Measurement of In-vivo Local Shear Modulus by Combining Multiple Phase Offsets
MR Elastography

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Abstract

To provide realistic surgical simulation, haptic feedback is important. In the existing surgical simulators, the fidelity of the deformation and haptic feedback is limited because they are based on the subjective evaluation of the expert-user and not on an objective model-based evaluation. To obtain elastic modulus of in-vivo human tissues, magnetic resonance elastography (MRE) was developed. MRE is a phase-contrast-based method that can visualize propagating strain waves in materials. The quantitative values of shear modulus can be calculated by estimating the local wavelength of the wave pattern. Low frequency mechanical motion must be used for soft tissue-like materials, because strain waves rapidly attenuate at higher frequency. Therefore, wavelength in MRE is long. It is difficult to estimate local wavelength with high spatial resolution especially from noisy MRE with long wavelength. To encode the acoustic strain wave, the motion-sensitizing gradient (MSG), an essential component of MRE imaging, was used like a phase contrast MR angiography sequence [5]. MRE with multiple initial phase offsets can be generated with increasing delays between the MSG and mechanical excitation.

This paper deals with the measurement of local shear modulus by combining multiple initial phase offsets MRE. Using the MRE system, we investigate some of the characteristics of shear wave propagation in gel phantoms and in-vitro and in-vivo tissues.

Materials and Methods

Acquirement of magnetic resonance elastography

In order to acquire MRE images, experiments were performed with a 1.5 Tesla whole-body MR scanner (MAGNETOM Vision Plus, Siemens AG). Acoustic strain waves were generated at the surface of the object using an electro-mechanical actuator. The direction of the motion was set parallel to the object surface. The waveform of the MSG was sinusoidal, and synchronized with externally applied mechanical cyclic excitation at the tissue surface. MRE with multiple phase offsets were generated with increasing delays between the MSG and mechanical excitation. Typically, MSG was 80 to 400 Hz and peak
amplitude of the vibration was one micrometer. Other typical parameters are repetition time: 100 to 500 msec, echo time: 34 to 47 msec, and slice thickness: 10mm. MRE images were obtained for tissue-simulating poly vinyl alcohol (PVA) hydrogel phantoms, excised porcine liver and in-vivo human calf muscle. Mechanically excited wave numbers were controlled for each sample to avoid reflections from the far anterior surface that could interfere with wavelength measurements.

Post-processing of the acquired MRE data

When choosing a method for measuring local wavelength, one must consider that MRE has a long wavelength relative to the required spatial resolution and includes much noise and artifacts. Differential operations are usually used to obtain high spatial resolution maps. However, these are sensitive to noise. If high-cut filters were used to moderate the noise effect, the resolution of the wavelength would become worse. The window-function method is usually used in time series analyses and this method needs a long wave series to accurately analyze the frequency component. In principle, the spatial resolution is equal to the width of the window function. Thus, these methods could not be applied to MRE data analysis. An algorithm for estimating local wavelength [6] using for MRE was reported by Manduca, et al [7]. This method uses the Gaussian on logarithmic scale filters. It is robust to the noise, but it dose not represent boundary between hard and soft medium sufficiently. Another algorithm for MRE is the instantaneous frequency method which uses the Hilbert transform [8-10]. These methods can not measure a local wavelength shorter than one cycle of the acoustic strain wave.

Estimating local wavelength by combining multiple phases offsets MRE

We developed a new algorithm to measure local wavelength at a higher spatial resolution by combining multiple phase offsets MRE. The algorithm is described below.

Shear modulus, \( \gamma \), is given by

\[
\gamma(y) = \rho(y) f \lambda(y)^2
\]  

(1)

where \( y \) is the depth from the surface of the object attached to the oscillator, \( f \) is the externally applied mechanical excitation frequency, and \( \rho(y) \) and \( \lambda(y) \) are the density of the object and the local wavelength of transverse acoustic strain waves at depth \( y \), respectively. The shear wave at time \( t \) is described by

\[
S(t, y) = A \sin(2\pi f t - \phi(y))
\]

(2)

\[
\phi(y) = 2\pi \int_0^1 \frac{1}{\lambda(y)} dy
\]

(3)

where \( A \) is the peak amplitude of MRE and \( \phi(y) \) is the phase delay from the object surface. Here we abbreviate attenuation parameter for simplification.

A series of snapshots of the mechanical wave propagating within the material were obtained with increasing delays between the mechanical excitation and the MSG waveform. If the delay is set to \( 1/(Nf) \), observed shear waves are described by equation 4 (Figure 1a).

\[
S(n/Nf, y) = A \sin(2\pi n/N - \phi(y)) \quad \{ n = 0,1,\ldots,N-1 \}
\]

(4)

We make a patchy wave by combining each sampled phase offset wave at the same depth, like a patchwork [11]. The patchy wave \( J \) (Figure 1b, c, d) is described by

\[
J(y, y_0, W, N) = \sum_{n=0}^{N-1} S(n/Nf, y) h(y, y_0, W/N)
\]

(5)

\[
h(y, y_0, \Delta y) = \begin{cases} 
1 & \frac{y_0 - \Delta y}{2} \leq y < y_0 + \Delta y/2 \\
0 & \text{else}
\end{cases}
\]

(6)

where \( W \) is the assumed local wavelength around the depth \( y=y_0 \), \( h \) is a window function and \( \Delta y \) (=W/N: spatial resolution) is the window size. When the assumed wavelength \( W \) approximates the local wavelength (Figure 1c), the power spectrum of \( J \) is localized at a fundamental wavelength.

Figure 1- The algorithm for estimating local wavelength. (a) Sinusoidal waves of multiple phase offsets (for example wavelength = 40, phase offset = 0, \( \pi/2 \), \( 3 \pi/2 \)). Synthesized waves (b-d) are combined with these patches, and power spectrums are shown in (e-g), respectively. When the synthesized wavelength is close to the original wavelength, the relative power of first harmonics becomes maximized.

Figure 2- Assumed wavelength and simulated wave (initial phase offset 0)
frequency (Figure 1f). When the assumed wavelength $W$ does not approximate the local wavelength (Figure 1b,d), the power spectrum of $J$ is distributed widely and not localized at the fundamental frequency (Figure 1e,g). Using these properties, one can measure the likelihood estimate of the local wavelength at $y_0$ by maximizing the ratio of fundamental component of $J$, that is

$$C(W) = \frac{\text{power of fundamental frequency}}{\text{total power}}$$

(7)

Using this algorithm, the spatial resolution improves in proportion to the number of phase offsets.

**Evaluation of proposed algorithm by computer simulation**

To evaluate frequency characteristics of the proposed algorithm, computer simulation was performed. In the simulation, we used the parameters as an actual condition. The shear modulus of the human body was reportedly 5 to 77 kPa [4, 12, 13]. The height of the region is 40 pixels and the wavelength is around 10 to 20 pixels when the mechanical cyclic motion is 125 or 250 Hz. Therefore, in this simulation the depth dependent wavelength, $\lambda(y)$, was defined as,

$$\lambda(y) = 5\sin(2\pi y / 40) + 15$$

(8)

where $\kappa$ is the wave number ($\kappa=1$ to 19). An example of $\lambda(y)$ at $\kappa=1$ (black line) and the corresponding simulated shear waves whose amplitude is 1000 under these conditions (gray line) are shown in Figure 2. The proposed algorithm was applied to the simulated shear waves in each condition ($\kappa=1$ to 19, $N=1$ to 16), and to calculate root mean square error (RMSE) between $\lambda(y)$ and estimated local wavelength at a depth of 10 to 30.

To evaluate the algorithm on noise characteristics, we added zero-mean Gaussian noise with a standard deviation of 20 to 80 to the simulated shear wave data. A patchy wave with 16 phase-different images was used in this experiment. For comparison, local wavelength was calculated by the instantaneous frequency method.

In the actual measurement, reflection of the shear wave was observed at the interface of the sharp differences of shear modulus. The local wavelength of the simulated wave which reflected off the bottom of a phantom was compared with the value obtained with the proposed algorithm and the instantaneous frequency method.

**Evaluation of shear modulus from actual MRE using the proposed algorithm**

We applied this method to actual MRE. The first objects were five (5, 6, 7.5, 9 and 10%) homogeneous cylindrical PVA hydrogel phantoms. The second object was a heterogeneous phantom, comprised of a horizontal slab of stiff 10% PVA hydrogel resting on a horizontal slab of soft 5% PVA hydrogel (Figure 3a). Heights and diameters of these objects were 0.11m. The third object was an excised porcine liver (Figure 4a). It was held in a cylindrical container, 0.10m high and 0.15m in diameter. The fourth object was an in-vivo human calf muscle (Figure 4c). In these experiments, a total of 4 to 16 phase-different images were acquired.

To confirm absolute quantitative measurements, shear modulus values of the PVA phantoms measured by the MRE method were compared to those measured directly by conventional mechanical methods. In the calculations for these PVA phantoms, homogeneous density, $\rho$, measured directly from actual weight and volume, was used. For the measurement of the shear modulus of the tissues, we simply applied $10^3$ kg/m$^3$ as the value of tissue density.

**Results**

**Computer simulation**

Frequency characteristics of the proposed algorithm are shown in Figure 5a. As the spatial frequency becomes high, the error (RMSE) value becomes large. The spatial

![Figure 3- 10% and 5% double-decker PVA hydrogel using MRE with 16 phase offsets.](image)

(a) 10% and 5% PVA MRI (T2) image. (b) 10% and 5% PVA hydrogel MRE image with 125Hz mechanical cyclic motion. (c) A small strip, shown in (b) by dotted lines, extracted from an MRE image with 16 phase offsets. (d) shear modulus map of 10% and 5% PVA hydrogel using MRE with 16 phase offsets

![Figure 4- in-vitro and in-vivo tissue images.](image)
in-vitro porcine liver images (a) MRI, (b) MRE (125Hz), in-vivo human calf images (c) MRI, (d) MRE (100Hz) resolution was improved using multiple phase offsets. If the
estimated local wavelength is equal to the average wavelength, 15, independent of the depth, the error becomes 0.79. Noise characteristics of the proposed method are shown in Figure 5b. The error is linearly proportional to the noise. The value for wavelength estimated using the proposed algorithm and 16 phase offsets including a normal distribution of noise with SD=80 was better than that obtained with the instantaneous frequency method using data that included a normal distribution of noise with SD=20 (equivalent to 16 average of SD=80 data) at almost all spatial frequencies.

Figure 6 shows the local wavelength of the simulated wave that reflected from the bottom of the phantom compared to the value obtained with the proposed algorithm using the instantaneous frequency method. The local wavelength in the domain (Depth=0 to 14) not distorted by reflection was measured exactly by the proposed method. The wavelength measured by the instantaneous frequency method, however, oscillated around the true value. This is because the instantaneous frequency method uses all the depth domain data, and the error caused by reflection is distributed over the entire depth domain.

Evaluation of shear modulus using the proposed algorithm

In the first set of experiments, with 5 to 10% PVA hydrogel, the shear modulus map was analyzed by the proposed method using MRE with 4 to 16 phase offsets. The shear moduli ranged from 4.7 to 46 kPa. Figure 7 shows that the values obtained with MRE and the mechanical method were similar despite that viscous effects were ignored (regression coefficient =1.054, interception =0.058, coefficient of determination (r²)=0.986). In the second set of experiments, with double-decker PVA hydrogel (Figure 3a) and 16 phase offsets (Figure. 3b, c), the edge between 10% and 5% PVA hydrogel was well represented by the proposed method using MRE with 16 phase offsets (Figure 3d). The measured shear modulus in the 5% PVA phantom was same as homogeneous one, but the shear modulus in the 10% PVA phantom was different from the values for the first set of experiments because of influence of reflection from the boundary. The spatial resolution of the map was sufficiently high despite the long local wavelength.

In the third set of experiments, with excised porcine liver, the shear modulus was analyzed by the proposed method using MRE with 16 phase offsets. The average of the shear modulus was 10.6 (SD=2.8) [kPa]. In the fourth set of experiments with in-vivo human calf muscle, the average of the shear modulus was 5.1 (SD=0.9) [kPa] using MRE with 8 phase offsets. The shear moduli for the tissue samples of excised porcine liver and in-vivo human muscle were in previously reported ranges [4, 12, 13].

Discussion

The proposed method could measure local wavelength from MRE with multi phase offsets. It measures local wavelengths shorter than one cycle of the acoustic strain wave and it is robust to the noise. To avoid reflection effect to the target region, mechanically excited wave numbers was controlled. As the acquisition time of MRE is linearly proportional to the number of phase offsets, it takes time to obtain high spatial resolution, but error is fewer than instantaneous frequency method in case of same imaging.
time. Theoretically, the more phase offsets used for the calculation, the higher the spatial resolution. Whereas, for MRE, the data are discrete and the spatial resolution is finite. The highest resolution of shear modulus is depend on the MRE spatial resolution.

In the experiments described in this paper, local wavelength was measured rather than shear modulus. Equation (1) could be used to convert wavelength to shear modulus and it dose not account for viscosity. Thus, the results cannot always be compared directly to direct measurements of shear moduli obtained by traditional force-displacement methods. For the PVA phantom study, we confirmed that the shear moduli measured by MRE and by the mechanical method were well correlated despite that viscous effects were ignored. Thus, in this PVA study, the viscous effects could be negligible. However in actual tissue, the viscous effects would have to be taken into account, so viscoelastic modeling should be considered as a next step.

Conclusion

The quantitative values of shear modulus can be calculated by estimating the local wavelength of the wave pattern of the MRE. In this paper, we described a method of measuring local wavelength with high spatial resolution by combining multiple phase offsets MRE. To confirm the reliability of this method, a computer simulation and phantom study were performed. Measurements done with various elastic objects were in good agreement with those obtained by MRE and the mechanical method. The shear modulus of excised porcine liver and in-vivo human calf muscle were also analyzed by this method. In the in-vitro and in-vivo study, though propagated shear waves had long local wavelengths and sometimes propagated less than the unit wavelength, the algorithm could still estimate the shear modulus. These results suggest the estimation of local wavelength using an algorithm makes it possible to measure the shear modulus with high resolution using MRE.

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References


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