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Accuracy of a Mitral Valve Segmentation Method Using J-Splines for Real-Time 3D Echocardiography Data

Andrew W. Siefert, MS¹, David A. Icenogle, MS¹, Jean-Pierre Rabbah, BS¹, Neelakantan Saikrishnan, PhD¹, Jarek Rossignac, PhD², Stamatios Lerakis, MD^{1,3}, and Ajit P. Yoganathan, PhD¹

¹Wallace H. Coulter Department of Biomedical Engineering, Georgia Institute of Technology and Emory University, Atlanta, GA

²College of Computing, Georgia Institute of Technology, Atlanta, GA

³Division of Cardiology, Emory University School of Medicine, Atlanta, GA

Abstract

Patient-specific models of the heart's mitral valve (MV) exhibit potential for surgical planning. While advances in 3D echocardiography (3DE) have provided adequate resolution to extract MV leaflet geometry, no study has quantitatively assessed the accuracy of their modeled leaflets versus a ground-truth standard for temporal frames beyond systolic closure or for differing valvular dysfunctions. The accuracy of a 3DE-based segmentation methodology based on J-splines was assessed for porcine MVs with known 4D leaflet coordinates within a pulsatile simulator during closure, peak closure, and opening for a control, prolapsed, and billowing MV model. For all time points, the mean distance error between the segmented models and ground-truth data were 0.40 ± 0.32 mm, 0.52 ± 0.51 mm, and 0.74 ± 0.69 mm for the control, flail, and billowing models. For all models and temporal frames, 95% of the distance errors were below 1.64 mm. When applied to a patient data set, segmentation was able to confirm a regurgitant orifice and post-operative improvements in coaptation. This study provides an experimental platform for assessing the accuracy of an MV segmentation methodology at phases beyond systolic closure and for differing MV dysfunctions. Results demonstrate the accuracy of a MV segmentation methodology for the development of future surgical planning tools.

Key Terms

Surgical Planning; Computational Methods; In Vitro Simulation; Heart Valve; Medical Imaging; Mitral Regurgitation

Introduction

Mitral valve disease is the most common heart valve ailment within the US population.²⁹ Dysfunctions occurring from this disease can be functionally classified with clinical and surgeon specific factors influencing the decision to repair or replace the mitral valve (MV).^{3,4} The ability to classify MV dysfunctions and pre-operatively assess potential repair techniques has been improved by real-time 3D echocardiography (rt-3DE) whose data sets provide full-volume temporal information for patient MV function.^{30,31,34,35} These

information rich data sets provide ample opportunity for both qualitative and quantitative analyses whose use and clinical potential are under active exploration.^{7,8}

In recent years, a growing number of studies have aimed to create patient-specific MV surgical planning models based on rt-3DE data sets.^{1,2,6,15,35} In theory, these models may inform which surgical technique may be best for a given patient's MV dysfunction.²² When combined with finite element methods, these models can provide information regarding the stress state in the MV. Identified stress concentrations can contribute to the design of MV repairs that avoid excessive loading of the leaflet tissue, mitral annulus, and surgical sutures.^{1,12,22,28} These insights may not only improve MV surgery but additionally individualize repairs by providing mechanistic insights for improving surgical procedures.⁵ Before reaching these eventual goals, many challenges remain for these computational models.

A significant challenge for these models is not only recreating the complex geometry of the MV but accurately segmenting it from the rt-3DE.² The reconstruction of the MV's leaflet geometry has relied on both automated and manual approaches with acceptable inter- and intra-user variability.^{1,15} Beyond user variability, evaluating the accuracy of these segmented models is an important first-step to not only validating the segmentation methodology but providing higher confidence in subsequent simulations of surgical repair and finite element analyses.

To this end, the aim of this study is to assess the accuracy of a newly developed rt-3DE-based segmentation methodology against excised porcine MVs with known 4D leaflet coordinates within a pulsatile left heart simulator and to create a platform for which similar tools can be tested. The segmentation methodology is based on user controlled J-splines and butterfly mesh interpolation. The accuracy of the segmentation method is assessed during MV closure, systolic closure, and opening for three leaflet geometries including a control, anterior leaflet flail, and anterior leaflet billowing model. To assess the ability of the segmentation methodology to analyze a patient rt-3DE data set, a patient MV was segmented both pre- and post-intervention at systolic closure. Multiple leaflet measurements are assessed at both time points demonstrating the unique capabilities of the developed segmentation methodology.

Methods

Segmentation Methodology

A segmentation tool for rt-3DE based upon user-controlled J_0 -splines was developed and implemented in Matlab (The Mathworks, Inc, Natick, MA). This tool can segment any 4D Cartesian data set by scaling the data to 0.5 mm voxels and orienting the segmentation planes across the MV in the septal-lateral direction (Figure 1). The MV annulus and leaflets were segmented in 1.5 mm slices from commissure-to-commissure. In each segmentation slice, the annulus was selected first, followed by the anterior and posterior leaflets. The use of J_0 -splines to connect the user-defined points significantly aided segmentation by providing local fitting to match the leaflet curvature. These steps were repeated for each slice and temporal frame in the data set.

To create a triangular mesh between each slice without extreme features, each segmented leaflet curve was sampled to have equally spaced points while keeping the original endpoints at the annulus and leaflet free edge. The number of points was determined by dividing by curve length by the slice spacing and rounding to the nearest whole number. Based on these conditions, the number of equally spaced points on each leaflet ranged from

4 to 15. After this was completed for each leaflet curve, an ordered triangular mesh was generated between each slice.

To reduce the segmentation time and to smooth the appearance of the virtual leaflets, butterfly mesh refinement was employed.⁹ Butterfly mesh refinement interpolates new points in the mesh based upon a weighted average of the three-dimensional positions of surrounding points (Figure 2). In this method, a new point (denoted as the letter 'P' in Figure 2) is placed at a weighted position on each side of the original triangular elements. To generate new points near the boundaries, neighboring points are mirrored over the annular circumference. Using this method, butterfly mesh refinement smoothly interpolates new points in the triangular mesh while maintaining the position of the original user-defined vertices. This reduces segmentation time and ensures the user-selected segmentation is not modified during mesh interpolation. Using these methods, average segmentation time was approximately 15–20 minutes per time point.

In addition to capturing the annular and leaflet geometry, the segmentation tool also allowed for separate segmentation of coaptation and regurgitant zones. Following manual segmentation, the J_0 -splines on each slice were sampled using constant length spacing while maintaining the original endpoints. Upon curve sampling, the data were triangulated and the resulting mesh was used to calculate annular area, annular dimensions, regurgitant orifice areas, tenting height, tenting area, coaptation area, and coaptation length as a function of intercommissural distance.

In Vitro Mitral Valve Simulator

In vitro simulation was conducted in the extensively studied Georgia Tech left heart simulator (GTLHS) (Figure 3).^{14,19,20,24–27,33} This closed-loop simulator allows for precise control of annular and subvalvular MV geometry at physiological left heart hemodynamics. Excised porcine MVs are sutured to a flat static annulus (orifice area of 12.2 cm²) and the PMs are sutured to two mechanically adjustable control rods capable moving them independently in the apical, lateral, and posterior directions. Transmitral flow was measured upstream of the atrium using an electromagnetic probe (Carolina Medical Electronics, FM501D, East Bend, NC). Transmitral pressure was monitored with static pressure transducers mounted in the atrium and ventricle (Validyne DC-40, Northridge, CA). The simulator's primary chamber is constructed from transparent acrylic allowing for excellent visual and echocardiographic access to the mounted MV.

Dual Camera Stereo-Photogrammetry

Dual camera stereo-photogrammetry has been successfully used in previous studies to measure MV leaflet motion and strains *in vitro*.^{14,16,19} This method was used within the present study to dynamically determine the 4D coordinates of the mitral leaflets through the entire cardiac cycle. In this method, tissue dye (Thermo Scientific, Waltham, MA) was used to mark the atrial surface of the anterior and posterior leaflet with a 1.5 mm × 1.5 mm square array. Each of the dye markers on each leaflet were approximately 0.5 mm in diameter. Two synchronized high-speed cameras (Basler 510K; Basler Corp, Exton, PA) with Nikon macro lenses (105mm, f2.8; Nikon, Melville, NY) were used to image the marker array throughout the cardiac cycle at 250 Hz.

Prior to each experiment, a previously established calibration method was used to calculate the 4D position of the leaflet markers using direct linear transformation (DLT).²³ In this method, a 10 mm steel cube was positioned within the volume occupied by the MV leaflets such that each high-speed camera could image 7 of the cube's corners. These calibration images were digitized within a custom MATLAB program. Using the cube calibration

images and those recorded during each experiment, DLT was used to calculate the 4D coordinates of each marker.^{14,19} Based on the magnification of the high-speed cameras, pixel size, and calibration cube, the 3D leaflet marker coordinates can be determined to an accuracy of 68 μm . This accuracy is in good agreement with previous investigations using these methods.^{14,16,19}

In-Vitro Protocol

Fresh porcine hearts were obtained from a local abattoir (Holifield Farms, Covington, GA) and MVs were excised preserving their annular and subvalvular anatomy. Selected MVs (N=2) were sutured to the simulator's annulus using a Ford interlocking stitch. During valve suturing, care was taken to place each suture just above the valve's natural hinge and not directly through the leaflet tissue. Additionally, normal annular-leaflet geometric relationships were respected - anterior leaflet occupying 1/3rd of annular circumference and commissures aligned in the 2 and 10 o'clock positions.

After annular suturing, each PM was attached to the PM control rods. Each PM was carefully positioned and fine-tuned to establish the control MV geometry as previously described.²⁰ Transmitral human pulsatile conditions were simulated (Cardiac Output 4.9 L/min, 70 beats/min, 120 mmHg transmitral pressure). After establishing the control valve geometry, 3D echocardiography and dual camera high-speed images of the MV were acquired. A Philips iE33 (Philips Medical Systems, Andover, MA) echocardiography system with an X7-2 matrix array transducer was used for this study. This probe exhibits the same operating characteristics and image capabilities as the transesophageal x7-2t probe. Triggered 3D full-volume images were acquired at depths of 10–14 cm. After acquisition, the highest quality DICOM images were imported into Matlab using a proprietary algorithm (Philips Medical Systems) and transformed into a 4D Cartesian data set for segmentation.

Due to limitations in the simulator's design (echocardiography probe obstructed the viewing plane of the high-speed cameras), echocardiography and high-speed camera images were acquired at separate cardiac cycles. During each acquisition, transmitral hemodynamics was carefully maintained to ensure intra-cycle repeatability. Because the echocardiography and high-speed systems operate at differing sampling frequencies, the image corresponding to systolic closure was defined as the middle frame between initial valve closure and initial valve opening. The MV closing and opening phases were similarly defined as midpoints between the valve's full open state and initial valve closure and initial valve opening.

Using the described protocol, three different valve models were simulated: control, billowing anterior leaflet, and flail anterior leaflet. Valve 1 simulated the normal and flail MV models while valve 2 simulated a billowing anterior leaflet. The billowing anterior leaflet condition was created by extending both anterior strut chordae with sutures, while the flail anterior leaflet condition was created by transecting both sets of anterior strut and marginal chordae. 2D echocardiographic images of these models are shown in Figure 4.

Assessing the Accuracy of the Segmented Models

High-speed camera images were time matched with the acquired rt-3DE images using the peak systolic frame from each data set. A 3D correction scheme was applied to the *in vitro* segmented data sets to account for refraction and acoustic speed differences in the experimental setup. Spatial registration of the segmented leaflets and 3D leaflet marker coordinates was performed using the best-fit alignment sub-routine within the Geomagic Studio 12 software package (Geomagic USA, Morrisville, NC). Using this function, the segmented leaflet surface was automatically translated and rotated in three-dimensional

space to minimize the square distances between the virtual model surface and the 3D leaflet marker points

To quantify the match between the virtual model and reconstructed markers, a custom MATLAB script (MathWorks, Natick, MA) was implemented to determine the distance error between each marker and the segmented leaflets. For each marker, the closest vertex in the virtual model was determined. The 6 triangular surface elements surrounding the vertex were then analyzed for which triangular element exhibited the shortest distance to the reconstructed marker. The minimum perpendicular distance from the identified triangular surface element to the reconstructed marker was then calculated. This distance error was calculated for each of the fiducial leaflet markers that were visible to the high-speed cameras during MV closing, systolic closure, and opening. Error distances for each valve and phase are reported as a mean $\pm$ 1 standard deviation. The frequency of errors was additionally determined with the relative distribution and 95th percentile error calculated for each MV model and phase. All of the errors for each valve and time point were grouped together into a single data set for the overall 95% error to be calculated.

Clinical Demonstration of Segmentation Methodology

After *in vitro* assessment, the tool was applied to a clinical case to test the capability of the tool to segment a patient rt-3DE data set. Transesophageal rt-3DE data sets were collected from patients at Emory University Hospital (Atlanta, GA). Institutional Review Board approval to review de-identified images was obtained for this study. A 76 year old female with severe functional mitral regurgitation (MR) was imaged using a Philips iE33 ultrasound machine and an X7-2t probe before and after MV repair. Full-volume and color Doppler images were acquired. Using the described segmentation methodology, the patient MV was segmented both pre- and post-intervention at systolic closure.

Results

Echocardiography Segmentation vs. 3D Leaflet Coordinates: Normal Model

The accuracy of the segmentation methodology for a simulated normal MV geometry was assessed at three time points: closing, peak systolic closure, and opening. Among these temporal phases, the average distance error between the echocardiography segmentations and ground-truth marker data sets was 0.40 ± 0.32 mm. The distance errors for each time point of the normal MV model are presented in table 1. Between the segmented models and marker data, good qualitative agreement can be observed (Figure 5). In each of the temporal phases, the distribution of distance errors were positively skewed with 95% of the absolute distance errors falling below 1.17 mm, 0.82 mm, and 1.04 mm for the closing, peak systolic, and opening phases, respectively. Distance errors were the greatest during the opening and closing phases.

Echocardiography Segmentation vs. 3D Leaflet Coordinates: Flail Model

For the flail model, the average distance error between the echocardiography segmentation and 3D leaflet coordinates for all time points was 0.52 ± 0.51 mm. The errors for each time point are presented in table 1. Similar to the normal MV model, good qualitative agreement can be observed between the segmented and ground-truth data set with the distribution of distance errors exhibiting a rightward skew (Figure 6). When assessing the peak distance errors for each cyclic phase, 95% of the absolute distances errors fell below 1.87 mm (closing phase), 1.1 mm (peak closure), and 1.33 mm (opening phase).

Echocardiography Segmentation vs. 3D Leaflet Coordinates: Billowing Model

In comparison to the normal and flail MV models, the average distance error between the echocardiography segmentation and ground-truth marker data for the billowed model was the largest (0.74 ± 0.69 mm). The average distance error between the segmentation and 3D leaflet coordinates were larger for each time point in comparison to the control valve (table 1). Similar to the control valve, the distribution of absolute distances between the echocardiography segmentation and the marker data were positively skewed but less than the normal valve comparisons. Of the distance errors, 95% fell below 2.12 mm (closing phase), 1.27 mm (peak closure), and 2.61 mm (opening phase) respectively. Each of which exceed the peak values observed in the control and flail MV models.

Clinical Application

The patient dataset segmented using the developed methodology showed a dilated mitral annulus pre-operatively (systolic area = 8.5 cm^2) exhibiting a septal-lateral and commissure-to-commissure distance of 2.85 cm and 3.75 cm, respectively. The resulting coaptation was poor, with a maximum coaptation length of 3.6 mm and coaptation area of 40 mm^2 (Figure 7). The largest leaflet tethering was observed near the A2-P2 diameter with a tenting height of 9 mm and tenting area of 2.08 cm^2 . The severe tethering disposed the leaflets to a centrally located MR jet that was verified by a segmented regurgitant orifice area of 4.2 mm^2 .

At surgery, the patient received a size 28 Medtronic CG Future annuloplasty ring. Mitral annulus reconstruction improved the maximum coaptation length to greater than 6 mm and a total coaptation area of 106 mm^2 . A direct comparison of coaptation length as a function of valvular position is presented in Figure 7. While improvements in coaptation were achieved, residual mitral regurgitation (grade 1+) was observed near the A3-P3 diameter. Compared to pre-operative measures, A3-P3 tenting height (6.1 mm preoperative vs. 7.6 mm postoperative) and area (0.94 cm^2 preoperative vs. 1.23 cm^2 postoperative) were worsened with annuloplasty.

Discussion

3D echocardiography can provide information rich data sets with several advantages over 2D acquisitions. Rt-3DE data sets have been suggested to better correlate with intra-operative findings during MV repair and do not suffer from 2D alignment errors.^{10,11,13,21} These advantages have provided a platform for the development of virtual MV models ultimately aimed to assist in surgical planning and improve MV surgery. While many challenges remain for reaching these goals, assessing the accuracy of these rt-3DE-based virtual models against ground-truth data sets is an obstacle that can be currently overcome. In spite of the much-improved data provided by rt-3DE, the lack of validated methodologies of segmenting and displaying these data has dampened enthusiasm for their use in routine clinical practice.

Assessing the accuracy of echocardiography segmentation models is a critical step in the development of virtual surgical planning models. In 2004, Bashein and colleagues assessed a novel 2D echocardiography segmentation method against laser scanned casts of 10 healthy porcine hearts.² The mean distance error between the segmented and cast MVs during systolic closure was 0.65 mm with 95 percentile errors approaching 1.5 mm. In the present study, the mean errors described herein were lower than the previous study (0.33 vs. 0.65 mm). Building on the previous work, this study was the first to evaluate segmentation errors beyond systolic closure. Evaluating the accuracy of opening and closing resulted in modest increases in segmentation errors (table 1).

Among the tested valve conditions, the anterior leaflet flail and billowing models resulted in the greatest mean errors when compared to simulating the normal model. These larger errors are a result of acquiring the echocardiography and high-speed camera images during different cardiac cycles. For the normal valve, coaptation geometry is relatively regular and cycle-to-cycle variations are minimal. For the flail and billowing models however, cycle-to-cycle variability in the anterior leaflet is slightly greater due to the transected chordae (flail model) and extension of anterior strut chordae using sutures (Billowing model). The resulting cycle-to-cycle variability in leaflet geometry therefore translates to larger errors in comparison to the normal MV model. Despite these challenges, the observed errors in the disease models remained relatively low and demonstrate the intra-cycle repeatability of the simulator and the accuracy of the segmentation methodology. These errors may be reduced in future evaluations by acquiring the echocardiography and high-speed images simultaneously.

Beyond repeatability, assessing the accuracy of a segmentation methodology within a pulsatile simulator possesses several unique advantages. The simulator may be used to evaluate the ability of a segmentation methodology to capture MV repair geometries or accurate representations of functional diseases.^{25,27,33} Moreover, geometries may be evaluated at time points beyond systolic closure but is currently limited to time points in which the tissue dye markers may be visualized. These measurements may be combined with several biomechanical measurements to provide additional boundary conditions for finite element analyses.^{14,19,20,22,24} To complete these analyses with more complex MV geometries (flail in Figure 6), the leaflet free edges may be smoothed to ease subsequent surface or volume meshing. Recent advances in multimodality simulators may additionally provide detailed fluid dynamic measurements required for fluid-structure interaction models.²⁶

Assessing the accuracy of segmentation methodologies is required given small perturbations in MV geometry can lead to large differences in valvular mechanics. Small changes in annular height have been shown to result in large changes in leaflet curvature and reductions in leaflet stress.^{19,32} Similar changes in leaflet geometry have been shown to shift chordal tethering profiles and papillary muscle force.^{17,20,24} Changes in the saddle height of annuloplasty rings have additionally demonstrated significant reductions in forces acting in the apical-basal direction in these devices.¹⁸

For the clinician, an accurate MV segmentation can provide a potentially more quantitative view of the leaflets and coaptation. As evaluated in the clinical case, the coaptation length can be mapped across the commissural axis. Areas of malcoaptation can be targeted for surgeon-selected repair strategies. Moreover, accurate MV segmentations can be combined with finite element methods to simulate loading of the valve under different disease and repair conditions. These data will aid in the selection of annuloplasty rings that may reduce excessive loading of the leaflet tissue, mitral annulus, and surgical sutures.^{1,12,22,28}

The demonstration of the segmentation methodology for patient use was limited to a single patient. Postsurgical analyses were unable to detect the orifice responsible for the postoperatively observed regurgitation jet (Figure 7). We hypothesize this orifice was missed due to either limitations in image resolution or the distance (1.5 mm) between segmentation slices. Future investigations will focus on evaluating the effect of segmentation slice interval on reconstructive accuracy and ability to detect small changes in valve leaflet geometry. Moreover, evaluate how the resolution of echocardiography may prohibit the ability to detect small orifice areas. Together, these will provide a strong platform for the extension of these methodologies for use in finite element and surgical planning simulations.

To estimate the errors associated with our clinical based measurements, the mean distance errors were analyzed for all three in-vitro valve models at systolic closure. During this phase, the mean distance error was 0.34 ± 0.30 mm for 726 evaluated leaflet markers. Assuming the high error bound, 0.64 mm would represent a conservative estimated error of our clinical measurements. While this is slightly greater than what may be expected with echocardiography (~0.25 to 0.5 mm), this is a systematic error. If a valve was simulated from a disease to a repair state in a surgical planning model, the error between each state would be the same and the change in the clinical metrics would be most informative. To the authors' knowledge, no decision-shifting clinical measurements require a mitral leaflet measurement with an accuracy below 1 mm. Mitral repairs aiming to restore coaptation target a range of 5–8 mm giving allowance for relative measurement error.⁵ Other measures such as coaptation depth and annular diameters are much greater than 0.64 mm, and for these reasons we believe the conservative estimated error of our clinical based measurements is acceptable.

Despite the advantages of the presented MV segmentation approach, several limitations are associated with the methods and results of this study. Assessing the accuracy between the echocardiographic segmented model and the dual-camera stereo measurements is limited to time points for which the markers on the leaflets can be imaged. This limits the ability to compute the error in coaptation length between the 4D marker data and segmented model. While clinical measures above the coaptation zone could be evaluated against those measured in the segmented model, an unsuitably large sample size would be required to account for valve-to-valve variations in the flail and billowing MV models. During rt-3DE imaging within the GTLHS, peripheral acoustic interference was observed and dampened our ability to segment the MV leaflets near the anterolateral and posteromedial commissures (Figure 5). The J-spline segmentation methodology was semi-automatic and is currently undergoing several improvements to allow for automated segmentation. Automation would potentially decrease the time required to segment each temporal frame and improve the program's potential for clinical use.

The present study provides a novel platform for assessing the accuracy of MV segmentation methodologies. It is the first MV segmentation method to have its accuracy assessed at time points other than systolic closure and for greatly differing MV leaflet geometries. The methods presented herein could have application in a variety of image segmentation problems whose methods may be extended in future studies. The presented method is capable of segmenting *in vitro* and *in vivo* MV rt-3DE data sets and can be applied to these types of data to better quantify MV geometry under normal, diseased, and repaired states. Combined, these results demonstrate the accuracy of a 3DE-based MV leaflet segmentation methodology towards the development of future surgical planning tools.

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Abbreviation, Symbols, and Terminology

MV	mitral valve
3DE	three-dimensional echocardiography
rt-3DE	real-time three-dimensional echocardiography

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FIGURE 1. Overview of the developed segmentation methodology with representative images of illustrating segmentation of the mitral leaflets.

FIGURE 2.

Schematic representation of butterfly mesh refinement where a point P is interpolated from the weighted three-dimensional positions of the surrounding points

FIGURE 3.

Left: schematic drawing the Georgia Tech left heart simulator with components identified;
 Right: Atrial view of a mitral valve mounted within the simulator which was inked with tissue dye for stereo-photogrammetry.

FIGURE 4. 2D echocardiography images of each of the mitral valve models with leaflets segmented during systolic closure and mid diastole.

FIGURE 5.

(A) Marker data (dots) are superimposed on the segmented mitral valve leaflets, (B) distance error maps between the valve segmentation and stereo-photogrammetry data, (C) frequencies of distance errors are plotted with the total number (N) of evaluated marker points

FIGURE 6.

Marker data (dots) are superimposed on the segmented mitral valve leaflets with graphical representations of the frequencies of distance errors for the flail and billowing mitral valve models.

FIGURE 7. Pre- and post-operative mitral leaflet geometries providing locations of regurgitant orifice areas.

TABLE 1

Mean $\pm$ 1 standard deviation distance errors expressed in millimeters between the echocardiography segmentations and recorded marker data for each of the mitral valve models, the total number of evaluated points to calculate the mean distance error is shown in parentheses.

		Temporal Phase During the Cardiac Cycle		
		Closing	Peak Closure	Opening
Mitral Valve Model	Normal	0.45 $\pm$ 0.37 (289)	0.33 $\pm$ 0.25 (251)	0.41 $\pm$ 0.32 (288)
	Billowing	0.85 $\pm$ 0.63 (305)	0.52 $\pm$ 0.39 (255)	0.82 $\pm$ 0.89 (311)
	Flail	0.62 $\pm$ 0.65 (266)	0.38 $\pm$ 0.40 (224)	0.56 $\pm$ 0.41 (236)