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Three-Dimensional Regional Left Ventricular Deformation from Digital Sonomicrometry

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Abstract—**Understanding how the left ventricle deforms in 3D and how this deformation is altered with coronary occlusion may lead to the development of non-invasive imaging techniques to determine the extent of permanent injury. To determine regional 3D strains in the left ventricle of the heart we employed digital sonomicrometry, with high temporal and spatial resolution. Two cubic arrays of 8 omni-directional transceiver crystals were implanted in two regions of the left ventricle in an open chest canine preparation ($n = 6$). Additional crystals were used to define a fixed external reference space and the long axis of the ventricle. Using ultrasound transit time the distances between all the crystals were recorded. A multidimensional scaling technique was then applied to transform the distances to 3D crystal coordinates. A least squares fit of the displacement field was applied to calculate homogeneous strains for each cube. Cardiac specific directions were determined and strains rotated into the local coordinate space. This technique was applied pre- and post- coronary occlusion. Alterations in strain patterns were evident in the ischemic region and subtle temporal changes in the control region. Thus, digital sonomicrometry, with high temporal and spatial resolution, enhances our ability to analyze regional left ventricular 3D strain patterns.**

Keywords— **Coronary occlusion, Myocardial deformation, Strain measurement, Sonomicrometry**

I. Introduction

Understanding how the left ventricle (LV) deforms in 3D may have major implications for defining the extent of injury following coronary artery occlusion. Understanding how myocardial ischemia alters 3D deformation will be vital to the development of non-invasive imaging approaches for the assessment of myocardial viability. Developments in 3D Magnetic Resonance Imaging (MRI) techniques such as MR tagging [2], [1] and shape based boundary tracking [3], [9] are promising. However, these techniques employ beat averaging and long imaging times. Therefore, these approaches might miss crucial temporal changes in strains. They also have low spatial resolution compared to sonomicrometry. Biplane radiography using radiopaque markers is another technique to measure 3D LV strains. Implanted marker positions and strains are calculated using triangulation technique. The radiopaque marker technique offers a relatively high temporal resolution (120 Hz) and spatial resolution ($\sim$0.2 mm) and has been successfully employed to determine regional LV strains [6]. Digital sonomicrometry provides both improved temporal resolution (>125 Hz) and spatial resolution (0.024 mm). Ratcliffe *et al* demonstrated that sonomicrometry can accurately localize specific myocardial locations in 3D space using a custom multidimensional scaling algorithm [8]. Digital sonomicrometry has the advantage of portability and availability that both MR and biplane radiography are lacking.

We have employed a commercially available multidimensional scaling algorithm (Sonometrics Corporation) along with the use of digital sonomicrometry to determine 3D crystal locations in small regions of the LV. Analysis of the crystal displacements over the cardiac cycle permits calculation of regional LV strains for an individual heart beat. Digital sonomicrometry provides the high temporal and spatial resolution needed to appreciate the subtle changes in strain patterns we expect. The use of fixed reference crystals enabled us to compare strains from different experimental states. The use of an additional internal cardiac reference allowed us to determine cardiac specific strains. We applied this technique to estimate *in vivo* regional LV strain before and after coronary artery occlusion.

II. Methods

Surgical Preparation. All animal experiments were performed with the approval of the Yale Animal Care and Use Committee and in compliance with the guiding principles of the American Physiological Society on research animal use. 6 canines were surgically instrumented under anesthesia. LV pressure and aortic pressure were measured using micromanometers (Millar 7F, Houston, TX). A thoracotomy was performed in the fifth intercostal space. The heart was suspended in a pericardial cradle. A segment(s) of the left anterior descending artery (LAD) was dissected for the placement of snare occluder(s). With the aid of an implantation device constructed in our laboratory an 8 crystal cubic array of crystals (4 subepicardial, $\sim$2.0 mm diameter; 4 subendocardial, $\sim$0.7 mm diameter) was placed in the central ischemic injury region and the remote control region. To define the LV long axis a crystal was implanted in the LV apex and at the base of the LV near the bifurcation of the left main coronary artery. Finally, to define a fixed coordinate space, 3 crystals attached to a plexi-glass frame were secured in the pericardial space under the right ventricle. We applied our approach to experimental canine models of coronary occlusion, allowing us to evaluate both the temporal changes in LV deformation following coronary

occlusion and the impact of the extent of the ischemic injury on regional LV deformation.

Data Acquisition. Digital Sonomicrometry employs the time of flight principal of ultrasound to measure the distance between a transmitter and a receiver. A high speed digital counter is started when the transmitter is fired, and stopped when the first peak of the ultrasound wave is detected. Knowing the speed of ultrasound in tissue, the transit time is converted to a scalar distance. A total of 21 crystals are used in each study. The distances between all possible pairs of crystals are recorded along with LV and aortic pressure at a sampling frequency of greater than 125 Hz.

Signal Processing. Due to a variety of technical issues the recorded distances must be filtered to remove noise. This is a two step process. The first step is automated. Occasionally, the system triggers on the second or subsequent ultrasound waves, rather than on the first, and a "level shift" of the data trace occurs. This level shift is a brief and rapid increase in distance corresponding roughly to a multiple of the wavelength of the ultrasound signal. The detected distance is therefore the true distance plus a positive constant. Another type of error, a dropout, results when the system is triggered by noise before the first peak reaches the receiver. Both of these errors can be automatically detected by examining the continuity of the data trace. The true distance data is a continuous and smooth trace of points. The continuity of the trace is detected by first and second order derivatives. The transition point of the level-shift is detected and the minimum level-shift step (approximately the wavelength of ultrasound) is estimated statistically over the entire trace. The level-shift segment is then shifted down to its correct level. The dropout points are detected and eliminated since they are below the true distance. The eliminated dropout points are interpolated with a tenth order least-squares polynomial. Because there occasionally are multilevel-shifts and dropouts near the level-shifts both are eliminated interactively in forward and backward trace directions. It is estimated that the automatic filter algorithm corrects over 90% of the data trace defects. The second step is a manual check using software developed by Sonometrics Corporation. This software allows the user to correct any remaining noise or eliminate any crystal pair trace that has a signal which is not correctable.

Once the distances are filtered they are passed to the 3D calculation program. First, four crystals are defined by the user to define the local coordinate system. One crystal is designated as the origin, a second defines the x-axis, a third defines the x-y plane and the fourth defines the positive z direction. The x, y, z coordinates of all the others are referenced to this coordinate system. Simple triangulation is used to obtain the first estimate of the crystal coordinates, which are then subsequently refined through iterative filtering using a statistical algorithm called "multidimensional scaling". This algorithm iteratively adjusts the x, y, z coordinates of each point and minimizes the total error between the original measured distances and the same distances obtained from the reconstructed 3-D data set. Simulated annealing technique is used to explore the entire solution space and avoid being trapped in any local minimum.

After conversion to 3D coordinates, individual heart beats are further divided into isovolumic, ejection, and diastolic phases, using an automated technique developed in our laboratory, which is applied to the LV pressure and aortic pressure signals. These beats are then passed to the strain calculation program.

At each temporal frame, cardiac specific local coordinate system is established for each crystal cube. The apex-base crystal pair defines the longitudinal direction. The circumferential direction is defined by the intersecting line between the estimated epicardial plane (from the epicardial crystals) and the plane which is perpendicular to the longitudinal direction and passing through the centroid of the epicardial crystals. The radial direction is the cross product of the longitudinal and circumferential directions. The global coordinates of the crystals at end-diastole and the current time are transformed into this local reference frame. Displacement vectors are calculated for all crystals of the cube, and a continuous displacement field is estimated from these vectors in a weighted least square fashion. Cardiac specific strains (longitudinal, circumferential, radial, and three shear strains) as well as three principal strains and their directions are calculated from the displacement field.

III. Results

Dynamic 3D crystal positions were viewed qualitatively in an interactive cine format on a Silicon Graphics workstation. Regional deformations for both the ischemic injury and remote control crystal arrays were viewed from data acquired before and after LAD occlusion. Regional LV deformation was analyzed relative to the fixed external reference and the long axis of the heart. Review of these cine loops permits visualization of complex regional deformations. A representative static display of the 3D crystal configuration is illustrated in Fig. 1. 3D locations of the 21 crystals are shown at end diastole and end systole, the two extreme phases of the cardiac cycle. The 3D crystal configurations for this dog are shown before and 1 hour after LAD occlusion. The 3 crystal external reference plane can be seen at the bottom of each image. Note that the external reference remains fixed, suggesting that the algorithm reproducibly calculates these crystal positions. The apex to base crystal pair defines the long axis of heart. Also displayed are the cubic array of crystals in central ischemic injury region and the remote control region. In this example, regional deformation in the ischemic injury region and the remote control region are comparable before coronary occlusion. Note the obvious change in deformation of the ischemic injury region following LAD occlusion (see Fig. 2). To appreciate more subtle temporal alterations in deformation quantitative display of strains are required.

Cardiac specific strains were computed over the entire cardiac cycle and referenced to end diastole. Fig. 3 illustrates a representative set of strain curves segmented into 3 cardiac phases (isovolumic systole, ejection systole, and diastole). Changes in normal cardiac specific strains and
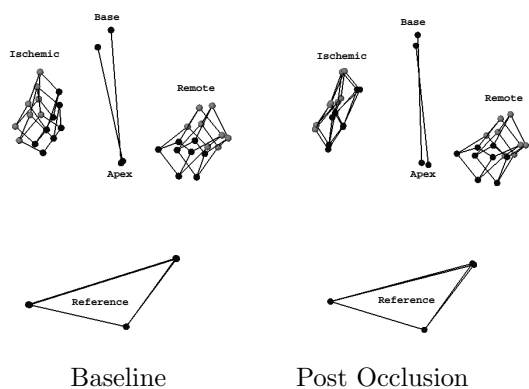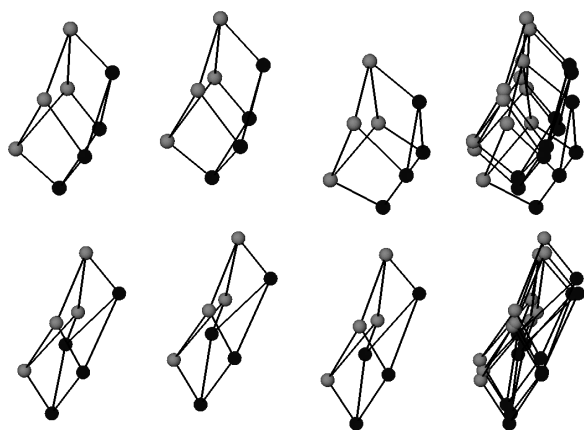
Baseline   Post Occlusion

Fig. 1.   Projection of 3D crystal locations. End-diastolic and end-systolic locations are shown at baseline (left) and after LAD occlusion (right). (Epicardial crystals - light gray; endocardial crystals - dark gray).

End-Diastole End-Isovolumic End-Systole Combined

Fig. 2.   Changes in regional myocardial deformation in central ischemic cubic array. Crystal coordinates are shown before (top) and after (bottom) LAD occlusion. Three phases of the cardiac cycle are shown separately and in combination.
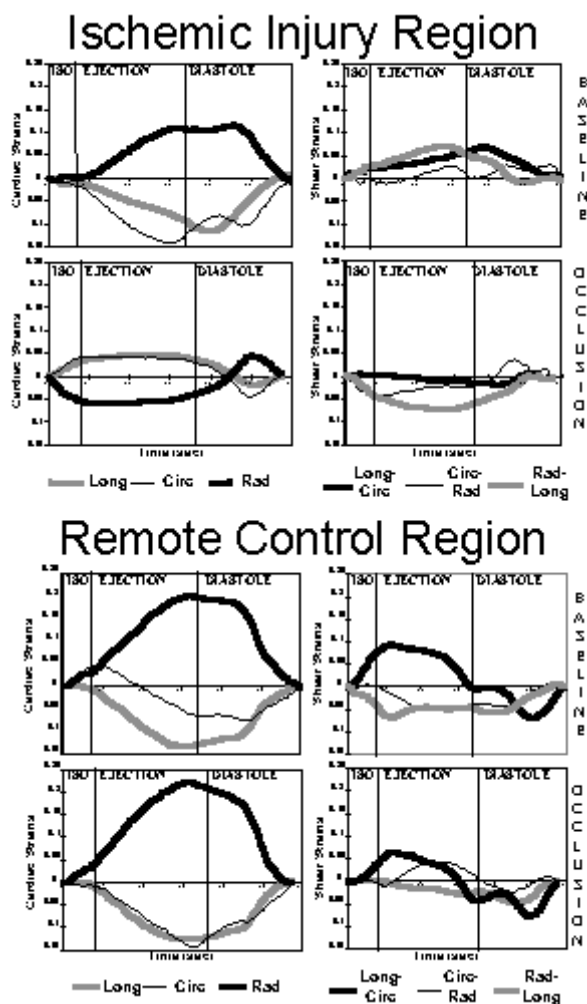

Fig. 3.   Cardiac specific strains. Strains from the central ischemic injury region are on the top and from the remote control region on the bottom. The top row for each region represents baseline strains, while bottom row represents strains post LAD occlusion (radial - Rad; circumferential - Circ; longitudinal - Long). Shear strains are shown on the right. The cardiac cycle has been segmented into isovolumicic, ejection, and diastolic phases.

cardiac shear strains in ischemic injury region and the remote control region before and after LAD occlusion are shown for one representative cardiac cycle for the crystal configuration above. Lengthening was expressed as positive and shortening as negative. Under baseline conditions, there is appropriate radial lengthening and circumferential and longitudinal shortening. After LAD occlusion, in the ischemic injury region, all the cardiac specific strains have changed their signs(i.e. lengthening to shortening). The region remote from the ischemic insult also shows a change in cardiac specific strains and shears. The most dramatic change in the remote region was the loss of isovolumic circumferential lengthening and a change in the circumferential -radial shear (shortening to lengthening).

IV. Discussion

We have successfully implanted arrays of sonomicrometers into the myocardium of 6 dogs for the serial assessment of regional LV deformation. We have shown that from the scalar distances measured we can accurately reconstruct

the relative 3D coordinates of the crystals in relationship to a fixed external reference. Inspection of cine loops of the crystals positions over the cardiac cycle enables us to visually appreciate complex changes in regional deformation following coronary occlusion. Regional homogeneous cardiac specific strains were calculated relative to local internal cardiac reference system, with both high temporal and spatial resolution. Our approach using digital sonomicrometry allows for the identification of subtle temporal changes in regional myocardial deformation, and offers a unique method for defining complex cardiac deformations.

Gorman *et al* recently showed that digital sonomicrometry can accurately and reproducibly localize specific myocardial locations in a chronic ovine model to look at the mitral valve [5]. Although they used the same acquisition system they did not implant the crystals within the myocardium. They sutured the crystals to the myocardial surfaces. In addition, these investigators used an alter-

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native multidimensional scaling algorithm. In the current analysis we employed both an external and internal reference system to generate cardiac specific myocardial strains. We observed no significant change in 3D coordinates of the external reference crystals over multiple cardiac cycles demonstrating our ability to accurately determine 3D crystal locations. The return of each crystal coordinates to the same end diastolic position also supports that we were able to reproducibly localize the crystals in the small territory required to quantify regional deformation.

Much of the information gained regarding 3D deformation of the left ventricle comes from analysis of implanted radio-opaque markers using biplane cine angiography. While this approach has certain merits, there are also significant limitations. One obvious concern is the effect of bead implantation. Fenton *et al* reported an average flow decrease of 25% within 5 mm of marker implantation [4]. These investigators implanted three columns of lead spheres (five 1 mm diameter lead beads per column). More importantly there are errors associated with localization of the markers in a 3D space [4], [7]. This error is due to pincushion effect, cone effect, and identification of the marker centroids.

Less invasive magnetic resonance imaging approaches (i.e. radial tagging, SPAMM, phase contrast imaging) offer an alternative approach. MR imaging employing a variety of these methodologies [2], [1], [3], [9] is able to accurately quantify LV deformation. MR imaging has the advantage of being able to measure strain over the entire LV as opposed to just regionally. While these techniques hold great promise, their relatively low spatial resolution and the fact that they employ beat averaging and not real time imaging, might not allow detection of important although subtle temporal changes in deformation. This would prevent adequate sampling to detect changes during critical short phases in the cardiac cycle, like isovolumic contraction. In addition, MR tagging does not permit tracking of a myocardial element over the entire cardiac cycle (secondary to signal decay), and also does not permit tracking of deformation over extended periods of time, as is the case with ventricular remodeling.

One of the major limitations of digital sonomicrometry is the enormous volume of data that must be manually filtered. This analysis can become a time consuming process when 21 crystals are employed, since a total of 420 measured distances must be computed. Three to five seconds of data acquired at ~125 Hz took approximately 6-8 hours to filter. However, once the signals were filtered we were able to easily analyze multiple cardiac cycles. Another possible limitation is the potential for damage of the local tissue when implanting the crystals. This should be minimal since the crystals we are using are ~0.7 mm as compared to the radiopaque beads used by McCulloch *et al* [6].

V. Conclusion

Digital sonomicrometry, with high spatial and temporal resolution, when combined with multidimensional scaling can be used to accurately determine 3D regional LV strains.

This technique allows for the determination of cardiac specific strains. The high temporal and spatial resolutions allow for the investigation of subtle changes in strain patterns associated with coronary artery occlusion.

While we have successfully developed the methodology for measuring 3D regional LV deformation we are still developing the tools to fully analyze and understand the observed strain patterns. There are obvious changes in the region of ischemic injury. Changes in strains over time may permit determination of the extent of permanent damage. Also, the subtle temporal changes in the remote control region may predict late ventricular remodeling and provide risk stratification.

Once we understand the regional 3D deformation of the LV in response to a coronary occlusion we hope to use this information to assist in the development of non-invasive MR imaging approaches, to determine the extent of irreversible injury. The results from our digital sonomicrometry may reveal the most appropriate parameters to analyze with MR imaging. Alternatively, we might be able to derive tissue properties that can be passed into the computer models used to derive strains from MR images.

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