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Executive Summary

Project Category: Research

Project Title: Manual Realignment of Short Axis 2DE Images Provides Stable Reference Point for Wall Motion Analysis

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Introduction

Two-dimensional echocardiography (2DE) is widely used for detecting wall motion abnormalities (WMAs) during cardiac stress testing. Diagnosis from these images relies on qualitative interpretation by a cardiologist, which leads to large inter-observer variability. Quantitative measures of wall motion should provide a more objective, consistent basis for diagnosis, but have been limited by an inability to define a coordinate system for analysis robust to both translation of

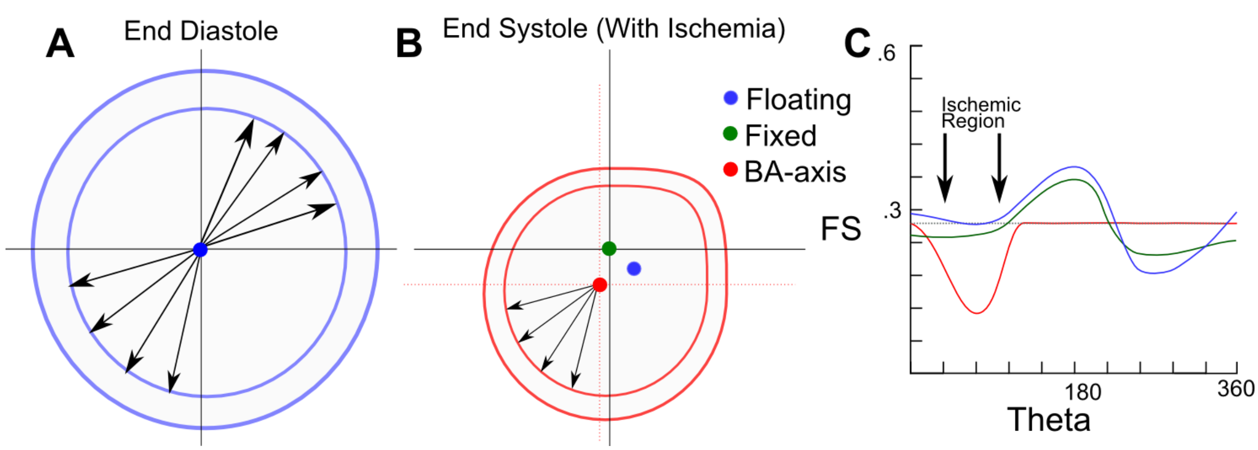

Fig 1 The short axis of the LV at end diastole (a) and end systole (b) when a WMA is present. The floating centroid is the center of mass (COM) of the short axis view and is calculated at ED and ES. The COM shifts causing overestimation of FS in the AWM region (b,c). The fixed centroid is the center of mass calculated at ED and is assumed to stay in the same place from ED to ES, resulting in issues when the heart translates during contraction (b,c). The BA-axis point is defined by distant user-defined landmarks at both end diastole and end systole.

the heart and the presence of WMAs. Recently, using three-dimensional (3D) echocardiography, our lab developed a quantitative measure of wall motion that relies on user-defined landmarks remote from potential WMAs and successfully identifies ischemic regions. We hypothesize that manually realigning 2DE images can provide most of the benefit of this 3D analysis using more widely available 2D images. The goal of this study was to determine how potential errors in manual alignment will affect subsequent quantitative wall motion analysis. This information was used to develop a program that allowed a physician to realign 2DE images in three-dimensions. Our method was found to be the best quantitative method for detecting WMAs from standard 2DE images.

Project Motivation

Two-dimensional echocardiography is used for detecting WMAs during cardiac stress testing. WMAs indicate a region of underlying ischemia. Ischemia occurs when a tissue does not get enough oxygen, due to inadequate blood flow. When this occurs in the heart, the cells do not function properly, and worsen its ability to pump blood to the body. During cardiac stress testing, a patient must exercise or be infused with a drug that increases contractility and heart rate. During these tests, cells in the heart have an increased demand for oxygen, and more blood flows to those cells. If a patient has a clot or blockage in a coronary artery, not enough oxygen can get to the tissue, and the pump function of these cells is reduced.

Ultrasound is used to record the motion of the heart during stress testing. The method of diagnosis has long required physicians to look at the images of the heart and subjectively determine whether there WMAs are present. This method has a high rate of interobserver variability and provides no measure of severity of the WMA.

Quantitative methods have been developed to address the issue of diagnosing regional ischemia through WMAs, however, they have struggled to gain widespread acceptance due to high error rates, or high cost of the ultrasound technology. Regional endocardial shortening and myocardial

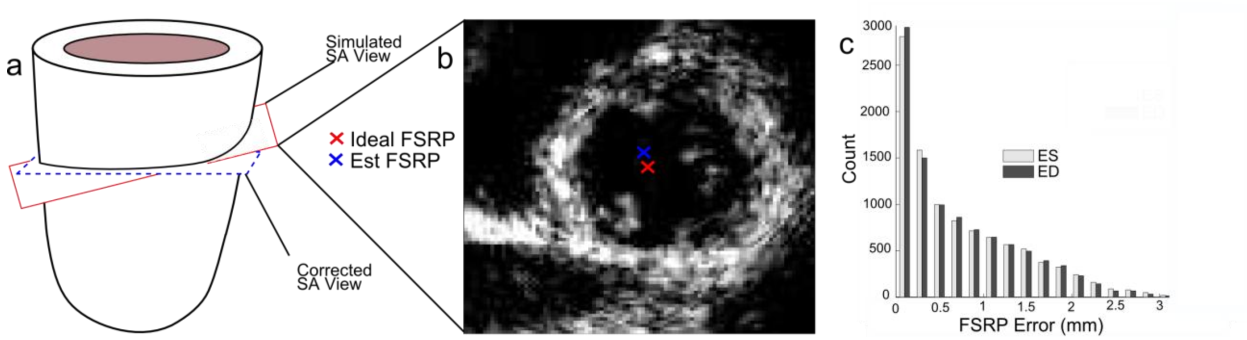

Fig 2 (a) A translation (tilt, rotation and base-apex shift) was applied to produce a view that simulated error in transducer position (red). The obtained view was placed horizontally at the correct base-apex axis position (dotted blue). The calculated FSRP error (b) is the difference between the intersection of the base-apex axis with the red plane and the blue plane. (c) Distribution of the error in the FSRP after z-position correction of 10,000 randomly generated slices through the 3D datasets. The slices were used to simulate variations in the acquisition of an ultrasound technician. These translations included rotation about the ultrasound viewing axis (±15°), tilting of the transducer (±15°) and base-apex directional shifts (±15mm). The resulting histogram shows small FSRP errors (ED average = .73 ± .64 mm; ES average = .70 ± .63 mm).

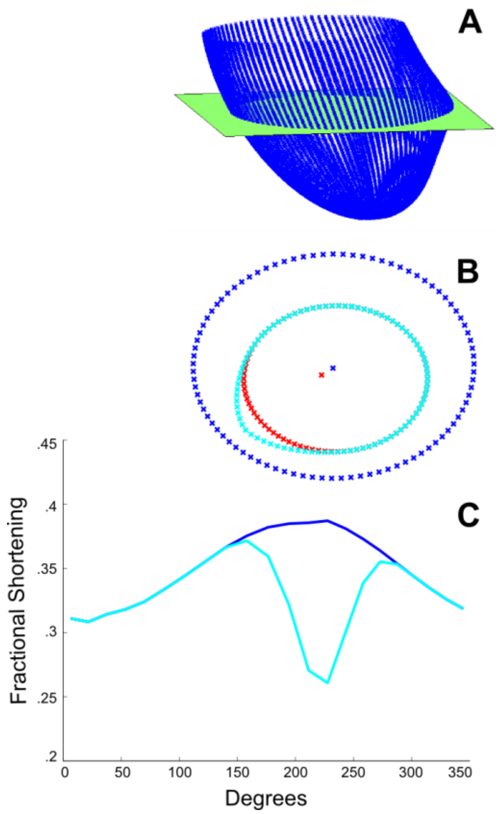

Fig 3 (a) model of left ventricle in 3D with SA slice through midwall green plane). (b) cross section of midwall slice with ED (blue), normal ES (red) and infarct ES (cyan) endocardium. Blue and red x marks represent FSRP positions. (c) output radial position in degrees vs. FS.

fractional thinning has been measured from a centroid point throughout the cardiac cycle using standard 2DE images[1-3]. Centroid methods have high error rates, because there is no way of finding a point in two dimensions that is robust to both translation and regional WMAs (Fig 1). More recently, a method called speckle tracking imaging (STI) has been successfully used[4]. However, this method is unrealistic to implement broadly because of the cost of the equipment. Three-dimensional echocardiography has also had success in finding WMAs[5,6], however, these machines are found primarily in academic facilities and the method requires a few hours of a physician's attention to complete. We have developed a method that allows a user to realign 2DE images in three dimensions; this provides the advantages of having a three-dimensional coordinate system while requiring only a 2DE machine. This is a method that can be employed by any physician who has access to a computer and a standard 2DE device.

Approach

Realignment Program: A method for analyzing realigned 2DE images was developed, which requires the selection of two mitral leaflet hinge points and one apex point on each of the three standard long axis views (four-chamber, three-chamber, and two-chamber) at end systole (ES) and end diastole (ED). When these views are aligned in 3D, an axis that intersects the center of the mitral valve ellipse (called the base) and the apex can be defined. The intersection of this axis with a standard short axis (SA) view is the fractional shortening reference point (FSRP), and changes in distances from this point to the endocardial surface are used to quantify wall motion. In order to determine the error in the FSRP due to errors in short-axis realignment, 1,000 SA views were extracted from each of 10 clinical 3D echocardiography datasets at locations and orientations simulating expected variations in the tilt, rotation and base-apex axis position of the transducer during 2DE image acquisition (Fig 2a). The intersection of the base-apex axis with each simulated SA view represented the ideal FSRP for that view. Each SA view was then corrected for position along the base-apex axis, but not tilt or rotation (Fig 2a). The intersection of the base-apex axis with this corrected plane represented an estimate of the FSRP. The error in FSRP was calculated as the distance between the ideal and estimated FSRPs at both ED and ES (Fig 2b).

Cardiologist Realignment: A cardiologist performed three realignments on each of the ten clinical datasets. The user was allowed to fully correct the long axis views, but was limited to correcting only the height of the short axis view. The difference between the cardiologist's FSRP and the ideal FSRP is the measure of error. The amount of time the cardiologist took to realign the images was also recorded.

Model Effect of FSRP Error on WMA Detection: To determine the effect of the FSRP error on the ability to detect WMAs, a model of the left ventricle was developed[6]. The left ventricle was modeled as an open ellipsoid (Fig 3). The model inputs included the base-apex distance, short-axis diameter and FSRP error to create a dataset-specific model. The prescribed ischemic region was 50% of the circumference and 50% of the height of the modeled LV. The severity or extent of WMAs was varied to simulate a range of loss of function. The WMA was modeled as a cosine function circumferentially. The scale of the cosine function varied based on vertical distance from the center of the WMA. Sensitivity and specificity measures were made for the FSRP method, as well as the fixed and floating centroid methods.

Results and Analysis

Tilt and Rotation and FSRP Error: The results indicate that the tilt and rotation of the short axis slices have little influence on the error in the FSRP (Fig 2c). The mean error in the FSRP was found to be small for both ED (.73 ± .64 mm) and ES (.70 ± .63 mm). The reason for the small effect is slightly different for tilt and rotation. The small errors indicate that a user does not need to correct for tilt and rotation when realigning the images.

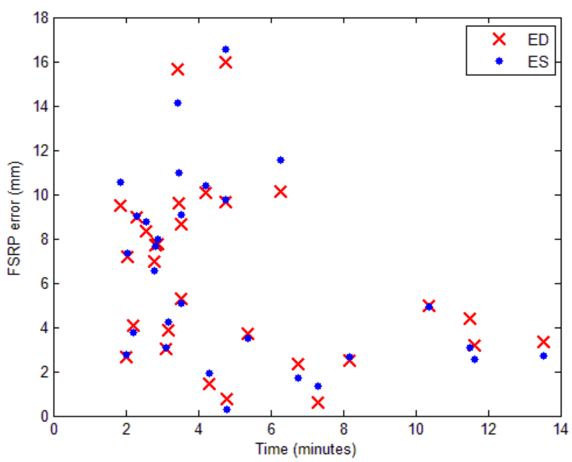

Fig 4 Shows FSRP error as a function of the amount of time it takes the cardiologist to realign the images. The FSRP error appears to be smaller when the user takes longer to realign the images.

Cardiologist FSRP Realignment Error: The average FSRP error for all trials is 6.38 ± 3.95 mm for the ED FSRP and 6.43 ± 4.12 mm for the ES FSRP (Fig 4). The error is closely related to the amount of time the cardiologist spends realigning the images. The average FSRP error for trials where the cardiologist spends more than seven minutes is 3.17± 1.53 mm and 2.88 ± 1.61 mm for the ED and ES FSRPs, respectively. The error and standard deviation are much larger, however, when the cardiologist took less than seven minutes.

Model Effect of FSRP Error on WMA Detection: The average FSRP error is ~21% of the diameter at systole, however, we hypothesized that the difference between the ES and ED error vectors matters more than the ES and ED errors independently. Areas under the curve from a ROC analysis are .96, .95 and .93 for FSRP, fixed and floating methods, respectively (Fig 5). The differences in specificities at 95% sensitivity differ greatly, with 80%, 69% and 45% for FSRP, fixed and floating methods, respectively. These results indicate that the base-apex axis method performs better than the fixed and floating centroid methods, even when there are large errors in ED and ES FSRPs.

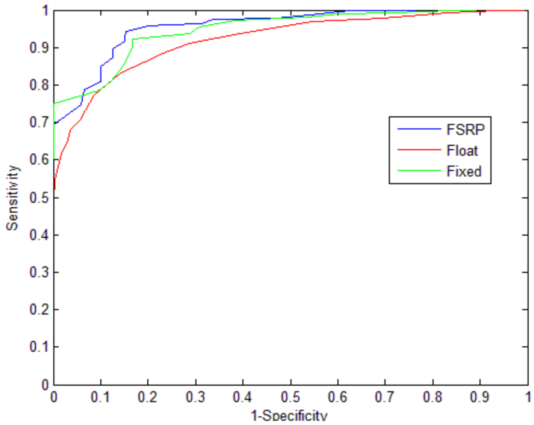

Fig 5 Shows a ROC curve for the three 2DE methods. The FSRP method has an 80% specificity at 95% sensitivity. Fixed and floating methods have a 69% and 45% specificity at 95% sensitivity.

Conclusions

Based on the findings, limiting a user to only base-apex adjustments provides for a good estimate of the FSRP while also streamlining the realignment process. The ability of a user to realign an image is dependent upon the amount of time he/she spends. Despite large FSRP errors, the model indicates that our novel FSRP method outperforms other methods used for quantitative identification of WMAs from 2DE images.

Before broad implementation, further testing should be done to see how the program performs with WMAs of different circumferences. Additionally, the method is only employed on the short axis of the LV. Because of this, the likeliness of a WMA showing up on the short axis must be found. A commercial version of this program could be implemented in any hospital that has a 2DE machine. Additionally, the program could be used by ultrasound technicians or nurses. If diagnosis of WMAs required only a 2DE machine and a nurse, cardiac stress testing could become available to a much greater portion of the population. Early diagnosis of diseases like coronary artery disease and life-threatening coronary artery blockages could be found before it is too late.

List of References

1. Force, T. *et al.* Overestimation of infarct size by quantitative two-dimensional echocardiography: the role of tethering and of analytic procedures. *Circulation* **73,** 1360–1368 (1986).
2. Wiske, P. S., Pearlman, J. D., Hogan, R. D., Franklin, T. D. & Weyman, A. E. Echocardiographic definition of the left ventricular centroid. II. Determination of the optimal centroid during systole in normal and infarcted hearts. *J. Am. Coll. Cardiol.* **16,** 993–999 (1990).
3. Zoghbi, W. A. *et al.* Quantitative assessment of left ventricular wall motion by two-dimensional echocardiography: validation during reversible ischemia in the conscious dog. *J. Am. Coll. Cardiol.* **11,** 851–860 (1988).
4. Amundsen, B. H. *et al.* Noninvasive myocardial strain measurement by speckle tracking echocardiography: validation against sonomicrometry and tagged magnetic resonance imaging. *J. Am. Coll. Cardiol.* **47,** 789–793 (2006).
5. Herz, S. L., Ingrassia, C. M., Homma, S., Costa, K. D. & Holmes, J. W. Parameterization of left ventricular wall motion for detection of regional ischemia. *Ann. Biomed. Eng.* **33,** 912–919 (2005).
6. Herz, S. L. *et al.* Quantitative three-dimensional wall motion analysis predicts ischemic region size and location. *Ann. Biomed. Eng.* **38,** 1367–1376 (2010).

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