Ultrasound strain imaging for quantification of tissue function: cardiovascular applications

Chris L. de Korte[a], Richard G.P. Lopata[b], Hendrik H.G. Hansen[a]
[a]Medical UltraSound Imaging Centre (766 MUSIC),
Radboud University Medical Centre, POBox 9101, 6500HB Nijmegen, The Netherlands
[b] Biomedical Engineering, Eindhoven University of Technology, Eindhoven, The Netherlands

ABSTRACT

With ultrasound imaging, the motion and deformation of tissue can be measured. Tissue can be deformed by applying a force on it and the resulting deformation is a function of its mechanical properties. Quantification of this resulting tissue deformation to assess the mechanical properties of tissue is called elastography. If the tissue under interrogation is actively deforming, the deformation is directly related to its function and quantification of this deformation is normally referred as 'strain imaging'. Elastography can be used for atherosclerotic plaques characterization, while the contractility of the heart or skeletal muscles can be assessed with strain imaging.

We developed radio frequency (RF) based ultrasound methods to assess the deformation at higher resolution and with higher accuracy than commercial methods using conventional image data (Tissue Doppler Imaging and 2D speckle tracking methods). However, the improvement in accuracy is mainly achieved when measuring strain along the ultrasound beam direction, so 1D. We further extended this method to multiple directions and further improved precision by using compounding of data acquired at multiple beam steered angles.

In arteries, the presence of vulnerable plaques may lead to acute events like stroke and myocardial infarction. Consequently, timely detection of these plaques is of great diagnostic value. Non-invasive ultrasound strain compounding is currently being evaluated as a diagnostic tool to identify the vulnerability of plaques. In the heart, we determined the strain locally and at high resolution resulting in a local assessment in contrary to conventional global functional parameters like cardiac output or shortening fraction.

Keywords: Ultrasound, Elastography, Strain imaging, Heart, Carotid.

1. INTRODUCTION

After the introduction of ultrasound imaging for medical applications [1, 2] it has always been used to assess the morphological as well as functional information of organs. With ultrasound imaging the geometry can be visualized and quantified with excellent accuracy. Furthermore, the velocity of blood particles can be assessed using ultrasound Doppler imaging. Since the time required for acquiring a 2D image is only in the order of 10-50 ms, images can be acquired at high temporal resolution making it the ultimate technique for imaging rapidly moving or deforming structures. These advantages have positioned ultrasound imaging as the most frequently used modality for cardiovascular applications.

Cardiovascular disease is one of the leading causes of death in Western Society [3]. For optimal treatment, geometric and functional imaging is of paramount importance. Echography or ultrasound (US) imaging is the most used imaging modality for diagnosis of cardiovascular disease [3]. US imaging is non-invasive, easily applicable, and has no potentially harmful radiation hazard. The great advantage of 2D US is the excellent temporal resolution which makes it especially suited for studying dynamic processes like, for example, closing of the heart valves .

With the increase in computational power and the inherent high temporal resolution, in the last two decades many new developments were introduced to assess and quantify tissue motion and deformation in order to quantify its function or mechanical properties. During the last decade, two major breakthroughs occurred in ultrasound imaging: firstly, real-time 3D cardiovascular imaging became available as a clinically useful tool. With the introduction of 2D matrix array transducers not just one longitudinal plane but a whole volume can be scanned by transmitting the echo pulses in a pyramid shaped volume [4]. In this way, the whole heart, or a substantial part of the vasculature, can be imaged in 3D. In

Medical Imaging 2013: Ultrasonic Imaging, Tomography, and Therapy, edited by Johan G. Bosch, Marvin M. Doyley,
Proc. of SPIE Vol. 8675, 867502 · © 2013 SPIE · CCC code: 1605-7422/13/$18 · doi: 10.1117/12.2001595

particular for imaging of the heart with its complex deformation pattern not confined to a single plane, real-time 3D scanning is beneficial [4].

Secondly, new kinds of functional US imaging became feasible with the introduction of strain (deformation) imaging and motion tracking techniques [5]. Ultrasound strain imaging or elastography was first described in 1991 by Ophir and colleagues [5]. Elastography provides a strain image that is a representation of the elastic (mechanical) properties of the tissue. Since tumors have mechanical properties deviating significantly from surrounding tissues like breast or liver, elastography is in principle an excellent technique to identify and characterize these tumors. For this reason, in the last decade of the last century this technique was mainly focused on tumor detection. But a tendency towards cardiac and vascular applications can be observed over the last 10 years [6-10]. In case of the heart, the strain images do not represent the mechanical properties of the tissue but are representing the contractile properties of the heart muscle. Since high resolution (2D) strain images are generated with these techniques, local dysfunction of the heart muscle can be identified and quantified. Commercial strain estimation software is based on tracking dominant image features: echograms are characterized by a 'noisy' appearance called speckles, and these speckles can be tracked in 2D and 3D datasets [11]. However, basic elastography studies have demonstrated that the deformation of tissue can be determined much more accurately by using the radio frequency (RF) ultrasound data. In contrary to the echo image, the RF signal is containing both amplitude and phase information and especially the phase information is very beneficial for tracking small displacements accurately [12]. The displacement of tissue is mostly determined by calculating the cross-correlation function of successively acquired RF data. It appeared that the cross-correlation value is also a valuable parameter to distinguish between the heart muscle and the fast flowing blood in the cavities. Therefore, this information can additionally be used to segment the heart muscle [13].

A relatively new application of strain imaging is vascular elastography to identify atherosclerotic plaque components. This method uses the principle that the pulsatile blood pressure deforms the vessel wall and plaque. The magnitude of the strain is not only related to tissue composition but is also a strong indicator of weak spots in the plaque surface [14]. This method was initially developed using intravascular ultrasound catheters [15] and is currently being transformed into a non-invasive technique [16].

In this paper, the application of different techniques to quantify cardiac as well as skeletal muscle deformation will be reviewed. Furthermore, the application of strain compounding using beam steering to characterize atherosclerotic plaques will be discussed.

2. CARDIAC STRAIN IMAGING

2.1 Tissue Doppler Imaging

In the nineties, assessment of myocardial function became feasible by means of Tissue Doppler Imaging[17]. By acquiring the Doppler signal produced by the moving myocardial tissue instead of the blood, an estimate of the tissue velocity became available. The hypothesis was that affected myocardial tissue would have a decreased velocity or an asynchronous velocity pattern in respect to normal myocardial tissue. This technique could be implemented easily in commercial ultrasound systems since it is based on Doppler techniques. The disadvantage of the velocity of the tissue is that non contracting myocardial tissue that is surrounded by still functional contracting tissue will have a similar velocity pattern as the normal tissue since it will be moved by the surrounding tissue. To overcome this problem, the next step was to determine the deformation of the myocardial tissue. Hans Torp and colleagues [18] introduced Doppler based strain imaging. By taking the difference between two velocity estimates along a Doppler trace and dividing it by the distance between them, the strain rate was assessed. Integrating this strain rate estimates over the cardiac cycle results in the strain curve. Since the strain in the cardiac muscle can only be determined along the ultrasound line this technique is inherently one dimensional. In this way, in particular regions the longitudinal strain can be determined using apical acquisitions and circumferential and radial strain using parasternal views.

2.2 Speckle tracking techniques

Nowadays, non-Doppler techniques are the most used techniques for cardiac and vascular applications [4;5]. Since high resolution (2D) strain images can be acquired at high temporal resolution, local dysfunction of the heart muscle can be identified and quantified by tracking dominant image features. Echograms are characterized by a 'noisy' appearance called speckles, and these speckles can be tracked [11]. Although the speckle presence changes with tissue deformation and motion, the correlation between subsequently acquired echo frames is high due to the high frame rates available. For cardiovascular applications, a frame-rate of 60 to 80 frames per second is considered sufficient to maintain proper correlation between the frames. Different techniques have been developed to adequately track the tissue displacement. The main difference are in the regularization techniques applied after displacement estimation. The strain is determined by taking the finite difference, which amplifies the noise. Consequently, temporal filtering as well as using *a priori* information on tissue incompressibility and tissue motion over the cardiac cycle are applied to convert the noisy displacement estimates into a strain value. This might be the reason that strain values measured with multiple systems on the same patients differ substantially for different systems [19, 20]. Therefore, a sensitive and accurate technique is required to enhance the clinical applicability and making strain estimation vendor independent.

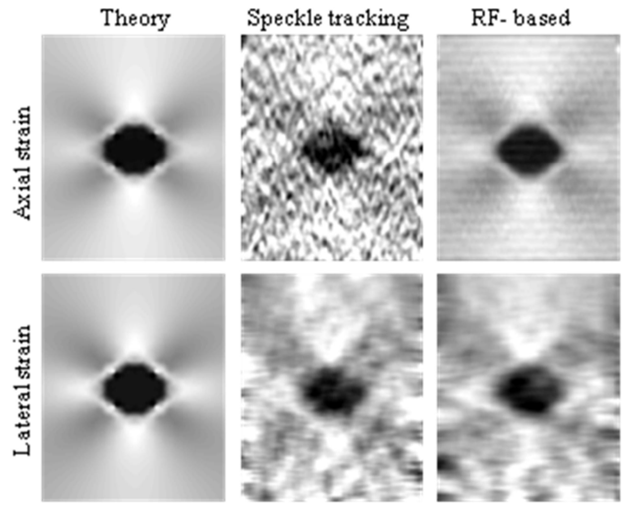

Figure 1: The benefit of RF-based 2D strain estimation.

2.3 RF based techniques

Speckle tracking techniques are less computationally demanding than RF-based strain estimation techniques that are used in elastography. However, basic studies have demonstrated that the deformation of tissue can be determined much more accurately by using the RF signal [21]. In contrary to the echo image, the RF signal contains both amplitude and phase information and especially the phase information is very beneficial for tracking small displacements accurately. The displacement of tissue is mostly determined by calculating the cross-correlation function of successively acquired RF data. This approach was for the first time applied by Konofagou and d'Hooge [9] and was further developed for 2D strain estimation by Langeland et al. [10].

We implemented an iterative 2D and 3D correlation-based algorithm [12, 22]. Displacements were calculated from the temporal position of the peak of the 2D, or 3D, cross-correlation function. To obtain sub-sample and sub-line resolution, 1D parabola's were fitted in three orthogonal directions through the peak of the cross-correlation function by solving analytical expressions. To increase elastographic resolution, the window size was decreased using previous (interpolated) estimates as offset values (coarse-to-fine strategy). A short median filter was applied to remove outliers in the displacement images and the 2 or 3 orthogonal components of the strain were obtained using a least squares strain estimator [23].

RF- based techniques are still in experimental phase and are not commercially available. We evaluated the 2D and 3D strain estimation techniques using matrix array transducers: a 4 MHz (X4) connected to a SONOS 7500 or a 7 MHz (X7-2) with an iE33 real-time 3D system (both Philips Medical Systems, Bothell, USA). Both systems were equipped with an RF-interface. All RF data were first stored in memory and then transported to a workstation for off-line processing. For experimental verification, a phantom was made of 8.0 % gelatine (1.0 % agar) with a hard cylindrical inclusion (3.0 % agar, approximately four times stiffer). The phantom (10 cm x 10 cm x 10 cm) was compressed with a large plate compressor by applying a stepwise displacement of 0.5 mm (leading up to a total of 10.0 % strain in 20 steps).

The technique was further evaluated in an animal study in which dogs (n=4) with an induced valvular aortic stenosis were monitored over time. At an age of 8 weeks, a stenosis was created resulting in a pressure gradient as measured with Doppler ultrasound of 35 mmHg. This stenosis developed in 3 months into a pressure gradient of 20, 100, 120, and 200 mmHg, for the four animals, respectively. The created valvular aortic stenosis results in a chronic pressure overload of the left ventricle leading to hypertrophy (and eventually fibrosis) of the myocardial tissue, except for the stenosis with a gradient of 20 mmHg that can be considered to be insignificant. Using ECG-triggered BiPlane imaging with the SONOS 7500, frame-to-frame deformations were obtained over the heart-cycle for manually segmented regions-of-interest (ROIs) of the lateral wall in both the short-axis (SAX) and long-axis (LAX) planes [24]. The results of these experiments revealed that the radial strain as measured in the SAX and LAX planes are similar, underlining the accuracy of the technique. The circumferential and longitudinal strain as measured in the SAX and LAX planes respectively show increased standard deviation of the strain estimate with respect to the radial strain estimates. This can be explained by the fact that these strain components are determined from the envelope of the ultrasound signals instead of the RF-data that is used for the radial strain estimates. Comparison of strain profiles of hearts with different valvular aortia stenosis rates

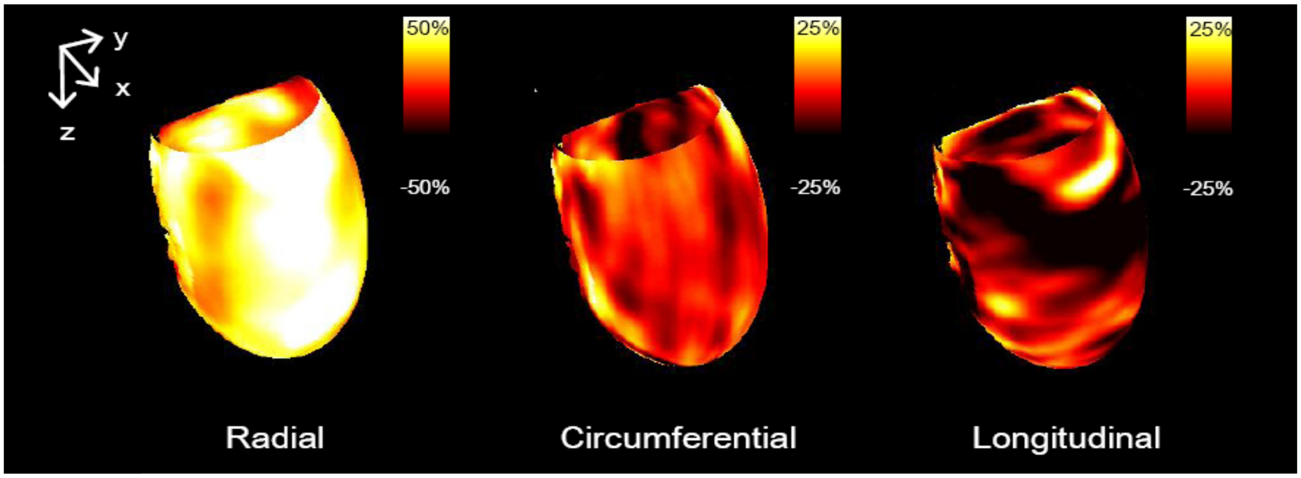

Figure 2: Full volume 3D strain imaging of the left ventricle of a normal child during systole showing thickening in radial direction and extension in circumferential and longitudinal direction.

reveals decreasing strain values for increasing stenosis rates. Furthermore, for severely stenotic valves, not only both systolic strain rate and maximum (end-systolic)strain decreased but also prolonged intervals of increased strain were found in the diastolic phase, indicating diastolic failure.

Clinical evaluation was performed using full volume RF data acquired in nine healthy children at the age of 6 -14 years with a Philips iE33 ultrasound machine. The full volume dataset was acquired in 7 consecutive heart beats and resulted in a volume acquisition rate of approximately 50 Hz [25]. The 3D strain images representing the 3 orthogonal directions of the strain in a healthy child are presented in figure 2 and demonstrate that full 3D RF-based strain estimation using commercially available volume rates is feasible. However, during the heart cycle, the error in the strain estimate increases, especially in parts of the heart cycle with high deformation rates. Consequently, increased volume rates would be beneficial for RF-based strain estimation.

3. VASCULAR STRAIN IMAGING

In multi-dimensional strain imaging it is known that the optimal performance is obtained along the ultrasound beams. In this direction, the phase of the ultrasonic RF signal is also present and, especially when using the phase, small displacements can be quantified very accurately. Consequently, the accuracy in the axial direction (along the ultrasound beam) is 5 to 10 times better than in the lateral and azimuthal directions, i.e., orthogonal to the axial direction. When performing non invasive elastography of arteries, this results in poor radial strain estimates in regions where the ultrasound beam and radial strain are almost perpendicular [26]. Strain estimation in these regions was improved by strain compounding [27, 28]. Using multiple data sets acquired with different beam steered angles, the lateral strain can be determined from the axial displacement estimates [29, 30].

The benefit of strain compounding is demonstrated using a vessel with a soft plaque. From figure 3, it is clear that the strain estimate is much more accurate using compounding (right panel) than using conventional strain imaging (middle panel). Especially in the area's where the lateral component is dominating (at 3 and 9 o'clock), the improvement is substantial. Qualitative assessment by merely looking at the images already reveals that the improvement due to compounding is dramatic. Quantification of the improvement was performed by calculating the elastographic signal tot noise ratio (SNRe) and the elastographic contrast to noise ratio (CNRe). Compounding resulted in a 4dB improvement of the SNRe whereas the CNRe increased with almost 10 dB.

Evaluation of vascular strain compounding was performed in healthy volunteers. That study demonstrated that strain compounding is feasible while using the natural pulsatile pressure as excitation source. It became evident that strain compounding resulted in more precise strain estimates when compared to conventional strain imaging. Currently, the method is validated in patients. Compound strain acquisitions are performed in symptomatic patients the day before an endarterectomy procedure of the carotid is performed. During the endarterectomy procedure, the plaque is kept intact and is taken out allowing to perform histologic validation of the carotid elastograms.

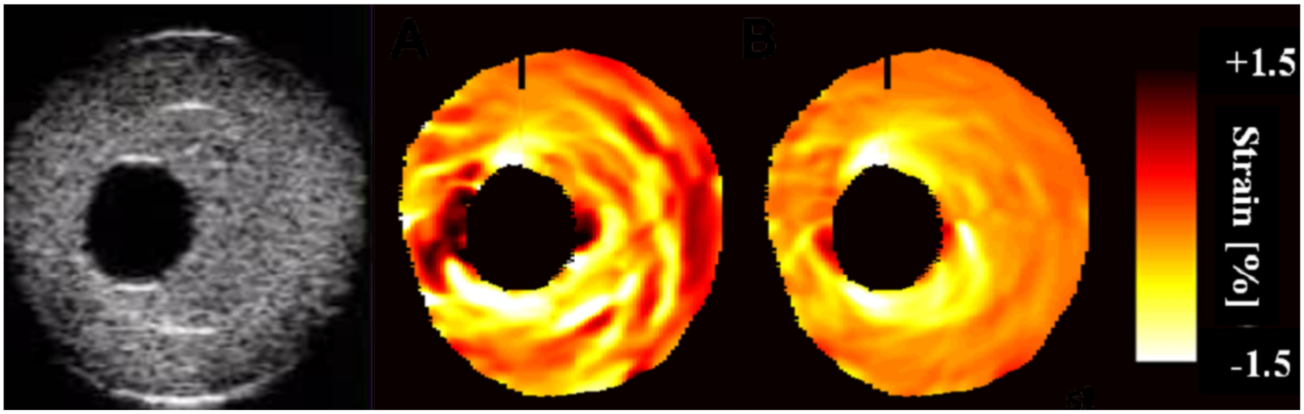

Figure 3: Non invasive vascular elastography with strain compounding (right) and conventional strain imaging (middle) of a vessel phantom with soft eccentric plaque with corresponding echogram (left).

Initial results show excellent agreement between elastograms and histology (data not shown). The presence of large regions with high strains showed to be a good predictor with high sensitivity and specificity for the presence of macrophages in the vicinity of the lumen and the presence of large amounts of fatty material in the plaque

4. CONCLUSION

Ultrasound strain imaging is an excellent method to assess cardiac function and to identify vulnerable plaque in arteries. RF-based strain imaging outperforms conventional strain imaging methods using only the gray scale images. Implementation of RF-based techniques in commercial echo systems is required to establish the clinical benefit of these techniques.

REFERENCES

[1] I. Edler and C. H. Hertz, "Application of echo ranging techniques to the determination of structures of biological tissues," *K.Fysiogr.Sallst.Lund Forshung,* 24, 1-19, (1954).

[2] I. Edler and C. H. Hertz, "The use of the reflectoscope for the continuous recording of the ovement of heart walls," *K.Fysiogr.Sallst.Lund Forshung,* 24, 40-58, (1954).

[3] P. Libby, R. O. Bonow, D. L. Mann, and D. P. Zipes, *Braunwald's Heart Disease - a textbook of cardiovascular medicine*8th. Philadelphia, PA: Saunders, Elsevier, (2008).

[4] M. Ahmad, "Real-time three-dimensional echocardiography in assessment of heart disease," *Echocardiography.,* 18, 73-77, (2001).

[5] J. Ophir, I. Céspedes, H. Ponnekanti, Y. Yazdi, and X. Li, "Elastography: a quantitative method for imaging the elasticity of biological tissues," *Ultrason.Imaging,* 13, 111-134, (1991).

[6] C. L. de Korte, H. H. G. Hansen, and A. F. W. van der Steen, "Vascular ultrasound for atherosclerosis imaging," *Interface Focus,* 1, 565-575, (2011).

[7] J. A. Schaar, C. L. de Korte, F. Mastik, R. Baldewsing, E. Regar, F. P. de, C. J. Slager, A. F. van der Steen, and P. W. Serruys, "Intravascular palpography for high-risk vulnerable plaque assessment," *Herz,* 28, 488-495, (2003).

[8] A. F. W. van der Steen, C. L. de Korte, and E. I. Céspedes, "Intravascular ultrasound elastography," *Ultraschall in Medizine,* 19, 196-201, (1998).

[9] E. E. Konofagou, J. D'Hooge, and J. Ophir, "Myocardial elastography--a feasibility study in vivo," *Ultrasound Med.Biol.,* 28, 475-482, (2002).

[10] S. Langeland, J. D'Hooge, P. F. Wouters, H. A. Leather, P. Claus, B. Bijnens, and G. R. Sutherland, "Experimental validation of a new ultrasound method for the simultaneous assessment of radial and longitudinal myocardial deformation independent of insonation angle," *Circulation,* 112, 2157-2162, (2005).

[11] M. Leitman, P. Lysyansky, S. Sidenko, V. Shir, E. Peleg, M. Binenbaum, E. Kaluski, R. Krakover, and Z. Vered, "Two-dimensional strain-a novel software for real-time quantitative echocardiographic assessment of myocardial function," *J.Am.Soc.Echocardiogr.,* 17, 1021-1029, (2004).

[12] R. G. P. Lopata, M. M. Nillesen, H. H. G. Hansen, I. H. Gerrits, J. M. Thijssen, and C. L. de Korte, "Performance Evaluation of Methods for Two-Dimensional Displacement and Strain Estimation Using Ultrasound Radio Frequency Data," *Ultrasound in Medicine and Biology,* 35, 796-812, (2009).
[13] M. M. Nillesen, R. G. Lopata, H. J. Huisman, J. M. Thijssen, L. Kapusta, and C. L. de Korte, "Correlation based 3-d segmentation of the left ventricle in pediatric echocardiographic images using radio-frequency data," *Ultrasound Med.Biol.,* 37, 1409-1420, (2011).
[14] C. L. de Korte, G. Pasterkamp, A. F. W. van der Steen, H. A. Woutman, and N. Bom, "Characterization of plaque components using intravascular ultrasound elastography in human femoral and coronary arteries in vitro," *Circulation,* 102, 617-623, (2000).
[15] C. L. de Korte, H. P. J. Buschman, S. W. E. van der Poll, A. F. W. van der Steen, G. J. Puppels, and A. van der Laarse, "Vascular plaque characterization using intravascular ultrasound elastography and NIR Raman spectroscopy in vitro. ," in *Proceedings SPIE Medical Imaging*, San Diego, CA, USA, 2000, 180-186.
[16] H. H. G. Hansen, T. Idzenga, and C. L. de Korte, "Noninvasive Vascular Strain Imaging: from Methods to Application," *Current Medical Imaging Reviews,* 8, 37-45, (2012).
[17] W. N. McDicken, G. R. Sutherland, C. M. Moran, and L. Gordon, "Color Doppler Velocity imaging of the myocardium," *Ultrasound in Medicine and biology,* 18, 651-654, (1992).
[18] A. Heimdal, A. Stoylen, H. Torp, and T. Skaerpe, "Real time strain rate imaging of the left ventricle by ultrasound," *Journal of the American Society of Echocardiography,* 11, 1013-1019, (1998).
[19] L. P. Koopman, C. Slorach, W. Hui, C. Manlhiot, B. W. McCrindle, M. K. Friedberg, E. T. Jaeggi, and L. Mertens, "Comparison between Different Speckle Tracking and Color Tissue Doppler Techniques to Measure Global and Regional Myocardial Deformation in Children," *J.Am.Soc.Echocardiogr.,* (2010).
[20] L. P. Koopman, C. Slorach, C. Manlhiot, B. W. McCrindle, M. K. Friedberg, L. Mertens, and E. T. Jaeggi, "Myocardial tissue Doppler velocity imaging in children: comparative study between two ultrasound systems," *J Am.Soc.Echocardiogr.,* 23, 929-937, (2010).
[21] J. Ophir, B. Garra, F. Kallel, E. Konofagou, T. Krouskop, R. Righetti, and T. Varghese, "Elastographic imaging," *Ultrasound Med Biol,* 26 Suppl 1, S23-9, (2000).
[22] R. G. P. Lopata, M. M. Nillesen, H. H. G. Hansen, I. H. Gerrits, J. M. Thijssen, and C. L. de Korte, "Performance of Two Dimensional Displacement and Strain Estimation Techniques Using a Phased Array Transducer," *Ultrasound in Medicine and Biology,* 35, 2031-2041, (2009).
[23] R. G. P. Lopata, H. H. G. Hansen, M. M. Nillesen, J. M. Thijssen, and C. L. De Korte, "Comparison of One-Dimensional and Two-Dimensional Least-Squares Strain Estimators for Phased Array Displacement Data," *Ultrason Imaging,* 31, 1-16, (2009).
[24] R. G. P. Lopata, M. M. Nillesen, C. N. Verrijp, S. K. Singh, M. M. Lammens, J. A. van der Laak, H. B. van Wetten, J. M. Thijssen, L. Kapusta, and C. L. de Korte, "Cardiac biplane strain imaging: initial in vivo experience," *Phys.Med.Biol.,* 55, 963-979, (2010).
[25] R. G. Lopata, M. M. Nillesen, J. M. Thijssen, L. Kapusta, and C. L. de Korte, "Three-Dimensional Cardiac Strain Imaging in Healthy Children Using RF-Data," *Ultrasound Med.Biol.,* 37, 1399-1408, (2011).
[26] H. Ribbers, R. G. Lopata, S. Holewijn, G. Pasterkamp, J. D. Blankensteijn, and C. L. de Korte, "Noninvasive two-dimensional strain imaging of arteries: validation in phantoms and preliminary experience in carotid arteries in vivo," *Ultrasound Med.Biol.,* 33, 530-540, (2007).
[27] C. L. de Korte, "Strain estimation and/or hardness imaging of tissue or tissue structures," PCT Patent 60.708.879, (2005).
[28] H. H. G. Hansen, R. G. P. Lopata, and C. L. de Korte, "Noninvasive Carotid Strain Imaging Using Angular Compounding at Large Beam Steered Angles: Validation in Vessel Phantoms," *IEEE Trans Med Imaging,* 28, 872-880, (2009).
[29] H. H. G. Hansen, R. G. P. Lopata, T. Idzenga, and C. L. de Korte, "An Angular Compounding Technique Using Displacement Projection for Noninvasive Ultrasound Strain Imaging of Vessel Cross-Sections," *Ultrasound in Medicine and Biology,* 36, 1947-1956, (2010).
[30] H. H. G. Hansen, R. G. P. Lopata, T. Idzenga, and C. L. de Korte, "Full 2D displacement vector and strain tensor estimation for superficial tissue using beam-steered ultrasound imaging," *Phys Med Biol,* 55, 3201-3218, (2010).