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Model-Based Screening of Wall Motion Measures for Detection of Ischemia in Three-Dimensional Cardiac Images

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Abstract—**Quantitative measurement of left ventricular wall motion can improve clinical diagnosis by providing a more objective approach than qualitative analysis, which is subject to large inter-observer variability. We have developed novel techniques for quantifying left ventricular wall motion in three-dimensional image data sets. In this study, finite element models simulating regional ischemia in the left ventricle were used to screen potential wall motion measures for their capability to detect and evaluate the size of an ischemic region. Preliminary experimental results showed that wall motion analysis of real-time three-dimensional echocardiographic images successfully detected ischemia. Our four-dimensional wall motion analysis system provides an objective and quantitative approach for detecting and assessing the severity of disease.**

I. Introduction

Left ventricular (LV) wall motion analysis is useful for studying regional cardiac function and identifying diseased or dysfunctional myocardium [1]. In acutely ischemic myocardium, regions of the LV receiving insufficient blood flow rapidly switch from active contraction to passive stretching during ventricular systole. This change in regional mechanics is visible in ultrasound images as a change in regional wall motion.

While visual identification of wall motion abnormalities in echocardiograms is currently used, qualitative analysis such as this can lead to large inter-observer variability [2]. Systematic quantification of wall motion should greatly improve diagnosis and provide valuable information that can be used to track the progress of disease in a patient.

Real-time three-dimensional (RT3D) echocardiography has become increasingly popular because it enables rapid acquisition of volumetric image data of the entire left ventricle. The additional information available from 3D images improves quantitative analysis of wall motion by allowing for new solutions to classic problems that have limited quantitative analysis in two-dimensional images.

We previously demonstrated a novel approach to measuring wall motion in prolate spheroidal coordinates [3], and have recently extended this methodology to four dimensions. This parameterization allows for definition and computation of many different measures of endocardial surface motion. Here, we demonstrate the use of finite element models of the canine LV to screen candidate measures for their anticipated utility in a particular diagnostic application, in this case identifying and quantifying regional ischemia. Finite element models provide an excellent platform for evaluating potential wall motion measures because it is possible to simulate a disease state and systematically vary the location and severity of disease. Multiple measures of regional LV function can be calculated from the models and compared to one another. We also report here preliminary experimental results for one wall motion measure that performed well in finite element simulations.

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II. Methods

A. Finite Element Model

Using Continuity [4], a three-dimensional (3D) finite element model simulating temporary occlusion of the left anterior descending (LAD) and left circumflex (LCx) coronary arteries in the canine left ventricle was employed to screen candidate wall motion measures [5]. In the model, an anisotropic exponential constitutive law governed passive filling and active contraction was defined using a time-varying elastance model. A fully transmural ischemic region was simulated in the LAD or LCx perfusion beds [5].

The size of this ischemic region was varied to test the ability of several wall motion measures to quantify the extent of ischemia. The ischemic regions covered between 6.5% and 41% of the endocardium in the simulation of LAD occlusion, and between 7% and 37% in the simulation of LCx occlusion.

B. Experimental Data Acquisition

A single canine study was performed under a research protocol approved by Columbia University's Institutional Animal Care and Use Committee. The animal was anesthetized with isoflourane and underwent a lateral thoracotomy and median sternotomy and the heart was supported in a pericardial cradle. RT3D echocardiograms were acquired using a SONOS 7500 ultrasound system (Philips Medical Systems, Best, the Netherlands). Epicardial echocardiograms were obtained from the apex of the heart at baseline and during temporary occlusions (2 minutes duration) of the proximal LAD and mid LCx coronary arteries. The LV endocardial border was manually traced in the images using custom Matlab (Mathworks, Natick, MA) routines.

C. Three-Dimensional Wall Motion Analysis

A parametric representation of the LV endocardial surface in prolate spheroidal coordinates (λ, μ, θ) was obtained from the finite element model and the experimental data [3]. The coordinate λ is analogous to a radius in spherical coordinates. A surface was fit to the digitized endocardial data at ED and at ES. This parametric representation enabled calculation of several measures of regional LV function. Each measurement was displayed using a Hammer projection map and color-coded to display abnormal regions in dark gray and black.

Three-dimensional fractional shortening (3DFS), a measure of wall motion comparable to two-dimensional fractional shortening used for wall motion analysis in echocardiography, was calculated by comparing the position of the endocardial surface at end diastole and at end systole using the equation [3]:

$$3DFS = (\lambda_{ED(ENDO)} - \lambda_{ES(ENDO)}) / \lambda_{ED(ENDO)} \quad (1)$$

In the finite element model, several measures of regional LV function were compared to 3DFS to test their ability to quantify the size of ischemic region prescribed in the model including: three-dimensional wall thickening (3DWT), radial strain and circumferential strain. These measures were selected for comparison with 3DFS because they have been shown to be useful in identifying abnormal regional LV function in the literature. In particular, wall thickening, when compared with motion analysis in MRI, has been reported to better differentiate between ischemic and normal myocardium [6]. Others have shown radial strain, calculated from MRI tagged images, to be a good measure of regional LV function [7]. Evidence based on the mechanics of ischemic myocardium, as measured from implanted markers, suggested that circumferential strain should be most sensitive for identifying ischemic myocardium in some situations [8].

D. Four-Dimensional Wall Motion Analysis

Four-dimensional (4D) measures (3D + time) of wall motion were considered to determine whether incorporating the timing of LV contraction into the analysis improved the detection of ischemia. Four-dimensional fractional shortening (4DFS), analogous to 3DFS, was measured by comparing the end-diastolic position of the endocardium to the location of peak inward excursion achieved by each point on the endocardium:

$$4DFS = (\lambda_{ED} - \lambda_{MIN}) / \lambda_{ED} \quad (2)$$

The rate of change of the coordinate λ was also studied because it has been found that ischemic myocardium exhibits rapid early systolic stretching in contrast with gradual shortening found in normal tissue [9] and finite element modeling suggested that non-contracting myocardium should show positive $\partial\lambda/\partial t$ during isovolumic systole. Specifically, we investigated maximum systolic $\partial\lambda/\partial t$ ($\max(\partial\lambda/\partial t)_{SYS}$) in one experimental RT3D echocardiographic data set. This data set consisted of manually digitized endocardial data for one entire cardiac cycle that was fitted using a bicubic Hermite basis function in space and a cubic Lagrange polynomial in time. We shaded positive values indicating outward motion during systole dark gray and black on Hammer projection maps.

III. RESULTS

Parameter maps for a large and small simulated LCx ischemic region are shown in Figure 1. 3DFS, 3DWT, and radial strain were classified as normal and color-coded white for values greater than 0.25, hypokinetic (light gray) for values between 0.05 and 0.25, akinetic (dark gray) for values between –0.05 and 0.05, and dyskinetic (black) for values less than –0.05. Circumferential strain was classified using

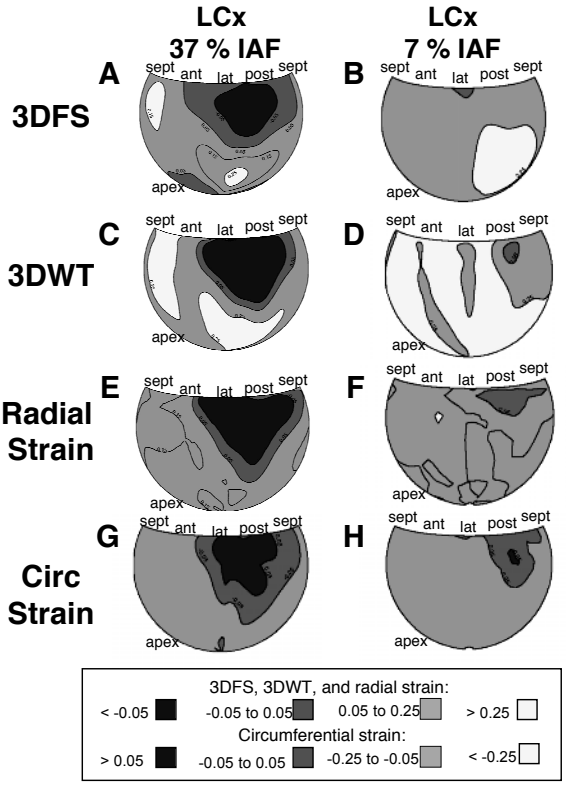

Fig. 1. Four different measures of regional LV function tested on computational simulation of regional ischemia in the LCx perfusion territory for a large (37% ischemic area fraction – left panel) and small (7% ischemic area fraction – right panel) ischemic region. Hammer map displaying three-dimensional fractional shortening (3DFS) in the finite element model with a large and small simulated occlusion of the LCx coronary artery (**A** and **B,** respectively). Three-dimensional wall thickening (**C, D**), radial strain (**E, F**), and circumferential strain (**G, H**) are shown.

the opposite sign of the cut-off values for the categories used with the other measurements. For the large ischemic region, there was a similar pattern in maps of all four measures of regional ventricular function. For the small ischemic region, a small abnormal area remained present in the LCx perfusion bed for 3DWT, radial strain and circumferential strain, but not 3DFS.

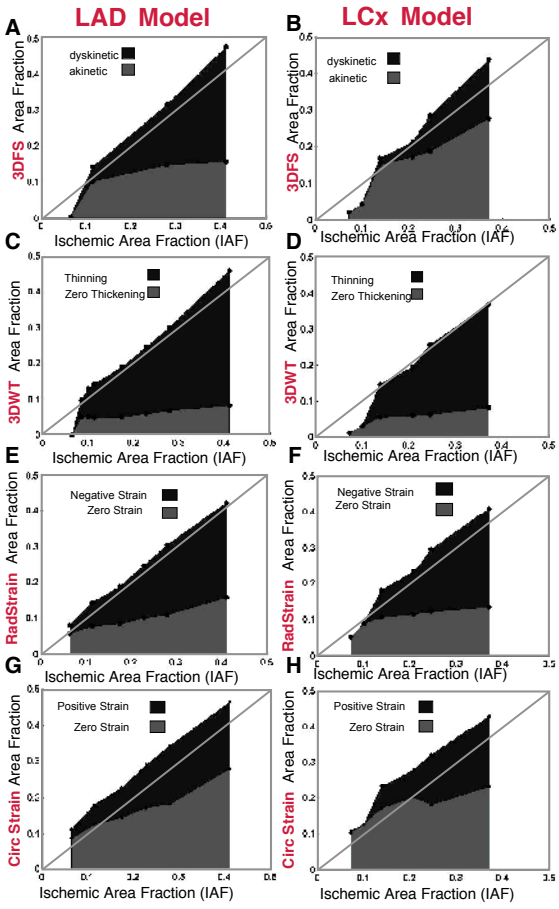

Fig. 2. Comparison of four different measures of wall motion calculated for a range of sizes of LAD (left panels) and LCx (right panels) coronary artery occlusions. The fraction of the LV endocardial surface with zero or less wall motion vs. the fraction of endocardial surface that was prescribed ischemic in the model is shown. Relationships for 3DFS (**A, B**), 3DWT (**C, D**), radial strain (**E, F**), and circumferential strain (**G, H**) are displayed here.

Relationships between the size of the ischemic region prescribed in the finite element model and the fraction of the endocardial surface that showed akinesis or dyskinesis are shown in Figure 2 for both simulated LAD and LCx occlusions. These relationships were nearly linear with a slope very close to one. These results indicated that each one of these measures was a good predictor of the ischemic region size. For 3DFS and 3DWT, there appeared to be a threshold below which a very small ischemic region did not induce a detectable wall motion abnormality. This threshold is likely present because the ischemic myocardium is tethered to healthy normal tissue. Such thresholds appear to be smaller or absent for radial and circumferential strain.

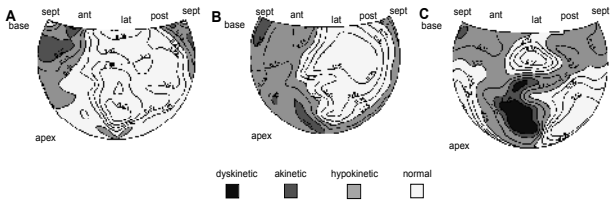

Fig. 3. Maps of 3DFS measurements from RT3D echocardiograms of a single open-chest anesthetized canine. Baseline echocardiographic data shows normal 3DFS throughout most of the LV and some hypokinesis and akinesis in the basal-septum (**A**). Echocardiographic data during proximal LAD occlusion shows hypokinesis and akinesis in the septum and lateral walls from the base to the apex (**B**). Data acquired during LCx occlusion shows dyskinesis in the lateral wall from the mid-ventricle level to the apex (**C**).

The 3DFS analysis results from the canine experimental data are shown in Figure 3. 3DFS successfully identified regions of abnormal wall motion corresponding to the occlusion sites.

Three- and four-dimensional analyses of echocardiograms acquired during mid LCx occlusion of the canine experiment are shown in Figure 4. Figure 4A shows data adapted from Reference [9] demonstrating that normal myocardium shortens during systole, but ischemic myocardium exhibits rapid longitudinal stretching during early systole. A graph of λ versus time for the same location in the LV in the dog at baseline and during ischemia is shown in Figure 4B. There was inward motion during systole at baseline, shown by an initial negative slope, and outward motion during systole in the presence of ischemia, shown by an initial positive slope. The 3DFS map showed dyskinesis in the lateral wall from the mid ventricle to the apex of the LV (Figure 4C). This map also showed hypokinesis and akinesis in the septum close to the base in a region where there was no ischemia. The map of

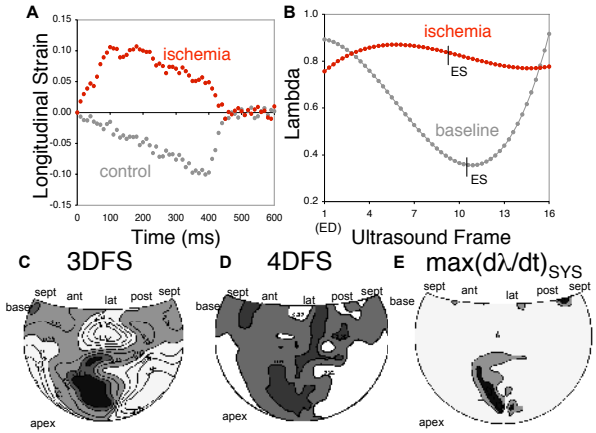

Fig. 4. Three-dimensional and four-dimensional wall motion analysis of echocardiographic data acquired during mid LCx occlusion of a canine. Villarreal et al. [9] showed longitudinal stretching during early systole in the ischemic region and longitudinal shortening in the normal myocardium (**A**). The coordinate λ is plotted versus the ultrasound frame number at the same location on the ventricle of the dog at baseline and during LCx occlusion (**B**). 3DFS analysis highlights the ischemic region in the lateral wall and some non-ischemic myocardium in the basal-septum (**C**). The 4DFS map shows a very similar pattern of wall motion as 3DFS (**D**). $\max(\partial\lambda/\partial t)_{SYS}$ identifies only the ischemic region as abnormal (**E**).

4DFS showed a very similar pattern to the 3DFS result. The map of maximum systolic $\partial\lambda/\partial t$ showed outward motion during systole ($\max(\partial\lambda/\partial t)_{SYS} > 0$) in the lateral wall between the mid ventricle and the apex. This abnormal motion, highlighted in dark gray and black, aligned well with the ischemic region.

IV. CONCLUSIONS

We present here a model-based approach to screening candidate wall motion measures for specific clinical applications. Results from the modeling studies indicate that 3DFS, 3DWT, radial and circumferential strain are good predictors of the ischemic region size. It is possible that radial and circumferential strain may perform better at detecting very small ischemic regions. To confirm this, further studies need to be performed to simulate ischemic regions covering less than 6% of the left ventricle.

We demonstrate that 3DFS successfully identifies ischemic regions in experimental RT3D echocardiograms. Initial results of four-dimensional analysis of wall motion suggest that incorporating the timing of contraction into the analysis may provide a more specific identification of ischemic regions. One such measure, $\max(\partial\lambda/\partial t)_{SYS}$, shows great promise in identifying ischemic myocardium based on initial outward motion during isovolumic contraction. Four-dimensional indices of wall motion have the potential to improve the detection of ischemia over 3D measures such as regional wall thinning and systolic bulging. For example, an ischemic region that shows a different temporal pattern of contraction may not be fully characterized by a 3D analysis that considers only two time frames; in this case, a 4D analysis of the entire cardiac cycle may provide more useful information.

The wall motion analysis techniques presented here can be applied to any set of 3D or 4D cardiac images including RT3D echocardiography and magnetic resonance imaging (MRI). Measures of wall motion such as 3DFS and $\max(\partial\lambda/\partial t)_{SYS}$ are well suited for analysis of RT3D echocardiograms because these measures only require that the position of the endocardium be visible throughout the cardiac cycle. In order to analyze 3DWT, visualization of the endocardial and epicardial border is required. MRI tagging may be more appropriate for analysis of radial and circumferential strain.

Parameterizing the LV in prolate spheroidal coordinates facilitates quantification of LV wall motion. Our wall motion maps provide a simple and clear display of abnormalities. This quantitative analysis technique fully utilizes the three-dimensional information available in the images providing a more objective and rapid approach to evaluating regional left ventricular function. The methods are versatile and can be applied to several types of imaging modalities that yield four-dimensional (3D + time) data sets.

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REFERENCES

[1] C. Beeder, Y. Charuzi, I. K. Loh, H. Staniloff, and H. J. Swan, "Relationship between segmental abnormalities and global left ventricular function in coronary artery disease: validation of a theoretical model," *Am Heart J*, vol. 102, pp. 330-4, 1981.

[2] M. S. Dolan, K. Riad, A. El-Shafei, S. Puri, K. Tamirisa, M. Bierig, J. St Vrain, L. McKinney, E. Havens, K. Habermehl, L. Pyatt, M. Kern, and A. J. Labovitz, "Effect of intravenous contrast for left ventricular opacification and border definition on sensitivity and specificity of dobutamine stress echocardiography compared with coronary angiography in technically difficult patients," *Am Heart J*, vol. 142, pp. 908-15, 2001.

[3] S. L. Herz, C. M. Ingrassia, S. Homma, K. D. Costa, and J. W. Holmes, "Parameterization of left ventricular wall motion for detection of regional ischemia," *Ann Biomed Eng*, vol. 33, pp. 912-9, 2005.

[4] A. D. McCulloch, "Continuity 6. <http://www.continuity.ucsd.edu>," 2006.

[5] R. Mazhari, J. H. Omens, J. W. Covell, and A. D. McCulloch, "Structural basis of regional dysfunction in acutely ischemic myocardium," *Cardiovasc Res*, vol. 47, pp. 284-93, 2000.

[6] H. Azhari, S. Sideman, J. L. Weiss, E. P. Shapiro, M. L. Weisfeldt, W. L. Graves, W. J. Rogers, and R. Beyar, "Three-dimensional mapping of acute ischemic regions using MRI: wall thickening versus motion analysis," *Am J Physiol*, vol. 259, pp. H1492-503, 1990.

[7] P. Croisille, C. C. Moore, R. M. Judd, J. A. Lima, M. Arai, E. R. McVeigh, L. C. Becker, and E. A. Zerhouni, "Differentiation of viable and nonviable myocardium by the use of three-dimensional tagged MRI in 2-day-old reperfused canine infarcts," *Circulation*, vol. 99, pp. 284-91, 1999.

[8] J. W. Holmes, J. A. Nunez, and J. W. Covell, "Functional implications of myocardial scar structure," *Am J Physiol*, vol. 272, pp. H2123-30, 1997.

[9] F. J. Villarreal, W. Y. Lew, L. K. Waldman, and J. W. Covell, "Transmural myocardial deformation in the ischemic canine left ventricle," *Circ Res*, vol. 68, pp. 368-81, 1991.