r_c, & \Delta r \leq r_t \\ -r_t/r_c, & \Delta r > r_t \end{cases}$$

Where r_t is the transition point from a linear slope to a slope of zero, representing random correlations beyond this length. The correlation length (r_c) was determined to be the reciprocal of linear slope. We fit function $f(\Delta r)$ to determine both r_c and r_t, for each point in the image using nonlinear least squares in Matlab. These values were found for each individual image axis: x and y in-plane and z through-plane across slices for each MEG direction (x, y, z) separately. Boxplots were generated for the correlation lengths for each MEG direction and x and y in-plane and z through-plane across slices. The average correlation length and 95% confidence intervals across all subjects were reported for the data. Differences in correlation lengths between Im, ImPhys, and ImPhysVib noise were assessed with paired, one-sided t-tests.

Experiment 2: Cardiac-Induced Physiological Noise

Physiological noise due to the cardiac cycle was further assessed to determine if cardiac-induced brain motion resulted in increased physiological noise. Three subjects were scanned (2F/1M, 22-

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25 years old) with a similar protocol to the physiological noise condition described above, with MEGs at 70 mT/m and applied vibration off. Here, the scan included only 8 slices with 9 mm gap and reduced TR of 1120 ms to allow for 250 repetitions to be acquired. All other parameters are the same as described previously: FOV 240 x 240 mm^2, matrix size 80 x 80, GRAPPA R = 3, TE = 65.0 ms, and resolution 3.0 x 3.0 x 3.0 mm^3. Scans were performed with different MEG directions separately, and each of the three scans were 4 minutes and 47 seconds in duration. During the scan, a Siemens pulse-oximeter measured the participant's pulse at the fingertip via oxygen saturation, which was recorded along with the timing of the MRE sequence.

The pulse-oximeter signal was adjusted to have a range between 0 to 1 to normalize across individual subjects (24). The timing of peaks of the cardiac cycle were determined through the "findpeaks" Matlab function (24). The pulse-oximeter data was sub-divided into 10 equal bins based on time between peaks, with each bin representing one-tenth of the cardiac cycle, and the corresponding MRE images were sorted into one of the ten bins based on when the acquisition occurred relative to the pulse. Bin 1 was assigned as the bin containing the highest noise in order to account for delays between the pulse-oximeter, blood flow, and electronic communication (31). The average noise and standard deviation across images within a bin were computed. The in-plane correlation length for slices from bins 1 and 7 were also found following the protocol in *Experiment 1*. The average correlation length and the 95% confidence interval were reported, and differences in average noise and correlation lengths were assessed with paired, one-sided t-tests between bins 1 and 7.

Experiment 3: Effects of Correlated Noise on Mechanical Property Estimation

An additional set of noise scans were acquired for one subject (M, 23 years old) following the protocols of *Experiment 1* but with higher spatial resolution with 2.0 x 2.0 x 2.0 mm^3 voxels for use in simulations (modified parameters: matrix size 120 x 120, TR/TE = 6720/78 ms). These protocols included the full MRE scan and the three noise scans, all with the same co-registered FOV.

Whole brain MRE simulations with realistic wave propagation patterns were created from the 2 mm MRE data with 8 phase offsets, and used to study the effects of different noise types on

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property inversion (32). A finite element model was created from the brain mask and forced displacement boundary conditions were assigned from MRE measurements at the boundary. Complex-valued viscoelastic shear moduli were assigned as G* = (2.4 + i1.1) kPa for the overall brain tissue, with bilateral subcortical structures (nucleus accumbens, amygdala, caudate, hippocampus, pallidum, putamen, and thalamus) assigned using realistic values (32). Near-incompressibility was assumed with bulk modulus of 1.0 GPa and density 1000 kgm^{-3}. This allowed for a set of idealized noise-free motions with realistic wave and viscoelastic mechanical property values, to which various patterns of noise could be added. Profiles of Im, ImPhys, and ImPhysVib noise, extracted from the 2 mm MRE scan as described in *Experiment 1*, were applied at random to each slice and image in the MRE dataset. We created 50 simulated datasets per each type of noise, adding varying levels of noise by using different scaling factors to produce datasets with a range of signal-to-noise ratios. Gaussian noise was also added to a separate set of simulations as a comparison to real MRE noise profiles. Simulations with added noise were converted into mechanical property maps through the nonlinear inversion algorithm (NLI), returning maps of the storage and loss moduli, G' and G", which are configured into property maps of shear stiffness, $\mu = 2|G^*|^2/(G' + |G^*|)$ and damping ratio, $\xi = G''/2G'$ (16). For each simulated dataset with added noise, the octahedral shear strain-based signal-to-noise ratio (OSS-SNR) was also calculated (21), and the simulated datasets had OSS-SNR ranging from 2 to 15.

A low-noise simulation was created and assigned as the reference data set for all analyses. We used a virtually no noise simulation with OSS-SNR of 111.56 as the reference rather than the ground truth to remove the unavoidable effects of limited contrast recovery that occur due to the regularization required to maintain stability with in vivo data and instead focus on the effect of additional noise. The average normalized root-mean-square error (NRMSE) for the simulation with added noise, $\tilde{\mu}$, was compared to the reference simulation stiffness, μ, ($NRMSE(\tilde{\mu}) = \|\mu - \tilde{\mu}\|_F/\|\mu\|_F$). The average NRMSE for the damping ratio of the simulation with added noise, $\tilde{\xi}$was also compared to the reference simulation stiffness, ξ, $\left(NRMSE(\tilde{\xi}) = \|\xi - \tilde{\xi}\|_F/\|\xi\|_F\right)$. The errors were then plotted relative to OSS-SNR and fitted with a two-term exponential model ($y = a\exp(bx) + c\exp(dx)$) to visualize trends for the effects of Im, ImPhys, and ImPhysVib noise.

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RESULTS

Experiment 1: Quantification of Noise from Physiomechanical Sources

Average noise was calculated for each of the three image conditions: Im, ImPhys, and ImPhysVib noise; Figure 1 illustrates this noise in one representative subject (other subjects can be found in Supplemental Information, Figures S1 and S2). When MEG and vibration are off to isolate image noise, the average absolute Im noise across all subjects is 0.020 radians, which is consistent for each of the MEG directions (Table 1). When the MEGs are on, but vibration is off, the average ImPhys noise was 0.043 radians, which is double observed Im noise ($p = 0.022$) and may be attributed to encoding of spurious physiological motion or table vibration. For this condition (MEG on and vibration off), the MEG direction z (superior-inferior, SI) exhibited the most noise. When both MEG and vibration are on, the average ImPhysVib noise across subjects is 0.043 radians, which is a 48% increase as compared to ImPhys noise ($p = 0.040$). The most ImPhysVib noise is again observed in the MEG z direction (Table 1).

The FWHM for Im, ImPhys, and ImPhys noise distributions were found for each MEG direction (Figure S3 and Table 1). A wider FWHM in ImPhys (0.13 radians) and ImPhysVib noise (0.21 radians) indicates that observations with greater noise are more likely. The FWHM of ImPhysVib noise was greatest for MEG z (SI), followed by MEG y (AP) and MEG x (LR). The wider distribution of values for MEG y and z are likely due to spurious motion from the applied vibration, which occurs primarily in the anterior-posterior direction, but also induces displacement in the superior-inferior direction owing to rotation about the left-right axis with the neck as a pivot (33). ImPhysVib noise FWHM was significantly greater than ImPhys noise ($p = 0.014$) and Im Noise ($p = 0.002$).

The phantom experiments confirmed the trends of increasing noise in the Im, ImPhys, and ImPhysVib average absolute noise and their noise distributions (Figure S4). ImPhys noise was greater than Im noise ($p = 0.001$), and ImPhysVib noise was greatest primarily in the MEG y direction, which is the same direction as the applied vibration (Table S1). ImPhysVib noise was significantly greater than both Im noise ($p = 0.004$) and ImPhys noise ($p = 0.012$). The increase in ImPhys noise (when the MEG is turned on, but vibration remained off) was less than what was seen in the brain, due to the lack of physiological processes in the phantom, and is likely attributed

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to small table motion that is caused by gradient switching (25,34). The FWHM remained similar between Im and ImPhys noise, averaging 0.023 and 0.024 across the MEG directions for each noise type, unlike the brain (Figure S5). There was then a 36% increase in the FWHM between ImPhys and ImPhysVib noise indicating a greater distribution of large noise observations. This difference was significant for both Im noise ($p = 0.019$) and ImPhys noise ($p = 0.018$).

Figure 2 demonstrates the correlation of noise observations and Figure 3 shows the subsequent determination of correlation length. Correlation of noise in-plane noise decays gradually away from the point until it becomes more random indicating a lack of correlation (Table 2). Conversely, correlation of noise through-plane decays immediately due to EPI data being acquired as separate 2D slices. Figure 4 exemplifies in-plane correlation length differences. Im noise is the least correlated, with all three MEG directions averaging in-plane correlation lengths of 5.37 mm (95% CI: 5.32-5.43 mm), which is approximately 1.5 voxels in this experiment and thus is effectively not correlated. ImPhys and ImPhysVib noise had long correlation lengths in plane, averaging in-plane 26.54 mm (95% CI: 26.22 – 26.86 mm) and 28.94 mm (95% CI: 28.6 – 29.27) across all MEG directions, each significantly greater than from Im noise ($p = 0.009$ and 0.012, respectively). Correlation lengths for ImPhys noise was greatest in the MEG z direction in comparison to MEG x and MEG y. ImPhysVib noise exhibited short average correlation lengths in MEG x and MEG z, but long correlation lengths in MEG y. For all noise conditions, through-plane noise correlation length remained small, averaging 5.50 mm (95% CI: 5.45 – 5.54 mm) for ImPhysVib noise.

Experiment 2: Cardiac-Induced Physiological Noise

Figure 5A shows ImPhys noise measured at different points in the cardiac cycle. The cardiac bin assignments were made in post-processing after a delay based on the bin that contained the most noise as well as the timing of physiological delays between the pulse-oximeter signal and physiological brain motion. We observed that the noise in the resultant 10 bins followed a similar trend to the pulse oximeter signal. Cardiac bin 1 with the most noise averaged 0.083 radians across all three MEG directions, which suggests that this is likely when there is the most blood flow in the brain corresponding to systolic events (Table S2). This is double the average noise observed in bin 7 (0.048 radians; $p = 0.014$) which is likely when there are the smallest tissue displacements due to cardiac pulsation. In bin 1, the noise in the MEG z direction was greater, likely because

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brain tissue moves in the superior direction as an effect of systole. However, in bin 7, with the smallest amount of overall noise, the observations were similar across all MEG directions. Therefore, more ImPhys noise was found in bins expected to exhibit greater tissue changes due to brain pulsation. Note that these noise levels are higher than reported in Experiment 1 (Table 1), as we used a short TR to achieve sufficient sampling across the cardiac cycle in Experiment 2, and thus have a higher baseline Im noise component.

Bins that are likely to be related to increased pulsatility not only had the most noise, but also had the most variability in noise between images across all slices (Figure 5B). Bins where more ImPhys noise was observed (i.e. bins 1-3) had both the largest magnitude of noise, and the most variability in noise between images across all slices, which indicates variability in tissue displacement from cardiac pulsation. Likewise, more variability was observed in the MEG z (SI) direction which corresponds to the direction of cardiac pulsation movement in the brain.

We also considered whether the physiological noise from cardiac pulsation was spatially correlated by computing correlation lengths from noise observations in different bins (Figure 6 and Table S3). The noise in bin 1 is highly correlated averaging 30.88 mm (95% CI: 30.54-31.21) across all MEG directions, and greater than in bin 7 where the average correlation length is only 8.47 mm (95% CI: 8.37 – 8.57 mm) ($p = 0.031$). This confirms that cardiac pulsation not only results in more noise, but that this is the source of high correlation of ImPhys noise observations as seen in *Experiment 1*.

Experiment 3: Effects of Correlated Noise on Mechanical Property Estimation

Figure 7 demonstrates that correlated noise added to simulated MRE images influences mechanical property estimation. As the amount of ImPhysVib noise increases, the recovered property maps degrade, especially at low OSS-SNR values near 3. This is in contrast to purely Gaussian, uncorrelated noise that has less of an impact on recovered property maps even for similar OSS-SNR values. How correlated the added noise is also affects the recovered properties: Im noise (Figure S6) had less of an effect than ImPhys noise (Figure S7), which were both less than ImPhysVib noise. These qualitative observations are supported by quantitative error metrics for a range of simulated OSS-SNR values for each condition, demonstrating how lower OSS-SNR

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values result in greater error as compared to the reference simulation (Figure 8). Each fit for NRMSE vs. OSS-SNR for the different noise components exhibited R^2 values exceeding 0.96, demonstrating an appropriate fit was applied to the data. At low OSS-SNR values NRMSE increases exponentially, which confirms the trends occurring visually in the stiffness and damping ratio maps.

DISCUSSION

This study examined correlated noise and how it affects the estimation of mechanical properties. Physiological motion and spurious vibration become encoded along with the desired motion in the phase of MRE images, which contributes to errors in estimated mechanical property maps. We quantified the noise that arises from different sources and how spatially correlated the noise is. It was demonstrated through simulation that correlated noise has a greater impact on mechanical properties estimated with the nonlinear inversion MRE algorithm. These trends were consistent across subjects and between phantom experiments. This is the first systematic characterization of noise in brain MRE data.

Broadly, we investigated contributions to noise from image, physiological, and vibration sources. Image noise in MRI is often assumed to be Gaussian, though this is generally not true in practice. The use of multiple receiver coils in MR acquisition contributes to noise correlations through coupling coil elements in an array or configuring eddy currents on similar paths (35–37). Subsequently, physiological and vibration noise are much larger contributors to noise in MRE. Physiological noise results from tissue displacements due to processes including cardiac pulsation, as pulsatile tissue displacements in the brain will cause regions of tissue to move together. On the other hand, vibration noise arises from slight variability in applied motion from the actuator. It is important to note that our experiments do not actually isolate these individual components. Our physiological noise scans also contained image noise as it is impossible to decouple the two, because noise is random, we cannot isolate a particular type of noise. Similarly, our vibration noise scan included both physiological and image noise, as would be present in an MRE study in practice. However, we used this methodology to estimate these components of MRE noise to better characterize the origin and influence of correlated signal noise, and future work may build on these results to try and further decompose the noise into its components.

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One of the dominant sources of physiological noise is the cardiac cycle, which is linked to intracranial pressure and fluid flow, and thus it can alter the blood pressure over the course of the cardiac cycle and induce pulsatile motion in the brain, which has previously been reported to be as much as 187 μm (28,38). To analyze only the effects of cardiac pulsation on physiological noise, we sorted noise measurements based on pulse oximeter reading and designated the grouping with the most noise as "Bin 1". This process showed that there is an increase in physiological noise in observations that likely correspond to systole, which produces a pulse wave that dissipates into surrounding tissue microvasculature (38,39). Subsequently, observations in bins exhibiting less noise and short correlation lengths are likely attributed to blood returning to the heart during diastole for the next contraction (39). Spatial distributions of physiological noise also resemble pulsatile brain motion measurements taken with cardiac gated motion-sensitized MRI sequences (29,40); specifically, the spatial distribution of the noise patterns in Figure 5A are consistent with a pulsating brain. The MEG y (AP) shows stretching in bin 1 (top moving up and bottom moving down), switching to compressing by bin 3. MEG x (LR) shows a similar stretching in bin 1 as the left side moving left and the right side is moving right. This also switches to compression by bin 4-5. These trends demonstrate how the ImPhys noise observed from the motion encoding is can be linked to cardiac physiological processes.

A typical MRE sequence is not synchronized to the cardiac cycle, and thus each excitation and acquisition that together comprise a full dataset will occur at a random point in the cardiac cycle. If the acquisition occurs near systole, the MEG will capture the most pulsatile motion, while during diastole there will be less noise. Other sources of physiological noise are breathing and subtle subject motion, including from table vibration, which would similarly be encoded as spurious noise signal. Though we did not thoroughly investigate these other sources of noise, it is likely that they also contribute to noise measured in the experiments with motion encoding on. Table vibration has been demonstrated to result from low-frequency changing of imaging gradients (34), and large gradient amplitudes result in more motion during a scan (25). We likely observed this contribution of table shaking to ImPhys noise in phantom experiments as there was a slight increase in the average absolute noise in this condition over Im noise, though these increases in the phantom from table shaking are much less than those in the brain that likely also result from physiological

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sources. We note that we used a lower gradient strength in the phantom experiments since phantoms are generally actuated easier and we sought to avoid excessive phase accumulation, making it difficult to compare table shaking between phantom and brain experiments, as phantoms also affect and respond to table shaking differently. Breathing is another periodic process that may contribute to head motion, as respiration displaces the brain approximately every 5000 ms (41,42) and inspiration produces compression in the brain, with reported strains upwards of -28×10^{-3} (40). During breathing, the diaphragm moves several centimeters and the chest wall can move several millimeters, causing magnetic field changes that result in distortions in acquired images across space and time (43) and which may appear as physiological noise in MRE images. These physiological motions are generally at frequencies lower than the vibration frequency, so the frequency-selective MEGs are not very sensitive to these motions. However, these motions are large and MRE gradients retain some sensitivity at low frequencies (44), resulting in meaningful phase being accumulated.

The vibration noise experiments are most indicative of true noise distribution and correlation lengths of MRE data as both MEG and vibration are on. In Experiment 1, the MEG y direction with vibration had a correlation length of 25.8 mm which means that noise is correlated within 8-12 pixels depending on resolution. Because the MEG y direction is the same direction that the actuation takes place, these errors are likely due to variations in mechanical actuation, due to the force of the pneumatic actuator moving the weight of the head, which can alter the motion such that it is no longer perfectly harmonic and thus does not have a consistent amplitude or frequency. (18,45,46). However, we also note that these correlation lengths are estimates based on our fitting of how points in space are correlated. In this analysis we fit correlations in each spatial direction separately and assumed that at some distance the points become effectively uncorrelated. A more sophisticated fitting approach, considering decay in correlations in all directions together, may improve accuracy of correlation length estimates.

The simulations in Experiment 3 confirm that the noise observed is correlated and our hypothesis that this correlated noise leads to increased errors in NLI calculations, with greater error from more correlated noise sources even at the same OSS-SNR. OSS-SNR is an estimate of the error in the strain to measure the quality of MRE data, which is determined by residuals from the Fourier

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transform through time; therefore, noise is assumed to be Gaussian distributed in space and across phase offsets, which we have demonstrated here is not true due to its highly correlated nature. The minimization process of NLI uses an objective function based on unweighted least squares which is optimal when all measurements have approximately the same variance, and there is no covariance between measurements, thus making its estimates susceptible to the physiological and vibration noise described here. Our group has often used an OSS-SNR of 3 as the threshold for data quality that would result in stable inversion results with NLI (13,47); the simulation experiments presented here indicate this instability point occurs between OSS-SNR of 2 and 3. We also note that above that threshold there is still some voxel-wise error, including the asymmetry present in estimated properties in Figure 7 and S7 that is likely due to local characteristics of the wave field and noise present. While the global OSS-SNR threshold has been used extensively, the effects of local OSS-SNR on regional properties has not yet been rigorously explored, and measuring repeatability of estimated properties is still recommended even for data with high OSS-SNR.

Noise suppression techniques should be considered for MRE, however traditional approaches to limit physiological noise in MRI may not necessarily translate for MRE (48). Cardiac gating has been implemented in diffusion encoding to trigger motion encoding away from cardiac cycle peaks, such that data is only collected during diastole (24). However, the beat-to-beat variability of the cardiac cycle may interfere with the typical MRE actuation scheme that uses continuous or near-continuous application of harmonic motion. Other approaches instead could entail adding navigator echoes to measure and correct phase errors (49–51) as have been used in multishot MRE sequences previously (18,52). The noise components examined here are also often considered as interslice phase discontinuities (due to high correlation in-plane but not through-plane), which has been identified as a reason for using 2D inversion algorithms instead of 3D algorithms that are more appropriate for brain (53), and several post-processing approaches have been proposed to remove or minimize this effect (19,54). Finally, opportunities exist to explicitly consider correlated noise in the formulation of inversion algorithms for estimating properties. For instance, use of weighted least squares in NLI can addresses the case when noise is correlated, and a strong candidate for the weighting matrix is the inverse prior covariance matrix. The noise levels and correlation lengths in each direction determined in this paper can be used to efficiently build an

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approximation of the prior covariance matrix for the displacement measurements without additional scan time, which will allow implementation of weighted least squares in NLI to improve results in the presence of spatially correlated measurement errors (55). This approach is specific to NLI, however, similar strategies may be possible in commonly used direct inversion techniques.

In this study, only noise observed with the 2D EPI MRE sequence was analyzed; in other MRE sequences, noise may appear more or less correlated due to differences in acquisition. In 3D sequences, the observed effect of low correlation of noise through plane may not hold true as slices are acquired as part of a single volume (56,57), while multislab or multiband sequences will likely present more complex noise behavior as slices are acquired in multiple volumes (52). Multishot sequences may also have different behavior because images are solved using data acquired from multiple excitations, and thus may include different noise observations. This phenomenon is the same as motion-induced phase error that can be addressed during image reconstruction (18,52), but the effect on remaining noise in the reconstructed image is not yet known. In the future, the methods outlined here can be implemented to identify and account for MRE noise during the inversion process. Furthermore, depending on the MRE actuation frequency used, other sources of signal noise, such as breathing, table shaking, or different actuator types, should be assessed for their effects on MRE data.

CONCLUSION

Through this study, we have characterized signal noise in MRE from three types of sources: image, physiological, and vibration noise. We have implemented the correlation length as a method of measuring the extent noise contribute to errors in MRE images and have demonstrated that correlated signal noise contributes to errors in MRE inversions. Adding real signal noise to simulated data demonstrated that increasingly correlated noise, captured through the motion encoding gradient, contributes to increased errors in mechanical property calculations at a given SNR. MRE is a sensitive tool to assess brain health and detect subtle differences to brain mechanical properties. The ability to accurately characterize MRE signal noise will result in improved mechanical property maps and thus contribute to the advancement of MRE as a tool for brain health.

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TABLES

Table 1. Mean and standard deviation of average absolute noise and FWHM of noise distributions across all subjects.

	Average Noise (radians)			Noise FWHM (radians)		
	Im	**ImPhys**	**ImPhysVib**	**Im**	**ImPhys**	**ImPhysVib**
MEG X	0.020±0.006	0.044±0.014	0.053±0.013	0.080±0.019	0.121±0.019	0.168±0.019
MEG Y	0.022±0.005	0.037±0.009	0.068±0.018	0.084±0.007	0.126±0.013	0.222±0.026
MEG Z	0.020±0.007	0.047±0.013	0.068±0.023	0.080±0.019	0.151±0.025	0.239±0.033

Table 2. Average correlation lengths and 95% confidence intervals in mm for noise observations across all subjects.

	Im Noise		
	MEG X	**MEG Y**	**MEG Z**
In-Plane X	4.82 (4.78 - 4.86)	5.32 (5.26 - 5.37)	4.80 (4.74 - 4.85)
In-Plane Y	5.57 (5.51 - 5.63)	6.14 (6.07 - 6.20)	5.58 (5.53 - 5.64)
Thru-Plane Z	3.13 (3.10 - 3.15)	3.16 (3.14 - 3.18)	3.11 (3.09 - 3.13)
	ImPhys Noise		
	MEG X	**MEG Y**	**MEG Z**
In-Plane X	19.53 (19.27 - 19.78)	19.27 (19.1 - 19.45)	35.69 (35.21 - 36.16)
In-Plane Y	23.71 (23.45 - 23.97)	19.54 (19.29 - 19.79)	41.50 (41.02 - 41.99)
Thru-Plane Z	2.95 (2.93 - 2.97)	3.00 (2.98 - 3.03)	3.15 (3.13 - 3.17)
	ImPhysVib Noise		
	MEG X	**MEG Y**	**MEG Z**
In-Plane X	18.64 (18.45 - 18.83)	30.67 (30.28 - 31.07)	28.40 (28.12 - 28.68)
In-Plane Y	20.54 (20.34 - 20.75)	38.29 (37.79 - 38.78)	37.07 (36.65 - 37.48)
Thru-Plane Z	3.85 (3.82 - 3.88)	7.20 (7.14 - 7.26)	5.44 (5.40 - 5.49)

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FIGURE CAPTIONS

Figure 1. Average absolute average noise observed in one subject, demonstrating how the noise increases and spatially varies for Im, ImPhys, and ImPhysVib noise components. Similar plots for additional two subjects can be seen in Supplementary Figures S1 and S2.

Figure 2. Visual comparison of noise and noise correlation in three imaging directions. Noise is shown for one repetition of a slice alongside the corresponding correlation coefficient computed for a single point. Correlation coefficients indicate the degree of correlation of noise observations across the image with respect to the point indicated by the star.

Figure 3. Log-linear plots of correlation coefficients for a single voxel of interest indicated by the star in Figure 3. Correlation coefficients are fitted in space to determine correlation lengths. Plots demonstrate long correlation lengths in-plane versus through-plane, with reported values for each MEG direction. MEG directions are defined as x (left-right), y (anterior-posterior), and z (superior-inferior). In-plane and through-plane denominations refer to directions of correlations in space.

Figure 4. (A) Correlation lengths determined for different points in space for noise in the three MEG directions. (B) Box plots of correlation lengths from all three subjects. Top and bottom edges of box indicate 25^{th} and 75^{th} percentiles with center line indicating the median. Through-plane correlation lengths remain consistent across noise scans, while in-plane noise has long correlation lengths in ImPhys and ImPhysVib noise.

Figure 5. Qualitative assessments of ImPhys noise across cardiac bins and slices. (A) Average noise and (B) standard deviation of noise for one subject. There is a difference in the amount of noise between cardiac bins. Bins corresponding to systole have more noise compared to bins that correspond to the duration of diastole. This trend is consistent in all three MEG directions, with the MEG z direction having greater noise as compared to the other two directions.

Figure 6. Correlation lengths differ between cardiac bin 1 and bin 7 of ImPhys noise. (A) Qualitative comparison of noise in different cardiac bins. (B) Quantitative evaluation between bin

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1 and bin 7, demonstrating long correlation lengths in bin 1. Top and bottom edges of box indicate 25^{th} and 75^{th} percentiles and central line inside indicates median.

Figure 7. Simulation results for (A) Gaussian and (B) ImPhysVib noise. Simulated wave motion and OSS-SNR maps for datasets with noise to the simulation. Resultant estimated shear stiffness and damping ratio, and their differences to the low noise simulation. Image quality improves with gains in OSS-SNR. Results for simulations with Im and ImPhys noise added are shown in Supplementary Information (Figures S6 and S7).

Figure 8. Percent error (NRMSE) in property estimates for simulations with different OSS-SNR values from Gaussian, Im, ImPhys, and ImPhysVib noise added for (A) shear stiffness and (B) damping ratio. Two-term exponential fits are included to visualize trends. Error is reduced at higher OSS-SNR levels.

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SUPPLEMENTAL TABLE AND FIGURE CAPTIONS

Table S1. Mean and standard deviation of average absolute noise and FWHM of noise distributions across all phantoms.

Table S2. Mean and standard deviation of average absolute noise in cardiac bins 1 & 7 across all subjects in radians.

Table S3. Average correlation lengths and 95% confidence intervals in mm for noise observations in Cardiac Bin 1 & 7.

Figure S1. Average absolute noise for the second subject for Experiment 1.

Figure S2. Average absolute noise for the third subject for Experiment 1.

Figure S3. Histogram of noise observations for each MEG direction across all subjects. Greater spread of noise observed when MEG and vibration are on (ImPhysVib Noise), which is confirmed with larger FWHM. FWHM of distributions are reported in Table 1.

Figure S4. Average absolute noise for one phantom. Noise is overall smaller in comparison to noise in the brain. Reduced noise in the MEG y and z directions when the MEG is turned on and most noise observed in the MEG y direction with vibration.

Figure S5. Distribution of noise for phantom experiment. Noise distribution is similar amongst different MEG directions and types of noise. Decrease in peak frequency, particularly in the MEG y direction for ImPhysVib noise. FWHM is reported in Supplemental Table S1.

Figure S6. Results from simulation experiment for Im noise in Experiment 3.

Figure S7. Results from simulation experiment for ImPhys noise in Experiment 3.

Figure S8. Sagittal slices of Y-motion, real and imaginary components for ImPhysVib noise. Increased slice jitter is present at lower OSS-SNR.