Ultrafast vascular strain compounding using plane wave transmission


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ABSTRACT

Deformations of the atherosclerotic vascular wall induced by the pulsating blood can be estimated using ultrasound strain imaging. Because these deformations indirectly provide information on mechanical plaque composition, strain imaging is a promising technique for differentiating between stable and vulnerable atherosclerotic plaques. This paper first explains 1-D radial strain estimation as applied invasively in coronary arteries. Next, recent methods for noninvasive vascular strain estimation in a transverse imaging plane are discussed. Finally, a compounding technique that our group recently developed is explained. This technique combines motion estimates of subsequently acquired focused ultrasound images obtained at various insonification angles. However, because the artery moves and deforms during the multi-angle acquisition, errors are introduced when compounding. Recent advances in computational power have enabled plane wave ultrasound acquisition, which allows 100 times faster image acquisition and thus might resolve the motion artifacts. In this paper the performance of strain imaging using plane wave compounding is investigated using simulations of an artery with a vulnerable plaque and experimental data of a two-layered vessel phantom. The results show that plane wave compounding outperforms 0° focused strain imaging. For the simulations, the root mean squared error reduced by 66% and 50% for radial and circumferential strain, respectively. For the experiments, the elastographic signal-to-noise and contrast-to-noise ratio (SNRe and CNRe) increased with 2.1 dB and 3.7 dB radially, and 5.6 dB and 16.2 dB circumferentially. Because of the high frame rate, the plane wave compounding technique can even be further optimized and extended to 3D in future.

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1. Introduction

Ultrasound strain imaging or elastography is a technique introduced by Ophir et al. (1991) to differentiate between malignant and benign tissue based on the deformation pattern of a tissue in reaction to a force. The technique is now being used to detect malignancies in breast, prostate, and liver tissue (Cosgrove et al., 2013) and to assess the functionality of the cardiac muscle and skeletal muscles (Lopata et al., 2010, 2011; Okrasinski et al., 2012; Xu et al., 2010).

For vascular applications, strain imaging is also a very interesting technique, where it is mainly applied to differentiate between stable and vulnerable atherosclerotic plaques (de Korte et al., 2011). Usually, the naturally occurring deformations of the arterial wall and plaque are determined, which occur in response to changes in intraluminal pressure throughout the cardiac cycle. By measurement of these deformations, strain imaging indirectly provides mechanical information about the plaque composition. The vulnerability of a plaque is determined by its geometry and its composition (Davies, 1996; Falk et al., 1995; Finn et al., 2010).

Currently, only the geometry of the plaque and the degree of luminal narrowing it causes can be measured using conventional B-mode and Doppler ultrasound in the clinic, which explains why ultrasound strain imaging would be very useful. Histology studies have shown that plaques which contain a large lipid pool separated from the pulsating blood by only a thin fibrous cap and which are infiltrated by macrophages are responsible for most sudden cardiovascular events (Schaar et al., 2004a; Virmani et al., 2000). Plaques which mainly contain fibrous tissue are considered stable, even if they cause the same degree of luminal narrowing, because they are less prone to rupture suddenly. In an intravascular study of the coronary arteries, it was shown that strain imaging, or elastography or palpography, as it is also often called, enabled differentiation between vulnerable and stable plaques with a high sensitivity and specificity (Schaar et al., 2001). Furthermore, a good correlation was found between plaque phenotype and clinical symptoms (Schaar et al., 2004b). More regions with high deformation were identified in patients with unstable angina compared to patients with stable angina. The most high strain regions were observed in patients who previously suffered a myocardial infarction.

Intravascular strain imaging is explained schematically in Fig. 1. Radio-frequency (RF) ultrasound signals are acquired for different
acquisition angles at various blood pressure levels by transmitting and receiving ultrasound from a rotating transducer in the tip of a catheter. Next, a small 1D-kernel of RF data from within the vessel wall at a certain angle is selected and cross-correlated with a larger 1D kernel of RF data acquired at the same angle, but at a different pressure. The shift in the peak of the obtained normalized cross-correlation function yields the local displacement that occurred in the wall tissue, due to the pressure change. The radial displacement field of the entire vascular cross-section is obtained by repeating this procedure for all acquisition depths and angles. The first order spatial derivative of these displacements in the radial direction yields the radial strain field.

Since the intravascular approach is applicable only in patients which are already in the catheterization laboratory and since people often do not have clinical symptoms before the first, in many cases lethal, cardiovascular event, methods for early noninvasive vascular strain imaging have been developed (Cinthio et al., 2005; Hansen et al., 2012; Hasegawa and Kanai, 2009; Kim et al., 2004; Korukonda et al., 2013; Larsson et al., 2011; Maurice et al., 2004; Shi et al., 2008). As can be observed in Fig. 2a, the ultrasound beam direction for noninvasive strain imaging in the transverse imaging plane is not in line with the radial strain direction for the entire cross-section. To determine the radial strain, the displacements along the beam (axial) and perpendicular to the beam (lateral) need to be estimated, and converted into radial displacement and strain. To obtain both axial and lateral displacements from a noninvasive ultrasound acquisition, the cross-correlation is carried out using 2D kernels instead of the 1D kernels described for the intravascular case. These 2D kernels contain RF data from multiple adjacent image lines, which are matched in a larger 2D kernel containing RF data from the next ultrasound frame. With this approach, the axial displacement and strain can be estimated precisely. However, because of the lack of ultrasound phase information in the lateral direction and the approximately tenfold larger sampling distance (equal to the image line spacing), lateral displacement estimations are less precise. This results in local distortions of the radial displacement and strain field and also of any other displacement and strain component that requires the lateral displacement component as input, such as the circumferential strain.

Several methods have been developed for more accurate noninvasive strain estimation in the transverse imaging plane. In general, these methods either focus on an improved estimation of the lateral displacement component or focus on circumventing the use of lateral displacement for the derivation of radial, and in some cases circumferential strains. One of the first methods reported for accurate radial displacement estimation was the method proposed by Nakagawa et al. (2004). In this method, adjacent ultrasound beams were all steered through the center of the lumen by applying additional delays to the transducer elements. With the change in beam direction, the direction of phase information changes and the ultrasound beams become aligned with the radial direction for a small segment of the cross-section. Regular axial 1D displacement tracking and strain derivation can be performed to obtain accurate radial strains. This method is computationally efficient, since no conversions from axial and lateral strains to radial strains are required. A disadvantage of the technique is that radial strains can only be obtained for a small segment (±40°) of the cross-section. In 2009 and 2010 our group introduced two segment-based methods that enabled improved radial and circumferential strain estimation for the entire cross-section by using mainly axial information (Hansen et al., 2009, 2010a). Both methods acquire RF-data of the vessel cross-section at multiple beam steering angles. At each of these angles, axial displacements and strains were estimated only for those segments of the cross-section in which the beam’s axial direction was closely aligned to the radial or circumferential direction of the vessel wall. Because of this close alignment, the radial and circumferential strain could be approximated for those segments without use of the less accurate lateral displacement component. The segments were combined to form a strain image for the entire cross-section. The first method assumed incompressibility and isotropy of the tissue to compensate for the neglected lateral component.
(Hansen et al., 2009), while the second method assumed the absence of circumferential motion (Hansen et al., 2010a). When no circumferential motion is present, the second method outperforms the first, because it requires less contribution of lateral data. However, circumferential motion does exist for plaques with a complex heterogeneous composition. In that situation, the first method might be the most accurate.

Conventional 2D ultrasound images are constructed using line-by-line focused ultrasound acquisitions. First, an echo pulse is transmitted for a small aperture centered around the imaging line. Next, the system switches to receiver mode until the scattered and reflected signal of the maximum desired depth has returned to the transducer. This sequence is repeated for all lines to build up the image. It is, however, also possible to transmit an unfocused plane wave or spherical wave into the tissue, receive the signal on each transducer element, and perform the reconstruction of the full image (Jensen et al., 2006; Kruizinga et al., 2012; Sandrin et al., 1999; Tanter et al., 2002). Korukonda et al. implemented and compared several of such ‘full view’ transmission methods for radial and circumferential strain estimation in vessels (Korukonda and Doyley, 2012; Korukonda et al., 2013). One of the techniques introduced by Korukonda et al. combined several spherical wave acquisitions using synthetic aperture imaging to reduce the lateral width of the point spread function and improve the lateral displacement estimation accuracy. To increase the intensity of the transmitted spherical waves, multiple transducer elements were activated for the generation of these waves (sparse array technique). The results of this technique were compared to those obtained with coherent plane wave compounding. Coherent plane wave compounding also aims at decreasing the lateral width of the point spread function by averaging RF data obtained after multiple sequential plane wave transmissions at various beam steering angles (Montaldo et al., 2009). In their most recent paper, Korukonda et al. showed that synthetic aperture imaging with sparse arrays gives higher elastographic signal-to-noise and contrast-to-noise ratio’s compared to coherent plane wave compounding in phantoms (Korukonda et al., 2013). In vivo, the strain results of the coherent compounding method are visually better. This is probably because the echo-intensity in the tissue is less for the synthetic aperture method than for the coherent plane wave compounding method.

The latest method developed by our group allows accurate estimation of all 2D components of the strain tensor for the entire cross-section by compounding axial displacement components estimated from three different beam steering angles, as shown in Fig 2b (Hansen et al., 2010b). Briefly, beam-steered ultrasound RF data for all imaging lines are successively acquired for three alternating focused beam steering angles of approximately +20°, 0° and −20°. For each beam steering angle the axial displacement field is estimated by cross-correlation with the RF data of the previously acquired frame from that beam steering angle. This implies that for each angle, a different projection of the displacement field can be acquired with high accuracy. A more accurate reconstruction of the 2D displacement can be obtained by combining, or compounding these projections. The main advantage of this method compared to our previous methods (Hansen et al., 2009, 2010a) is that no assumptions regarding tissue isotropy, compressibility or circumferential motion are required. Although the methods compared by Korukonda et al. enable a considerable improvement of the lateral displacement estimates, our compounding method might be more accurate, since it only uses axial displacement estimates and no lateral displacement estimates at all. With respect to conventional 0° radial strain imaging, this method improved the elastographic signal-to-noise ratio (S/NR) and contrast-to-noise ratio (CRN) by 4.0 dB and 9.8 dB, respectively, in an experimental setting with a pressurized vessel-mimicking phantom. The compound strain imaging method assumes that the imaged tissue is quasi-static between the images acquired at the different angles, however, in reality the tissue is in motion in between the frames which leads to erroneous displacement vector estimates when using conventional focused imaging.

A possible solution to reduce motion artifacts is plane wave imaging, which is very fast, since it requires only one transmit for the reconstruction of an entire ultrasound image. Thus, instead of line-by-line transmission this implies image-by-image transmission, enabling an increase in frame rate by a factor of 100–300. Because of this increase in frame rate, it is possible to record data for the various beam-steering angles nearly simultaneously, which will minimize the motion artifacts. Of course there is also a drawback to plane wave imaging, due to the unfocused transmission, the lateral resolution of the ultrasound data decreases. A previous plane wave imaging study demonstrated a decreased signal-to-noise ratio for lateral strain imaging (Park et al., 2007), but the effect on axial displacement and axial strain imaging was reported to be minor. Since our compounding method only utilizes the axial displacement component, we expect that a combination of compounding and plane wave imaging might be ideal for fast and accurate strain imaging in arteries. In this study, the performance of plane wave displacement compounding for vascular strain imaging is investigated. First the performance will be assessed using in silico simulations of a vulnerable plaque model. Next, the performance will be investigated in experiments with a pressurized vessel-mimicking phantom which represents a vessel wall with a soft plaque.

2. Materials and Methods

2.1. Simulations

Radiofrequency (RF) data of a carotid artery with a vulnerable plaque were simulated before and after deformation using the Field II ultrasound simulation program (Jensen, 1996; Jensen and Svendsen, 1992). As inputs, Field II requires a definition of a transducer, a scanning sequence, and a matrix containing the 3D coordinates of scatterers that mimic the tissue. The simulated transducer had the same properties as the L5–12 ATL transducer used for the experiments. It consisted of 192 elements with a pitch of 198 μm, an element width of 173 μm, and an element height of 4 mm. A center frequency of 9 MHz was used and the speed of sound c was assumed to be 1540 m/s. Two scanning sequences were implemented: one for plane wave transmission and one for focused transmission. For both scanning modes, simulations were performed for beam steering angles of −20°, 0°, and +20°. The excitation and impulse responses used were similar to those used by the experimental transducer. More details on the implemented scanning sequences can be found in Appendix A of the Supplemental data. The simulations resulted in ultrasound RF data for each separate transducer element sampled at a frequency of 36 MHz. These RF element data were combined to form RF (image) lines. This “beam-forming” was performed using the delay-and-sum methods as described in Appendix B of the Supplemental data. The displacement and strain estimation described later on was also performed on this beam-formed RF data. Beam-forming is an essential step in ultrasound imaging, because it allows the reconstruction of ultrasound image lines from the signals received by the various transducer elements. Traditionally, beam-forming was implemented in hardware, however with recent advances in computational power it has become possible to carry it out in real-time using the software.

Two 3D matrices of scatterers were defined using a finite element model (FEM) of a carotid artery with a vulnerable plaque. The scatter matrices represent the artery before and after an intraluminal pressure increase of 10 mmHg. The FEM is an upscaled version of a previously published FEM model for coronary artery atherosclerosis (Baldewsing et al., 2004). As can be observed (Fig. 1a), the model resembles a typical vulnerable plaque with a large lipid pool that is separated from the lumen by only a thin fibrous cap (Schaar et al., 2004a; Virmani et al., 2000). To define the initial matrix scatterer (before the pressure increase), one million scatterers were randomly distributed over the vessel wall area. The geometry and Young’s modulus values of the different layers are presented in Fig. 3. The lumen center was located at a depth of 2 cm. The amplitude of all scatterers was set equal to one. The positions of the scatterers after the pressure increase were obtained by adding the axial and lateral displacements from the finite element model solution to the scatterer positions of the initial matrix. The FEM was
constructed using the partial differential equation toolbox of Matlab R2010b (The MathWorks, Natick, MA, USA) and consisted of over 20.000 triangular finite elements. All elements were assumed to be nearly incompressible (Poisson’s ratio, $\nu = 0.495$) and isotropic and a plane strain situation was assumed. A very soft ($E = 1$ Pa) compressible ($\nu = 0.001$) surrounding layer of 2 mm thickness was added to avoid rigid body translation during the FEM calculation. This layer was not considered during the rest of the analysis. Band-limited noise was added to the simulated RF data to make the data more realistic using the procedures described before (Hansen et al., 2013). Noise was added to the plane wave data and the focused data until a signal-to-noise ratio of 13 dB and 27 dB was reached, respectively. These values were obtained from the experimental data by determining the intensity of the RF signal inside the vessel wall with respect to the level of the noise outside the vessel wall.

2.2. Phantom experiments

To compare the various acquisition modes in a more realistic setting, a vessel-mimicking phantom was created that consisted of two layers. The outer diameter of the phantom was 1.3 cm and it had an eccentric lumen with a diameter of 0.7 cm. The phantom was created in two steps. First the outer layer was created by pouring a 15% polyvinylalcohol (PVA) solution with scatterers in a mold with a diameter of 1.3 cm after concentric placement of a rod of 1 cm in diameter. To create the solution, a mixture of 2.5 g of SiC scatterers (15–40 μm, E. Merck, Darmstadt, Germany), 37.5 g of PVA (Boom, Meppel, The Netherlands), and 210 g of cooling liquid (Koelvloeistof Basic Safe, Halfords, The Netherlands) was heated to ~90 °C in a closed cylinder until a homogeneous liquid was formed. After pouring the solution in the mold, it was freeze thawed once. The cooling liquid was used to reduce the generation of tissue inhomogeneities caused by the increased pressure that is usually generated by inward freezing that occurs when water instead of cooling liquid is used. After freeze thawing once, the concentrically placed rod was removed and replaced by an eccentric rod of 0.7 cm in diameter. The created void was then filled with a similar PVA solution, however now with only 10% PVA to create a soft inner layer. The mold with the stiff outer layer and the new solution was subjected to another freeze-thaw cycle for solidification. The geometry of the phantom is presented in Fig. 4a. Young’s modulus of the soft layer and the stiff layer were estimated to be 8.1 kPa, and 98.8 kPa, respectively, see also Fig. 4e. To obtain these values, two additional homogeneous phantoms with a concentric lumen were created from 10% and 15% PVA solutions. Ultrasound recordings of these phantoms were acquired for various intraluminal pressure levels and the diameter was plotted as a function of the intraluminal pressure. From the slope of these curves Young’s modulus was estimated using a previously published procedure (Hansen et al., 2010a).

After creation, the soft plaque phantom was placed in a water tank with the transducer mounted above it and facing down. The vessel phantom was attached to a pump that generated a sinusoidal pulsating flow at a frequency of 1.5 Hz (90 BPM) with a minimum pressure of 20 mmHg and a maximum pressure of 26 mmHg. At this pressure change, the maximum cumulative strains were in the order of 10% and the maximum interframe strains were approximately 1.5%, which is similar to a real carotid artery. The pressure was monitored using a disposable pressure sensor (Ohmeda). Ultrasound RF data were acquired using the same two ultrasound acquisition modes as used in the simulations: plane wave acquisition, and focused acquisition. RF data were again recorded for beam steering angles of $\theta = 0^\circ$, $-20^\circ$ and $20^\circ$. Ultrasound B-mode images of the vessel phantom for the various angles and acquisition modes are shown in Fig. 4. A Verasonics 4-board system, equipped with an L5-12 transducer, was used to record the RF data. All settings in transmission were equal to those used in the simulations and delay-and-sum beam-forming was performed in receive as described in Appendix B. A frame rate of 59 Hz was used for focused imaging which is similar to frame rates achieved in conventional vascular 2D imaging. For each beam steering angle, ultrasound acquisitions were performed for 95 image lines with the center line crossing the lumen center. To obtain RF data for a full sweep from minimum to maximum pressure without memory overload, the system was paused after each acquisition of three angles before acquiring a new set of three angles. This pausing resulted in a compound acquisition frame rate of 15 Hz. For plane wave imaging the frame rate was set to 2000 Hz. Although possible, higher frame rates were not used in this acquisition mode to limit the computational load and the amount of memory required for storage of the data.

2.3. Strain estimation

Before displacement estimation, a region of interest (ROI) was selected based on a 0° focused image acquired at minimum pressure. Displacement estimation was performed within this ROI for all beam steered acquisitions. For each acquisition angle, axial displacements were calculated using 2D cross-correlation kernels. The displacements were estimated iteratively, using a coarse-to-fine 2D cross-correlation method which was described in (Lopata et al., 2009). Briefly, in iteration one, the method starts by estimation of ‘coarse’ displacements using large RF data kernels of $1 \times 1$ mm². In iteration two, more local ‘finer’ displacement estimates are obtained by using decreased kernel sizes of $0.5 \times 1$ mm². In the last iteration, subsample aligning was used to more accurately find the cross-correlation peak at subsample level (Lopata et al., 2009). The ‘coarser’ displacement estimates of each
preceding iteration were used as an initial guess. A window overlap of 40% was used in the axial direction and of 80% in the lateral direction which resulted in a displacement estimate, or pixel, for approximately every $200 \times 200$ µm$^2$. In between iterations, those displacement estimates that were considered as outliers were median filtered using a window of $7 \times 7$ displacement pixels. Outliers were defined as displacement values that had a corresponding normalized cross-correlation peak lower than 0.7.

To be able to derive the complete 2D strain tensor, two independent displacement components ought to be estimated. As aforementioned, our compounding technique estimates the horizontal and vertical displacement component separately by using axial displacement estimates obtained at the various beam steering angles (Hansen et al., 2010b). The 0° axial displacement provides a direct estimate of the vertical displacement component. The axial displacements obtained from the +20° and –20° beam-steered acquisition are combined to derive the horizontal displacement ($u_{\text{hor}}$) component:

$$u_{\text{hor}} = \frac{u_{\text{ax}+\theta} - u_{\text{ax}-\theta}}{2 \sin \theta}$$

(1)

here, $u_{\text{ax}+\theta}$ and $u_{\text{ax}-\theta}$ are the axial displacements, estimated at beam steering angles of +20° and –20°, respectively. These horizontal and vertical displacement estimates were cumulated over all pressure steps using a custom made tracking algorithm created in Matlab 2010b (Matlab, the Mathworks, Natick, MA, USA). Briefly, the coordinates of each point within the ROI with respect to the starting frame are recalculated for each new frame using the estimated displacements. Since the displacements do usually not correspond to an integer amount of displacement pixels, bilinear interpolation was used to find the displacement values at coordinates in between displacement pixels. For each frame, the difference of the tracked coordinates of the points in the ROI was determined with respect to their coordinates in the first frame. The differences of the x-coordinates and the y-coordinates provided the cumulative axial and lateral displacements, respectively. 1D least-squares strain estimators (LSQSE) with a size of 9 displacement pixels were then applied to these cumulative displacements to obtain all 2D strain components (Kallel and Ophir, 1997). Principal component analysis resulted in the principal strains.

### 2.4. Analyses

For the simulation, the root-mean squared error (RMSE) of the estimated radial strains and circumferential strains with respect to the FEM strains was determined to compare the strain estimation precision for the various transmission methods. For comparison, also the results for 0° focused imaging and 0° plane wave imaging are presented. For these 0° cases, the horizontal displacement component corresponded to the lateral displacement estimate obtained directly from the 2D normalized cross-correlation procedure.

For the eccentric two-layered phantom, the strain images were compared by calculating the elastographic signal-to-noise ratio ($SNRe$) and the elastographic contrast-to-noise ratio ($CNRe$). In order to calculate the $SNRe$ and $CNRe$, two regions of interest corresponding to the inner and outer layer were manually selected. $SNRe$ and $CNRe$ were calculated following

$$SNRe = 20 \log \frac{\mu_1}{\sigma_1}$$

(2)

$$CNRe = 20 \log \frac{2(\mu_1 - \mu_2)^2}{(\sigma_1^2 + \sigma_2^2)}$$

(3)

here, $\mu_1$ and $\mu_2$ are the mean and $\sigma_1$ and $\sigma_2$ are the standard deviations of the strain values in the two vessel layers (index 1 = inner layer, index 2 = outer layer). Besides $SNRe$ and $CNRe$, also the mean deviation from zero for the cumulated radial and circumferential strains after one pressure cycle was calculated. This parameter is called the residual strain. Because the vessel returns to its initial state after each pressure cycle, the residual strain value gives an indication of the cumulative error that is generated for the various transmission methods over an entire pressure cycle. Finally, the estimated strain images of the phantom were also visually compared with theoretical strain images determined by finite element modeling. The FEM was constructed using the geometry and Young’s moduli presented in Fig. 4 and using the same Matlab toolbox and assumptions as were used for the construction of the FEM in the simulations. The difference between the FEM deformation fields at intraluminal pressures of 20 mmHg and 26 mmHg was taken as the theoretical strain field.

### 3. Results

#### 3.1. Simulations

The constructed radial and circumferential strain images for the simulated phantom are presented in Fig. 5. As can be observed, the radial strains (top row) are negative in sign and the circumferential strains (bottom row) are positive in sign, which is as expected because the intraluminal pressure was increased. Furthermore, it can be observed that the strain images obtained with focused compounding and plane wave compounding match the theoretical FEM solution better than the images obtained with 0° imaging. As expected, compounding provides better estimates in the 3 and 9 o’clock regions of the radial strain images, and in the 6 and 12 o’clock regions of the circumferential strain images, because the lateral component normally dominates the estimates in these regions when using 0° imaging. A striking result is that the images obtained with plane wave acquisition and focused acquisition are almost similar despite the poorer lateral resolution of the plane wave ultrasound image. Table 1 shows the results of the RMSE analysis, which quantitatively support this qualitative observation. The RMSE values for plane wave compounding and for focused compounding are approximately the same: 0.33% for the radial and ~0.40% for the circumferential component. The RMSE values for 0° focused imaging and 0° plane wave imaging are also similar, except for the radial strain image obtained with 0° focused imaging, which has an RMSE value which is 1.31 times the RMSE of the 0° plane wave image (0.97% versus 0.74%). Compounding clearly outperforms 0° imaging. With respect to 0° focused imaging with RMSE values of 0.97% for radial strain and 0.76% for circumferential strain, plane wave compounding reduced the RMSE by 66% and 50%, respectively.

#### 3.2. Experiments

Fig. 6 shows the calculated strain images for the experiment with the two-layered vessel mimicking phantom at various
moments during the pressure cycle. As can be observed, focused compounding and plane wave compounding again results in less errors than 0° imaging. The results obtained with focused acquisition are again visually similar to those obtained with plane wave acquisition. At the end of the pressure cycle, strain values deviate from zero in the 3 and 9 o’clock regions of the radial strain images, and in the 6 and 12 o’clock regions of the circumferential strain images obtained by 0° imaging. Because the phantom returns to its initial state after each pressure cycle, zero strain is expected over the full cross-section. Therefore, these deviations from zero can be considered as errors. As can be observed, these errors are not present in the images obtained with compounding. With compounding, a band of increased strain values can clearly be distinguished in the soft layer of the vessel region indicated in Fig. 6, which is dominated by errors in the 0° images. This band is most clearly visible when the intraluminal pressure is maximum (t=0.6 T). The increased strain levels in that region with respect to the rest of the cross section can also be observed in the theoretical strain images that were obtained by the finite element modeling, Fig. 7. Overall, the estimated strain images have the same pattern as the FEM-based theoretical strain field, although the absolute value of the FEM-based strain is lower. Table 2 shows the results of the SNR, CNR, and residual strain analysis. As expected, the SNR and CNR values for the compounded images are much higher than for the 0° acquisitions. For plane wave compounding, the SNR and CNR of the radial strain were 4.0 dB and 2.8 dB and the SNR and CNR for the circumferential strain were 6.4 dB and 0.5 dB. Compared to the 0° focused acquisition this is an increase in radial SNR and CNR of 2.1 dB and 3.7 dB, respectively, and an increase in circumferential SNR and CNR of 5.6 dB and 16.2 dB, respectively. An increase in SNR of ~6 dB implies a twofold reduction (10^6/20) in the standard deviation of the strain estimates considered that the average strain measured in the region of interest is the same. An increase in CNR of 16 dB roughly indicates a 6 times (10^16/20) better discrimination of the strain values of the two selected regions. Focused compounding performed slightly better than plane wave compounding. On average, the SNR and CNR are 1.7 dB and 2.5 dB higher for focused compounding. The residual strain results reveal a similar performance: the residual strain for focused compounding is less than for plane wave compounding. Compounding again clearly outruns the performance of 0° imaging. The residual radial and circumferential strains reduced from 2.4% and 5.0% for plane wave compounding to 1.3% and 1.1% for 0° focused imaging.

Table 1
The root mean squared-error (RMSE) values for the radial and circumferential strain images constructed for the simulated vulnerable plaque model for the investigated ultrasound acquisition methods.

<table>
<thead>
<tr>
<th>RMSE (%)</th>
<th>0° Focused imaging</th>
<th>Focused compounding</th>
<th>0° Plane wave imaging</th>
<th>Plane wave compounding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radial strain</td>
<td>0.97</td>
<td>0.33</td>
<td>0.74</td>
<td>0.33</td>
</tr>
<tr>
<td>Circumferential strain</td>
<td>0.76</td>
<td>0.41</td>
<td>0.75</td>
<td>0.38</td>
</tr>
</tbody>
</table>

Fig. 6. The left four columns show radial strain images constructed for the various acquisition modes for the eccentric two-layered experimental phantom. The remaining columns present the circumferential strain images constructed for the various acquisition modes. From top to bottom, the cumulative strain images recorded at various acquisition times during the pressure cycle are shown.

Fig. 7. The theoretical radial and circumferential strain images for the two-layered phantom obtained using finite element modeling. An intraluminal pressure increase of 20 mmHg to 26 mmHg was assumed.
4. Discussion

For both simulations and experimental data, plane wave compounding provides a major improvement in the strain estimation accuracy with respect to 0° focused imaging. In the simulations, the plane wave compounding results are approximately equal to those obtained with focused compounding. For the experimental data, the focused compounding results were slightly better in terms of SNRe and CNRe, compared to the plane wave compounding results, although this difference in performance was hardly observable in the actual strain images (Fig. 6). On average, the SNRe and CNRe were 1.7 dB and 2.5 dB higher for the focused acquisitions. In terms of residual strain, only the radial strain revealed an improvement of focused imaging over plane wave imaging. The improved performance in terms of SNRe and CNRe might be explained by the fact that the ultrasonic signal-to-noise ratio of focused ultrasound imaging is higher than the ultrasonic signal-to-noise ratio of plane wave imaging, as can also be observed in Fig. 4. It should however be kept in mind that only data for one vessel cross-section were considered in this study. The improvement might thus not be statistically significant. The plane wave and focused acquisition were performed after each other, which might also have lead to small variations in the experimental setup and thus in the strain measurements. Next to that, for the calculation of SNRe and CNRe, officially two regions with homogeneous strain values should be considered. This was not possible in this study because of the natural strain decay from the inside to the outside of the vessel wall, which is also visible in the FEM based strain profiles of Fig. 7. The lower strain levels for the FEM with respect to the estimated strains would either indicate an underestimation of the intraluminal pressure difference or an overestimation of Young’s moduli. The pressure sensor has an accuracy of at least 0.1 mmHg. Therefore, we expect that Young’s moduli were overestimated. The phantom we used in the experiments had been stored in a refrigerator in a closed tank with water for some time before the experiments were performed. Therefore, it might be that the phantom had softened a bit, due to the absorption of water. Next to that, the PVA-solutions for the two-layered phantom and the homogeneous phantoms were created at different times, thus small variations in the concentration of the solution might also have been present. Aside from the discussion whether focused compound strain estimation is slightly better than plane wave compound strain estimation, it should be kept in mind that the frame rate for plane wave imaging is a factor of ~100 higher in 2D. This provides a lot of opportunities to improve the strain estimation. For instance, the quality of strain estimation might be improved further by averaging of strain images. Adding acquisitions using more beam steering angles might also be an option. In several studies it has been illustrated that compounding with more acquisition angles further improves the strain estimation quality (Rao and Varghese, 2009; Techavipoo et al., 2004).

The high frame rates reached with plane wave imaging also bring 3D vascular strain estimation within reach. If a 2D matrix array would already exist with the possibility to record a 100 by 100 imaging lines using focused imaging, frame rates would be around 1 Hz, thus approximately 1 image per pressure cycle. Thus, too low to perform 3D vascular elastography. For plane wave transmission frame rates would be the same in 2D as in 3D, since only one transmission is required to image an entire 3D volume. The step from 2D to 3D is very important for vascular applications, because it reduces operator dependency by imaging a large volume instead of one cross-section. Furthermore, since the artery translates and deforms in the longitudinal direction, it can move out of the imaging plane during 2D strain estimation. This will result in artifacts for 2D strain estimation but for the 3D case, this motion can be quantified and corrected for. Next to further enhancement of the strain estimation and extension of the technique to 3D, it would also be interesting to see how the technique performs in vivo and to compare the estimation quality with other proposed techniques like synthetic aperture imaging and coherent plane wave compounding.

Finally, some discussion about the application of ultrasound, plane wave imaging and plane wave compound strain imaging in the clinic. Because ultrasound is fast, easily applicable, non-ionizing, relatively cheap, and has a higher temporal resolution than MRI, CT, and PET, it is the imaging modality of choice for diagnosis of vascular disease. A drawback of ultrasound is that the image quality depends on what tissue the ultrasound signal has to travel through before reaching the tissue of interest. In vascular applications, calculations can seriously reduce image quality and with that make it difficult to diagnose. In case no proper diagnosis can be made based on ultrasound, usually other imaging modalities are used. Another way of avoiding the calculations would be to screen for vulnerable plaques at an earlier stage of atherosclerosis, when plaques hardly contain any calcifications. In this stage, vulnerable plaques are often non flow limiting and, therefore, not considered as dangerous based on current ultrasound Doppler-based parameters. Strain imaging however, might highlight regions with increased strains within the vessel wall, indicating the presence of vulnerable plaque. With respect to plane wave imaging, we expect application in the clinic soon, because plane wave transmission can be carried out using the same ultrasound transducers as are being used for focused imaging now. The change from focused transmission to plane wave transmission can be performed by software adjustments only. Plane wave imaging at full frame rates and for several seconds is however not possible yet on most existing ultrasound systems, because it puts extra demands on data transfer rates and on data storage capacity. Nevertheless, to successfully perform plane wave strain compounding for arterial deformation estimation, it is not required and not advisable to scan at maximum frame rates for a long period of time without interruption, because the motion in between two frames would be too small to be successfully estimated. We propose a combination of high and low frame rates

<table>
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<tr>
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<th>Focused imaging</th>
<th>Focused compounding</th>
<th>Plane wave imaging</th>
<th>Plane wave compounding</th>
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<tbody>
<tr>
<td>Radial strain</td>
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<tr>
<td>SNRe (dB)</td>
<td>1.9</td>
<td>5.9</td>
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<tr>
<td>CNRe (dB)</td>
<td>−6.5</td>
<td>−0.5</td>
<td>−12.0</td>
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<tr>
<td>Residual (%)</td>
<td>2.4</td>
<td>0.6</td>
<td>3.0</td>
<td>1.3</td>
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<tr>
<td>SNRe (dB)</td>
<td>0.8</td>
<td>7.8</td>
<td>1.1</td>
<td>6.4</td>
</tr>
<tr>
<td>CNRe (dB)</td>
<td>−15.7</td>
<td>3.1</td>
<td>−14.1</td>
<td>0.5</td>
</tr>
<tr>
<td>al</td>
<td>5.0</td>
<td>1.1</td>
<td>4.6</td>
<td>1.1</td>
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for optimal performance of the plane wave compounding technique. A high frame rate (> 1000 Hz) to acquire the RF data at the multiple beam steering angles in a certain state of deformation, and a low frame rate (> 30 Hz) in between each set of beam steered acquisitions to generate strains in the arterial wall that can be optimally estimated.

In conclusion, compound plane wave strain estimation outperforms strain estimation based on focused imaging. Strain images were visually similar to images obtained with focused compounding for both simulated as well as experimental data. Because frame rates are more than 100 times higher for plane wave acquisitions, there is room for further enhancement of the strain estimation accuracy. Furthermore, due to the high frame rates and promising accuracy, the compound plane wave strain estimation technique is expected to enable accurate noninvasive 3D vascular strain estimation in future.

Conflict of interest statement
There is no potential conflict of interest to declare.

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Appendix. Supplemental Data
Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.jbiomech.2014.01.015.

References
