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Cardiac biplane strain imaging: initial in vivo experience

R G P Lopata¹, M M Nillesen¹, C N Verrijp², S K Singh³, M M Y Lammens², J A W M van der Laak⁴, H B van Wetten³, J M Thijssen¹, L Kapusta⁴ and C L de Korte¹

¹ Clinical Physics Laboratory, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands
² Department of Pathology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands
³ Department of Cardiothoracic Surgery, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands
⁴ Pediatric Cardiology, Department of Pediatrics, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

E-mail: R.Lopata@cu.kz.umcn.nl

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Abstract
In this study, first we propose a biplane strain imaging method using a commercial ultrasound system, yielding estimation of the strain in three orthogonal directions. Secondly, an animal model of a child’s heart was introduced that is suitable to simulate congenital heart disease and was used to test the method in vivo. The proposed approach can serve as a framework to monitor the development of cardiac hypertrophy and fibrosis. A 2D strain estimation technique using radio frequency (RF) ultrasound data was applied. Biplane image acquisition was performed at a relatively low frame rate (<100 Hz) using a commercial platform with an RF interface. For testing the method in vivo, biplane image sequences of the heart were recorded during the cardiac cycle in four dogs with an aortic stenosis. Initial results reveal the feasibility of measuring large radial, circumferential and longitudinal cumulative strain (up to 70%) at a frame rate of 100 Hz. Mean radial strain curves of a manually segmented region-of-interest in the infero-lateral wall show excellent correlation between the measured strain curves acquired in two perpendicular planes. Furthermore, the results show the feasibility and reproducibility of assessing radial, circumferential and longitudinal strains simultaneously. In this preliminary study, three beagles developed an elevated pressure gradient over the aortic valve (∆p: 100–200 mmHg) and myocardial hypertrophy. One dog did not develop any sign of hypertrophy (∆p = 20 mmHg). Initial strain (rate) results showed that the maximum strain (rate) decreased with increasing valvular stenosis (−50%), which is in accordance with previous studies. Histological findings corroborated these results and
showed an increase in fibrotic tissue for the hearts with larger pressure gradients (100, 200 mmHg), as well as lower strain and strain rate values.

1. Introduction

Congenital malformations of the heart may lead to a reduced function of the myocardium. Resulting non-ischemic heart failure is already described in childhood and adolescence. In children with a valvular aortic stenosis, a pressure overload in the left ventricle will be present. In time, this pressure overload is an important factor that may lead to myocardial hypertrophy, followed by fibrosis (Sasayama et al 1976). Consequently, non-invasive diagnostic methods for monitoring myocardial damage might be an important tool to evaluate therapies that are aiming at reducing the risk of chronic heart failure. Although echocardiography is a well-established clinical tool in pediatric cardiology (Kiraly et al 1997, Sahn and Vick 2001, Langeland et al 2006), it does not provide quantitative information on locally disturbed functional properties of the myocardium. Currently, the pressure gradient across the stenotic valve as assessed with Doppler ultrasound is used as a diagnostic standard. However, this technique only yields information on the severity of the flow gradient and provides neither quantitative information on cardiac function nor on the functional composition of the heart muscle (Pacileo et al 2003, Khalid et al 2006). Hence, it is of crucial importance to obtain quantitative information about the heart function.

Cardiac ultrasound strain imaging is a technique that uses two-dimensional (2D) echo data to estimate the local deformation of the heart. Cardiac tissue velocity and strain can be quantified using various approaches. In general, the displacement of signal segments is tracked using a pattern matching algorithm. Cardiac strain can be quantified using Tissue Doppler Imaging (TDI)-based strain imaging (Heimdahl et al 1998) or 2D speckle tracking (Kaluzynski et al 2001, Leitman et al 2004). The first approach has a high sensitivity in the axial direction, but it is a one-dimensional technique. The second approach, i.e. speckle tracking, provides strain values in two dimensions. Two-dimensional data windows were used to estimate the displacements in both directions (Bohs and Trahey 1991, Chaturvedi et al 1998). Recent studies revealed that 2D cardiac strain imaging is feasible using 2D speckle tracking (Kaluzynski et al 2001, Leitman et al 2004). Speckle tracking yields robust displacement and strain estimation. However, robustness is gained at the cost of sensitivity to changes in the ultrasound data caused by small deformations (Cho et al 2006).

One can also use the raw, radio frequency data (RF). This approach has proven to yield enhanced performance compared to 2D speckle tracking techniques (Lopata et al 2009b). RF-based strain imaging is used for a wide variety of clinical purposes, for instance for detecting tumors and lesions (Céspedes et al 1993), atherosclerotic plaques (de Korte et al 2000) and blood clots (Xie et al 2004). In most of these applications, quasi-static or external compression of tissues is used. However, the tissue deformation in the heart is caused by an active contraction/relaxation process repeating itself each heart cycle. One-dimensional strain imaging was successfully applied in actively deforming tissue like skeletal muscle (Kallel et al 1998) and the heart (D’hooge et al 2000, Konofagou et al 2002, Sutherland et al 2004). Several 2D methods using RF data have been proposed (Konofagou and Ophir 1998, Chen et al 2004, Langeland et al 2004, Lopata et al 2009c) and were applied to cardiac data (Langeland et al 2006, Lee et al 2007).

A limitation of 2D cardiac imaging is simply the lack of the third dimension. The orientation of muscle fibers is not confined to one single plane, and the heart has a complex 3D structure and geometry. The ‘out-of-plane motion’ is therefore an important source of
Cardiac biplane strain imaging

error in 2D strain measurements (Konofagou and Ophir 1998, Konofagou et al 2002), and the full three-dimensional (3D) strain tensor cannot be estimated from 2D data. In other words, the available 2D information is not sufficient for a full assessment of heart geometry and dynamic function. Since 3D ultrasound imaging is on the rise, new techniques became available for estimating strain in more than two dimensions (Yoshikawa et al 2005, Chen et al 2005). However, one of the established problems in this field is the sub-optimal temporal resolution of 3D + time datasets.

Adequate spatial information and resolution are obtained at the cost of the temporal resolution. This issue results in contradictory interests. On one hand, adequate spatial information and resolution are required for accurate strain imaging within the entire 3D volume of the heart. At the same time, temporal resolution is also required because high deformation rates decrease the signal correlation significantly. High de-correlation of post-deformation signals may cause inaccuracies and biased strain estimates (Alam and Ophir 1997). Besides, large translations of signal segments will cause problems for smaller search windows. Therefore, a relatively high frame rate is required to be able to solve these issues. Several publications indicated that a frame rate of 200–300 Hz is required (Kanai et al 1997, Langeland 2007). Also Konofagou and coworkers based their results on data with a high temporal resolution system using a non-standard ECG-gated acquisition protocol (Luo et al 2007). Recently, Chen et al (2009) reported that the frame rate should be ten times higher than the heart rate when using RF data. However, this seems optimistic and the maximum applied strains in the phantom study were relatively low (<5%).

Insufficient spatial and temporal resolution have prohibited a widespread application of 3D RF-based strain imaging, although some studies report (preliminary) results using either 3D speckle tracking (Saito et al 2008, Crosby et al 2009), RF data (Patil et al 2007, Lopata et al 2007) or registration (Elen et al 2008). A first step toward full 3D strain imaging is biplane strain imaging. This commercially available technique enables the measurement of cardiac strain in two orthogonal planes simultaneously. Hence, the strain can be measured in two orthogonal directions for a segment of the left ventricle in both the short-axis and long-axis view. It must be noted that the full 3D strain tensor can only be estimated along the line that is formed by the boundary between the planes and that out-of-plane motion is still present.

In the present paper, the feasibility of cardiac strain imaging using biplane RF data was examined. Phased array biplane imaging was used as a fast technique to image two orthogonal planes in the myocardium simultaneously (see figure 1). Contrary to previous studies using mechanical semi-3D arrays (Yoshikawa et al 2005), a matrix array transducer was available and used. However, the system allows biplane acquisition at a maximum frame rate of only 100 Hz. As stated before, this is considered to be relatively low for RF-based strain imaging, but it is two to three times higher than the frame rate available for 3D full volume data.

The aims of this study were twofold. First, the technical challenge was to perform RF-based 2D displacement and strain estimation by 2D kernel matching using a commercial ultrasound system with a matrix array transducer and get reproducible results in vivo in subjects with a wide range of heart rates. The system’s temporal and spatial resolutions were limited and it was examined whether cardiac strain imaging would be feasible. The second aim was to evaluate the method in vivo in subjects with different pathology of the heart muscle. Both aims were achieved using data acquired in a canine model of a child’s heart. This particular animal model was chosen because the geometry and size of the heart resemble that of a small child (Willmann et al 2009). A valvular aortic stenosis was surgically induced in the beagles. The effects of an elevated pressure gradient were studied using biplane ultrasound (strain) imaging. Histological evaluation of the myocardial tissue was performed. The animal model and imaging technique are proposed as a framework to monitor the development of
hypertrophy in the heart due to valvular aortic stenosis using strain imaging. The preliminary findings are reported.

2. Materials and methods

2.1. Materials

In a pilot animal study, four dogs (beagles) with a surgically induced valvular aortic stenosis were studied. Early and recent reports in the literature revealed that pathological effects developed during growth in this animal model caused by a valvular aortic stenosis (Sink et al 1980, Hori et al 2008). During the intervention, one of the three cusps of the aortic valve was plicated, resulting in a bicuspid valve. As a result, a pressure gradient ($\Delta p$) of approximately 30 mmHg over the stenotic valve was present in all dogs directly after the intervention. This pressure gradient normally develops progressively in the young dogs, yielding a chronic pressure overload of the left ventricle. Consequently, the heart muscle becomes hypertrophic. As a result of this chronic condition, fibrosis gradually develops.

All four dogs of this pilot animal study were used for demonstrating the feasibility of the proposed strain estimation technique in vivo. In one particular animal, the surgical creation of a valvular aortic stenosis failed to develop a chronic pressure overload. This was demonstrated using Doppler echocardiography that revealed that the pressure gradient over the valve reduced from 30 mmHg (immediately after the intervention) to 20 mmHg within 2 months. It remained at this level during the follow up, and the geometry of the heart also showed no signs of hypertrophy. This animal was considered to be a valid ‘reference’ model. The other dogs developed a mean pressure gradient of 100, 120 and 200 mmHg, respectively. The dogs were followed up for 9 months and terminated after the last examination for histological analysis. All the animal experiments were performed according to the national ethical rules and permission was obtained from the local animal ethics committee.

2.2. Two-dimensional strain estimation

When using 3D ultrasound techniques, large volumes of the heart are imaged. Therefore, vast amounts of data are generated. Also for biplane imaging, the amount is enormous
when the deformation of the heart is followed up during several heartbeats. To decrease the computational load significantly, a fast correlation and interpolation algorithm is required. For 2D strain estimation, an iterative correlation-based coarse-to-fine strain algorithm (Shi and Varghese 2007) was developed using a 2D parabolic approximation with an additional step of local aligning and local axial stretching (Lopata et al 2009b).

The coarse-to-fine algorithm estimates displacements parallel and perpendicular to the ultrasound beam simultaneously, using the cross-correlation function of 2D pre- and post-compression kernels. First, large kernels of demodulated RF data (so-called signal ‘envelope’ or ‘speckle’ data) are correlated and the cross-correlation is used to find a coarse 2D displacement field by detecting its peak (figure 2). In consecutive iterations, RF data are used and the kernel size is decreased. This results in higher precision and resolution of the displacement estimates. Smaller data kernels can be used, since the initial displacement field is used as an initial guess. For all steps, the pre-compression kernel was correlated with a larger kernel in the post-compression area, automatically defining (and limiting) the possible measured axial and lateral displacements (figure 2). To obtain sub-sample resolution in both the axial and lateral direction, a 2D parabolic function was fitted to the peak of the 2D cross-correlation function. It was shown that this method performed equally well or even better than other interpolation techniques and also proved to be a fast alternative to interpolation of RF lines (Céspedes et al 1995, Lopata et al 2009b). To enhance the correlation between pre- and post-compression windows, the signal kernels were ‘re-correlated’ by aligning the windows on sub-sample level in both the axial and lateral direction using interpolation (see figure 2). Finally, the data are compressed or stretched using strain estimates of the previous iteration (‘stretching’) in order to increase correlation in areas with high strain (Lopata et al 2009b, 2009c).

The performance of this method was previously evaluated using linear array ultrasound data in phantoms (Lopata et al 2009b). However, 2D and biplane echocardiographic data are often acquired with phased array transducers. The resulting sector scan data are stored in a polar coordinate system and have non-equidistant line spacing in the Cartesian system. The applicability of the method on phased array data was demonstrated and its performance was quantified using simulations and phantom studies (Lopata et al 2009c). This study revealed that strain estimation using 2D data kernels outperformed 1D kernel matching for sector scan data. The strain quality was quantified in a commonly used inhomogeneous tissue phantom. The signal-to-noise ratio (SNR) of the strain images was found to be 30 dB (axial) and 20 dB (lateral) in a simulation study, but was 5 to 7 dB lower in experimental data. Furthermore, it was shown that the use of local aligning and stretching improved the SNR of the strain images by 5 to 20 dB for a range of strains of 0.5–5.0%. Again, phased array sector scans operate in a polar coordinate system and strains are not measured in the vertical or horizontal direction. The axial displacements and strains are measured along the direction of beam propagation. The so-called in-plane displacements and strains are measured perpendicular to the ultrasound beam and are the lateral displacements and strains. Since biplane data consist of two perpendicular planes, the lateral strain is measured in two directions, the azimuth and elevational direction.

The 2D strain algorithm used a decreasing radial pre-compression kernel size from coarse (6.0 mm) to fine scale (1.0 mm) with a fixed pre- and post-compression lateral kernel size of five scan lines. The post-compression kernels (i.e. search area in the next frame) were two times larger in both directions (see table 1). After coarse-to-fine displacement estimation, aligning and stretching were performed. The axial displacements were smoothed with a sliding-window median filter of (5.0 mm × 5 lines). The lateral displacement estimates are noisier because of under-sampling and the lack of phase information in this direction. Hence, a
Figure 2. Schematic overview of the 2D (biplane) strain method. This iterative procedure starts off at coarse scale, using large 2D kernels of envelope data. During consecutive steps, the axial kernel size is decreased and radio-frequency data are used to increase both resolution and precision. Finally, the data are re-correlated using so-called aligning and stretching for further improvement of the 2D displacement fields. After obtaining the displacement estimates, the myocardial tissue is tracked using these data and the cumulative strain images are generated.

A filter of $5.0 \, \text{mm} \times 11$ lines was used for the lateral displacements. The spatial derivatives of the axial and lateral displacements were calculated in the axial and lateral direction, respectively, using a 1D least-squares (LSQ) strain estimator (Kallel and Ophir 1997) with a kernel size of 11 displacement estimates.

2.3. Experimental data acquisition

Data were acquired with a Philips SONOS 7500 live 3D US system and an X4 matrix array transducer with a center frequency of 2.5 MHz and a bandwidth of 1–4 MHz (Philips Medical...
Figure 3. Biplane image of a canine heart in short- and long-axis view. The total tracked region-of-interest in the lateral wall is indicated with the gray line (dashed) in both images. The used region for strain analysis is the region within the white line (solid). The direction of the measured strain components is indicated in the lower part (arrows).

Table 1. Used settings of the strain estimation method for each iteration.

<table>
<thead>
<tr>
<th></th>
<th>Coarse</th>
<th>Middle</th>
<th>Fine</th>
<th>Aligning</th>
<th>Stretching</th>
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<td>2 mm</td>
<td>2 mm</td>
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<td>RF data</td>
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<tr>
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<td>Lateral window (post)</td>
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<tr>
<td>Median filter (axial)</td>
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<tr>
<td>Median filter (lateral)</td>
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Systems, Bothell, USA). The system was equipped with an RF interface that transferred the radio frequency data to a regular PC workstation using USB 2.0. The RF data were digitized at 19.5 MHz. The compression and gain settings did not change or influence the RF data. Using a smaller imaging plane (angle of 40° instead of 90°, imaging depth of 10 cm) in the parasternal view, a frame rate in the order of 100 Hz (96–104 Hz depending on echo depth) was achieved. The sector was large enough to image the total region of interest in the infero-lateral wall of the myocardium (see figure 3). The electrocardiographic (ECG) signal was captured during the acquisition. RF acquisition was triggered on the R-wave of the ECG signal.

Each animal was imaged monthly over a period of 6 months. Depending on the heart rate of the animals (70–140 bpm) and due to the limited data storage capacity of the system (200 images), this resulted in at least one complete cardiac cycle. In retrospect, the experiments yielded four suitable datasets for each animal. Using biplane imaging and the proposed strain estimation method, frame-to-frame deformations of the infero-lateral wall in the short-axis plane (Sax) and the long-axis plane (Lax) were obtained over the heart-cycle (see figure 3). Considering the orientation of the myocardium in the image sector, the measured axial strains within the infero-lateral wall were assumed to be parallel to the radial strains ($R$).
The lateral strains in the Sax and Lax planes were relatively parallel to the circumferential ($C$) and longitudinal ($L$) strain, respectively (see figure 3). Combination of these two views with 2D strain estimation and with the previous assumptions yielded the deformation of the heart muscle in radial, circumferential and longitudinal directions for the middle segment of the left ventricle. The myocardial tissue was manually segmented by a trained observer (figure 3). Instead of tracking the contour of the ROI, all windows within the segmented ROI were tracked using the measured displacements (Lopata et al. 2009a). The least squares strain estimator was used again to estimate the radial (Sax and Lax), circumferential (Sax) and longitudinal (Lax) strains. The cumulative strain values were determined for all pixels within the ROI for all strain components during the heart cycle. For comparison between dogs, a small region within the myocardium was defined (figure 3, white solid lines). The cumulative strain curves, the maximum strain rate and maximum strain were measured.

2.4. Histopathological examination and statistics

After removal of the heart, the left and the right ventricle were opened to allow free drainage of blood. The hearts were cut in slices (thickness $= 1\text{ cm}$) perpendicular to the long axis. The slice originating at 1 cm below the aortic valve and corresponding to the short-axis view echo data (figure 1) was removed for histological examination and fixed in a 10% buffered formalin solution. After 5 days of fixation, this slice was photographed, divided into anatomically marked portions and completely embedded in paraffin. Tissue samples (thickness $= 5\mu m$) were stained with hematoxylin/eosin (HE) and Masson trichrome for histopathological examination. The HE staining was used for general histological evaluation of the tissue and Masson to evaluate the fibrotic component. However, the latter stain was also used for digital image analysis as it permits to quantify the fibrotic component.

For quantitative measurement, the paraffin blocks including the lateral wall were selected, and $5\mu m$ thick sections were stained with 1% acid Fuchsin. The percentage fibrosis was assessed by digital image analysis, as described by Van der Steen et al. (1994). For each beagle, 100 microscopic fields of view of the lateral wall with exclusion of the papillary muscle and 35 fields of the papillary muscle were measured, with a pixel size of $1.3\mu m \times 1.3\mu m$ (image size $= 0.7\text{ mm}^2$).

Quantification of the area occupied by fibrosis was performed fully automatically, using a KS400 image analysis workstation (Carl Zeiss, Germany). Collagen belonging to blood vessels was interactively excluded from the analysis, whereas ischemic infarction zones in the papillary muscle were included. All statistics were performed using SPSS for Windows (SPSS Inc., Chicago, IL, USA, version 16.0.2). Because data from histometry show a skewed distribution, deviating from the normal distribution, log-conversion was also applied. To study differences between different beagles, ANOVA was used with Dunnett post hoc testing in case of a significant main effect. Statistical differences were considered significant for $p < 0.05$.

3. Results

An example of the deformation (i.e. strain) of the heart during the cardiac cycle can be appreciated in figure 4. The biplane cardiac strain images are shown (figures 4(a)–(d)). Furthermore, the cumulative strain was determined for a region in the infero-lateral wall for all three components of the strain (figures 4(f), (g)). The strain range for this particular example is from $-30$ to $30\%$. The positive radial strains reveal thickening of the myocardial wall in the systolic phase and thinning in the diastolic phase (Sax and Lax, figures 4(a), (b)). The circumferential and longitudinal strain components are negative, representing shortening of
Figure 4. Cumulative strain in the animal model at several time points (I–V) of the cardiac cycle within the ROIs in the infero-lateral wall of the left ventricle. The strains are projected on the B-mode images (a) short-axis radial strain, (b) long-axis radial strain; (c) circumferential strain and (d) longitudinal strain; (e) the measured ECG signal, the vertical dashed lines indicate the time points I–V; (f) the cumulative radial strain curves; (g) the cumulative mean circumferential and longitudinal strain curves.
the muscle during contraction, followed by lengthening in the diastolic phase (figures 4(c), (d)). Radial strain images as determined for both planes (figures 4(a), (b)) show similar behavior and ‘match’ at the intersection of the biplane. It may be noted that the radial strain images roughly return to their initial value in diastole, but a small residue of strain remains (see section 4). This residue is higher for the components C and L due to noise accumulation.

In figures 4(f), (g), the mean cumulative strain curves are shown for a central ROI in the myocardial wall (figure 3, white solid line). Again, both radial strain curves are similar in magnitude and shape. The radial strain has a maximum expansion value of approximately 50% in both curves. The circumferential and longitudinal strain curves have a maximum contraction value of $-14\%$ and $-33\%$, respectively. This corresponds to figures 4(c) and (d), where the level of contraction in the Lax view is higher.

As an example, all four strain curves for the beagle with the lowest pressure gradient are shown in figure 5. Here the error bars are added to indicate the variance of the strain measurements within the ROI for each phase of the cardiac cycle. Again, the radial strain curves of both planes are similar and also the error bars have an almost equal magnitude. The error on circumferential and longitudinal strain is higher as can be expected. This is caused by the lower spatial resolution and the absence of phase information in this direction.

The four beagles developed pressure gradients over the aortic valve of 20, 100, 120 and 200 mmHg, respectively. The radial strain curves, obtained in the beagles with 20 and 200 mmHg, are shown to illustrate that the difference in shape is reproducible (figures 6(a), (b), (d) and (e)). The radial strain of the pathological dog ($\Delta p = 200$ mmHg) shows a different shape and lower maximum strain values. Furthermore, the images of the myocardial tissue
Figure 6. Both short-axis (a) and long-axis mean radial strain curves (b) for the beagle with the lowest pressure gradient ($\Delta p = 20$ mmHg); (c) a tissue sample of the myocardium is shown after staining of fibrosis (black structures). The mean radial strain curves (d-e) and histology (f) for the beagle with the highest pressure gradient ($\Delta p = 200$ mmHg).

revealed more fibrosis for this beagle (figure 6(f)). A more extensive analysis of the differences between the four beagles is given in figures 7 and 8. In figure 7, the mean maximum, end-systolic, strain (left) and the maximum systolic strain rate (right) for all three directions are shown for the four beagles. The strain and strain rate traces were averaged for all pixels within the ROIs. The median values are also indicated (black horizontal lines). The maximum radial strain rate decreases for dogs with a higher pressure gradient. The trend in maximum radial strain seems less evident but the measurements are less scattered. The longitudinal strain and strain rate also decrease in magnitude. However, the circumferential strain shows little difference, and no distinct correlation with the present pressure gradient can be depicted.

Histological analysis of the dog with the lowest pressure gradient revealed no signs of hypertrophy nor of dilation of the left ventricle. No formation of fibrosis was found (see figure 6(c)), except for some sub-endocardial fibrosis in a papillary muscle and in the septum and in a microscopic old infarction at the junction of the septum and the posterior wall. Still, this dog may be considered to be a reference model, as in the lateral wall no fibrosis was observed. The other dogs with an elevated pressure gradient revealed diffusely increased fibrotic tissue in the myocardium, both interstitial and in the perivascular spaces. The beagle with a $\Delta p = 200$ mmHg had a more intense, sometimes multifocal interstitial fibrosis in the papillary muscles. This beagle presented several small, partly fibrotic ischemic infarctions. One of them, lying in the posterior wall, was already partly calcified. On morphometric examination, the variance of the fibrosis seemed to increase with the pressure gradient.

The dogs with an elevated pressure gradient of 100 and 200 mmHg revealed a higher percentage of fibrotic tissue in the myocardium (see figure 8). Log-conversion of the data facilitated comparison. Again, the variance of fibrotic tissue seems to increase with the pressure gradient. However, the amount of fibrosis in the beagle with a $\Delta p = 120$ mmHg seems relatively low compared to the other dogs, especially the dog with $\Delta p = 100$ mmHg.
Statistically, a significant lower amount of collagen was found in the dog with $\Delta p = 20$ mmHg compared to the dog with $200$ mmHg ($p < 0.001$). The beagle with $\Delta p = 100$ mmHg also had less collagen compared to the dog with $\Delta p = 200$ mmHg ($p = 0.003$). However, the fibrotic tissue present in the beagle with $\Delta p = 120$ mmHg was surprisingly lower compared to the other dogs ($p < 0.001$).

4. Discussion

In this paper, the feasibility of biplane cardiac strain imaging was investigated. The primary objective was to investigate if three orthogonal strain components can be measured using a commercial ultrasound machine with a standard acquisition protocol. The technique was evaluated in vivo in four different beagles and preliminary findings of a pilot animal study on valvular aortic stenosis were reported.

The strain images in figure 4 provide a good overview of cardiac deformation of the infero-lateral wall during the cardiac cycle. The strain images provide local information of myocardial contraction and relaxation in semi-3D space and time. The independently measured radial strain images in both planes reveal a good similarity. This is even more clearly shown in the mean cumulative strain curves in figure 4(f) and figures 5 and 6. The shape of the presented radial strain curves is in accordance with previous studies in humans.
Figure 8. Histology results of the four dogs: Box-and-whisker plots of the amount of fibrotic tissue within short-axis slice of myocardial tissue (a) and of the papillary muscle (b). The Box and whisker plots of the log-converted data are also shown for the myocardial tissue (c) and the papillary muscle (d).

(Kowalski et al 2003) and animals (Langeland et al 2006). The results show that cardiac strain estimation from biplane imaging is feasible and reveal the reproducibility of the method (figures 4–7) in the three directions within the encountered range of heart rates and for the different pathologies.

However, the time-dependent behavior and translational and rotational movement of the infero-lateral wall make it difficult to interpret these strain images in terms of local contraction and relaxation. Furthermore, the noisy character of the circumferential and longitudinal strain images makes analysis even more complex. Despite the loss of information after averaging of the strain values, the mean strain curves of a fixed ROI in the infero-lateral wall demonstrated to reveal information of myocardial function in time during contraction and relaxation of the heart. These curves are useful in assessing hypertrophy or cardiac failure (Weidemann et al 2002, Ganame et al 2008). The differences in circumferential and longitudinal strain are not fully understood yet, but corroborate the need for the extension of current techniques to a full 3D approach. The choice of ROI will influence the shape and magnitude of the strain curves. Hence, a region in the middle of the myocardium was chosen. However, this choice of ROI might have caused the low circumferential strain values.
One could question whether normalization of the measured strain curves is necessary for comparison of strain measurements in time. No significant correlation between strain (rate) and heart rate was found in this study. However, heart rate, cardiac output and pressure determine the functional and mechanical properties of the heart during contraction and relaxation and thus the strain profiles. Therefore, a more parametrical approach for the interpretation of strain images is unavoidable.

The maximum strain values showed a decrease for higher pressure gradients but the reference animal ($\Delta p = 20 \text{ mmHg}$) had relatively average radial strain values (56%) compared to the other dogs (36–62%). However, the strain rate results revealed a negative correlation between maximum systolic strain rate and pressure gradient, which could be an indication of myocardial stiffening. The systolic radial strain decreased from 675 to 330% s$^{-1}$ (median values, see figure 7). The longitudinal strain was halved and the strain rate decreased from $-410$ to $-140$% s$^{-1}$, although the values were more dispersed. However, the circumferential strain and strain rate did not reveal any significant trends or correlation with the pressure gradient. These results are in accordance with previous studies (Ganame et al 2008, Kowalski et al 2003) that also found a large decrease in radial/longitudinal strain and strain rate in different pathologies. Ganame et al found that the radial strain in control subjects was 60–65% and the strain rate was 500% s$^{-1}$. In patients with concentric hypertrophic cardiomyopathy, the radial strain and strain rate dropped to 40–45% and 300% s$^{-1}$, respectively. In these studies it was also shown that the longitudinal strain (rate) decreased significantly. However, the strain was measured by acquiring data from a different position.

Although the pressure gradient is a good measure of the development of hypertrophy, the left ventricular pressure would be ideal for normalization purposes. However, measuring the LV pressure in patients (or animals) is too invasive and stresses in the myocardial wall cannot be measured. Furthermore, the range of heart rates was quite large, since the animal’s heart rate is not easily controlled. The impact of the pressure gradient correlated with the percentage of fibrosis as measured on histological examination of the lateral wall of the left ventricle. There was no perfect correlation however, probably partly due to the presence of more ischemic lesions that were seen as infarctions in the papillary muscle. Another reason could be an increased perivascular fibrosis both in the papillary muscle and in the external part of the lateral wall of the ventricle. The effect of the pressure gradient was better detectable in the papillary muscles (figure 8(b)) than in the outer part of the ventricle wall (figure 8(a)). Although in the lateral wall of the dog with the lowest pressure gradient no obvious fibrosis was found, it remains debatable if this dog can be considered to be an ideal reference model due to the presence of a small infarction.

The authors are aware of the limitations of this study. First of all, a follow-up, large-scale study is needed, including a control group of healthy dogs for reference. Secondly, only four suitable measurements were available for each dog due to numerous practical reasons and problems. In a follow-up study, the echo exams have to be extended, including reproducibility measurements per date. The lack of multiple measurements makes it more difficult to assess the influence of growth on the strain analysis and to monitor the development of hypertrophy and the formation of fibrosis in time.

Extension of the current technique to a full 3D approach is still desirable, considering the ability to measure the full 3D strain tensor within 3D space and following the tissue in 3D space. Since these datasets have a reduced frame rate compared to biplane imaging, the low frame rate limit will determine the feasibility of 3D strain imaging. However, full 3D strain imaging will enable the algorithm to account for out-of-plane motion and will allow 3D tracking. The advantage of 3D strain estimation might also lie in the possibility to measure torsion during the
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contraction of the heart muscle. Torsion may become an important parameter to characterize local heart function (van der Toorn et al 2002).

5. Conclusion

Cardiac strain imaging is feasible using the biplane phased array RF data on a commercial US system. The algorithm allowed strain imaging in both orthogonal planes simultaneously at moderate frame rates. The feasibility of the technique was evaluated in an animal model. Preliminary results of this pilot study indicated that different strain values were found in animals with a severe stenosis with respect to a reference animal. However, a large-scale animal study is required to further validate the animal model. In a follow-up study, a large group of patients will be imaged to demonstrate the clinical applicability of the proposed method.

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References

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