

Utilizing MR Elastography to Visualize Higher Harmonic Components of Wave Propagation in Phantoms with Interfaces

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Synopsis

While MRE can be used to calculate mechanical properties of tissue, bio-interfaces can cause distortions in the shear-wave propagation patterns which are difficult to account for with current MRE techniques. Therefore, we utilized three specialized MRE sequences to visualize the first three harmonics of wave propagation in phantoms with simulated bio-interfaces. We were able to measure the doubling and tripling of wave number in the phantoms excited at the fundamental vibration frequency using this optimized MRE protocol. We characterized differences in wave propagation at higher harmonics along phantom interfaces, and observed substantial differences in wave characteristics based on adhesion level.

Introduction

Most tissues consist of multiple layers, membranes, and abnormalities such as tumors, all of which interact through bio-interfaces. Techniques such as MR Elastography (MRE)¹ are meant to calculate homogenized properties such as compliance and loss factors of biomaterials in vivo but fail to predict the essential mechanics of and around bio-interfaces due to distortions in the shear-wave propagation patterns. Therefore, developing more accurate models for wave propagation near bio-interfaces (especially low-adhesion interfaces) would be of prime importance for mechanical parameter estimation. Additionally, using more complex analysis techniques of wave propagation, such as investigating the reflection and refraction of higher harmonics of applied waves, could allow us to create metrics for adhesion in-vivo (e.g., tumor tissue interface)². In this study, we therefore used phantom models with interfaces of various adhesion levels, along with specialized MRE sequences, to visualize wave propagation of the first, second, and third harmonic of applied vibration to investigate changes in wave propagation.

Methods

Using Knox gelatin, three different 3.5% w/w phantom configurations were made in 4in. cube containers. The first configuration was a single solid block that was allowed to cure in a 4°C refrigerator overnight. For the two layered configurations, two of the 4in. cube containers were filled halfway with the liquid phantom mixture before being cured. These phantoms were then stacked on top of each other, one after being pat dry (to create a sticky interface) and the other with oil added between the layers (to create a slippery interface). MRE³ was then performed on these phantoms using a Siemens 3T Prisma MRI scanner with a 48-channel head coil (Siemens Healthineers), and a custom piezoelectric actuator^{4,5} with 50 Hz mechanical vibration applied perpendicular to the layer boundary (Figure 1). Three custom MRE sequences were used, all with 2.5 mm isotropic resolution, 20 phase offsets, GRAPPA 3, TR 6720 ms, TE 69 ms, and encoding frequency 50 Hz.

The first sequence was used to capture the main harmonic of vibration (50 Hz, as applied by the mechanical actuator) over one period in all three orthogonal directions, while the second and third were used to capture the second harmonic of vibration over two periods (100 Hz) and third harmonic of vibration over three periods (150 Hz) respectively. This was accomplished, despite not changing the mechanical vibration frequency, by using an encoding frequency of 50 Hz but a fractional encoding factor of 0.5 (or 0.35 for third harmonic) with 2 encoding gradients (or 3 for third harmonic) such that a full 50 Hz period could be captured, but this period would be encoded with two (or three) abutting 100 Hz (or 150 Hz) encoding gradients. In doing this, we maximize sensitivity of the encoding to 100Hz or 150Hz while keeping phase offsets the same. We then visualize both the spatial wavelength of vibration in all three of our phantoms at the first, second, and third harmonic (Figure 2), as well as the temporal frequency response in all cases (Figure 3).

To determine the effect of boundary conditions on wave propagation, we investigated a region of interest above and a region below the boundary (or just one region at the top of the phantom and one region below for the case with no interface) by taking the average amplitude of the frequency response both locations. We then took the ratio of top region amplitude to bottom region amplitude to determine any differences in wave transmission for the given harmonics (Table 1).

Results

We were able to measure the doubling and tripling of wave number in the phantoms excited at the fundamental vibration frequency using this optimized MRE protocol (Figure 2). From the frequency response plots, the main component is the first harmonic in our first sequence, while for the second sequence, the main component is the second harmonic; in the third sequence, while the main component is the first harmonic (likely due to spectral leakage), the third harmonic component is amplified over all other components (Figure 3). There are also trends of either increased or decreased wave amplitude on either side of the interface based on adhesion level and harmonic (Table 1). For instance, oiled and sticky interfaces have 38% and 14% more third harmonic wave propagation compared respectively to the no interface phantom (in the direction of wave propagation).

Discussion

In the future, we plan to further analyze this data and attempt to by investigating transmission and reflection coefficients of shear-horizontal wave scattering in each encoding direction. As demonstrated here, we observed an increased level of higher harmonics in phantoms with lower adhesion levels, which implies that we can potentially use these wave propagation characteristics to quantify the level of adhesion in phantoms and tissues. We also have plans to create 3-D printed phantoms with well-defined boundary conditions to further investigate this topic and create a pipeline for determining boundary conditions using MRE.

Conclusion

By altering MRE parameters to encode multiple periods of the higher harmonics of a single applied mechanical vibration frequency, we can analyze wave propagation of these higher harmonic components to identify boundary layers and potentially boundary mechanical properties.

Acknowledgements

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Figures

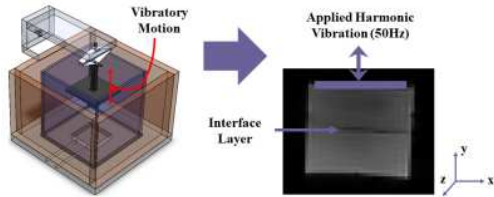


Figure 1: The MRE and Phantom Setup Used in this Study. We used a piezoelectric actuator at vibration frequency 50 Hz to apply mechanical vibration to the top of the phantom via a plate-like end effector. The vibration was applied perpendicular to the interface (the x-direction).

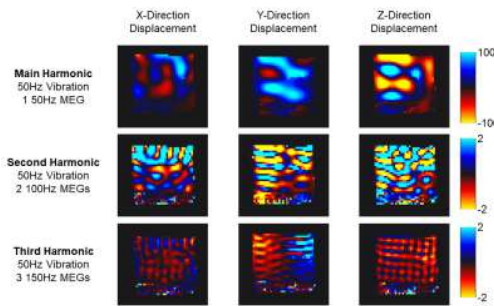


Figure 2: The First, Second, and Third Harmonic Wave Propagation using only 50 Hz applied harmonic vibration. Using 50 Hz encoding frequency with a fractional encoding of 1, 0.5, or 0.35 and number of MEGs of 1, 2, and 3 were used to capture the first (50 Hz), second (100 Hz), and third (150 Hz) harmonic respectively. We can see a doubling and tripling of wave number with one-half and one-third of the wavelength for the second and third harmonic images respectively.

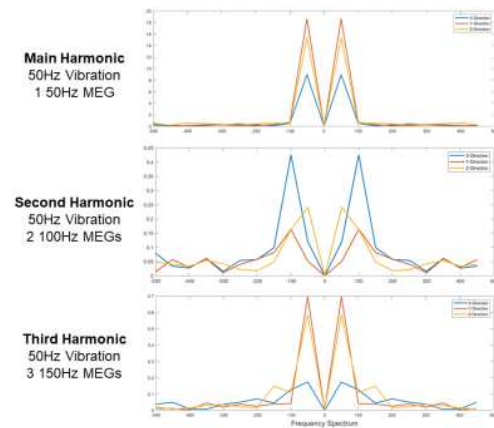


Figure 3: Frequency plots Over Entire Center Slice of Phantom Volume. Our method allows us to still visualize the main harmonic in the second and third sequence type as our first frequency ‘bin’, but primarily encodes the second or third harmonic of vibration, which is visualized in our second or third frequency ‘bin’.

Harmonic	Interface Type	X-Direction	Y-Direction	Z-Direction
First Harmonic	No Interface	1.03	1.06	1.01
	Sticky Interface	0.95	1.75	1.42
	Oiled Interface	0.83	1.24	0.99
Second Harmonic	No Interface	1.30	0.94	0.88
	Sticky Interface	1.12	1.19	1.16
	Oiled Interface	1.06	1.32	0.97
Third Harmonic	No Interface	0.91	1.17	0.88
	Sticky Interface	1.15	1.03	1.13
	Oiled Interface	1.50	0.85	1.51

Table 1: Ratio of Top ROI Amplitude to Bottom ROI Amplitude (in the frequency domain) for each interface type in each direction. We see a decrease in wave propagation from top to bottom of interface with decreased interface adhesion in the x-direction third harmonic, y-direction second harmonic, and z-direction third harmonic. We see the opposite trend in the x-direction first and second harmonic, y-direction third harmonic, and z-direction second harmonic.