Published in final edited form as:

J Biomech. 2012 March 15; 45(5): 903–907. doi:10.1016/j.jbiomech.2011.11.033.

Semi-Automated Mitral Valve Morphometry and Computational Stress Analysis Using 3D Ultrasound

Alison M. Pouch, Chun Xu, Paul A. Yushkevich, Arminder S. Jassar, Mathieu Vergnat, Joseph H. Gorman III, Robert C. Gorman, Chandra M. Sehgal, and Benjamin M. Jackson

Abstract

In vivo human mitral valves (MV) were imaged using real-time 3D transesophageal echocardiography (rt-3DTEE), and volumetric images of the MV at mid-systole were analyzed by user-initialized segmentation and 3D deformable modeling with continuous medial representation, a compact representation of shape. The resulting MV models were loaded with physiologic pressures using finite element analysis (FEA). We present the regional leaflet stress distributions predicted in normal and diseased (regurgitant) MVs. Rt-3DTEE, semi-automated leaflet segmentation, 3D deformable modeling, and FEA modeling of the in vivo human MV is tenable and useful for evaluation of MV pathology.

Introduction

Mitral valve (MV) disease is common in humans and not infrequently fatal. Mitral regurgitation, in particular, demonstrates a strongly-graded relationship between severity and reduced survival.¹ MV surgery, both repair and replacement, are commonly exercised treatment options for mitral regurgitation. Imaging and assessment of the mitral valve has traditionally been achieved by qualitative 2D ultrasound image analysis. Recently, real-time three-dimensional transesophageal echocardiography (rt-3DTEE) has become widely available and implemented. 3D image-based modeling of the mitral valve is increasingly useful, and finite element analysis (FEA) has been applied to the MV frequently over the last 20 years.^{2,3,4,5}

To date, the majority of valve morphometry studies have employed manual tracing to reconstruct valve geometry from 3D echocardiographic image data.^{6,7,8,9,10,11} Therefore, the first objective of this paper is to introduce an alternative semi-automated approach to valve morphometry based on a simple and rapid approach to user-initialized image segmentation that exploits the contrast between the mitral valve tissue and surrounding blood pool in rt-3DTEE images. The valve is subsequently modeled using 3D continuous medial representation to obtain localized thickness maps of the mitral leaflets.

Our laboratory has recently provided a framework for the application of *in vivo* MV geometry and FEA to human MV physiology, pathophysiology, and repair.¹² Therefore, the second objective of the current study is to demonstrate that the semi-automated 3D MV model can be loaded with physiologic pressures using FEA, yielding reasonable and

© 2011 Elsevier Ltd. All rights reserved.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

meaningful stress and strain magnitudes and distributions. Furthermore, we endeavor to demonstrate this capability in both healthy and diseased human mitral valves.

Methods

Image acquisition

Intra-operative rt-3DTEE data sets were obtained from two patients, one with severe ischemic mitral regurgitation (IMR) and one without mitral valve disease. The electrocardiographically gated images were acquired with an iE33 scanner (Philips Medical Systems, Andover, MA) using a 2 to 7 MHz transesophageal matrix-array transducer over four consecutive cardiac cycles. The frame rate was 17 to 30 Hz with an imaging depth of 14 to 17 cm. The image volumes were exported in Cartesian format ($224 \times 208 \times 208$ voxels), with an approximate isotropic resolution of 0.7 mm. From each rt-3DTEE data series, an image volume delineating the mitral valve at mid-systole (a single time point in the cardiac cycle) was selected for analysis.

Semi-automated image analysis

User-initialized segmentation—Segmentation of the mitral leaflets has two steps: user-initialized region of interest (ROI) extraction, and 3D active contour segmentation based on region competition.¹³ User-initialized ROI extraction begins with construction of a 2D maximum intensity projection image along the axial dimension of the image volume. Adaptive histogram equalization¹⁴ is applied to the projection image to enhance the annular rim and leaflet coaptation zone of the mitral valve. In this enhanced projection image, a user outlines the valve and marks the leaflet coaptation curve in 2D. This information is then used to initialize 3D segmentation. The user selects a soft threshold for region competition, and a level set method¹⁵ is used to perform the final segmentation. The segmentation process is illustrated in Figure 1, and the anterior and posterior leaflet segmentations of the normal and diseased subjects are illustrated in Figure 2(a).

Mitral valve geometric modeling—Once 3D binary images of the anterior and posterior leaflets are obtained, our technique models the shape of each mitral leaflet using 3D continuous medial representation (cm-rep).^{16,17} Unlike a surface representation that describes an object's boundary geometry, medial representation is a compact representation of shape. First introduced by Blum,¹⁸ a shape's medial axis is defined as the locus of centers of maximal inscribed balls (MIBs), where each ball is tangent to the object's boundary at a minimum of two points. In three dimensions, a medial representation is a locus of tuples $(\mathbf{m}, R) \in \mathbb{R}^3 \times \mathbb{R}^+$, where $\mathbf{m}$ is the medial manifold formed by the centers of the MIBs and R refers to the radii of the MIBs centered at those points or, equivalently, to the distance between the medial axis and object surface. For reference, a 2D diagram of medial representation is presented in Figure 3. Medial representation is exploited in this work for its ability to assess local variations in leaflet thickness, derived from the radial thickness field R .

In the cm-rep framework, geometric representations of the mitral leaflets are obtained by fitting a deformable medial model, also referred to as a template, to its binary segmentation by Bayesian optimization. Each leaflet is treated as a separate shape, so the valve is modeled as two separate cm-reps, where each leaflet is a *simple* object whose skeleton consists of a single medial manifold. The medial manifold of each leaflet is represented by a mesh with 500 to 600 nodes and 900 to 1000 triangulated elements and is associated with a triangulated boundary mesh that represents the surface of the leaflet. Template fitting, or mesh deformation, consists of three stages: one alignment stage, one multi-resolution fitting stage, and a final deformation stage where both leaflets are simultaneously fitted to the leaflet

segmentations. (1) During the first stage, Jenkinson's FLIRT affine registration tool^{19,20} is used to obtain a similarity transform that aligns the leaflet templates with their corresponding segmentations. (2) The leaflet medial models are then independently deformed to fit the binary leaflet segmentations at three different resolutions. The objective function minimized during deformation incorporates the volumetric overlap error between the medial model and binary segmentation, as well as regularization terms and inequality constraints required by inverse skeletonization.¹⁷ (3) Finally, to correct for any intersection of the leaflet models, the medial models of the two leaflets are combined into a single model during the third stage of fitting. During the simultaneous fitting of both leaflets, a leaflet intersection penalty term is used to correct and prevent intersection of the leaflets' medial models. For increased efficiency during the last two steps of template fitting, the Laplace eigenfunction basis is defined on the medial template such that it can be deformed smoothly by modifying the coefficients of a small number of basis functions rather than all vertices of the template mesh.¹⁶ The results of model fitting are shown in Figure 2(b), and the radial thickness field R mapped to the medial manifold of each leaflet is shown in Figure 2(c) for both the normal and diseased valves.

In this study, the atrial surface of the fitted boundary mesh of each leaflet is used for finite element analysis. At each node of the mesh, localized leaflet thickness is quantified as chord length, i.e. the distance between the two boundary patches $\mathbf{b}^+$ and $\mathbf{b}^-$ associated with each point $\mathbf{m}$ on the medial manifold, as shown in Figure 3.

Finite Element Analysis

To obtain high-quality meshes for complex shapes such as mitral leaflets, the atrial sides of the leaflet surfaces acquired from semi-automated image analysis were first imported into HyperMesh 10.0 (Altair Inc.) as triangular elements, where raw nodal points were added, suppressed, or replaced to refine the leaflets' topological details without changing geometrical shape. The mesh quality criteria included element Jacobian, element size, minimum and maximum angles, and skewness. The refined triangulated leaflet surfaces were modeled as thin shells (type S3R). The thickness measurements acquired from the rt-3DTEE data were interpolated and assigned to each node in the refined leaflet mesh using Matlab (the Mathworks, Natick, MA). Leaflet tissue was assumed to be orthotropic and linearly elastic, with a Poisson's ratio of 0.49, and Young's modulus determined from excised porcine tissue data (Table 1).² The coaptation area between the anterior and posterior leaflet was defined as an interface pair with coefficient of friction $\mu=0.3$. Thirty-two chordae originating from each papillary muscle tip were inserted symmetrically into the anterior and posterior leaflets along the free edges of the leaflets (primary chordae), or more peripherally (secondary chordae). Papillary muscle tips were modeled as single points hinged in space associated with rotational freedom only. Chordae tendinae were represented by strings connecting the papillary muscle tips to the insertion points on the leaflets, and modeled by a tension-only truss element (type T3D2). Commercial FEA software (ABAQUS/Explicit 6.9, HKS Inc. Pawtucket, RI) was used to analyze the deformation and resulting stress distribution in the MV models, as previously described.¹² Systolic loading was accomplished via application of an 80 mmHg pressure gradient across the MV. Stress, strain and displacement were recorded as output variables.

Results

The mean and maximal AL and PL thicknesses derived from 3DE are reported in Table 2, for both the normal and the diseased MV. The regurgitant orifice of the diseased valve was clearly imaged and depicted in the 3D model, as demonstrated in Figure 4.

The pressure-load-induced von Mises stress fields predicted by FEA are presented in Figure 5, for both the normal and diseased MV. The regurgitant orifice of the diseased valve is evident in the loaded valve, though some conformational change (deformation) has occurred. The peak and mean stresses in the bellies of the AL and PL's of each valve were similar (Table 3). Note that for both MVs, the peak AL belly stress was larger than the peak PL belly stress, and the mean AL stress was significantly larger than the mean PL stress ($P < 0.001$ in both the normal and the diseased valve).

Discussion

A semi-automated and integrated methodology for imaging, segmenting, modeling, and deriving computationally-predicted pressure-derived MV leaflet stresses is presented herein, and points the way towards intraoperative and periprocedural guidance from morphometric and stress modeling of the MV.

The current study describes an approach to valve morphometry that provides a comprehensive, automated assessment of 3D valve geometry – in both normal and diseased MVs – by ultrasound image analysis. This is accomplished using an efficient segmentation strategy that exploits the contrast in 3D transesophageal images and uses projections of 3D data to eliminate the need for the user to navigate a 3D image volume during initialization. Though not emphasized in this report, the incorporation of deformable registration with cm-rep allows for a compact parametric representation of valve shape, from which a number of clinically significant features can be automatically derived. In addition, with the ability to establish points of correspondence on valves of different subjects and on the same valve at different time points, deformable modeling with cm-rep lays the foundation for statistical studies of time-dependent valve morphology.

A further advantage of the image analysis and segmentation algorithms described is that an objective measure of local MV leaflet thickness is provided. While these measurements have not been validated *in vivo*, our laboratory is in the process of doing so. *Ex vivo* human MV leaflet thicknesses have been described, and our image-derived thicknesses are generally consistent with those pathologic measurements²¹ and with prior echocardiographic measures of leaflet thicknesses in normal human MVs.²² This work presents the first FEA simulation of the MV incorporating high resolution *in vivo* measurements of leaflet thickness.

The ability to reliably estimate patient-specific mitral leaflet and chordal stresses *in vivo* has important clinical implications. Repair failure as manifest by the development of recurrent mitral regurgitation has recently been demonstrated to be far more common than originally believed.^{23,24} Recent studies have also shown that repair failures often result from stress related phenomenon such as chordal rupture, leaflet suture line disruptions and annuloplasty ring dehiscence.^{24,25} The ability to assess leaflet and chordal stresses in repaired valves will, with clinical experience, likely lead to improved surgical results by identifying patients with high stress valves in the early post-operative period. Such patients could either have re-repair or valve replacement before ever leaving the operating room, or could be subjected to closer postoperative clinical follow-up.

There are some evident limitations of the current work. First, the stress maps derived have not been tested against *in vivo* experimental results. However, this deficit is characteristic of all prior work on the stress and strain behavior of the mitral valve apparatus: it is difficult or impossible to measure *in vivo* strains of heart valves except in discrete matrices of transducers or markers.^{26,27} Second, the FEA utilizes a less-than-comprehensive MV model: whereas the leaflet surface profile and papillary muscle tips are accurately determined by rt-3DTEE, the chordae tendinae were not reliably imaged and so their incorporation in

the model is, at best, heuristically motivated. This solution is admittedly suboptimal, but similar to that adopted in prior noninvasive MV FEA studies.⁵ Prot et. al. used *ex vivo* examination of porcine valves to determine the number and insertions of secondary chordae,⁴ but this approach is clearly impossible in most human studies. In addition, the material properties model (linearly elastic) used is relatively simplified; however, the closed mitral valve has been shown to have a linear stress-strain relationship over the physiologic range of pressures.²⁸ Finally, homogeneous and uniform material properties were used throughout this work. It is reasonable to presume that leaflet material properties will be different in diseased and healthy MVs, and may vary regionally in a single valve. Nevertheless, the current research emphasizes the dependence of mechanical stress on geometric derangements in the diseased MV.

Recently, we have demonstrated that FEA modeling of the *in vivo* human MV using high-resolution 3D imaging is reasonable and useful for stress prediction in MV pathologies and repairs.¹² The current work extends and amplifies those results, and promises near-real-time stress analysis in the human MV using automated 3DE image analysis and modeling, and FEA. Therefore, we believe that a rational approach to *in vivo* MV stress analysis incorporates realistic empiric material properties of leaflets and chordae, 3D imaging, semi-automated valve segmentation and modeling, and FEA.

References

1. Trichon BH, Felker GM, Shaw LK, Cabell CH, O'Connor CM. Relation of frequency and severity of mitral regurgitation to survival among patients with left ventricular systolic dysfunction and heart failure. *Am J Cardiol.* 2003; 91(5):538–43. [PubMed: 12615256]
2. Kunzelman KS, Cochran RP, Chuong C, Ring WS, Verrier ED, Eberhart RD. Finite element analysis of the mitral valve. *J Heart Valve Dis.* 1993; 2:326–340. [PubMed: 8269128]
3. Kunzelman KS, Einstein DR, Cochran RP. Fluid-structure interaction models of the mitral valve: function in normal and pathological states. *Philos Trans R Soc Lond B Biol Sci.* 2007; 362:1393–1406. [PubMed: 17581809]
4. Prot V, Haaverstad R, Skallerud B. Finite element analysis of the mitral apparatus: annulus shape effect and chordal force distribution. *Biomech Model Mechanobiol.* 2009; 8:43–55. [PubMed: 18193309]
5. Votta E, Caiani E, Veronesi F, Soncini M, Montecvecchi FM, Redaelli A. Mitral valve finite-element modeling from ultrasound data: a pilot study for a new approach to understand mitral function and clinical scenarios. *Philos Transact A Math Phys Eng Sci.* 2008; 366:3411–3434. [PubMed: 18603525]
6. Jassar AS, Brinster CJ, Vergnat M, Robb JD, Eperjesi TJ, Pouch AM, Cheung AT, Weiss SJ, Acker MA, Gorman JH 3rd, Gorman RC, Jackson BM. Quantitative mitral valve modeling using real-time three-dimensional echocardiography: technique and repeatability. *Ann Thorac Surg.* 2011; 91:165–171. [PubMed: 21172507]
7. Levine RA, Handschumacher MD, Sanfilippo AJ, Hagege AA, Harrigan P, Marshall JE, Weyman AE. Three-dimensional echocardiographic reconstruction of the mitral valve, with implications for the diagnosis of mitral valve prolapse. *Circulation.* 1989; 80:589–598. [PubMed: 2766511]
8. Ryan LP, Jackson BM, Enomoto Y, Parish L, Plappert TJ, St John-Sutton MG, Gorman RC, Gorman JH 3rd. Description of regional mitral annular nonplanarity in healthy human subjects: a novel methodology. *J Thorac Cardiovasc Surg.* 2007; 134:644–648. [PubMed: 17723812]
9. Sugeng L, Chandra S, Lang RM. Three-dimensional echocardiography for assessment of mitral valve regurgitation. *Curr Opin Cardiol.* 2009; 24:420–425. [PubMed: 19593121]
10. Vergnat M, Jassar AS, Jackson BM, Ryan LP, Eperjesi TJ, Pouch AM, Weiss SJ, Cheung AT, Acker MA, Gorman JH 3rd, Gorman RC. Ischemic mitral regurgitation: a quantitative three-dimensional echocardiographic analysis. *Ann Thorac Surg.* 2011; 91:157–164. [PubMed: 21172506]

11. Yamaura Y, Watanabe N, Ogasawara Y, Yamamoto K, Kawamoto T, Toyota E, Akasaka T, Yoshida K. Geometrical demonstration and three-dimensional quantitative analysis of the mitral valve with real-time three-dimensional echocardiography: Novel anatomical image creation system. *J Echocardiography*. 2004; 2:99–104.
12. Xu C, Brinster CJ, Jassar AS, et al. A novel approach to in vivo mitral valve stress analysis. *Am J Physiol Heart Circ Physiol*. 2010; 299(6):1790–1794.
13. Zhu SC, Yuille A. Region competition: Unifying snakes, region growing, and Bayes/MDL for multiband image segmentation. *IEEE Transactions on Pattern Analysis and Machine Intelligence*. 1996; 18:884–900.
14. Zuiderveld, K. Contrast Limited Adaptive Histogram Equalization, *Graphic Gems IV*. Academic Press Professional; San Diego: 1994. p. 474–485.
15. Sethian, JA. Level set methods and fast marching methods: Evolving interfaces in computational geometry, fluid mechanics, computer vision and material science. Cambridge University Press; Cambridge: 1999.
16. Yushkevich PA. Continuous medial representation of brain structures using the biharmonic PDE. *Neuroimage*. 2009; 45:S99–110. [PubMed: 19059348]
17. Yushkevich PA, Zhang H, Gee JC. Continuous medial representation for anatomical structures. *IEEE Trans Med Imaging*. 2006; 25:1547–1564. [PubMed: 17167991]
18. Blum, H. A Transformation for Extracting New Descriptors of Shape. In: Wathen-Dunn, W., editor. *Models for the Perception of Speech and Visual Form*. MIT Press; Cambridge: 1967. p. 362–380.
19. Jenkinson M, Bannister P, Brady M, Smith S. Improved optimization for the robust and accurate linear registration and motion correction of brain images. *Neuroimage*. 2002; 17:825–841. [PubMed: 12377157]
20. Jenkinson M, Smith S. A global optimisation method for robust affine registration of brain images. *Med Image Anal*. 2001; 5:143–156. [PubMed: 11516708]
21. Sahasakul Y, Edwards WD, Naessens JM, Tajik AJ. Age-related changes in aortic and mitral valve thickness: implications for two-dimensional echocardiography based on an autopsy study of 200 normal human hearts. *Am J Cardiol*. 1988; 62(7):424–30. [PubMed: 3414519]
22. Louie EK, Langholz D, Mackin WJ, Wallis DE, Jacobs WR, Scanlon PJ. Transesophageal Echocardiographic Quantitation of Mitral Leaflet Thickness in Patients with Mitral Valve Prolapse. *J Am Coll Cardiol*. 1995; 25(1):191A.
23. McGee EC Jr, Gillinov AM, Blackstone EH, Rajeswaran J, Cohen G, Najam F, Shiota T, Sabik JF, Lytle BW, McCarthy PM, Cosgrove DM. Recurrent mitral regurgitation after annuloplasty for functional ischemic mitral regurgitation. *J Thorac Cardiovasc Surg*. 2004; 128:916–24. [PubMed: 15573077]
24. Flameng W, Meuris B, Herijgers P, Herregods M. Durability of mitral valve repair in Barlow disease versus fibroelastic deficiency. *J Thorac Cardiovasc Surg*. 2008; 135:274–82. [PubMed: 18242250]
25. Zegdi R, Sleilaty G, Latrémouille C, Berrebi A, Carpentier A, Deloche A, Fabiani J. Reoperation for Failure of Mitral Valve Repair in Degenerative Disease: A Single-Center Experience. *Ann Thorac Surg*. 2008; 86:1480–4. [PubMed: 19049735]
26. Padala M, Hutchison RA, Croft LR, Jimenez JH, Gorman RC, Gorman JH 3rd, Sacks MS, Yoganathan AP. Saddle shape of the mitral annulus reduces systolic strains on the P2 segment of the posterior mitral leaflet. *Ann Thorac Surg*. 2009; 88(5):1499–504. [PubMed: 19853100]
27. Krishnamurthy G, Ennis DB, Itoh A, Bothe W, Swanson JC, Karlsson M, Kuhl E, Miller DC, Ingels NB Jr. Material properties of the ovine mitral valve anterior leaflet in vivo from inverse finite element analysis. *Am J Physiol Heart Circ Physiol*. 2008; 295(3):H1141–H1149. [PubMed: 18621858]
28. Krishnamurthy G, Itoh A, Bothe W, Swanson JC, Kuhl E, Karlsson M, Miller DC, Ingels NB Jr. Stress–strain behavior of mitral valve leaflets in the beating ovine heart. *J Biomech*. 2009; 42:1909–1916. [PubMed: 19535081]

Figure 1.

Semi-automated segmentation algorithm. (a) The user initializes a region of interest (ROI) in a long-axis cross-section of the 3DE image volume, identifying the valve along the axial dimension. (b) The user initializes annular points in a projection image depicting the valve from an atrial perspective. (c) The user shifts posterior annular points into the coaptation zone, forming an outline of the anterior leaflet. (d) The user initialization is used to automatically generate a 3D ROI containing the valve in the image volume. (e) A final segmentation of the valve is obtained by thresholding and 3D active contour evolution. (LA = left atrium, LV = left ventricle, AL = anterior leaflet, PL = posterior leaflet)

Figure 2. Reconstructions of mid-systolic diseased (left) and normal (right) mitral valves from 3DE image data, including (a) the results of image segmentation, (b) the fitted medial models, and (c) the radial thickness field R mapped to the medial manifold of each leaflet. Note that, by definition, the medial manifold does not extend to the leaflet boundary, as there is a distance R between the manifold and leaflet surface. (AL = anterior leaflet, PL = posterior leaflet)

Figure 3.

Two-dimensional diagram of medial geometry. The red curve represents the medial surface (skeleton) m . The maximally inscribed circle centered at the black dot on m has radius R , with two spokes (arrows) pointing to two points, b^+ and b^- , on the object boundary shown in blue. The vector $\nabla_m R$ lies in the tangent plane of m and points in the direction of greatest change in R . In this work, thickness is measured as chord length, illustrated by the dotted line spanning the distance between b^+ and b^- .

Figure 4. Finite element models of mid-systolic diseased (A, C) and normal (B, D) mitral valves reconstructed from rt-3DTEE, in transvalvular (A, B) and oblique (C,D) views. (Nodes and elements have been reduced for visualization purposes.)

Figure 5. von Mises stress contour maps of diseased (left) and normal (right) MVs. Note the persistent orifice between the anterior and posterior leaflets in the regurgitant valve despite some conformational change (deformation) with pressure loading.

Table 1

Mitral valve material properties used in FEA model

Parameter	Anterior leaflet	Posterior leaflet	Primary chordae	Secondary chordae
Cross-sectional Area (mm ²)	-	-	0.4	0.7
E _{circumferential} (Pa)	6.20×10 ⁶	2.35×10 ⁶	4.20×10 ⁷	2.20×10 ⁷
E _{radial} (Pa)	2.10×10 ⁶	1.887×10 ⁶	-	-
Poisson's Ratio	0.49	0.49	0.49	0.49
Density (kg/m ³)	1.04×10 ³	1.04×10 ³	1.04×10 ³	1.04×10 ³

Table 2

Mitral valve leaflet thicknesses

	Mean (mm)	Maximum (mm)	Nodes in mesh
Anterior leaflet (normal)	2.6	4.7	13735
Posterior leaflet (normal)	2.3	4.8	9148
Anterior leaflet (diseased)	2.4	5.1	9235
Posterior leaflet (diseased)	2.4	4.2	4125

Table 3

von Mises stress

	Mean (kPa)	P-value	Peak (kPa)
Anterior leaflet belly (normal)	97.1 ± 37.2		215.5
Posterior leaflet belly (normal)	37.6 ± 14.4	<.001	85.5
Anterior leaflet belly (diseased)	81.7 ± 19.2		192.8
Posterior leaflet belly (diseased)	39.2 ± 16.3	<.001	134.8