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Waveguide effects and implications for cardiac magnetic resonance elastography: A finite element study

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Abstract

Magnetic resonance elastography (MRE) is increasingly being applied to thin or small structures in which wave propagation is dominated by waveguide effects, which can substantially bias stiffness results with common processing approaches. The purpose of this work was to investigate the importance of such biases and artifacts on MRE inversion results in: (i) various idealized 2D and 3D geometries with one or more dimensions that are small relative to the shear wavelength; and (ii) a realistic cardiac geometry. Finite element models were created using simple 2D geometries as well as a simplified and a realistic 3D cardiac geometry, and simulated displacements acquired by MRE from harmonic excitations from 60 to 220 Hz across a range of frequencies. The displacement wave fields were inverted with direct inversion of the Helmholtz equation with and without the application of bandpass filtering and/or the curl operator to the displacement field. In all geometries considered, and at all frequencies considered, strong biases and artifacts were present in inversion results when the curl operator was not applied. Bandpass filtering without the curl was not sufficient to yield accurate recovery. In the 3D geometries, strong biases and artifacts were present in 2D inversions even when the curl was applied, while only 3D inversions with application of the curl yielded accurate recovery of the complex shear modulus. These results establish that taking the curl of the wave field and performing a full 3D inversion are both necessary steps for accurate estimation of the shear modulus both in simple thin-walled or small structures and in a realistic cardiac geometry when using simple inversions that neglect the hydrostatic pressure term. In practice, sufficient wave amplitude, signal-to-noise ratio, and resolution will be required to achieve accurate results.

Keywords

cardiac elastography; cardiac MRE; elastography; finite element modeling; MR elastography; myocardial stiffness; shear waves; waveguide

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

1 | INTRODUCTION

Magnetic resonance elastography (MRE) non-invasively measures mechanical material parameters, such as shear modulus, in soft tissue. In MRE, an external source generates shear waves in a tissue of interest. A phase contrast based MRI technique then measures the vibrational displacements as they propagate through the tissue. Finally, the displacement field is inverted to generate a map of material properties.^{1,2} MRE has proven clinically useful in liver^{3–5} and is showing promise for clinical applications in the brain,^{6–8} and many other possible applications are being explored.

In some of these applications, thin or small structures are being investigated.^{9–11} Waveguide or boundary effects can dominate wave propagation in such structures as the ratio of the thinnest dimension to the wavelength falls below unity, in which case the propagation of the mechanical wave depends critically on geometry as well as on the underlying material properties. In particular, cardiac MRE, which is being investigated by several groups,^{12–16} is prone to these waveguide effects. The thickness of the myocardium is smaller than MRE wavelengths at current MRE driving frequencies, and waveguide behavior is clearly present. Many MRE processing approaches that do not properly account for the hydrostatic pressure term can yield biased results in these situations.

It is known that applying the curl operator to the displacement field can in principle remove waveguide effects due to longitudinal waves, leaving only a field that propagates at the shear wave speed, although at the expense of noise amplification.^{17–20} The purpose of this work is to investigate the importance of biases and artifacts due to waveguide effects on MRE inversions based on the Helmholtz equation in: (i) various idealized 2D and 3D geometries with one or more dimensions that are small relative to the shear wavelength; and (ii) both a simplified and a realistic cardiac geometry. We focus primarily on comparing results with and without applying the curl operator and with and without bandpass filtering, and testing both 2D and 3D processing for the realistic cardiac geometry.

2 | THEORY

Elastography is exceptionally difficult in the diastolic left ventricular myocardium, which has a wall that is normally between 8 and 13 mm thick.²¹ Since the thickness of the myocardium is smaller than typical MRE shear wavelengths at common driving frequencies, waveguide effects dominate the wave propagation, and incorrect stiffness estimates may result if these are not accounted for.

The equation of motion for homogeneous, isotropic, linear viscoelastic materials under harmonic excitation is

$$G \nabla^2 \mathbf{u} + (\lambda + G) \nabla (\nabla \cdot \mathbf{u}) = -\rho \omega^2 \mathbf{u}$$

where $\mathbf{u}$ is the harmonic displacement vector, ρ is the density of the material, ω is the angular frequency of the mechanical oscillation, and λ and G are the Lamé parameters.² If the material is purely elastic, only two types of wave can propagate inside the material:

longitudinal (compressional) waves that propagate with a wave speed of $c_L = \sqrt{(\lambda + 2G)/\rho}$ and shear waves that propagate with a wave speed of $c_s = \sqrt{G/\rho}$. If the material is viscoelastic, the wave speeds are affected by the viscosity, e.g. the shear wave speed becomes $c_s = 1/\text{Re}(\sqrt{\rho/G^*})$, where G^* is the complex shear modulus. The real part of the complex shear modulus G^* is usually denoted as the storage modulus, G' , while the imaginary part is the loss modulus G'' .

Soft tissue is almost incompressible, and $\lambda \gg G$, and $c_L \gg c_s$. In general, the wavelength of the longitudinal wave is very long in soft tissues, and $\nabla \cdot \mathbf{u}$ is very small. This makes accurate estimation of λ very challenging. However, λ is large, and in general $\lambda(\nabla \cdot \mathbf{u})$ is not negligible.¹⁷ Thus this term, sometimes called the pressure or hydrostatic pressure term, must be accounted for or its contribution removed from the displacement data to accurately estimate G . While some MRE inversions attempt to properly account for this term,^{22,23} these approaches tend to be computationally intensive, and simpler inversions that neglect this term are more commonly used, such as those described below.

If the $\nabla \cdot \mathbf{u}$ term is neglected, the equation above reduces to the Helmholtz equation, on which many common MRE inversions are based²:

$$G \nabla^2 \mathbf{u} = -\rho \omega^2 \mathbf{u}$$

Ignoring the $\nabla \cdot \mathbf{u}$ term is also implicit in methods that estimate the wave speed or wavelength, such as local frequency estimation (LFE) or phase gradient (PG), as well as more fundamental approaches such as direct inversion (DI) that are based on the equations of motion. For all such methods, the longitudinal wave must be removed to obtain an accurate estimate of G . Obtaining a correct answer thus becomes a question of how to process the wave field to remove the longitudinal contribution before presenting it to the inversion algorithm.

It is possible to partially filter out the effects of the longitudinal wave, since its wavelength is usually long and thus its contributions are at very low spatial frequency. This is typically done by applying a spatial frequency filter to the displacement data, to remove longer wavelengths that are considered to be due to the longitudinal waves, while keeping shorter wavelengths considered to represent shear waves. Typically, very short wavelengths that are considered to be noise are also removed, making the filter a bandpass filter.²⁴ This approach often works only to a limited extent, partly because soft tissue is viscoelastic and the spatial frequency spectra of the waves expand and overlap. In practice results are often sensitive to the exact filter shape and cutoffs used.

Contributions from longitudinal waves (often called hydrostatic effects) can also be eliminated in principle by applying the curl operator to Equation 1, leaving simply

$$G \nabla^2 (\nabla \times \mathbf{u}) = -\rho \omega^2 (\nabla \times \mathbf{u})$$

and then inverting the curled displacement field.^{17,18,25–28} This is theoretically correct in a homogeneous isotropic object, since the part of $\mathbf{u}$ due to compressional waves is curl free, and taking the curl of $\mathbf{u}$ leaves only contributions due to shear waves. However, in practice, noise-corrupted empirical estimates of $\mathbf{u}$ are used when solving for stiffness, in which case this equality is not expected to hold exactly. As both the curl and Laplacian are comprised of differential operations, noise amplification is a practical concern that must be addressed.

The above analysis is true in objects of any size. Near a boundary, or in small or thin objects with at least one dimension smaller than the wavelength, waveguide or boundary effects can dominate wave behavior and the propagation of the mechanical wave depends on geometry as well as on the underlying material properties. For example, Lamb waves in a thin plate have their own characteristic displacement pattern, and propagate at the Lamb wave speed, different from either the longitudinal or shear wave speeds above. However, inside the material, only longitudinal and shear waves with their characteristic wave speeds are possible. Guided waves must therefore represent combinations of longitudinal and shear waves with amplitudes, phases and propagation directions set by the boundary conditions. This applies even close to the boundary, as long as one is far enough inside that local derivatives can be taken from data entirely within the object. Waveguide effects due to longitudinal waves can thus be eliminated in principle by inverting the curl of the displacement field.^{17–20} Since the remaining wave field represents only shear waves with amplitudes, phases, and propagation directions set by the boundary conditions, but all moving at the shear wave speed, stiffness estimates based on these wave fields are free from waveguide artifacts except where the remaining wave field has nodes.

3. | METHODS

3.1 | Finite element models

The finite element models (FEMs) were created in COMSOL 5.0 (COMSOL, Burlington, MA, USA) for the 2D geometries and ANSYS 16.1 (ANSYS, Canonsburg, PA, USA) for the 3D cardiac geometry models (ANSYS was required for its memory efficient parallel solver capability for large systems of equations). A linear viscoelastic material was defined for both approaches based on a complex shear modulus G^* of $4 + 1i$ kPa (thought to be close to the properties of the diastolic heart),^{16,29} Poisson's ratio of 0.499995, and mass density of 1 g/cm^3 . In COMSOL, the inputs for complex shear modulus were entered directly into the linear elastic material definition for Young's modulus, and in ANSYS a tabular input was defined using the "tb,expe" option of the linear viscoelasticity Prony series method of input, with the real component defined as the shear storage modulus and the imaginary component defined as the shear loss modulus. Isotropic materials were assumed for simplicity. The equivalent of each software's direct linear equation solver was used to solve the system of equations at each requested frequency using a full harmonic analysis approach. FEM simulations were run at driving frequencies of 60, 80, 100, 140, 180, and 220 Hz.

3.1.1 | 2D finite element models—The 2D FEM geometries were modeled with the plane strain approximation and consisted of rectangles of varying dimensions (5×5 , 10×10 , 20×20 , 10×200 , 20×200 , 100×200 and 200×200 ; all dimensions in mm). Element

types consisted of the hybrid formulation (mixed) with second order displacement and linear pressure terms. The analyses employed a hybrid element formulation that includes hydrostatic pressure as an independently solved variable. This mixed displacement-pressure formulation helps to stabilize the calculated nodal displacements for nearly incompressible materials. The element spacing of 0.1 mm was chosen based on successive mesh refinements of the smallest rectangle model (5 mm $\times$ 5 mm) until the inversion results were unaffected by additional refinements. Two sets of boundary condition constraints were considered for each rectangle geometry (“free” and “fixed”), where “free” refers to the case where no nodes were constrained at the non-excited boundaries, and “fixed” refers to the case where all nodes on the non-excited edges were fully constrained. Since the actual forces on the myocardium wall are unknown, these two extremes were chosen to bracket the harmonic response and explore how sensitive the inversion results were to the boundary conditions. Three different types of harmonic displacement were applied at the left-hand edge: shear displacement with 0.05 mm amplitude, longitudinal displacement with 0.05 mm amplitude, and both of these together (“mixed driving”). The models ranged from about 2500 elements with 46 000 degrees of freedom for the 5 mm $\times$ 5 mm cases to about 1 million elements with about 18 million degrees of freedom for the 100 mm $\times$ 200 mm cases. The 2D simulations were conducted on an HP Z840 20-core workstation with 96 GB of memory.

3.1.2 | 3D finite element models—The 3D FEM geometries consisted of: (i) a hollow hemispherical geometry with internal partition wall (“simplified heart geometry”); and (ii) a two-chamber realistic cardiac geometry derived from patient anatomy (“realistic heart geometry”), which is further described below. The hemispherical geometry had an outer diameter of 90 mm and the wall thickness of both the hollow hemisphere and partition wall was 5 mm. The model consisted of quadratic tetrahedral elements of varying sizes, ranging from about 0.35 mm resolution in one sector of the heart (the area to be analyzed) to 2 mm resolution in areas far away from this sector, meant to simply capture overall behavior to establish reasonable boundary conditions for the high-resolution sector. The resulting mesh contained about 2.5 million nodes with about 10.3 million degrees of freedom. The displacement results were interpolated onto a 0.5 mm Cartesian grid. The boundary conditions were chosen such that each of the three degrees of freedom was fixed on the flat upper surface of the hemispherical geometry, with free boundary conditions elsewhere. A group of exterior nodes at the base of the sphere representing the apex of the heart was selected and defined as the excitation nodes, and driven with either shear or longitudinal harmonic displacement of 0.05 mm.

The 3D realistic geometry of the ventricles was obtained from a segmented ECG-gated computed tomography image volume of a patient’s heart in diastole. The scan was of a 36-year-old female who was asymptomatic with hyperlipidemia but no other cardiac history.¹⁵ The CT scan of the patient was performed on a Somatom Definition scanner (Siemens Medical Systems, Erlangen, Germany) after 5 mg oral metoprolol, 0.4 mg of nitroglycerine sublingual, and intravenous injection of 80 mL of Omnipaque 350 (GE Healthcare, Milwaukee, WI, USA). Scan parameters were gantry rotation = 330 ms, kVp = 100, mA = 451, FOV = 200 mm, collimation = dual source 64 $\times$ 0.6, slice thickness = 0.75 mm, and increment = 0.4 mm. The cardiac geometry was segmented from the CT scan with a

threshold level sufficient to distinguish it from the surrounding air using Mimics software (Materialise, Leuven, Belgium), and this was used as the input geometry to the FEM models. The model consisted of linear hexahedral elements converted directly from the segmented CT voxels with $0.29 \text{ mm} \times 0.29 \text{ mm} \times 0.2 \text{ mm}$ resolution and contained about 7 million nodes with about 22 million degrees of freedom. Boundary conditions consisted of fully constraining the nodes on the most superior face of the heart wall geometry in all degrees of freedom, with free boundary conditions elsewhere. A harmonic displacement excitation with 0.05 mm amplitude was applied in either a shear or longitudinal direction to a group of exterior nodes at the base of the geometry at various frequencies from 60 to 220 Hz.

The 3D FEM mesh configurations discussed above represented the highest resolution grid that could be solved on our high-performance computing server (Penguin Computing Relion 1900 server with 24 computational cores and 768 GB of random access memory). To confirm that the element formulations and mesh sizes chosen were providing sufficiently accurate displacement results for the frequency range of interest, the meshes were unrefined once to confirm that MRE inversions showed inversion result differences of less than 0.01 kPa between the different grid sizes across the range of frequencies.

3.2 | Inversion algorithm

The shear modulus was calculated by direct inversion (DI) of the Helmholtz equation on either the displacement, bandpass filtered, or curled wave field.² The data was smoothed with a 5×5 Gaussian filter, since, despite being the output of FEM simulations, it had a small amount of quantization noise and discretization error. Spatial derivatives for the curl and Laplacian were taken using a four-nearest- (2D) or six-nearest- (3D) neighbor kernel at the resolution of the FEM data (which varied with the type of simulation). A tissue density of 1 g/cm^3 was assumed. The DI algorithm solved the Helmholtz equation simultaneously in a least squares fashion for all components of motion as follows, similar to AIDE³⁰ or MDEV with a single frequency³¹:

$$G = -\rho\omega^2(\nabla^2 \mathbf{u})\mathbf{u} / (|\nabla^2 \mathbf{u}|^2 + \epsilon)$$

where G is the shear modulus, the $\mathbf{u}$ vector represents the 2D or 3D (2×1 or 3×1) displacement, filtered displacement, or curl components at a single voxel, ρ is the density (assumed to be equal to that of water), ω is the angular velocity, ∇^2 is the 2D or 3D Laplace operator, $*$ denotes the conjugate transpose, and ϵ is a Tikhonov regularization parameter to avoid division by very small numbers, which was set to 10^{-6} times the median value of $|\nabla^2 \mathbf{u}|^2$.

4 | RESULTS

4.1 | 2D thin rectangle results

In the 2D FEM models, results obtained without applying the curl were incorrect, with biased complex shear modulus values and many artifacts, while the results obtained by applying the curl were almost always uniform and correct. Sample results for one of the 10

mm x 200 mm 2D rectangular simulations are shown in Figure 1 (in all 2D figures, x is the horizontal direction and y is the vertical direction). Shear excitation across the entire left-hand side of the object was used, driven at an excitation frequency of 60 Hz, with free boundary conditions on the other three sides. The top row shows a sample displacement field in the actual object, while the second row shows the displacement field in a similarly sized central region inside a much larger object. The latter illustrates what we will term the “natural” wavelength of the simulated material, the wavelength inside a large homogeneous object of this material, far from the boundary, whereas the former shows that the apparent wavelength can vary dramatically with waveguide effects. The natural wavelength for this material ($G^* = 4.0 + 1.0i$ kPa, $|G^*| = 4.12$ kPa, wave speed = 2.05 m/s, density $\times$ wave speed squared = 4.19 kPa) is about 34.1 mm at 60 Hz, so the width of this object is less than one-third of the natural wavelength. The results obtained without the curl showed $|G^*|$ values generally much lower than the correct value, with artifacts on the side furthest from the driving source, and $|G^*|$ values inside the region of interest (ROI) shown in Figure 1(c) of 2.47 ± 0.24 kPa. Conversely, the $|G^*|$ results with the curl are uniform and correct, with the values inside the same ROI being 4.12 ± 0.08 kPa. The storage and loss modulus values are uniform and correct with the curl (4.00 ± 0.08 kPa and 1.00 ± 0.04 kPa), while the values without the curl are 2.41 ± 0.22 kPa and 0.46 ± 0.34 kPa.

Driving at higher frequencies decreased the biases associated with waveguide effects, though they were still present, while applying the curl continued to produce correct results. Figure 2 summarizes stiffness results for various 10 mm $\times$ 200 mm simulations at 180 Hz, with all combinations of free or fixed boundary conditions and shear or longitudinal driving. At this high frequency the waves often attenuated below the precision limit of the simulation well before propagating the length of the FEM rectangle, and beyond this point all inversions failed. Here the natural wavelength is about 11.4 mm, so the object is only slightly thinner than the natural wavelength, and waveguide effects are expected to be present but not as severe as in the 60 Hz case. For the case of shear driving with free boundary conditions (analogous to Figure 1), the results without the curl were much closer to the correct values than at 60 Hz, but were still biased and contained artifacts ($|G^*|$ values were 3.59 ± 0.24 kPa within the ROI shown), while results with the curl were correct (4.12 ± 0.004 kPa), although attenuation affected the results beyond about 100 mm. For shear driving with fixed boundary conditions, attenuation effects were much more severe, and results were only obtainable for about 30 mm, but again the curl result was correct in this area (4.12 ± 0.11 kPa) while the non-curl inversion had difficulty (4.52 ± 1.59 kPa). For longitudinal driving, the non-curl inversion performed poorly with free boundaries (3.66 ± 0.82 kPa), and very poorly with fixed boundaries (12.00 ± 4.37 kPa); in both cases, the curl-based inversion performed well up to the attenuation limit (4.09 ± 0.37 kPa and 4.12 ± 0.004 kPa respectively). Table S1 (all Tables are in the Supplementary Materials) shows the numerical results within the ROI (chosen to be within the attenuation limit in all cases) for the four simulations, including storage and loss modulus values, which show similar patterns.

Scenarios at intermediate frequencies between 60 and 180 Hz (not shown) behaved in the expected intermediate fashion: as one moved from lower to higher vibrational frequencies, the wavelengths became shorter, leading to reduced biases and artifacts from waveguide effects, and improved (but still incorrect) results without the curl, and the waves attenuated

more quickly. In all cases applying the curl led to correct results (including correct storage and loss modulus values) and much lower standard deviations than without the curl. Similarly, scenarios with wider rectangles (20 mm × 200 mm and 100 mm × 200 mm) behaved as expected, with inversions without the curl gradually improving as objects became wider, and inversions with the curl always giving accurate results.

4.2 | 2D small square results

Similar results were obtained in the 2D squares. Sample results for the 20 mm x 20 mm 2D square object are shown in Figure 3 at 60 Hz and 180 Hz, with shear driving across the bottom side and free or fixed boundary conditions on the other three sides. The natural wavelengths for the material modeled were about 34.1 mm at 60 Hz and about 11.4 mm at 180 Hz, so at 60 Hz the object size was about 0.6 times the natural wavelength. As before, inversions without the curl varied depending on the boundary conditions and driving method, but were inaccurate and contained artifacts in all cases. The artifacts were much worse at 60 Hz, while at 180 Hz, with the object size about 1.8 times the natural wavelength, the artifacts still existed but were more modest and concentrated near the edges. Inversions with the curl were accurate in all cases, although artifacts were observed in the 60 Hz fixed boundaries case, corresponding to the nodes of the standing wave. Table S2 shows the numerical results within the ROI for the four simulations, highlighting the incorrect results and much higher standard deviations obtained without the curl, particularly in the fixed boundary cases. Inversions with the curl were always within 0.01 kPa of the correct mean values, with standard deviations less than 0.003 kPa except for the difficult 60 Hz fixed boundary case (0.013 kPa). Inversions without the curl had mean values ranging from 2.86 ± 0.36 kPa to 4.28 ± 6.51 kPa.

Sample results for the 5 mm x 5 mm 2D square object are shown in Figure 4 at 60 Hz and 180 Hz. At 60 Hz the object size was about one-sixth of the natural wavelength, while at 180 Hz the object size was about one-half of the natural wavelength. As before, but amplified in this smaller object, inversions without the curl were very inaccurate and contained artifacts in all cases (1.87 ± 5.97 kPa to 5.30 ± 6.56 kPa at 180 Hz; much worse at 60 Hz). Inversions with the curl were remarkably good for the cases with free boundaries (means within 0.01 kPa of the correct value, standard deviations <0.06 kPa), and had problems in the 180 Hz fixed boundary case only in the areas of the nodes. In the 60 Hz fixed boundary case, these problems amplified, and significant noise was present in the solution (4.08 ± 1.59 kPa), indicating that the calculated FEM displacements were reaching the limits of accuracy (due to finite precision and spatial discretization) in modeling such a challenging situation of standing waves in a very small object. Table S3 shows the numerical results within the ROI for the four simulations, including the storage and loss modulus, and showing the difficulties the curl-based inversion had in the fixed boundary cases, particularly at 60 Hz, but also showing the very incorrect results and much higher standard deviations obtained without the curl in all cases.

4.3 | Simplified 3D hemispherical geometry results

In the 3D hemispherical geometry, inversions without the curl were inaccurate, while applying the curl yielded accurate results. The 3D hemispherical geometry results are shown

in Figure 5 for the shear excitation, 100 Hz case. As above, inversions without the curl had strong artifacts, and the $|G^*|$ values along the profile shown in Figure 5(c) were 2.93 ± 1.30 kPa. Applying the curl yielded much more uniform although slightly underestimated results of 3.97 ± 0.04 kPa for $|G^*|$ (and only slightly different results for the storage modulus) and 0.94 ± 0.03 kPa for the loss modulus. The slight underestimates were due to edge effects (which occur when the derivatives used in the curl and inversion extend beyond the edge of the object) due to the larger voxel spacing.

4.4 | Realistic 3D cardiac geometry results

Similar results were obtained in the 3D realistic cardiac geometry. Figure 6 shows the realistic cardiac geometry for longitudinal excitation at the apex at 100 Hz, and a sample displacement field. Red values signify positive $\times$ displacement and blue values signify negative $\times$ displacement. Figures 7 and 8 show results for this geometry at 80 Hz and 140 Hz, with the same longitudinal driving at the apex. Results without the curl (Figure 7) were incorrect and showed many artifacts, with both 2D and 3D inversions, with 3D inversions yielding systematically lower values. These results ranged from 2.28 ± 0.89 to 4.32 ± 1.87 kPa for an ROI consisting of the heart mask as shown, eroded by three additional pixels in 3D, and removing the upper quarter or so of the image. The results with the curl but using only 2D inversions, while somewhat improved compared with not using the curl, were incorrect with numerous artifacts (Figure 8, top; ROI results 3.96 ± 1.53 and 4.65 ± 2.38 kPa at 80 and 140 Hz respectively). Results with the curl with 3D inversion (Figure 8, bottom) were fairly uniform and report the correct mean value (4.13 ± 0.11 and 4.13 ± 0.06 kPa at 80 and 140 Hz) to within 0.1 kPa and with a standard deviation around 0.1 kPa. Storage and loss modulus results for the 3D inversions with the curl at 80 Hz are shown in Figure 9, and the values along the profile show accurate recovery of both parameters. Table S4 shows the numerical results for the ROI shown in Figure 8 for all of these cases, including storage and loss modulus results, which show similar patterns.

Figure 10 shows results with shear driving instead of longitudinal driving at the apex, at both 80 Hz and 140 Hz, with 3D inversions with and without application of the curl. The results, summarized in Table S5 for the same ROI as before, were similar to longitudinal driving: results without the curl were incorrect and showed many artifacts (4.03 ± 1.03 and 4.24 ± 0.99 kPa at 80 and 140 Hz), while results with the curl were accurate to within 0.1 kPa with a standard deviation around 0.1 kPa as before. As before, 2D inversions (not shown) were insufficient to recover accurate values, and 2D inversions after the curl performed particularly poorly, with very high standard deviations. Similar patterns in the results occurred with both types of driving at other frequencies (60–220 Hz, not shown), with biases being more severe at lower frequencies due to stronger waveguide effects.

4.5 | Bandpass filter results

An alternative to applying the curl operator that is sometimes employed to remove longitudinal waves is to perform spatial bandpass filtering, to filter out the very long wavelengths expected for longitudinal waves in soft tissue. This can work well in large homogeneous objects, although the results tend to depend on the exact filter cutoffs used. However, bandpass filters tend to have a large point spread function, and in these narrow

objects information from outside the object is likely to contaminate the data and confound the results. Figure 11 shows results for bandpass filtering on the 3D heart model, using a 3D fourth-order Butterworth filter with cutoffs of 11 and 440/m. Bandpass filtering instead of the curl yielded poor results (4.04 ± 6.74 kPa), and interestingly bandpass filtering in combination with the curl yielded poor results as well (1.64 ± 2.42 kPa). These results are representative, and results from varying the cutoffs or from performing only 2D direction filtering with eight equally angularly spaced filters were qualitatively similar. Table S6 summarizes results for all these cases and for storage and loss modulus as well.

Additional insight can be gained by considering the $10 \text{ mm} \times 200 \text{ mm}$ rectangles from Figures 1 and 2. Figure 11 shows the results of applying bandpass filtering (cutoffs of 11 and 440/m) to the shear driving, free boundary condition case of Figure 1 (60 Hz), with ROI results summarized in Table S7. Bandpass filtering again yielded poor results (2.49 ± 0.28 kPa), and results with the curl had very high standard deviations (4.24 ± 7.03 kPa). Again, these results are representative, and results with different cutoffs were similar.

5 | DISCUSSION

The study showed that waveguide effects lead to artifacts and biases in MRE DI inversions based on the Helmholtz equation in idealized 2D and 3D geometries with one or more small dimensions, and in a realistic cardiac geometry as well. Applying the curl operator to the displacement field leads to correct MRE DI inversion results in all these cases. Bandpass filtering did not lead to correct results, even when the curl was applied to the filtered displacement field.

To date, the removal of waveguide effects with the curl has only been validated to a limited degree, with analytical models and simple phantoms.^{17–20} Nenadic et al. showed that application of the curl to anti-symmetric Lamb waves in thin plates (which propagate at the Lamb wave speed) results in a wave field that propagates at the shear wave speed, and demonstrated this analytically, in simulations, and in experiments.^{18,19} This holds for Rayleigh waves as well, which are the limiting case of Lamb waves as the plate becomes thicker.¹⁹ Baghani et al. demonstrated analytically how axisymmetric waves in a cylindrical waveguide are composed of longitudinal and shear components, with the curl recovering the true shear wave speed.²⁰ Sinkus et al. demonstrated biased answers without the curl but correct answers with the curl in a set of simple FEMs of a 2D rectangle.¹⁷ The 2D results here confirm these findings, and additionally show that applying the curl operator can lead to correct recovery of complex shear modulus values even in remarkably small structures, with dimensions as small as one-sixth of the wavelength, and under a variety of boundary conditions and mechanical excitations. The only remaining artifacts due to waveguide effects are difficulties at nodes of the wave field (e.g. in Figures 3 and 4). Such artifacts can to a large extent be handled by acquiring and inverting multiple different wave fields, for which the nodes are in different locations.

Removal of waveguide effects with the curl has not been validated in complex, realistic geometries, and in particular in a geometrically accurate geometry of the human left ventricle. The results here show that substantial biases and artifacts due to waveguide effects

can occur in this geometry at current MRE driving frequencies. The effects become smaller at higher driving frequencies, as the wavelength becomes smaller relative to the myocardial thickness. However, attenuation will become more of a problem in realistic situations, and wavelengths small enough to be completely isolated from waveguide effects in a thin myocardium would require higher frequencies than are currently practical. Also, since MRI resolution is of the order of millimeters, such small wavelengths cannot be adequately sampled with current acquisition schemes. However, applying the curl and performing full 3D direct inversion allows accurate recovery of the complex shear modulus. This is the first demonstration that full 3D MRE can, in principle, give accurate shear modulus measurements for a geometrically accurate, diastolic cardiac geometry with strong waveguide effects, at vibration frequencies of 60–220 Hz, by applying the curl operator to the displacement field. Results without applying the curl, even with band-pass filtering, were biased and contained numerous artifacts, as were results with the curl but using only 2D inversion, or results with the curl applying band-pass filtering as well. These inaccurate results occurred even with noise-free data and very high spatial resolution.

These conclusions should apply to all techniques based on inversion of the Helmholtz equation of the acquired wave field, or any other techniques that neglect longitudinal waves. In addition to all types of direct inversion, this includes common processing algorithms such as local frequency estimation (LFE) or phase gradient (PG) after directional filtering.² An additional consideration with LFE and PG is that the point spread function of the filters used in LFE and the directional filters usually required for PG imply that data from outside the object may blur into and contaminate results well inside the object, so these techniques are not suitable for very thin objects. On the other hand, these techniques are potentially more resistant to noise, since they only take first derivatives of the wave field. MRE inversion techniques that solve the full equation of motion and explicitly account for the pressure term^{22,23} should handle waveguide effects correctly in principle, although this has not yet been demonstrated to our knowledge.

This study had several limitations. The models assumed a homogeneous object and isotropic material properties, which is of course highly simplified compared with actual physiology. The models assumed isotropic material properties, whereas the myocardium is composed of muscle fibers with anisotropic mechanical properties with the fiber directions varying in a complex manner. Most current cardiac MRE approaches assume an isotropic material and derive an overall “effective” stiffness, although it has been shown that such results can vary in anisotropic materials when different types of excitation are applied, leading to waves that propagate in different directions relative to the fibers.³² While some anisotropic MRE inversions have been proposed, this remains very much an area of research with limited validation, and to our knowledge no such techniques have been applied to the heart.

The mechanical excitation imposed on the models in our simulations consisted simply of longitudinal or shear driving at the apex, whereas in actual cardiac MRE the waves are applied to the surface of the body and the manner in which waves are excited in the heart is complex and not well understood. The simulations also considered only the case of free boundary conditions for the heart, since this was deemed more appropriate than fixed boundary conditions. In reality, the boundary conditions are complicated and the heart is

6. | CONCLUSIONS

This work has studied the impact of waveguide effects on the processing of MRE data when using simple inversions that neglect the hydrostatic pressure term, and particularly in a realistic cardiac geometry. Substantial biases can occur if waveguide effects are not taken into account, and these effects are worse at lower frequencies. The results show that in principle, in homogeneous, isotropic materials, applying the curl operator allows for accurate recovery of the complex shear modulus in objects with waveguide effects in a wide variety of geometries. This holds true even in quite small objects with dimensions only a small fraction of the wavelength. In a realistic cardiac geometry, these results establish that, at a minimum, taking the curl of the wave field and performing a full 3D inversion are both necessary (although not sufficient) steps for accurate estimation of shear modulus with such inversions. Simple bandpass filtering fails in all these cases, because the narrowness of the structures implies that information from outside the object contaminates the data. These results should generalize to small or thin-walled structures in general. Whether MRE driving and acquisition techniques can produce sufficient wave amplitude, SNR, and resolution to yield accurate results in practice remains an open question.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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FIGURE 1.

Sample results for the 10 mm $\times$ 200 mm phantom with free boundary conditions and shear driving across the entire left edge at 60 Hz: (a) the y displacement field at one time point, (b) the y displacement field from a central section of a much larger object at the same time point, (c) $|G^*|$ inversion results without and with applying the curl, (d) storage and loss modulus results applying the curl, and (e) profiles across these storage and loss modulus results

FIGURE 2.

Sample $|G^*|$ inversion results for the 10 mm $\times$ 200 mm phantom with free and fixed boundary conditions and driving across the entire left edge at 180 Hz: (a) the y displacement field for the object at one time point with shear driving and free boundary conditions, (b) the y displacement field from a central section of a much larger object at the same time point with shear driving and free boundary conditions, (c) results without and with the curl for shear driving with free boundaries, (d) results without and with the curl for shear driving with fixed boundaries, (e) results without and with the curl for longitudinal driving with free boundaries, and (f) results without and with the curl for longitudinal driving with fixed boundaries

FIGURE 3.

Sample $|G^*|$ results for the $20 \text{ mm} \times 20 \text{ mm}$ square, with shear driving across the entire bottom face: top row, 60 Hz excitation, fixed boundary conditions without and with the curl, free boundary conditions without and with the curl; bottom row, same simulations with 180 Hz excitation

FIGURE 4.

Sample $|G^*|$ results for the $5 \text{ mm} \times 5 \text{ mm}$ square, with shear driving across the entire bottom face: top row, 60 Hz excitation, fixed boundary conditions without and with the curl, free boundary conditions without and with the curl; second row, same simulations with 180 Hz excitation. The natural wavelength is about six times the size of the object in the 60 Hz case

Color scale in kPa (correct answer = 4.12 kPa for stiffness, 1.0 for loss modulus)

FIGURE 5.

Sample results for the hemispherical simplified cardiac geometry: (a) the model, showing regions with different FEM grid spacings; (b) a sample x-component displacement image for the model driven with shear excitation at 100 Hz (red, positive x displacement; blue, negative); (c) the $|G^*|$ results without the curl applied in a slice through the center of the 0.35 mm spacing sector; (d) the $|G^*|$ results with the curl applied; (e) the loss modulus results with the curl applied

FIGURE 6.
The realistic cardiac geometry, and the x component of the displacement field for the 100 Hz case with longitudinal driving at the apex

FIGURE 7.

$|\mathcal{G}^*|$ results from direct inversion without applying the curl operator to the displacement field at 80 and 140 Hz with longitudinal driving at the apex. The area shown has been eroded once to ensure that only information inside the object is used in the results shown. Numerous artifacts and systematic biases are present throughout both the 2D and 3D inversions

Inversion results with the curl operator

FIGURE 8.

$|\mathcal{G}^*|$ results from direct inversion after applying the curl operator to the displacement field at 80 and 140 Hz with longitudinal driving at the apex. The area shown is thinner than in Figure 7 since another pixel has been eroded to account for use of the curl. The answer is essentially correct with 3D inversion, while inaccuracies and artifacts remain in the 2D inversion

FIGURE 9.

The storage and loss modulus for the 80 Hz, with curl, 3D results in Figure 8, showing correct recovery of both quantities (true values = 4.0 and 1.0 kPa)

Inversion results with shear driving

FIGURE 10.

$|G^*|$ results from 3D direct inversion for simulations with shear driving at the apex at 80 Hz and 140 Hz. The curl results are thinner than those without the curl since another pixel has been eroded to account for the additional derivative operator. The answer is essentially correct with the curl, while inaccuracies and artifacts remain without the curl for both inversions

FIGURE 11.

$|G^*|$ results using bandpass filtering: first two rows, for the 80 Hz heart model from Figure 8–2D filtering (top left), 3D filtering (top right), 2D filtering followed by the curl (middle left), and 3D filtering followed by the curl (middle right); bottom row, for the 10 mm $\times$ 200 mm model from Figure 1 after 2D filtering, without and with the curl