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Preliminary Validation of Angle-Independent Myocardial Elastography Using MR Tagging in a Clinical Setting

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Abstract

Myocardial Elastography (ME), a radio-frequency (RF) based speckle tracking technique, was employed in order to image the entire two-dimensional (2D) transmural deformation field in full view, and validated against tagged Magnetic Resonance Imaging (tMRI) in normal as well as reperfused (i.e., treated myocardial infarction (MI)) human left ventricles. RF ultrasound and tMRI frames were acquired at the papillary muscle level in 2D short-axis (SA) views at nominal frame rates of 136 (fps; real time) and 33 fps (electrocardiogram (ECG)-gated), respectively. In ultrasound, in-plane, 2D (lateral and axial) incremental displacements were iteratively estimated using one-dimensional (1D) cross-correlation and recorrelation techniques in a 2D search with a 1D matching kernel. In tMRI, cardiac motion was estimated by a template-matching algorithm on a 2D grid-shaped mesh. In both ME and tMRI, cumulative 2D displacements were estimated and then used to estimate 2D Lagrangian finite systolic strains, from which polar (i.e., radial and circumferential) strains, namely angle-independent measures, were further obtained through coordinate transformation. Principal strains, which are angle-independent and less centroid-dependent than polar strains, were also computed and imaged based on the 2D finite strains with a previously established strategy. Both qualitatively and quantitatively, angle-independent ME is shown to be capable of 1) estimating myocardial deformation in good agreement with tMRI estimates in a clinical setting and of 2) differentiating abnormal from normal myocardium in a full left-ventricular view. Finally, the principal strains are suggested to be an alternative diagnostic tool of detecting cardiac disease with the characteristics of their reduced centroid dependence.

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Keywords

Circumferential; Cross-Correlation; Cumulative; Elastography; Incremental; Infarct; Magnetic Resonance Imaging (MRI); Myocardial; Principal; Radial; Radio-Frequency (RF); Recorrelation; Strain; Tagging

INTRODUCTION

Widely used in the clinic, echocardiography has important advantages over alternative imaging techniques for the detection of cardiovascular disease owing to its higher temporal resolution, low cost, portability and familiarity to cardiologists. Myocardial deformation (or, strain) has been proven to be a reliable measure of cardiac dysfunction and is of high recent interest in the echocardiography field. Strain estimation techniques range from Tissue Doppler Imaging (TDI) (Sutherland et al. 1994, Miyatake et al. 1995, Hoffmann et al. 2002), Strain Rate Imaging (SRI) (Kaluzynski et al. 2001, D'hooge et al. 2002a, D'hooge et al. 2002b, Chen et al. 2005) to Myocardial Elastography (ME) (Konofagou et al. 2000, Konofagou et al. 2001, Konofagou et al. 2002, Lee et al. 2007a). Among those, myocardial elastography, which is a radio-frequency (RF)-based ultrasound speckle tracking technique, has been shown capable of assessing normal myocardial deformation (Konofagou et al. 2002, Konofagou et al. 2007) and detecting abnormal myocardial function *in vivo* (Konofagou et al. 2001), as a result of ischemia or infarction, through estimation of the myocardial deformation resulting from the natural contraction of the myocardium in each cardiac cycle. Myocardial elastography has also been shown fundamentally capable of accurately estimating and imaging in-plane deformation in full short-axis views in a previously proposed theoretical framework (Lee and Konofagou 2006, Lee et al. 2007a), using an ultrasonic image formation model and an established three-dimensional (3D), finite-element canine left-ventricular model, in both normal and left-circumflex (LCx) ischemic states. Furthermore, using the same framework, myocardial elastography could reliably differentiate abnormal from normal myocardium based on angle-independent estimates. Not only was ME shown to accurately estimate and image the myocardial displacements and strains using the theoretical model, but it could also differentiate abnormal from normal cardiac muscle without a beam-to-muscle angle dependence (Fung-Kee-Fung et al. 2005, Lee and Konofagou 2006, Lee et al. 2007a, Zervantonakis et al. 2007) in full view.

As far as clinical applications are concerned, tagged Magnetic Resonance Imaging (tMRI) (Zerhouni et al. 1988, Axel and Dougherty 1989b) is still regarded as the noninvasive gold standard of assessing myocardial deformation. Tags function as virtual markers embedded in the myocardium, and the deformation of their shape during the cardiac cycles is associated with the myocardial motion. Since MR tagging was invented in the late twentieth century, efforts have been made to quantify the myocardial motion/strain from tagged images; ranging from tracking tag lines or grids (Guttman et al. 1994, Denney and Prince 1995, Amini et al. 1998, Park et al. 1999, Declerck et al. 2000, Qian et al. 2006) to extracting harmonic phase (HARP) information (Osman et al. 1999, Sampath and Prince 2007).

Several previous studies have compared the estimates from echocardiography with those from tMRI (Edvardsen et al. 2002, Konofagou et al. 2003, Helle-Valle et al. 2005, Notomi et al. 2005, Amundsen et al. 2006). Edvardsen et al. (2002) first validated echocardiographic strains using Tissue Doppler against MRI tagging and showed high correlation for radial strains ($r=0.96$) between the two modalities. However, this tissue Doppler method merely estimates one-dimensional (1D) strain component, namely radial strain and no 2D images were shown. In addition, their estimated systolic strains were defined as the percent change of the segment length, while the actual Lagrangian normal strain component includes the second order of the shear components. Konofagou et al. (2003) showed that axial displacement ($r=0.81$) and strain ($r=0.65$) estimated from B-mode based myocardial elastography were well correlated with those from 1D MR tagging in the septum in an apical four-chamber view of human left ventricles. Only the axial estimates, which coincided with the beam direction and were displayed in an M-mode format, were shown. Notomi et al. (2005) used an ultrasound B-mode based speckle tracking technique to measure the ventricular torsion and validated it against MRI tagging. Basal and apical short-axis images were acquired from human subjects using both ultrasound and MRI tagging. Their temporal average torsion profile proved that torsional deformation estimated from the ultrasound speckle tracking was in good agreement with that from the HARP analysis of MRI tagging images. Helle-Valle et al. (2005) also showed the feasibility that ultrasound speckle tracking could assess ventricular rotation in healthy human subjects with findings consistent with those using MRI tagging. Similar to the methods presented by Notomi et al., basal and apical level short-axis images were acquired, and B-mode speckle tracking and HARP were employed to analyze rotation in ultrasound and MRI tagging, respectively. Average mid-endocardial and sub-endocardial rotation values were estimated and compared during a cardiac cycle across the two imaging modalities. Amundsen et al. (Amundsen et al. 2006) proposed a B-mode based speckle tracking echocardiography (STE) technique to track the displacement of segment endpoints and to calculate strain from the change in wall thickness. Echocardiograms were acquired from two- and four-chamber apical views. The longitudinal strain measured using their B-mode-based STE was in good agreement with tMRI estimates.

Nevertheless, none of the aforementioned reports provided a one-to-one comparison of displacement and strain fields obtained in echocardiograms and tMRI in full view in a clinical setting. Our group has implemented myocardial elastography in a clinical setting, and preliminarily validated in-plane displacement (i.e., lateral and axial) and strain (i.e., lateral, axial, radial and circumferential) estimates against MR tagging estimates by color-coding and overlaying those estimates on both echocardiography and tagged MR images (Konofagou et al. 2007, Lee et al. 2007a, Lee et al. 2007b).

In this paper, we focus on the full depiction of the nonuniformity of 2D transmural myocardial displacement and deformation (i.e., strains) in short-axis (SA) views from the ME technique with the additional implementation of principal strain estimation in a clinical setting. In order to evaluate the myocardial motion and strain estimates, ME is compared against MR tagging.

MATERIALS AND METHODS

High frame-rate ultrasound data acquisition

A clinical echocardiography ultrasound scanner (General Electric (GE) Vivid FiVe, GE Vingmed Ultrasound, Horten, Norway) with a phased array probe (FPA 2.5MHz 1C) was used to acquire cardiac ultrasound in-phase and quadrature (I/Q) data in 2D SA views at the papillary level from normal (female, 28 y.o., heart rate 80 bpm) and abnormal (male, 69 y.o., heart rate 73 bpm) subjects (N=2) at a frame rate of 136 fps. The I/Q data were further upsampled to retrieve the RF signals. The lateral and axial resolutions are approximately 1.92 mm and 0.77 mm, respectively. The human subject study protocol was approved by the Institutional Review Board of Columbia University, and informed consent was obtained from all human subjects prior to scanning.

The frame rates of commercial ultrasound systems typically range between 30 fps and 70 fps. With this GE system, the maximum frame rate is 50 fps in a default setting. However, RF-based speckle tracking requires higher frame rates for myocardial motion estimation (Kaluzynski et al. 2001, D'hooge et al. 2002a, Konofagou et al. 2002). In order to increase the frame rate without sacrificing beam density or the region-of-interest (ROI) size, a novel electrocardiogram (ECG)-gated composite imaging, which assembled multiple small sector images into a full-view echocardiogram, was implemented by our group (Wang et al. 2007). Slightly different from the fully automated method proposed by Wang et al., five or six sectors with a reduced field of view (FOV) were selected manually and combined off-line based on the spatial (i.e., depth and angle) and ECG information to depict the entire cardiac short-axis view at 136 fps using the GE system. RF data within three cardiac cycles were acquired for each sector. All the sectors were done under different breath-holds and free-hand scanning, and the total acquisition time was approximately six minutes.

In addition, at the frame rate of 136 fps used, the decorrelation of RF signals resulting from through-plane motion was reduced. In other words, sufficiently high correlation between two consecutive RF frames was achieved (Luo et al. 2007). The theoretical framework, evaluating performance of myocardial elastography at multiple short-axis (SA) views, proposed by our group (Lee and Konofagou 2006, Lee et al. 2007a) also showed that myocardial elastography still retained its good performance, even at the presence of through-plane motion. Furthermore, the data presented in this paper were acquired at the papillary muscle level, which served as a marker for registration purposes in a standard echocardiographic short-axis view (Feigenbaum et al. 2005).

MRI tagging (tMRI) data acquisition

Tagged MR images were obtained on a Philips Intera 1.5T scanner (Philips Medical Systems, Best, The Netherlands) equipped with a five-channel SENSE cardiac coil and master gradients of strength 30 mT/m and slew rate 150 T/m/s. A multi-slice and multi-phase true SA tagged image was acquired under free-breathing with a combination of fast-field echo excitation and a multi-shot echo-planar readout (EPI-FFE) technique (Stuber et al. 1999) (FOV=350 mm, TE=4 ms, TR=30, NSA=4, resolution acquired/reconstructed =192/256, flip angle =13 degrees, EPI factor=3 and full ECG gating scan duration=4.77

min). Receiver bandwidth was 401.9 Hz, and the time to fill k-space was 23.85 seconds. Two-dimensional grid tagging was performed yielding a 9-mm, in-plane tag resolution. The SA orientation was also acquired at the papillary muscle level from the same subjects. The nominal frame rate was 33 fps.

The reason why we focused on short-axis views was that anterior, posterior, lateral and septal wall regions could be imaged at the same time and that angle-independent strains were estimated based on polar coordinates, which were more appropriately represented in short-axis views than other echocardiographic views, e.g. parasternal long-axis and apical views given the associated LV quasi-circular shape. In addition, preliminary studies indicated that higher contrast between normal and abnormal myocardial deformation could be depicted in short-axis views.

Myocardial elastography (ME)

Two-dimensional, in-plane orthogonal (lateral and axial) displacement components were estimated using one-dimensional (1D) cross-correlation and recorrelation of RF signals in a 2D search (Lee and Konofagou 2006, Lee et al. 2007a). The cross-correlation technique employed a 1D matching kernel of 7.7 mm and 80% overlap. In a preliminary study, several different 1D matching kernel sizes were tested. It was concluded that the larger the kernel, the less noisy the displacement estimates, and the lower precision of the estimates. Since the overlap was directly defined by the 1D matching kernel size, the larger the kernel, the lower the resolution of displacement estimates. In other words, the trade-off between precision and resolution of displacement estimates, owing to the kernel size, was identified. According to the results from clinical data, the optimal 1D matching kernel used was approximately 10 times higher than the wavelength. The 80% overlap can be adjusted according to the need of resolution of displacement estimates. In other words, the window shift was assumed to indicate the expected elastographic resolution as reported in the literature (Srinivasan et al. 2003). The reference and comparison frames contained the RF signals before and after deformation, respectively. The RF signal segment in the comparison frame corresponding to the maximum cross-correlation value was considered to be the best match with the RF signal segment in the reference frame. Cosine interpolation was then applied around the peak of the cross-correlation function for a more refined peak search (Konofagou and Ophir 1998). Thus, the lateral and axial shifts between the reference and comparison RF segments with the highest cross-correlated value were the lateral and axial displacements, respectively.

A correction (or, recorrelation) in the axial displacement estimation (Lee and Konofagou 2006, Lee et al. 2007a) was performed to reduce the decorrelation resulting from axial motion for improved lateral displacement estimation. It was implemented by shifting RF signal segments by the estimated axial displacement in the comparison frame, prior to the second lateral displacement estimation. This estimated lateral displacement was then further normalized using the actual beam spacing, which varied with depth owing to the polar coordinates used in the phased array configuration. This normalization is detailed in Appendix A.

The incremental 2D displacements that occurred from ED to ES were further integrated to obtain the cumulative 2D systolic displacement. For each pixel, appropriate registration

between consecutive displacement images was performed in order to ensure that the cumulative displacement depicted the motion of the same tissue region. The end-diastolic phase was pinpointed by the peak (i.e., R wave) of the QRS segment in the ECG signal.

MR tag tracking

A tagged MRI sequence generates two perpendicular sets of equally spaced parallel tagging planes as temporary markers within the myocardium through spatial modulation of the magnetization at end-diastole (ED) (Axel and Dougherty 1989a, 1989b). Imaging planes are perpendicular to the two sets of tagging planes so that the tags appear as dark grids on the MR images and deform with the underlying myocardium during the cardiac cycle *in vivo*. This yields detailed motion information of the myocardium.

In order to track the tagging grids and obtain the localized myocardial displacement and strain values, we implemented a template-based tracking algorithm on a 2D grid-shaped mesh to obtain the displacement vectors of the crossing points (or, nodes) on the tagging grids (Park et al. 1999, Haber et al. 2000, Qian et al. 2005, 2006). Each crossing point (or, node) on the mesh was tracked by calculating the similarity between templates, which were modeled using two tunable Gabor filters and the underlying images (Qian et al. 2005, 2006). The crossing points on the mesh were driven iteratively by forces from those neighboring image patches, whose texture patterns were the most similar to a reference template. The coordinates of the crossing points were further smoothed in a time sequence by a cubic spline function, and the displacements were thus calculated through subtraction. Finally, a cubic B-spline-based method was employed to obtain a dense displacement distribution throughout the myocardium (Sandwell 1987). The cumulative 2D systolic displacement was also obtained.

Note that polar and Cartesian coordinates are used in the ultrasound phased array configuration and MRI tagging, respectively. More information regarding the difference of the coordinate systems used in the two imaging modalities is provided in Appendix B.

Strain estimation

Cumulative 2D (i.e., lateral and axial) systolic Lagrangian finite strain was derived from the cumulative 2D displacement to evaluate the systolic function *in vivo* (Lai et al. 1993, Lee and Konofagou 2006). Positive and negative 2D strains indicate tension and compression, respectively. In ME, a least-squares strain estimator (LSQSE) (Kallel and Ophir 1997) with a kernel of 11.7 mm in both the lateral and axial directions was used in order to improve the signal-to-noise ratio (SNR) in the strain image. Table 1 summarizes the main image parameters for myocardial elastography and MR tag tracking used in this study. The SNR of the tagged MR images was around 5.45, while that of MR strain images was approximately 10.15.

However, the aforementioned 2D finite strain was dependent on the orientation of the ultrasound transducer relative to the ventricle and on the coordinates of the image systems. In addition, the coordinate systems used in the two modalities were different as shown in Appendix B. This angle dependence and the use of the coordinate system might complicate

the interpretation of the myocardial deformation in the left ventricle as well as the comparison between two imaging modalities. Therefore, angle-independent, polar (i.e., radial and circumferential) strains, were additionally obtained by defining an angle, θ , about the centroid of the left ventricle and by coordinate transformation of the 2D finite strain. Positive and negative radial strains indicated myocardial thickening and thinning, respectively, while myocardial stretching and shortening were represented by positive and negative circumferential strains, respectively.

Even though the polar strains are independent of the transducer orientation, the selection of the centroid is critical. Principal strains have been proven to be angle-independent as well as less centroid-independent than the polar strains (Fung-Kee-Fung et al. 2005, Zervantonakis et al. 2007). Considering a 2D short-axis slice of the myocardium, solving the eigenvalue/eigenvector problem using equation (1) for the 2D finite strain tensor could yield two principal strains (eigenvalues) corresponding to two principal axes (eigenvectors), which closely approximated strains in the polar directions.

$$\mathbf{E}^p = \begin{bmatrix} \varepsilon_1 & 0 \\ 0 & \varepsilon_2 \end{bmatrix}, \quad (1)$$

where $\mathbf{E}^p$ is the principal strain tensor, and ε_1 and ε_2 are the classified 1st and 2nd principal components, respectively. Note that the two principal strains were classified according to their angles between the principal (i.e., eigenvectors) and polar directions (Zervantonakis et al. 2007). The 1st and 2nd principal strains closely approximated radial and circumferential strains, respectively (Zervantonakis et al. 2007).

Automatic contour tracking

Segmenting the myocardium from the neighboring tissue is essential in the depiction and detection of the extent of the pathological myocardium. The myocardial segmentation on the elastographic images throughout the entire cardiac cycle was performed and extended from 1D (i.e., axial) to 2D using an automated method (Luo and Konofagou 2008). The endo- and epicardial contours on the initial echocardiogram (i.e., at ED) were manually traced with 20 points each as the reference, while those for the rest of the frames were automatically segmented according to the estimated 2D displacement components. The automated contour tracking was thus implemented using 2D elastographic estimates.

RESULTS

Only the cumulative systolic deformation (i.e., displacements and strains) from ED to ES is considered in this paper since only the systolic function is relevant to the active contractility of the myocardium and the analysis of tagged MR images during diastole are not feasible owing to tag fading. The cumulative lateral and axial displacement images from ED to ES estimated using tMRI and ME at the papillary muscle level in a SA view of a normal left ventricle are shown in Fig. 1(i) at the end-systolic phase. The anterior, lateral, posterior and septal walls are in the upper right, lower right, lower left and upper left regions, respectively. Positive displacement values indicate rightward or upward motion, while negative displacement values represent leftward or downward motion. Figure 1(ii) shows the

corresponding cumulative systolic lateral and axial strains estimated from tMRI ((a) and (c)) and ME ((b) and (d)). As expected for a normal left ventricle being imaged in an echocardiographic short-axis view, tension in the lateral direction appears in lateral and septal myocardial regions, and axial tension in the anterior and posterior walls. The cumulative systolic polar and principal strains estimated from both imaging modalities are shown in Figs. 2(i) and (ii), respectively. Figure 2 shows positive radial (i.e., myocardial thickening in (a) and (b)) and negative circumferential (i.e., myocardial shortening in (c) and (d)) strains. The maps of the polar and principal strains were visually identical.

The temporal axial displacement and 2D, polar and principal strain profiles in a posterior wall region of $7.5 \times 7.5 \text{ mm}^2$ which is indicated by the white rectangles in Fig. 1 during systole are shown in Fig. 3. The temporal lateral displacement profiles of tMRI and ME (Fig. 3(a)) are obtained from the white rectangles shown in Fig. 1(i) (a-b). Note that the error bars represent the transmural variations of displacements, or strains, within the white rectangle on each image in Figs. 1 and 4. Compared with the other myocardial regions, the posterior wall is within a sector and thus less affected by the composite imaging. However, posteroseptal region is more suitable for obtaining temporal lateral displacement profiles. Figures 3(a)-(d) show the temporal (i.e., from ED to ES) profiles of the cumulative lateral and axial displacements and strains. The magnitude and the increasing trend of cumulative ME lateral and axial displacement (Fig. 3(b)) during systole are in excellent agreement with the tMRI estimates. However, the lateral strain (Fig. 3(c)) from the two modalities has a larger discrepancy than the axial strain due to the inconsistent lateral displacement patterns shown in Figs. 1(a) and (b). The temporal axial (Fig. 3(d)), radial (Fig. 3(e)) and the 1st principal component (Fig. 3(g)) strain profiles show better agreement between tMRI and ME than the lateral (Fig. 3(c)), circumferential (Fig. 3(f)) and the 2nd principal strain components (Fig. 3(h)) in the normal case. This is because the lateral strain (Fig. 3(c)) contributes more to the circumferential and the 2nd principal strains and thus results in their larger disagreement (Fig. 3(f) and (h)) between two modalities. The strains obtained from ME are also higher than the equivalent tMRI values (Fig. 3(c-h)). Increased standard deviations in the ME with time and higher standard deviations of the ME estimates compared to those of the tMRI ones were noted in the normal left ventricle (Fig. 3).

An example of a reperfused left ventricular deformation is shown in Figs. 4 and 5. This human subject suffered a myocardial infarction caused by partial occlusion of the distal left anterior descending (LAD) coronary artery and subsequent motion abnormalities in both the septal and anterior walls. Figure 4 shows the estimated cumulative systolic 2D strains and indicates that the axial component has better agreement than the lateral one. Not only does the reperfused left ventricle (Fig. 4) show hypokinetic behavior in the post-infarcted (i.e., anterior and anteroseptal) region and hyperkinetics in the normal (i.e., lateral and lateral-posterior) wall region compared with the normal left ventricle (Fig. 1(ii)), but the 2D strain patterns of the reperfused one (Fig. 4) are highly asymmetric compared to those of the normal one (Fig. 1(ii)). The cumulative systolic radial (Fig. 5(i) (b)) and 1st principal (Fig. 5(ii) (b)) ME strain estimates for the reperfused left ventricle show myocardial thickening in the posterior and anterior-septal walls but not in the septum or anterior region. In contrast, the radial (Fig. 5(i) (a)) and 1st principal (Fig. 5(i) (a)) tMRI strains show thickening throughout the entire myocardium with augmented thickening in the posterior wall but with

reduced thickening in the other walls. The circumferential (Fig. 5(i) (d)) and 2nd principal (Fig. 5(ii) (d)) strain estimates from ME show myocardial shortening in the posterior wall and slight stretching in the other regions, while the tMRI estimates (Figs. 5(i) (c) and (ii) (c)) indicate slight stretching in the lateral, anterior and anterior-septal walls.

Similar to the normal human left ventricle, the temporal axial displacement and 2D, polar and principal strain profiles for the reperfused case in a posterior wall region of $7.5 \times 7.5 \text{ mm}^2$ which is indicated by the white rectangles in Fig. 4 during systole are shown in Fig. 6. The temporal lateral displacement profiles of tMRI and ME are obtained from a posteroseptal wall region of $7.5 \times 7.5 \text{ mm}^2$ and are shown in Fig. 6(a). Overall, the displacements and strains obtained from ME are higher than the equivalent tMRI values. Increased standard deviations in the ME estimates with time and higher standard deviations of the ME estimates compared to those of the tMRI ones were also observed in this perfused left ventricle (Fig. 6).

Figure 7, a and b, show the temporal 1st and 2nd principal strain profiles in an anterior wall region of $3.5 \times 3.5 \text{ mm}^2$ in the normal left ventricle, which is indicated by the white rectangles in Fig. 2(ii), respectively. Figure 7, c and d, show the temporal 1st and 2nd principal strain profiles in the anterior wall region of $3.5 \times 3.5 \text{ mm}^2$ in the reperfused left ventricle, respectively. The normal left ventricle appears to experience radial thickening (Fig. 7a) and circumferential shortening (Fig. 7b); in contrast, the reperfused one shows radial thinning (Fig. 7c) and circumferential stretching (Fig. 7d). This observation verifies that the abnormal myocardium undergoes opposite deformation process compared with the normal myocardium.

DISCUSSION

Imaging of the 2D transmural displacement and deformation (or, finite strain) components, from lateral and axial, polar to principal coordinates, in a full short-axis view in a clinical echocardiography setting was first shown. A comparison of 2D images of all aforementioned estimated displacements and strains between ultrasound and MRI tagging in a clinical setting was also performed for the first time to our knowledge. Qualitatively, all these estimates from ME are in excellent agreement with those from tMRI in both normal (Figs. 1–2) and treated (Figs. 4–5) human subjects. More specifically, the 2D displacements (Figs. 3(a) and (b)), axial (Fig. 3(d)), radial (Fig. 3(e)) and the 1st principal (Fig. 3(g)) strains estimated from ME are in good quantitative agreement with the tMRI estimates in the posterior wall region of the normal human left ventricle. As for the reperfused human left ventricle, axial (Fig. 6(d)) and 1st principal (Fig. 6(g)) strains across the two imaging modalities show better quantitative agreement than other estimates.

In the normal human left ventricle shown in Fig. 1, estimates from both tMRI and ME show physiological motion and deformation in the systolic phase. However, the orientation of the tMRI 2D displacements (Fig. 1(i), (a) and (c)) and strains (Fig. 1(ii), (a) and (c)) does not exactly match with that of the ME estimates (Figs. 1(i)-(ii), (b) and (d)). This may result from the fact that the image planes acquired using MR tagging and ultrasound were not co-registered and that the coordinate systems were different between these two imaging

modalities (Appendix B). Moreover, the size and the shape of the right ventricle shown in the tagged MR image (Fig. 1(i), (a) and (c)) do not correspond to those shown on the echocardiography images (Fig. 1(i), (b) and (d)). In order to reduce a discrepancy due to image misregistration between the use of the coordinate systems and to more fairly compare the estimates between two image modalities, polar (Fig. 2(i)) and principal (Fig. 2(ii)) strains were imaged, showing myocardial thickening and shortening during systole in the normal human left ventricle.

The temporal profiles of the tMRI radial (Fig. 3(e)) and 1st principal (Fig. 3(g)) strains show excellent agreement with the equivalent ME profiles, while the circumferential (Fig. 3(f)) and 2nd principal component (Fig. 3(h)) profiles show the lowest agreement. However, the 2nd principal strain shows a smaller discrepancy than the circumferential strain across the two modalities in the normal left ventricle shown here. In general, principal strains show comparable results to those of polar strains in the clinical cases shown, but the former can be used to further reduce the centroid dependence, and thus, may constitute a more reliable tool for the accurate depiction of myocardial deformation (Fung-Kee-Fung et al. 2005, Zervantonakis et al. 2007).

The tMRI and ME strain estimates in the posterior wall of the reperfused ventricle are higher than those in the anterior wall (Figs. 4 and 5). This may indicate that the post-infarcted (i.e., anterior and antero-septal) region experiences the reduced contractility and that the normal region (i.e., posterior) compensates the systolic function for the abnormal region (i.e., anterior) with hyperkinesia, i.e., larger motion and deformation. However, this phenomenon of compensation is more pronounced in the ME, not in the tMRI estimates. The cumulative systolic axial, radial and the 1st principal strain estimated from ME in the posterior wall are approximately on the order of 50%, while those estimated from tMRI range from 20% to 30% (Figs. 6(d), (e) and (g)). This large discrepancy may be due to the different short-axis planes acquired in the two imaging system and still needs to be under careful investigation. In addition, the reperfused left ventricle exhibits a more asymmetric geometry and deformation pattern than the normal case. This further complicates the comparison between the strain estimates from the two imaging systems, especially in the presence of imperfect image registration. The polar and principal strains still show comparable results, and the latter may be an alternative parameter of detecting abnormal myocardial deformation with its less centroid dependence.

In the case of the reperfused myocardium (Figs. 4 and 5), again manual composite RF sector data acquisition was employed to increase the frame rate, but this may have caused mismatches between neighboring sectors in the septal and outside the lateral walls due to free-hand scanning, inconsistency in breath-hold duration and volume, and different length of cardiac cycles involved. Thus, the tMRI and ME strain estimates in the septal region of this reperfused myocardium appeared to have larger discrepancy than those in the other regions due to the septal discontinuity in the ultrasound data (Figs. 4 and 5). Synchronizing breathholds with pathological subjects was more difficult than with normals, and additional trials for an optimized data acquisition were avoided in patients. Moreover, the example of the reperfused human left ventricle shown was the only one, which still showed myocardial

dysfunction after treatment from our patient pool and was therefore used here as an example to contrast the normal case.

Temporal principal strain profiles in the anterior wall region of both normal (Figs. 7(a) and (b)) and reperfused (Figs. 7(c) and (d)) left ventricles show similar systolic strain trends with both imaging methods. Smaller spatial variations of strain estimates in tMRI than in ME are still noted. Overall, increased radial thickening (Fig. 7a) and circumferential shortening (Fig. 7b) with time in the anterior wall of the normal left ventricle are observed. The slight radial thinning (Fig. 7c) and circumferential stretching (Fig. 7d) in the anterior region of the reperfused left ventricle confirms the myocardial abnormality in the anterior region cause by partial LAD occlusion. Compared with the posterior wall region, the anterior wall region in the reperfused left ventricle undergoes opposite deformation according to both the ME and tMRI estimates. This is consistent with the qualitative observation of the reduced and even opposite deformation in the anterior wall and of the hyperkinetic posterior wall in compensation for the loss of contractility in the pathological region, in the reperfused case. Moreover, the anterior wall region of the reperfused left ventricle was thinner than that of the normal one. Therefore, only 25% of the ROI in the normal case was used to obtain the temporal strain profiles for the reperfused case. The same kernel size in the least-squared strain estimator was used in both normal and reperfused cases. Therefore, the kernel size relative to the myocardial thickness determined the smoothness effect on the strains. Furthermore, ME presents more contiguous deformation owing to its higher temporal resolution than tMRI.

The spatial resolution (1.92 mm and 0.77 mm in the lateral and axial directions) of an RF ultrasound frame is higher than that (9 mm in both lateral and axial directions) of a tagged MR image. This constitutes a discrepancy in spatial resolution (and thereby spatial variability) of the strain estimates between the two modalities. Figures 3 and 6 show the average strain values with the standard deviations depicting the spatial variations of strain estimates in the posterior wall region. A larger number of original signal samples are available transmurally in ultrasound than in MR tagging. Therefore, the larger standard deviation of ME compared to that of tMRI (Figs. 3 and 6) indicates that the spatial strain variation increases with spatial resolution as expected. The higher the spatial resolution is, the more strain estimates can be obtained within the myocardium, and thus the larger the spatial strain variation is (Srinivasan et al. 2003). This spatial strain variation confirms transmural non-uniformity previously reported in the canine and human left ventricles (Waldman et al. 1985, Bogaert and Rademakers 2001). The temporal resolution of echocardiography is four times higher than that of tMRI in the cases studied, so smoother temporal profiles of cumulative displacements and strains are shown (Figs. 3, 6, and 7).

Overall, the trends of tMRI and ME temporal cumulative displacement and strain profiles are in very good agreement, while the strain values show less agreement. Around 10% (20%) discrepancy of the strains in normal (treated) subjects with ME compared to that with tMRI was observed. This discrepancy may have resulted from several reasons as indicated above, such as the lower SNR of the ultrasound RF signals, sector discontinuities due to manually performed composite imaging, inexact registration between ultrasound and MR images, and a low transmural tagging resolution.

Despite the fact that higher ME than tMRI strain values were observed here (Figs. 3 and 6), several groups (Bogaert and Rademakers 2001, Herbots et al. 2003, Hurlburt et al. 2007) have shown similar radial and/or circumferential strain values of normal human left ventricles with the ME estimates reported in this paper. Bogaert and Rademakers (2001) showed total wall thickening of $32.8\pm1.0\%$ during systole estimated from MR tagging in the normal posterior wall. Herbots et al. (2003) showed average peak radial strain of $62\pm11\%$ estimated with SRI, and their results were in good agreement with those estimated from both ultrasound and MRI Mmodes, in the basal infero-lateral wall. Hurlburt et al. (2007) presented average radial strains of $37\pm17\%$ and circumferential strains of $21\pm7\%$ using B-mode speckle tracking in the posterior wall region. Although the strains obtained from ME are overall higher compared with those from tMRI in both normal and reperfused left ventricles, these preliminary results show that the two imaging modalities are in good agreement and that ME is capable of differentiating abnormal from normal myocardium even in a post-infarction, treated left ventricle. Correct co registration and study of the role of inherent resolution and SNR differences across the two modalities are currently ongoing.

Several groups have validated their cardiac function assessment techniques in echocardiography against the direct measurement of sonomicrometry (Papademetris et al. 2001, Langeland et al. 2005, Sengupta et al. 2006). However, this cannot be used as the gold standard in a clinical study due to the requirement of an invasive procedure. Nonetheless, conducting a series of validation studies using sonomicrometry in animals is currently ongoing as part of a separate animal study. In terms of a non-invasive, clinical validation of myocardial elastography, MR tagging was selected as the gold standard given that the methods used have been more established and its findings validated. On the other hand, to confirm the validity of the new tag tracking method, as part of a separate study, the tagging sequence is being further optimized, and the tracking algorithm (Metaxas et al. 2003, Qian et al. 2003) is being evaluated against more established techniques such as HARP (Osman et al. 1999) and velocity-encoded MRI (Wedeen 1992).

Finally, since MR and echocardiography data were not necessarily acquired from exactly the same myocardial region or image plane, and were not accurately co-registered due to the lack of 3D data, the ROIs selected for plotting temporal strain profiles might not have represented the same material points across the MR images and echocardiograms. In this preliminary study, we mainly concentrated on the regional transmural deformation after a global match of the papillary-level short-axis view between the two imaging configurations. Ongoing investigations on image registration are currently being performed to optimize cross-modality comparisons.

CONCLUSION

Myocardial motion and deformation in two orthogonal directions were assessed accurately using angle-independent myocardial elastography. In-plane, 2-D transmural (lateral and axial) displacement and (lateral, axial, polar and principal) strain fields were comparable to those obtained with tMRI, in both normal and pathologic human hearts in vivo. Axial displacement as well as radial and 1st principal strain estimates depicted the strongest agreements between the two modalities in the normal case. Most importantly, the abnormal

anterior region in the reperfused left ventricle was successfully depicted by the qualitative and quantitative principal strain results, showing passive deformation behavior with during active contraction (i.e., systole). Principal strains did not appear to be superior but comparable to polar strains in the reperfused case, so they may serve as an alternative tool in the detection of abnormal myocardium. Although preliminary results show that higher strain values were obtained with ME compared to tMRI, the overall trends of the temporal cumulative displacement and strain profiles obtained from these two imaging modalities are in excellent agreement. The presented results constitute a preliminary validation of high-frame-rate RF ultrasound data acquisition, and subsequently 2D imaging of full-view, in-plane, orthogonal displacement and strain components against tagged MR imaging. To our knowledge, this is the first time that a side-by-side comparison of the displacement and strain images is performed between MRI and echocardiography; qualitative or not.

Ongoing work focuses on the correct co-registration of ultrasound and tagged MR images, the use of a fully automatic composite ultrasound imaging technique, assessment of the role of the sonographic SNR on the ME strain estimates and study of the tradeoff between spatial resolution and strain accuracy for precise quantification in both normal and acute infarction subjects.

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APPENDIX A

The unit of the initial lateral displacement estimates is the number of interpolated RF signals in the lateral direction. Thus, the actual lateral displacements (mm) need to be further obtained by multiplying the initial lateral displacement with the actual beam spacing, which increases with the depth and can be calculated as follows:

$$u_{us} = u_{tmp} \cdot r \cdot \beta,$$

where u_{tmp} and u_{us} are the initial and actual lateral displacements, r is the radius at an RF sample point, and β is the angular increment of the RF signals in radians in the azimuthal direction (Fig. A-1).

APPENDIX B

In an ultrasound system, the axial direction is defined as the beam direction, and the lateral direction is perpendicular to the axial direction. In a linear array configuration, the lateral and axial directions correspond to the abscissa (x -) and the ordinate (y -) axes in Cartesian coordinates, respectively. On the other hand, the lateral (x_{us} -) and axial (y_{us} -) directions in a phased array configuration (i.e., polar coordinates) coincide with the angular and radial axes, respectively (Fig. B-1). The lateral and axial coordinates/displacements (u_{us} - and v_{us} -) can be transformed into Cartesian ones using the following equation:

$$\begin{bmatrix} x \\ y \end{bmatrix} = \begin{bmatrix} \cos\theta & \sin\theta \\ -\sin\theta & \cos\theta \end{bmatrix} \begin{bmatrix} x_{us} \\ y_{us} \end{bmatrix} \quad \begin{bmatrix} u \\ v \end{bmatrix} = \begin{bmatrix} \cos\theta & \sin\theta \\ -\sin\theta & \cos\theta \end{bmatrix} \begin{bmatrix} u_{us} \\ v_{us} \end{bmatrix},$$

where θ is the counterclockwise angle between the two coordinate systems, and u and v are the Cartesian displacements (Fig. B-1).

Cartesian coordinates are used in MR tagging, and thus the horizontal and vertical axes are defined as the lateral and axial directions, respectively. Clearly, different coordinate systems which are used in these two imaging modalities result in the discrepancy of the 2D displacement and strain estimates.

Figure 1.

Cumulative systolic 2D (i) displacements and (ii) strains of a normal human left ventricle between ED and ES: (a) and (c) are the lateral and axial components from tMRI, respectively; (b) and (d) are the lateral and axial components from ME, respectively. All the displacement and strain images are acquired approximately at the papillary muscle level and shown at ES. The white rectangles indicate where the temporal displacement and strain profiles shown in Fig. 3 are obtained.

Figure 2.

Cumulative systolic (i) polar and (ii) principal strains of the same normal human left ventricle between ED and ES: (a) and (c) are the radial/1st principal and circumferential/2nd principal strains from tMRI, respectively; (b) and (d) are the radial/1st principal and circumferential/2nd principal strains from ME, respectively. The white rectangles in (ii) indicate where the temporal strain profiles shown in Figs. 7(a) and (b) were obtained.

Figure 3.

A normal human left ventricle: temporal displacement and strain profiles from ME and tMRI in the postero-septal or posterior wall region of 7.5 mm by 7.5 mm from ED to ES in the case of (a) lateral, (b) axial displacements, (c) lateral, (d) axial, (e) radial, (f) circumferential, (g) 1st principal, and (h) 2nd principal strains. The displacement profile is displayed between -2 mm to 6 mm. The strain profile is displayed between -0.3 to 0.5, namely -30% to 50% strain.

Figure 4.

Cumulative systolic 2D strains of a reperfused human left ventricle between ED and ES: (a) and (c) are the lateral and axial strains from tMRI, respectively; (b) and (d) are the lateral and axial strains from ME, respectively. All the displacement and strain images are acquired approximately at the papillary muscle level and shown at ES. The white rectangles indicate where the temporal strain profiles shown in Fig. 6 are obtained.

Figure 5.

Cumulative systolic (i) polar and (ii) principal strains of the same reperfused human left ventricle between ED and ES: (a) and (c) are the radial/1st and circumferential/2nd principal strains from tMRI, respectively; (b) and (d) are the radial/1st principal and circumferential/2nd principal strains from ME, respectively. The white rectangles in (ii) indicate where the temporal strain profiles shown in Figs. 7(c) and (d) were obtained.

Figure 6.

A reperfused human left ventricle: temporal displacement and strain profiles from ME and tMRI in the posteroseptal or posterior wall region of 7.5 mm by 7.5 mm from ED to ES in the case of (a) lateral, (b) axial displacements, (c) lateral, (d) axial, (e) radial, (f) circumferential, (g) 1st principal, and (h) 2nd principal strains. The displacement profile is displayed between -3 mm to 8 mm. The strain profile is displayed between -0.4 to 0.8, namely -40% to 80% strain.

Figure 7.

Temporal systolic ME and tMRI principal strain profiles in the anterior wall region of 3.5 by 3.5 mm² in the case of a normal human left ventricle: (a) 1st and (b) 2nd systolic principal strains and of a reperfused human left ventricle: (c) 1st and (d) 2nd principal strains.

Figure A-1.

(a) the coordinate system used in the ultrasound phased array configuration, where solid lines show the representative RF signals, x_{us} and y_{us} are the lateral and axial directions, respectively, solid blue arrow shows the motion vector of a material point, P_1 ; (b) the magnification of the motion vector in (a): x_{us} and y_{us} are the actual lateral and axial displacements, respectively, and β is the angle increment between two neighboring RF signals.

(a)

(b)

Figure A-2.

(a) the ultrasound phased array configuration with x_{us} and y_{us} being the lateral and axial directions, respectively, x and y composing Cartesian coordinates, and θ being the counterclockwise angle between two coordinate systems; (b) illustration of the Cartesian coordinate system used in the tagged MR images. (x, y) represent the Cartesian coordinates in both (a) and (b), and P1 indicates the same material point under both imaging modalities.

Table 1

Strain imaging parameters for both myocardial elastography and MR tag tracking.

	Myocardial elastography	MR tag tracking
Temporal resolution of strain elements (fps)	136	33
Lateral resolution of strains (mm)	1.76	9
Axial resolution of strains (mm)	1.38	9
Data acquisition temporal resolution (fps)	136	33