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Principal strain vascular elastography: simulation and preliminary clinical evaluation

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Abstract

It is difficult to produce reliable polar strain elastograms (radial and circumferential) because the center of carotid artery is typically unknown. Principal strain imaging can overcome this limitation, but suboptimal lateral displacement estimates measured with conventional ultrasonic imaging methods make this an impractical approach for visualizing the mechanical properties within the carotid artery. We hypothesize that compounded plane wave imaging can minimize this problem. To corroborate this hypothesis, we performed (a) simulations with vessels of varying morphology and mechanical behavior (i.e., isotropic and transversely isotropic), and (b) a pilot study with 10 healthy volunteers. The accuracy of principal and polar strain (computed using knowledge of the precise vessel center) elastograms varied between 7–17%. In both types of elastograms, strain concentrated at the junction between the fibrous cap and the vessel wall, and the strain magnitude decreased with increasing fibrous cap thickness. Elastograms obtained from healthy volunteers were consistent with those obtained from transversely isotropic homogeneous vessels; they were spatially asymmetric—a trend that was common to both principal and polar strains. No significant differences were observed in the mean strain recovered from principal and polar strains ($p > 0.05$). This investigation demonstrates that principal strain elastograms measured

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with compounding plane wave imaging overcame problems incurred when polar strain elastograms are computed with imprecise estimates of the vessel center.

Keywords

Anisotropy; Atherosclerosis; Plane Wave Imaging; Vascular Elastography; Principal Strain

Introduction

Vascular elastography visualizes normal strains (radial and circumferential) within the carotid artery. However, several investigators are now developing methods to visualize shear strains because (1) peak shear strains and the American Heart Association classification of atherosclerotic plaques (Stary, 2000) are correlated, and (2) cyclic shear strains in the adventitia could trigger neovascular proliferation and destabilize plaques (Wan et al., 2014; Majdoulina et al., 2014b; Keshavarz-Motamed et al., 2014). Unfortunately, coordinate dependency limits the performance of vascular elastography. We can remove this dependency by diagonalizing the 2D strain tensor because doing so will transform the measured values to a new coordinate system where the principal axes are the only directions along which strain is significant. Several investigators have investigated principal strain imaging (i.e., diagonalizing the 2D strain tensor). For example, Zervantonakis et al. (2007) used principal strain to reduce the dependence of strain on the transducer angle and the ventricular centroid. Jia et al. (2009) used principal strain vectors to highlight areas of ischemia. Lee et al. (2008) demonstrated that clinicians could use principal strains to differentiate abnormal from normal myocardium. However, suboptimal lateral displacement estimates have hindered the development of a practical ultrasonic approach for visualizing principal strains.

Von Mises coefficients (Maurice et al., 2002) and model-based elastography (Floc'h et al., 2010; Hansen et al., 2013; Huntzicker et al., 2014) also provide coordinate-independent mechanical parameters. Von Mises strain represents radial strain and thus does not provide any information about strains in the circumferential direction. Model-based elastography provides information about plaque composition (Richards and Doyley, 2011; Baldewsing et al., 2005) that can identify life-threatening plaques. However, most modulus estimation techniques are not suitable for real-time applications, a problem that shear wave imaging techniques should overcome (Ramnarine et al., 2014). Our long-term goal is to develop practical methods for estimating coordinate-independent mechanical parameters. Therefore, the focus of this paper is to demonstrate that compounded plane wave imaging can provide accurate high precision lateral displacement estimates, a pre-requisite for principal strain imaging.

Synthetic aperture ultrasound imaging systems produce high precision axial and lateral displacement estimates required to produce useful principal strains (Korukonda et al., 2013). Researchers have used the incompressibility condition to improve the quality of lateral displacements (Lubinski et al., 1996; Poree et al., 2015). However, incompressibility processing may not produce useful lateral displacements in transversely isotropic tissues

such as the carotid artery because the Poisson's ratios in the longitudinal and the circumferential directions are not equivalent and are typically less than 0.5. Researchers have also demonstrated that introducing lateral oscillation during beamforming (Basarab et al., 2009; Gueth et al., 2007; Anderson, 1998; Jensen and Munk, 1998) reduces the effective lateral beamwidth of RF echo frames, and improve the quality of lateral displacement estimates. Another approach is to use an advanced beamforming method to improve the point spread function (PSF) of synthetic aperture ultrasound imaging systems (Korukonda et al., 2013; Korukonda and Doyley, 2012; Hansen et al., 2010a, 2014; Poree et al., 2015). Synthetic aperture imaging systems (sparse array (SA) and plane wave (PW) imaging) acquire images with higher lateral resolution than those obtained with standard ultrasound systems. Sparse array imaging systems transmit spherical waves sequentially from each element in the array, whereas PW imaging systems use all elements to transmit plane waves (i.e., a single flash). Additionally, SA imaging systems apply focusing during both transmission and reception (two-way beamforming), whereas PW imaging applies focusing only on receive (one-way beamforming). Consequently, PW imaging produces images with high side-lobe levels and lower depth penetration, which reduces the precision of lateral strain estimates (Korukonda and Doyley, 2012). However, the low transmission power of SA imaging systems restricts clinical applications. Plane wave imaging does not suffer from this limitation because all elements are active during transmission (it has higher transmission power). Furthermore, researchers have demonstrated that spatial compounding reduces the side-lobe level incurred in PW imaging (Montaldo et al., 2009) because the compounding produces a synthetic transmit focus. We have observed that with appropriate beamforming, compounded plane wave (CPW) imaging can estimate lateral displacements precisely (Korukonda and Doyley, 2012), and thus is a viable approach for estimating principal strains.

In this paper, we hypothesize that CPW can visualize principal strains within the carotid artery. To corroborate this hypothesis, we performed three groups of studies: To assess (1) the performance of principal and polar strain elastograms computed with CPW imaging, we simulated stable and unstable plaques with varying geometries; (2) how complex mechanical behavior manifests in principal strain elastograms, we performed simulation studies with transversely isotropic vessels with fibrous cap thickness ranging from 112 μm to 480 μm ; (3) the performance of a prototype system of compounded plane wave vascular elastography, we performed a pilot study with 10 healthy volunteers.

Methods

The proceeding subsections describe methods used in both the simulations and the patient studies. These include beamforming, displacement and strain estimation, and data analysis.

Beamforming

We used the delay-and-sum method to reconstruct radio frequency (RF) echo frames (Korukonda and Doyley, 2012) on a 40 mm $\times$ 40 mm grid with lateral and axial sampling frequency of 52 lines/mm and 40 MHz. Several good references describe the principle of the delay-and-sum beamforming method (Van Trees, 2002); therefore, this subsection will

provide only a brief description of the approach. We compute the backscatter intensity (S) at a given point (x_0, z_0) in the beamformed image as follows:

$$S(x_0, z_0) = \sum_{i=1}^{N_{tx}} \sum_{j=1}^{N_{rx}} w_{ij} RF_{ij}(t - \tau(x_0, z_0)), \quad (1)$$

where N_{tx} and N_{rx} represent the total number of active transmission and reception elements, respectively; $RF_{ij}(t)$ represents the RF echo obtained when the i^{th} element transmits and j^{th} element receives; t represents the time of flight of the echo; $\tau(x_0, z_0)$ represents the time of flight of the acoustic wave traveling from the transmit element to point (x_0, z_0) and back to the receive element; and w_{ij} represents the apodization weight. We computed the time required to transmit a plane wave (τ_{tx}) at an arbitrary angle (θ) from a point (x_0, z_0) as follows:

$$\tau_{tx} = \left(x_0 \sin(\theta) + z_0 \cos(\theta) + \frac{W}{2} \sin(|\theta|) \right) / c, \quad (2)$$

where c and W represent the speed of sound, 1540 ms^{-1} , and the width of the transducer array. We computed the receive time (τ_{rx}) as follows

$$\tau_{rx} = \left(\sqrt{(x_j - x_0)^2 + z_0^2} \right) / c, \quad (3)$$

where x_j represents the location of the receiving element. The total round-trip time, τ , to and from the point (x_0, y_0) was

$$\tau(x_0, z_0) = \tau_{tx} + \tau_{rx}. \quad (4)$$

Estimating displacement and strain

To compute axial and lateral displacements, we applied a 2D cross-correlation echo tracking algorithm to the reconstructed RF echo data (i.e., the pre- and post-deformed RF echo frames) (Zahiri-Azar and Salcudean, 2006; Alam et al., 1998). All echo tracking was performed with 2D kernels ($0.8 \text{ mm} \times 0.8 \text{ mm}$), which overlapped by 75% in both coordinates. A 2D spline interpolator provided sub-pixel displacement estimates, and we used a median filter ($0.2 \text{ mm} \times 0.2 \text{ mm}$) to remove spurious axial and lateral displacement estimates. To compute the normal (ϵ_{zz} , ϵ_{xx}) and shear (γ_{xz} , γ_{zx}) components of the 2D strain tensor (ϵ), we applied the least square strain estimator (Kallel and Ophir, 1997) to the measured displacements (axial and lateral). Radial (ϵ_{rr}) and the circumferential strain ($\epsilon_{\theta\theta}$) elastograms were computed from the normal and shear strain as follows:

$$\varepsilon_{rr} = \frac{1}{x^2 + z^2} [x^2 \varepsilon_{xx} + xz(\gamma_{xz} + \gamma_{zx}) + z^2 \varepsilon_{zz}] \quad (5)$$

$$\varepsilon_{\theta\theta} = \frac{1}{x^2 + z^2} [z^2 \varepsilon_{xx} + xz(\gamma_{xz} + \gamma_{zx}) + x^2 \varepsilon_{zz}].$$

To produce artifact-free images, this transformation requires accurate estimation of the lumen center.

Estimating principal strain

Solving the Eigenvalue equation for the 2D case: $|\mathbf{e}_{ij} - \mathbf{e}^{(k)}\delta_{ij}| = 0$, where $k=1,2$ provided the magnitude (λ_1, λ_2) and direction (θ_{p+}, θ_{p-}) of the principal strain; and δ_{ij} is the Kronecker delta. We computed the two Eigenvalues representing the major (λ_1) and minor (λ_2) principal strains as follows:

$$\lambda_{1,2} = \frac{1}{2} [(\varepsilon_{11} + \varepsilon_{22}) \pm \sqrt{(\varepsilon_{11} - \varepsilon_{22})^2 + (\varepsilon_{12} - \varepsilon_{21})^2}]. \quad (6)$$

The principal strain directions (i.e., the Eigenvectors) were computed as follows:

$$\theta_{p+} = \tan^{-1} \left(\frac{\varepsilon_{11} - \varepsilon_{22}}{\varepsilon_{11} + \varepsilon_{22}} \right) / 2$$

$$\theta_{p-} = \theta_{p+} + \frac{\pi}{2}, \quad (7)$$

where $\mathbf{e}_{ij}$ denotes any pair of strain components, separated by $\theta = \pi / 2$ (i.e., axial, lateral or radial, circumferential, etc.).

Data analysis

We used the normalized root-mean-square-error (NRMSE) and the elastographic contrast-to-noise ratio (CNR_e) performance metric to evaluate the quality of polar and principal strain elastograms. The NRMSE of polar and principal strains was defined as follows:

$$NRMSE = \frac{\sqrt{\langle (\hat{\Theta} - \Theta)^2 \rangle}}{\max(\Theta) - \min(\Theta)}, \quad (8)$$

where $\hat{\Theta}$ represents the estimated quantity (principal or polar strains), and Θ represents that actual quantity. We computed NRMSE in the simulation studies where the actual strain

distributions were known. The CNRe performance metric was defined as follows (Bilgen and Insana, 1998):

$$CNRe = 2 \frac{(\mu_w - \mu_p)^2}{(\sigma_w^2 + \sigma_p^2)}, \quad (9)$$

where μ_w and μ_p represent the mean strain values in the vessel wall and plaque regions, respectively; σ_w and σ_p represent the standard deviations of the strain values in the corresponding regions. Rather than preferentially selecting the region of interests (ROIs), we define the plaque and the background region, and then randomly select the center of the ROI in each region.

Simulation Study

The goal of the simulation study was to evaluate the quality and accuracy of principal strains obtained from stable and unstable plaques of varying morphology and mechanical behaviors (transversely isotropic vs. isotropic). We used simple and complex heterogeneous vessels with cap thickness of 112 μm to 480 μm to assess the performance of principal and polar strains. These cap thickness were based on previously reported results (Redgrave et al., 2008). To simulate realistic displacement noise, we performed 2D echo tracking on synthetic RF echo frames that were synthesized by combining the finite element method (FEM) and the Field II (Jensen and Svendsen, 1992) ultrasound simulation environment. Randomly generated Gaussian noise was added to all simulated channel data (pre-beamformed echoes) to produce images with sonographic signal-to-noise ratio (SNR_s) of 20 dB. This value of SNR_s represents the noise level measured experimentally when our clinical prototype system of vascular elastography was operating in PW imaging mode. Axial and lateral displacements computed using the FEM (i.e., the output of the finite element package) was used to construct ideal principal and polar strain elastograms. Applying the strain and displacement estimation process described in the previous section to synthetic RF echo frames produced noisy elastograms (principal and polar strains). In the proceeding subsections, we describe the key stages of the RF echo frames synthesis process: mechanical and acoustic modeling. The mechanical properties of all vessels were based on previously reported results (Redgrave et al., 2008).

Mechanical model

We used the Abaqus/CAE (Dassault Systemes, Vellizy-Villacoublay Cedex, France) software package to create finite element models of healthy and diseased arteries (Fig. 1). The plane strain approximation was used to reduce the three dimensional elasticity problem to two dimensions.

We pressurized all vessels incrementally by applying uniform pressures of 70.01 mmHg, 68.06 mmHg, 65.91 mmHg, 63.75 mmHg, 61.99 mmHg, and 60.23 mmHg to the inner lumen. These correspond to the brachial pressure measured in the diastole phase of the cardiac cycle of a 60 year old volunteer. Displacement elastograms measured at each pressure increment were combined (average of five elastograms) to produce composite

images. Healthy vessels (model 1, Fig. 1a) were elastically homogeneous (Young's modulus of 40 kPa and Poisson's ratio of 0.495), with inner and outer diameters of 1.5 mm and 6 mm (Hansen et al., 2009). We simulated diseased arteries with two different morphologies: simple (idealized), and complex. Vessels with simple morphology (model 2, Fig. 1 (b)) had inner and outer diameters of 1.5 mm and 6 mm (Hansen et al., 2009; Huntzicker et al., 2014); and these vessels contained soft lipid-rich plaques encapsulated by thin fibrous caps. The vessel wall, plaque, and fibrous cap of vessels in this group had Young's modulus values of 50 kPa, 1 kPa, and 700 kPa. To simulate unstable, intermediate, and stable plaques, we created vessels with fibrous cap thicknesses of 150 μm , 250 μm , and 350 μm .

We used previously reported data (Ohayon et al., 2008) to model vessels with a complex plaque morphology (model 3, Fig. 1 (c)). More specifically, we used *in vivo* intravascular ultrasound (IVUS) images acquired from coronary arteries using a commercially available IVUS system (iLab; Boston Scientific, Watertown, MA, USA) and a 40 MHz Atlantis SR Pro 3.6F catheter (Boston Scientific, Watertown, MA, USA) to create finite element models with complex plaques. The finite element model represented the coronary artery rather than carotid artery; therefore, to simulate realistic displacements for the carotid artery, we scaled the measured displacements by a factor of 1.6 as discussed in (Redgrave et al., 2008). We assumed that the mechanical properties and boundary conditions of the carotid and coronary arteries are similar; therefore, differences in the mechanical response (i.e., displacement and strain) are due to disparities in the geometries (size). Table 1 summarizes the mechanical properties of this group of vessels. Since the fibrous cap was not visible in the IVUS images, it was not included in the finite element models; however, we varied the distance between lumen and necrotic core: 160 μm , 320 μm and 480 μm .

The final group of vessels (model 4, Fig. 1 (d) for morphology) was also constructed from previously reported data (Finet et al., 2004) vessel models had fibrous cap thickness of 112 μm , 189 μm , and 328 μm . We used *in vivo* intravascular ultrasound images obtained from the coronary arteries using Un-Scan-It software (Silk Scientific, Inc., Orem, Utah, USA) to create finite element models. We computed motion in the carotid artery by scaling the estimated displacements by a factor of 1.6 (Redgrave et al., 2008). Like model 3, this was modeled as a transversely isotropic vessel (see Table 2 for mechanical properties). In all models, we assume the vessels were linearly elastic.

Acoustic model

We used the ultrasound simulation platform Field II (Jensen and Svendsen, 1992) to simulate the plane wave response of a commercially available L14–5/38 linear array (Prosonic Corp., Seoul, Korea) operating at 5 MHz. The transducer parameters are summarized in Table 3. To simulate the acoustic response of the pre-deformed artery, point scatterers were randomly distributed (10 scatterers per wavelength) within the simulated vessel to generate fully developed speckle (Wagner et al., 1983). Redistributing the point scatterers of the pre-deformed arteries using displacement fields computed with the FEM provided the acoustic response of the post-deformed vessel. The speed of sound in all simulated vessels was 1540 ms^{-1} .

Patient Study

The goal of this pilot study was to evaluate strain elastograms (principal and polar) acquired with a clinical prototype system of CPW vascular elastography. We imaged the carotid arteries of 10 volunteers with no history of cardiovascular disease, with the approval of the University of Rochester Institutional Review Board (IRB). All volunteers provided written informed consent for the study.

We implemented the CPW imaging technique on a commercially available ultrasound scanner (Sonix RP, Analogic, Peabody, MA, USA). All echo imaging was performed at 5 MHz with a 128 element linear transducer array (L14-5/38 probe). We used a multichannel data acquisition system (Sonix DAQ, Analogic, Peabody, MA, USA) to acquire plane wave RF echo data from transmission angles of -14° to 14° in increments of two degrees (Korukonda and Doyley, 2012; Korukonda et al., 2013; Huntzicker et al., 2014). Radio-frequency echo data was acquired at a frame rate of 1000 fps; an ECG device (Model 7600, Ivy Biomedical, CT, USA) triggered the start of all acquisition at the beginning of systole. We sampled the received echo signal to 12 bits at 40 MHz, which was stored on a workstation for off-line analysis using the MATLAB (MathWorks Inc., Natick, MA, USA) programming language. We measured the pressure in the brachial artery of all volunteers in the supine position one hour before elastographic imaging.

Results

Simulation study results

Homogeneous vessel (Model 1, Fig. 1a)—Polar strain and principal strain were indistinguishable in concentric homogeneous vessels. Figure 2 shows examples of the principal (major and minor), radial, and circumferential strain distribution within a concentric homogeneous vessel. Principal major strain elastograms were similar to circumferential strain; similarly, principal minor strains were indistinguishable from radial strains. For this case, the principal Eigenvectors and the polar strain vectors were perfectly aligned. We expected this would occur because in the concentric homogeneous vessels, shear strains were negligible. All elastograms agreed with theoretical predictions (Fig. 2 (c,d,g,h)): they displayed radial symmetry and decayed with the inverse of radial distance (Fig 2 (i,j))—observations consistent with previously reported results (Korukonda and Doyley, 2012; Hansen et al., 2009).

Simple isotropic heterogeneous vessel (Model 2, Fig. 1b)—At the junction between the fibrous cap and normal vessel wall, the magnitude of principal strain elastograms were consistently larger than their polar strain counterparts. Figure 3 shows representative examples of the principal (a–f) and polar (g–l) strain distributions recovered from heterogeneous vessels with the simple morphology (Fig. 1 (b)) and fibrous cap thicknesses of 150 μm , 250 μm and 350 μm . In both types of elastograms (principal and polar), strain concentrated at the junction between the fibrous cap and the vessel wall, the weakest region of a plaque (Richardson et al., 1989; Schaar et al., 2006; Loree et al., 1992). In these critical regions, strain magnitude decreased with increasing cap thickness,

suggesting greater mechanical stability; however, the area of strain concentration was consistently larger in principal strain elastograms.

Principal major and minor strains consisted of circumferential and radial strains, except at the junction between the fibrous cap and vessel wall where shear strains were significant. Polar and principal strains were similar because the coordinate transformation process was complete. Specifically, polar strain did not contain any coordinate transformation artifacts because the vessel center was known precisely. In practice, polar and principal strains elastograms maybe visually different because of errors incurred when calculating the vessel's center (see Appendix A).

Figure 3 (m,n) demonstrates that in critical plaque regions, shear strains were prevalent (i.e., the principal Eigenvectors and the polar vectors were misaligned).

Simple transversely isotropic heterogeneous vessel (Model 2*, Fig. 1b)—

Anisotropy destroys the symmetry observed between the different strain components in isotropic vessels. Figure 4 shows representative examples of the principal elastograms obtained from anisotropic vessels with similar morphology to those shown in Fig. 1 (b). To minimize the effects of geometrical anisotropy, we kept the vessel morphology constant in both cases. More specifically, the fibrous cap thickness of the vessels were 150 μm , 250 μm , and 350 μm . Table 4 summarizes the mechanical properties of the simple transversely isotropic vessels. Like their isotropic counterparts, (a) strain concentrated at the junction between the fibrous cap and the vessel wall, and (b) the area of strain concentration was larger in principal strain elastograms. However, strains incurred in isotropic vessels were larger in magnitude than those incurred in the transversely isotropic vessels—both groups of vessels were identical except the mechanical properties were different (isotropic vs anisotropic). This occurred because strain depends on the mechanical properties (i.e., Young's modulus and Poisson's ratio). Specifically, we expected radial strains to be larger than circumferential strains, the direction with the lowest Young's modulus and Poisson's ratio. Similarly, we expected principal minor strains (representative of radial strain) to be larger than principal major strains.

Transversely isotropic vessels with complex morphology (Models 3 and 4, Fig. 1c and 1d)—

Strain in the necrotic core decreased with increasing distance between the necrotic core and the lumen. Figure 5 shows a more complicated vessel that exhibits both geometrical and transversely isotropic mechanical behavior (model 3). In this simulation, no fibrous cap was included because it was not visible in the sonograms. Strain concentrated in the lipid pool, and it decreased with increasing distance between the necrotic core and the lumen.

In this example, the tissue between the necrotic core and lumen behaves like a soft cap—strains were highest in these regions. Principal minor strains were highest in the upper portion of the vessel (i.e., between 10 o'clock and 2 o'clock); however, in the lipid pool there were higher compressive strains because the Young's modulus in the radial direction of the fibrotic tissue was an order of magnitude lower than that in the circumferential direction. Visually, radial and principal minor strain elastograms were comparable. Strain

concentration was not visible at the interface between the necrotic core and the fibrotic tissues, because the boundary between the two regions was relatively smooth.

Increasing the distance between the necrotic core and the lumen decreased the strain in the necrotic core. Figure 6 shows another example of transversely isotropic vessels with complex morphology (model 4). Unlike the example shown in Fig. 5, these vessels contained a fibrous cap.

Quantitative Analysis—Principal and polar strain can characterize both isotropic and anisotropic mechanical behavior. Figure 7 shows bar plots of the mean strain computed at the critical region within the elastograms shown in Figs. 3–6, plotted as a function of cap thickness. Principal major and circumferential strains were positive, and principal minor and radial strain were negative. For isotropic vessels (Fig. 8 a), principal major and principal minor strains were equal but of opposite sign—radial and circumferential strains also displayed a similar trend. However, this symmetry was not observed in anisotropic vessels (Fig. 7(b,c,d)). Strain increased with decreasing cap thickness, which was consistent with the elastograms; however, principal strains were noticeably larger than polar strains (radial and circumferential strain). We expected this would occur because principal strain represents the largest strain components, and in these critical vessel regions shear strain was greater. Principal and polar strain elastograms had similar accuracy.

Figure 8 shows bar plots of NRMSE of the elastograms shown in Fig. 3–6. The accuracy of the principal major elastograms varied from 7–14%; whereas the accuracy of the circumferential elastograms varied from 7–17%. Both techniques performed similarly because we used the same information (normal and shear strains) to compute principal and polar strains, and because precise location of the vessels were used to compute polar strain elastograms.

Figure 9 shows bar plots of the CNRe computed from the elastograms shown in Figs 3–6. CNRe of the principal strain elastograms were similar to those obtained from polar strain elastograms.

Patient studies

Table 5 summarizes the patient characteristics. Pulse pressure varied considerably between the 10 volunteers, which could be more related to when the measurements were made rather than any physiological reason. Specifically, pressure measurements were made during the pre-screening stage for all volunteers, which was done an hour before elastographic imaging. We plan to measure pulse pressure before and after elastographic imaging in future studies. Figure 10 shows representative examples of strain elastograms obtained from five healthy volunteers. Elastograms obtained from all 10 volunteers displayed a similar trend. As in the simulation studies, principal major (Fig 10 (b) and circumferential (Fig. 10 (c) strain elastograms were comparable. Similarly, principal minor (Fig. 10 (d) and radial (Fig. 10 (e) strain elastograms were equivalent. This occurred because in this case, fitting a circle to points manually selected on the vessel wall provided a good estimate of the lumen's center. There was poor symmetry between principal major and minor elastograms, which suggests the vessels were transversely anisotropic. Similarly, circumferential and radial strains were

asymmetric. Since the magnitude of radial strains were larger than circumferential strains, this suggests that either the Young's modulus or Poisson's ratio in the circumferential direction was different from that in the radial direction—a behavior consistent with transversely isotropic vessels. Although these results are encouraging, we plan to conduct further studies with *ex vivo* tissue samples and histological analysis to validate our *in vivo* findings.

Figure 11 shows box plots of normalized strains (principal and polar) measured in carotid arteries of 10 healthy volunteers. To assess whether the mean strains recovered from polar and principal strains were different, we performed a paired t-test. We observed no significant difference between the principal and polar strain ($p > 0.05$), which was consistent with simulation results.

Discussion

This study assessed the performance of principal and polar strain elastograms. Principal strain imaging overcame problems incurred when computing polar strain elastograms with imprecise estimates of the vessel center. Specifically, the accuracy and contrast-to-noise ratio of principal strain elastograms were comparable to polar strain elastograms computed with knowledge of the exact vessel center (Figs. 8 & 9). The patient study revealed that the carotid arteries of volunteers exhibited transversely isotropic mechanical behavior. We observed no statistically significant difference in principal and polar strains recovered from healthy volunteers between 50 and 60 y of age ($p > 0.05$).

Principal strain elastograms minimize errors incurred when transforming strains measured in Cartesian coordinates to the polar coordinate system. Clinicians typically acquire ultrasound images from the sagittal and transverse planes of the carotid artery. Vascular elastography techniques visualize strains in both the sagittal and transverse planes. Strains (axial and lateral) measured in the sagittal plane are equivalent to radial and longitudinal strains induced in the vessel wall (Rao et al., 2007, 2006; Techavipoo et al., 2004); however, this is usually not the case for strains measured in the transverse plane. Figures 3 and 6 demonstrate that transforming strains measured in the transverse plane to the vessel coordinate system (polar) overcame this problem, which is consistent with previously reported results (Korukonda and Doyley, 2012; Maurice et al., 2005; Hansen et al., 2010b). However, imprecise estimates of the vessel center can produce erroneous radial and circumferential strain elastograms (see Appendix, Figs A1 and A2). Shear wave imaging (Doherty et al., 2013) can also provide coordinate-independent mechanical parameter. An additional benefit of using shear wave imaging to visualize the carotid artery is that it is typically less operator-dependent than quasi-static elastography.

Poree et al. (2015) also demonstrated that PW imaging can measure principal strains within vascular tissues; however, our approach differs from theirs in that we optimized the displacement estimation process to produce high precision axial and lateral displacements gleaned from previous reported studies (Korukonda and Doyley, 2011; Konofagou and Ophir, 1997). Furthermore, we did not use incompressibility processing to estimate lateral displacements and strain because this assumption is incorrect for transversely isotropic

organs such as the carotid artery. To optimize performance, we reconstructed all RF echo frames on a 40 mm × 40 mm grid with axial and lateral sampling frequency of 40 MHz and 52 lines/mm.

Besides providing coordinate-independent parameters, principal strains can differentiate isotropic from anisotropic vascular tissues. Vascular tissues display transversely isotropic mechanical behavior (Timoshenko and Goodier, 1969); however, most elastography techniques presume vessels are isotropic. Figures 3 and 4 demonstrate that strain distribution within isotropic and anisotropic materials are noticeably different. Specifically, in isotropic vessels the strain components are equal in magnitude but differ in sign (Fig. 7); however, this is not the case for transversely isotropic vessels. Figure 10 demonstrates that healthy carotid arteries are transversely isotropic, which is consistent with previously reported results (Loree et al., 1992; Holzapfel et al., 2004); however, additional *ex vivo* and *in vivo* studies are needed to corroborate the clinical results and to better understand the mechanism that produces anisotropy in healthy carotid arteries. An important question is: what are the disastrous consequences of assuming a transversely isotropic vessel is isotropic? Two obvious consequences are that this could (a) degrade the diagnostic performance of vascular elastography, and (b) compromise the accuracy of the modulus and stress recovery process (Richards et al., 2015). Incorporating a transversely isotropic mechanical model (Sinkus et al., 2005) in the image reconstruction process would improve the accuracy of modulus elastograms. Besides studying the impact of assuming isotropy when reconstructing the mechanical properties of a transversely isotropic vessel, we plan to develop a metric from principal strains, similar to that used in diffusion tensor imaging (Kubicki et al., 2007; Jones and Leemans, 2011; Mori and Zhang, 2006) to characterize the degree of transverse isotropy and assess if this varies with pathology.

This study had three main limitations. First, we did not conduct any studies to corroborate our expectation that principal strain imaging would improve the diagnostic performance of vascular elastography, which was beyond the scope of this work. Second, we did not confirm whether principal strains would allow better plaque delineation (Majdouline et al., 2014a). It could also prove useful to assess how anisotropy varies during atherosclerotic plaque development (Idzenga et al., 2012). Clinicians could potentially use this information to either reverse or slow down the atherosclerotic process (Meaney et al., 2009). Third, the thickness of the vessels used in models 1 and 2 are not realistic, they were much larger than those observed in practice. Therefore, in future simulation studies we plan to use more realistic models.

Conclusions

This study demonstrates that principal strain elastography computed with compounded plane wave imaging reduces artifacts incurred when polar strains are computed with imprecise estimates of the vessel center. In this work, we also demonstrated that principal strain imaging could prove useful in characterizing transversely isotropic mechanical behavior.

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Appendix

We performed simulations to evaluate the impact of computing polar strains with imprecise estimates of the vessel center. Specifically, we use the Abaqus/CAE (Dassault Systemes, Vellizy-Villacoublay Cedex, France) software package to create a finite element (FE) model of a diseased artery with complex morphology (model 3, Fig 1 (c)). Polar strain elastograms were computed by applying Eq 5 to normal and shear strains computed in the Cartesian coordinate system. We applied offsets of 0 mm, 1 mm, and 2 mm to the true center of the vessel during the coordinate transformation process. Three cases were considered, where the offsets were applied to: (1) the x-coordinate only, (2) the z-coordinate only, and (3) both the x and z coordinates. Figure A1 shows representative example of polar strain elastograms computed for the three cases. Figure A1 [i (a, b)] shows the corresponding principal major and minor strain elastograms, respectively. The polar strain distributions within the vessel are displayed in Figs. A1 [ii–iv]. The top (a–c) and bottom (d–f) rows in Figs A1 [ii–iv], display the circumferential and radial strains, respectively. The columns (a,d), (b,e) and (c,f) correspond to polar strain elastograms with an offset of 0, 1 and 2 mm in the center coordinates, respectively. Errors incurred when estimating the center of the vessel affected the visual appearance of the polar strain elastograms. Specifically, they corrupted the strain elastograms. Figure A2 shows the normalized root mean square error (NRMSE) estimated from the elastograms shown in Figure A1. The NRMSE was dependent on the accuracy of the coordinate transformation process (i.e., how well the center of the vessel was known).

Figure A1: Demonstrating the effect of errors incurred when geometric transformation is performed with imprecise estimate of the lumen center. In these examples, an offset of 0 mm, 1 mm, and 2 mm was added to the actual center of the vessel. (i) Coordinate independent principal major (a) and minor strain (b) elastograms. (ii & iii) Circumferential (a–c) and radial (d–f) strains elastograms produced when the offsets were added only to the X-coordinate and Z-coordinate of the vessel center, respectively. (iv) Circumferential (a–c) and radial (d–f) strain elastograms produced when the offsets were added to both the X and Z-coordinate of the lumen center simultaneously.

Figure A2: NRMSE of principal and polar strain elastograms incurred when offsets of 0 mm, 1 mm, and 2 mm was added to the X-coordinate, Z-coordinate or both coordinates of the actual lumen center. Showing errors incurred when the offsets were added to only the X-coordinate (i), Z-coordinate (ii), and both the X and Z-coordinates (iii) of the vessel center.

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Figure 1.

Morphology of the simulated vessels: (a) homogeneous healthy vessels (model 1); (b) simple isotropic and transversely isotropic heterogeneous vessels with simple thin-cap atheroma (model 2); (c) complex transversely isotropic heterogeneous vessels with complex plaque consisting of necrotic core and fibrosis, but no fibrous cap (model 3); (d) transversely isotropic heterogeneous vessels with an advanced atheroma consisting of fibrous cap, large lipid pool, and fibrosis (model 4).

Figure 2.

Elastograms and strain profiles obtained from homogeneous vessels (model 1). Strain elastograms measured using compounded plane wave imaging: (a) principal major (ϵ_{p+}), (b) circumferential ($\epsilon_{\theta\theta}$), (c) principal minor (ϵ_{p-}), and (d) radial (ϵ_{rr}). The actual strain distribution: (e) principal major (ϵ_{p+}), (f) circumferential ($\epsilon_{\theta\theta}$), (g) principal minor (ϵ_{p-}), and (h) radial (ϵ_{rr}). Measured and actual profiles of (i) principal major and circumferential strain; and (j) principal minor and radial strains. Close-up of (k) principal major and (l) principal minor strains. The green and blue arrows represent the polar and principal vectors, respectively.

Figure 3. Strain elastograms obtained from heterogeneous isotropic vessels (model 2) with fibrous cap thickness of 150 μm , 250 μm , and 350 μm from left to right. Showing strain images of the measured (a–c) principal major (ϵ_{p+}), (d–f) principal minor (ϵ_{p-}), (g–i) circumferential ($\epsilon_{\theta\theta}$), (j–l) radial (ϵ_{rr}). Close-up of (m) principal major and (n) principal minor strain elastograms. The mean strains plotted in Fig. 7(a) were computed in the small rectangular regions. The green and blue arrows represent the polar and principal vectors, respectively.

Figure 4.

Strain elastograms obtained from simple transversely isotropic vessels (model 2*) with fibrous cap thickness of 150 μm , 250 μm , and 350 μm going from left to right. Showing strain images: (a–c) principal major (ϵ_{p+}), (d–f) principal minor (ϵ_{p-}), (g–i) circumferential ($\epsilon_{\theta\theta}$), (j–l) radial (ϵ_{rr}). Close-ups of (m) principal major and principal minor (n) strain elastograms. The mean strains plotted in Fig. 7(b) were computed in the small rectangular regions. The green and blue arrows represent the polar and principal vectors, respectively.

Figure 5.

Strain elastogram obtained from transversely isotropic vessels (model 3) with complex morphology and cap thickness 160 μm , 320 μm , and 480 μm going from left to right. Showing strain images: (a–c) principal major (ϵ_{p+}), (d–f) principal minor (ϵ_{p-}), (g–i) circumferential ($\epsilon_{\theta\theta}$), (j–l) radial (ϵ_{rr}). Close-ups of (m) principal major and (n) principal minor strain elastograms. The mean strains plotted in Fig. 7(c) were computed in the small rectangular regions. The green and blue arrows represents the polar and principal vectors, respectively.

Figure 6.

Strain elastograms obtained from transversely isotropic vessels (model 4) with advanced plaques and fibrous cap thickness of 112 μm , 189 μm , 328 μm going from left to right. Showing strain images: (a–c) principal major (ϵ_{p+}), (d–f) principal minor (ϵ_{p-}), (g–i) circumferential ($\epsilon_{\theta\theta}$), (j–l) radial (ϵ_{rr}). Close-ups of (m) principal major and (n) principal minor strain elastograms. The mean strains plotted in Fig. 7(d) were computed in the small rectangular regions. The green and blue arrows represents the polar and principal vectors, respectively.

Figure 7.

Mean strains (principal and polar) computed over the rectangular regions-of-interests (ROIs) defined in Figs. 3–6 plotted as function of cap thickness. The error bars represent ± 1 std. dev. Showing strains (%) recovered from (a) the simple isotropic vessel (model 2*), (b) simple transversely isotropic vessel (model 2), (c) transversely isotropic vessel with complex morphology and no fibrous cap (model 3), and (d) transversely isotropic with fibrous cap and advanced plaque (model 4).

Figure 8. NRMSE of principal (major (a) and minor (b)) and polar (circumferential (c) and radial (d)) strains elastograms computed for heterogeneous vessels with varying cap thickness, morphology, and mechanical behavior.

Figure 9. CNRe of principal (major (a) and minor (b)) and polar (circumferential (c) and radial (d)) strains elastograms shown in Figs 3–6. Showing how CNRe (dB) varies with cap thickness, and mechanical behavior.

Figure 10. Montage of sonograms (a), principal major (b) and circumferential strain elastograms (c), principal minor (d) and radial strain elastograms (e) obtained from five female volunteers. The elastograms represent the mean strains computed over three cardiac cycles.

Figure 11.

Box and whisker plot of the mean (a) principal major, (b) circumferential, (c) principal minor, (d) radial strains recovered from all 10 patients. Showing lines at the lower quartile, median, and the upper quartile. The plot reveals no significant difference in principal and polar strains.

Table 1

Mechanical properties of transversely isotropic diseased vessels with complex morphology (model 3).

Tissue	E_{rr} (kPa)	$E_{\theta\theta}$ (kPa)	V_r	V_θ
Artery	10	100	0.1	0.27
Fibrosis	115.6	2312	0.07	0.27
Necrotic core	1	1	0.495	0.495

Table 2

Mechanical properties of transversely isotropic vessel with advanced plaque and complex morphology (model 4).

Tissue	E_{rr} (kPa)	$E_{\theta\theta}$ (kPa)	V_r	V_θ
Adventitia	80	800	0.01	0.27
Media	10	100	0.01	0.27
Cellular Fibrosis	20	200	0.01	0.27
Dense Fibrosis	100	1000	0.01	0.27
Lipid Core	1	1	0.495	0.495

Table 3

Physical properties of the L14-5/38 linear transducer array used in simulated and experimental studies.

Property	Value
Number of Elements	128
Center Frequency	5.0 MHz
Fractional Bandwidth	65%
Element height	4 mm
Element width	0.279 mm
Element pitch	0.305 mm
Kerf	0.025 mm
Focus	16.0 mm

Table 4

Mechanical properties of simple transversely isotropic diseased vessels (model 2*). These vessels had the similar morphology to those in model 2.

Tissue	E_{rr} (kPa)	$E_{\theta\theta}$ (kPa)	V_r	V_θ
Fibrous cap	700	7000	0.01	0.27
Vessel Wall	50	5000	0.01	0.27
Lipid core	1	1	0.495	0.495

Table 5

Summary of patient characteristics.

Patient Index	Sex	Age	BMI	Pulse Pressure (mmHg)	Smoker	Heart Diseases	Family Heart Diseases
1	Male	64	26.51	44	No	No	No
2	Female	55	23.67	60	No	No	Yes
3	Male	52	32.85	48	No	No	Yes
4	Female	54	26.39	32	No	No	No
5	Male	70	29.52	54	Yes	No	No
6	Female	53	22.95	44	No	No	Yes
7	Male	61	32.75	44	No	No	Yes
8	Male	56	28.02	50	Yes	No	Yes
9	Female	65	22.80	56	No	No	Yes
10	Male	58	26.34	48	No	No	Yes