Experimental Validation of a New Ultrasound Method for the Simultaneous Assessment of Radial and Longitudinal Myocardial Deformation Independent of Insonation Angle

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Background—Strain and strain rate have been proposed as tools to quantify regional myocardial function. One of the major pitfalls of the current methodology is its angle dependency. To overcome this problem, we have developed a new method for the estimation of strain, independent of angle. The aim of this study was to validate this new methodology in an experimental setting using sonomicrometry.

Methods and Results—In 5 open-chest sheep, ultrasound data were acquired. The new methodology was used to perform simultaneous measurements of radial and longitudinal strain in the inferolateral wall. Segment-length sonomicrometry crystals were used as the reference. After baseline acquisitions, deformation was modulated by pharmacologically changing the inotropic state of the myocardium and by inducing ischemia. Ultrasonically estimated radial and longitudinal strain were validated against sonomicrometry by means of Bland-Altman analysis and the intraclass correlation coefficient. For both strain components, good agreements were found between the ultrasound and the sonomicrometry measurements as shown by Bland-Altman statistics. The intraclass correlation coefficients were found to be 0.72 and 0.80 for the radial and longitudinal components, respectively.

Conclusions—A new technique for the estimation of myocardial deformation was validated. It was shown that the current problem of angle dependency was solved and that 2 deformation components could be estimated simultaneously and accurately. Furthermore, the technique was less time-consuming, because anatomic tracking was performed automatically. This approach could potentially accelerate the clinical acceptance of ultrasound deformation imaging in cardiology. (Circulation. 2005;112:2157-2162.)

Key Words: echocardiography • strain • angle dependency

In recent years, ultrasonic strain and strain rate imaging (SRI)1 have been shown to be clinically useful tools for quantifying cardiac function.2 The currently available 1D SRI methodology has been validated extensively.3–6 However, because this methodology typically makes use of myocardial velocity estimates, the intrinsic angle dependency of the velocity estimates is inherited, whereby only velocities parallel to the ultrasound scan line can be estimated accurately. The current SRI method is thus angle dependent,7 which makes the clinical interpretation more difficult and requires a high level of operator expertise. Moreover, this approach implies that only 1 component of the true 3D deformation of a myocardial segment is measured within 1 acquisition, thus limiting the information available on the myocardial deformation. This is especially important for transesophageal echocardiography, in which the probe position cannot be changed appropriately to align the ultrasound beam with the deformation component to be measured.8 Finally, to obtain reliable deformation estimates, it is necessary at present to manually track a myocardial segment throughout the cardiac cycle. This makes the technique relatively time-consuming and therefore less clinically applicable.

As a solution to these problems, a new method for deformation imaging has been developed in our laboratory, called 2D strain echocardiography. The method not only allows simultaneous analysis of radial and longitudinal myocardial deformation, independent of insonation angle, but also avoids the time-consuming step of manually tracking a myocardial segment. The technique was initially shown to be applicable to the normal heart in vivo,9 has been further optimized after a series of simulations,10 and was recently validated in tissue-mimicking phantoms.11 The aim of the present study was to further validate this new 2D approach in an in vivo setup by comparing the deformation of the sheep heart as measured by this new methodology with the deformation measured by sonomicrometry.

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Figure 1. Microcrystals were placed to give an independent simultaneous measure of longitudinal and radial strain. The ultrasound and cardiac coordinate systems are shown with the axial \( r_a \) and azimuthal \( r_w \) and radial \( r \) and longitudinal \( t \) directions, respectively.

Methods

Animal Preparation

To validate the proposed methodology, an in vivo animal setup was used. Five sheep were premedicated with ketamine hydrochloride 10 mg/kg. Anesthesia was induced with intravenous sodium pentobarbital 8 mg/kg and piramidamide 1 mg/kg and maintained with sodium pentobarbital 3 mg · kg\(^{-1} \) · h\(^{-1} \) and piramidamide 1 mg · kg\(^{-1} \) · h\(^{-1} \). The lungs were mechanically ventilated with a mixture of oxygen and room air to maintain normocapnia and normoxia. Lactated Ringer’s solution was administered at a rate of 5 mL · kg\(^{-1} \) · h\(^{-1} \). A triple-lumen catheter was inserted via the right jugular vein. A fluid-filled catheter was advanced into the proximal aorta via the left carotid artery for monitoring of systemic arterial pressure. Similarly, a Millar catheter was introduced into the left ventricle via the right carotid artery for monitoring of left ventricular pressure and its first temporal derivative (dP/dt). A sternotomy was performed, and the heart was suspended in a pericardial cradle to maintain a normal anatomic configuration.

For sonomicrometry measurements, a Sonometrics Digital Ultrasonic Measurement System (Sonometrics Corporation) was used. Three segment-length ultrasound crystals (2 mm) were fixed to the myocardium in the inferolateral wall. Two crystals were sutured to the epicardium in a longitudinal direction (crystals 1 and 2 in Figure 1). One crystal (crystal 3 in Figure 1) was placed subendocardially just radially to crystal 2 through the myocardial wall. The latter was introduced in an oblique way to avoid damage to the myocardium to be studied. They enabled us to continuously measure wall thickening and longitudinal shortening at a time resolution of 1.7 ms and provided a continuous reference for the longitudinal and radial strain.

Data Acquisition

A Toshiba PowerVision 6000 equipped with a radiofrequency (RF) interface for research purposes was used to acquire ultrasonic RF data in a 45° sector format with a 5-MHz cardiac transducer (PSM-50AT) by placing the transducer directly on the contralateral epicardium. Parasternal long-axis-like images were acquired at a frame rate of 167 Hz. The acquired RF data were stored and transferred to a personal computer for further postprocessing. Owing to overlapping frequency bands for the microcrystal system and the ultrasound system, the microcrystal data were acquired immediately before the ultrasound data and then switched off while the ultrasound data were acquired.

To change the range of strain values, myocardial strain was modulated over 4 stages with differing challenges. After the baseline acquisitions, the inotropic state was reduced by an esmolol infusion and increased by a dobutamine infusion, and finally, ischemia was induced in the region under investigation by ligating a distal branch of the circumflex coronary artery. For the esmolol and dobutamine stages, a physiological target was set to a 50% reduction in dP/dt and a 100% increase in dP/dt relative to baseline for esmolol and dobutamine, respectively. For esmolol, this was achieved at an infusion rate of \( \approx 100 \mu g \cdot kg^{-1} \cdot min^{-1} \), whereas the dobutamine infusion rate was \( \approx 2.5 \mu g \cdot kg^{-1} \cdot min^{-1} \). In this way, 4 data sets were obtained in each animal.

Deformation Estimation

The method is based on estimating the velocity vector rather than the velocity component along the image line alone, as is currently the case for Doppler estimation. This can be obtained by a new methodology developed in our laboratory based on 2D tracking of RF image patterns. Briefly, the algorithm finds the velocity vector by tracking patterns in the RF image between consecutive frames, as illustrated in Figure 2. For each pixel in the image, angle-independent velocity estimation is performed by selecting a search pattern around that pixel in 1 frame (eg, “search pattern” in Figure 2) and looking for a matching pattern in a search region around that pixel of the following frame (“search region” in Figure 2). The search pattern is placed at different positions in the search region, and the similarity is measured for the overlapping area. The position where the highest similarity is found (illustrated as a solid rectangle in the “solution” image in Figure 2) determines the in-plane frame-to-frame displacement relative to its initial position (illustrated as a dashed rectangle in the “solution” image in Figure 2). For a more detailed description of this methodology, see Langeland et al.

From the velocity vector field, radial and longitudinal strain estimates were obtained in the following way: at the beginning of the heart cycle, the endocardial and epicardial borders of the region of interest were indicated on the conventional B-mode images reconstructed from the RF data. Then, a fine grid was automatically positioned within the selected region of interest with an intergrid point distance of 0.5 mm. For each frame, the position of each grid point was updated on the basis of the underlying velocity vector. In this way, the deformation of the grid followed the deformation of the underlying myocardium, and the radial and longitudinal strain could be estimated from the distance changes between grid points as a function of time. To have robust measurements, the whole width (10 mm) and length (10 mm) of the region of interest were used to calculate the radial and longitudinal strain, respectively. This gave an effective spatial resolution of 10 mm for both strain components. Because the method makes use of RF data, it is intrinsically independent of gain settings.

One heart cycle, defined as 1 RR interval on a synchronously recorded ECG, was analyzed for each data set. End systole was defined as aortic valve closure, determined as dP/dt\(_{\text{min}}\) - 20 ms. All postprocessing was performed with software (SPEQLE 2D) developed in our laboratory as an extension to existing custom-made software (SPEQLE).13

Statistical Analysis

For comparison of the strain curves throughout the cardiac cycle, 10 strain values were extracted during systole and diastole (20 values in total) at equidistant time points for both measurement methods. As recommended by Bland and Altman,14 the agreement between the methods was assessed by calculating the paired difference between...
the 2 methods for each measurement and by estimating the bias and 95% limits of agreement relative to the mean measurement of both methods. As appropriate for continuously changing variables, the mean value and limits of agreement were found with methods that accounted for such replicated measurements. The goal was to achieve an agreement equal to or better than the agreement found in a similar validation of the more conventional Doppler-based technique.

In addition to the Bland-Altman statistics, the intraclass correlation was calculated as a measure of consistency between the 2 methods. The variance between sheep (σs), the variance between the inotropic stages (σi, conditional on sheep), the variance between the 20 different time points (σt, conditional on sheep and stage), and the residual error, ie, variance between the 2 methods (σe, conditional on sheep, stage, and time point) were found with repeated-measures ANOVA that included stage, time point, and their interaction as fixed effects. The intraclass correlation coefficient (ICC) was then found as: ICC=(σs²+σi²+σt²) / (σs²+σi²+σt²+σe²), where s indicates stage, i indicate inotropic stage, t indicates time point, and e indicates residual error.

Results
Two data sets acquired during the dobutamine infusion were excluded because of poor image quality. This resulted in 18 remaining RF data sets. Examples of curves for baseline and ischemia are given in Figures 3 and 4, respectively. The Bland-Altman plots for replicated measurements in Figures 5 and 6 show the bias and the 95% limits of agreement for the radial (Figure 5) and longitudinal (Figure 6) strain estimates to be 2.0±9.3% and 0.4±5.5%, respectively. The intraclass correlation coefficients were found to be 0.72 and 0.80 for the radial and longitudinal strain, respectively. For a graphical representation, the scatterplots are shown in Figures 7 and 8, together with the line of unity.

Discussion
Ultrasound tissue deformation imaging has been shown to be an interesting new approach for the assessment of regional myocardial function. However, the angle dependency of the current implementation of the technique makes its clinical applicability more difficult, because an appropriate alignment of the ultrasound beam with the direction of deformation is often difficult owing to the limited number of acoustic windows through the human thorax. For transesophageal echocardiography imaging, this is an even more severe problem, because the position of the transducer is relatively fixed. To overcome this limitation, a method that allows the simultaneous estimation of both radial and longitudinal strain with ultrasound has been developed by our laboratory. In this study, this methodology was validated in an in vivo setup against sonomicrometry.

Strong correlations were found between the 2 methods for both the radial and longitudinal strain components. Both components could thus be estimated with the same accuracy,
which implies the angle dependency problem has been solved. This is also illustrated in Figures 3 and 4, in which Doppler-derived strain is markedly underestimated owing to angulation (see Figure 1). Moreover, because both components are estimated simultaneously, this could open new possibilities for investigation of the different response in radial and longitudinal function. Because subendocardial myocardial fibers are more susceptible to ischemia, it might be expected that longitudinal function is altered earlier than radial function,16 because subendocardial fibers are oriented longitudinally.17 This could have interesting clinical implications in quantifying inducible ischemia during stress echocardiography. Currently, stress echocardiography is performed by visually interpreting the motion and deformation of the myocardial walls in 2D gray-scale images. This makes stress echocardiography subjective, and a high level of expertise is required to obtain correct readings.18 In particular, the timing of the deformation is difficult to assess.19 For this reason, deformation imaging has been suggested as a tool to improve the quantification of stress echocardiography.20–22 A problem with the current methodology is that images from several transducer positions have to be used to assess the different deformation components. With the new methodology, only 1
Clinically acceptable limits. From the analysis of the radial component (eg, Figure 6) showed a better agreement than the longitudinal components can be obtained from the same data set. The transducer position is needed, because 2 deformation components were found in the Bland-Altman analysis. The longitudinal component (eg, Figure 6) showed a better agreement than the radial component (eg, Figure 5); however, both were within clinically acceptable limits. From the analysis of the radial strain (eg, Figure 5), it can be seen that the values were overestimated, because the bias was found to be 2.0%. This might be due to potential errors in the reference measurements. Indeed, to keep good contact between the subendocardial microcrystal (crystal 2 in Figure 1) and the myocardium throughout the cardiac cycle, the microcrystal could not be positioned perfectly subendocardially but rather had to be placed a bit more toward the mid-myocardial layer. Given that the highest strain occurs subendocardially, the strain measured by the microcrystals might underestimate the radial strain.

As can be seen in Figures 5 and 6, good agreement was found in the Bland-Altman analysis. The longitudinal component (eg, Figure 6) showed a better agreement than the radial component (eg, Figure 5); however, both were within clinically acceptable limits. From the analysis of the radial strain (eg, Figure 5), it can be seen that the values were overestimated, because the bias was found to be 2.0%. This might be due to potential errors in the reference measurements. Indeed, to keep good contact between the subendocardial microcrystal (crystal 2 in Figure 1) and the myocardium throughout the cardiac cycle, the microcrystal could not be positioned perfectly subendocardially but rather had to be placed a bit more toward the mid-myocardial layer. Given that the highest strain occurs subendocardially, the strain measured by the microcrystals might underestimate the radial strain.

The radial strain values as measured in the present study were found to be low compared with what has been found in other SRI studies. The value of radial thickening could be dependent on species and furthermore be influenced by the fact that an open-chest model was used in the present study. The aim of the present study was merely to validate the new ultrasound methodology, and thus, this was not considered a limitation, because good agreement with the microcrystal data was found to be most important.

Although interesting findings based on the current 1D SRI method have been presented in the literature, their migration into daily clinical practice has been tempered because the current method is relatively time-consuming owing to the fact that the region of interest has to be tracked manually over the cardiac cycle. It is also essential that the myocardial wall be well aligned with the ultrasound beam, which means that a high level of expertise is required for the data acquisition and analysis. The new approach proposed here solves both problems, because the tracking is intrinsic to the method, and no alignment of the wall with the ultrasound beam is needed. We thus believe that an angle-independent method should be an important factor in accelerating the clinical acceptance of ultrasonic deformation imaging in cardiology.

The problem of temporal drifting of strain curves, as reported in earlier work, is also present in this new methodology. As in other methods, drifting is compensated for by forcing all grid points to return to their initial positions at the end of the heart cycle. This drifting could be part of the cause of the discrepancy between the 2 methods seen in Figure 4.

The ultrasound data in the present study had a frame rate of 168 Hz. This is comparable to the current SRI methodology for images at a similar sector angle. The new methodology provides a temporal resolution similar to the current SRI technique. A high temporal resolution is required to resolve the timing of the strain curves, especially for the application in stress echocardiography.

**Study Limitations**

In the present study, only the longitudinal and radial strain components were assessed. However, by acquiring a parasagittal short-axis view, both circumferential and radial deformation can be measured. Currently, several companies are introducing 3D ultrasound imaging for cardiac applications. The method validated in the present study can easily be modified to estimate deformation in 3 dimensions, independent of angle, given an appropriate acquisition. This will allow for the estimation of radial, longitudinal, and circumferential strain from single data sets.

Because regular tissue Doppler data were not acquired in the present study, no direct comparison between Doppler-based strain imaging and this new methodology was performed. Therefore, the superiority of the new methodology over the Doppler-based method remains to be demonstrated.

Although rotation and shearing were not explicitly validated in the present study (because these fell outside the scope of this work), it would be expected that these could be measured given prior data reported in the literature with similar methodologies. These estimates have already been shown to have potential clinical applications.

The accuracy of radial and longitudinal strain could be dependent on the relative position of the transducer to the cardiac segment under investigation. In the present study, no attempt was made to compare different transducer positions.

**Conclusions**

A new technique for the estimation of myocardial deformation has been validated. It was shown that the current problem of angle dependency was solved and that 2 components of the deformation can be estimated simultaneously. Furthermore, the technique is less time-consuming because anatomic tracking is performed automatically. This could potentially accelerate the clinical acceptance of deformation imaging in cardiology.
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