Effect of Off-Frequency Encoding in Magnetic Resonance Elastography

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Introduction:

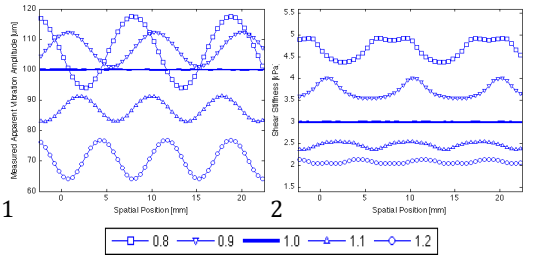
Magnetic Resonance Elastography (MRE) is an emerging, promising technique to noninvasively assess the mechanical properties of biological tissue by mapping the tissue kinematics using displacement-weighted MRI sequences [1]. In time-harmonic elastography, shear waves are generated in tissue at a certain driving frequency and are encoded using bipolar gradients that flip with the same frequency [2]. Having the encoding phase-locked to the actuation allows for a "filtering" of extraneous motion by maximizing contrast only for vibrations at that frequency. Encoding off-frequency from the vibration has been used to increase speed [3] or capture multiple frequencies [4], always with a known change in contrast [5], and results can be manipulated based on expected frequencies. For many applications of MRE, the insurgence of vibrations at a frequency other than the driving one is unlikely since the overall dynamic system can be considered linear. However, for brain elastography, under certain excitation modes, the dynamic system is nonlinear [6], which can result in extra frequencies being excited that will contaminate the encoded signal [7]. The purpose of this work is to investigate how unintended off-frequency encoding, stemming from nonlinearities in the dynamic system, will affect brain stiffness estimations from MRE.

Theory:

In MRE, wave motion is encoded using bipolar gradients, which results in a phase accumulation given by Equation (1) [1]. The motion itself is governed by the vibration frequency, ω_v, while the encoding frequency is represented as ω_g, the ratio between the two being Ω, which leads to Equation (2). In time-harmonic MRE, the temporal profile of the shear waves is captured by sampling at multiple, user-controlled phase offsets, θ. These offsets are generally chosen to span one vibration period evenly in order to achieve a spectral resolution equal to the encoding frequency when the temporal data is transformed to a frequency spectrum. Since the vibration and encoding frequencies are not assumed to be equal, the relationship between actual and desired phase offsets is $\theta_v = \Omega\theta_g$, and the encoded temporal signal will not repeat in time, causing errors with the Fourier decomposition. In addition to an incorrect assumption of the global vibration frequency, there will be variations in harmonic amplitude with wave number and spatial position. Since wave inversion algorithms employed in MRE utilize both the known vibration frequency and spatial changes in amplitude, both global (mean stiffness over entire tissue) and local (fluctuations of stiffness in space) errors in shear stiffness estimate will arise.

$$\phi = \gamma \int_0^{\tau} G(t) \cdot u_0 \cos(\mathbf{k} \cdot \mathbf{r} + \omega_v t + \theta) dt \qquad (1)$$

$$\phi = \frac{\gamma \cdot G \cdot u_0 \cdot \tau}{\pi\Omega} \sin(\theta - \pi\Omega)[1 - \cos(\pi\Omega)] \qquad (2)$$



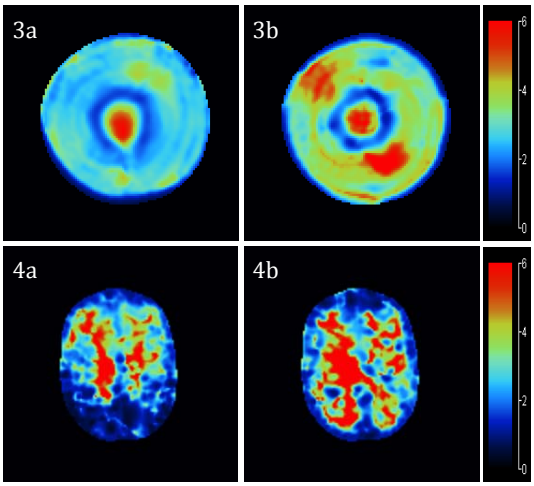
Methods:

Numerical simulations: Waves in a single dimension for a sample with constant stiffness and wave amplitude were modeled for various frequencies around the encoding frequency (Ω = 0.8 to 1.2). Encoding was simulated with phase offsets consistent to one period of the encoding frequency. The resulting temporal signal was decomposed using the Fourier transform, and the wave pattern of the first harmonic was used in the inversion algorithm to determine the shear stiffness of the sample.

Experiments: Similar to the simulations, MRE data was collected with varying frequency ratios for both a cylindrical agar gel phantom with stiffer center core and a human brain. Acquisitions were performed on Siemens 3T Allegra scanner using a single-shot EPI sequence, with 50 Hz bipolar gradients and 40 phase offsets. Other imaging parameters included TE/TR = 90/1000 ms, FOV = 240 mm (192 for phantom), matrix = 64x64, and 5 mm slice thickness. Wave images were inverted using a 2D LFE algorithm [9].

Results and Discussion:

The amplitude of the first harmonic of the simulated waves is shown for different spatial positions in Figure 1. Since the simulation modeled a constant stiffness of the sample and did not include any kind of attenuation factor, the wave amplitude should be constant in space, as demonstrated for the case where Ω = 1.0. These amplitude variations manifest themselves as variations in the reconstructed stiffness of the sample, as shown in Figure 2. For the different frequency ratios, the mean value of the stiffness increased by 56.6 % (Ω = 0.8) and decreased by 30.5 % (Ω = 1.2), due to the appearance of longer and shorter wavelengths, respectively. The local stiffness changes, resulting from incorrect assessment of wave amplitude, are also greater for lower frequency ratios, with fluctuations of up to 7.0 % compared to 3.5 % for Ω equal to 0.8 and 1.2, respectively. The measured stiffness of the cylindrical phantom and brain demonstrated similar phenomena for the different frequency ratios as well. The estimated stiffness maps are shown in Figures 3a and 3b for the phantom at Ω equal to 1.0 and 0.8, respectively, and figures 4a and 4b for brain at those ratios. For both experiments, it can be clearly seen that the mean stiffness across each tissue changes when the frequency ratio deviates from 1.0, as demonstrated in the simulations. There are also apparent changes in the stiffer structures in both the phantom and brain, which is a demonstration of the local variations in estimated stiffness with off-frequency encoding. These variations could be crucial when MRE is used in a diagnostic setting to look for stiff abnormalities such as tumors.



Figures: (1) Amplitude of first harmonic and (2) shear stiffness vs. spatial position in simulated data. Shear stiffness from data with frequency ratios of 1.0 and 0.8 for a phantom (3a and 3b) and brain (4a and 4b).

Conclusions:

The work presented here demonstrates how major errors in shear stiffness estimate using MRE can arise from small deviations between vibration and encoding frequencies. Much work in elastography assumes that the dynamic system is linear, thus eliminating the possibility of mode conversion, and also that the actuator will input a single, prescribed frequency to the system. Nonlinearities in the dynamic system or actuation can lead to the changes in frequency described above, with a 20% change in frequency resulting in an error in the stiffness estimate of up to 56.6%. For nonlinear dynamic systems, such as the human brain, modified methods concerning the mechanical actuation, imaging protocol, or processing tools [6,7,8] need to be utilized.

References: [1] Muthupillai, R., et al., *Science*, 1995. **269**(5232): p. 1854-1857; [2] Manduca, A., et al., *Med Image Anal*, 2001. **5**(4): p. 237-254; [3] Sack, I., et al., *Magn Res Med,* 2009. **61**(3): p. 668-677; [4] Klatt, D., et al., *Phys Med Biol,* 2007. **52**(24): p. 7281-7294; [5] Rump, J., et al., *Magn Res Med,* 2007. **57**(2): p. 388-395; [6] Johnson, C., et al., *Proc. ISMRM,* 2009. no. 718; [7] Sack, I., et al., *Magn Res Med*. 2004. **52**(4)**:** p. 842-850; [8] Sinkus, R., et al., *Proc. ISMRM,* 2002. no. 33; [9] Grimm, R., et al., MRE / Wave, 2006.