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Fluid-Structure Interaction Analysis of Ruptured Mitral Chordae Tendineae

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Abstract

The chordal structure is a part of mitral valve geometry that has been commonly neglected or simplified in computational modeling due to its complexity. However, these simplifications cannot be used when investigating the roles of individual chordae tendineae in mitral valve closure. For the first time, advancements in imaging, computational techniques, and hardware technology make it possible to create models of the mitral valve without simplifications to its complex geometry, and to quickly run validated computer simulations that more realistically capture its function. Such simulations can then be used for a detailed analysis of chordae-related diseases. In this work, a comprehensive model of a subject-specific mitral valve with detailed chordal structure is used to analyze the distinct role played by individual chordae in closure of the mitral valve leaflets. Mitral closure was simulated for 51 possible chordal rupture points. Resultant regurgitant orifice area and strain change in the chordae at the papillary muscle tips were then calculated to examine the role of each ruptured chorda in the mitral valve closure. For certain subclassifications of chordae, regurgitant orifice area was found to trend positively with ruptured chordal diameter, and strain changes correlated negatively with regurgitant orifice area. Further advancements in clinical imaging modalities, coupled with the next generation of computational techniques will enable more physiologically realistic simulations.

Keywords

chordae tendineae; mitral valve; comprehensive model; fluid-structure interaction; computer simulation; chordal rupture

Conflict of interest

No benefits in any form have been or will be received from a commercial party related directly or indirectly to the subject of this manuscript.

1. Introduction

The mitral valve (MV) is responsible for maintaining forward blood flow from the left atrium (LA) to the left ventricle (LV). It is composed of two leaflets: the anterior, which is comprised of one contiguous scallop, and the posterior, which is comprised of the smaller P1, P2, and P3 scallops. Numerous chordae tendineae, which attach the leaflets to the LV wall via the papillary muscles, connect to each leaflet both along its free edge (primary chordae) and across its ventricular face (secondary chordae) (Fig. 1). Some smaller chordae (tertiary) do not connect to the leaflet, but rather provide connections between adjacent chordae.

Competent MV closure during cardiac contraction depends on a well orchestrated force balance across these structures. Loss of function of one or more chordae disrupts the link between the MV and the LV. Chordal rupture is frequently observed clinically; it may be idiopathic, or a consequence of connective tissue disorders, trauma [1], infective endocarditis [2], rheumatic heart disease [3], or spontaneous rupture [4, 5]. Chordal rupture can lead to leaflet prolapse [6], which is a primary mechanism of mitral regurgitation (MR), the most common form of significant heart valve disease [7]. The specific leaflet segment that prolapses, and the severity of the resultant MR, vary according to the particular ruptured chorda. Individual chordae may be classified according to size, branch type, or position, however, the connection between chordal class and the valve's response to its rupture has yet to be studied. Systematic investigation into the loss of leaflet coaptation that results from specific classes of chordal rupture could provide insight into possible treatments and/or treatment planning.

To begin to understand the mechanics governing MV function, finite element analysis was introduced decades ago for normal [8], diseased [9, 10, 11], and surgically repaired states [12, 13, 14, 15]. More recently, we and others have utilized fluid-structure interaction (FSI) analysis to understand the complex dynamics of mitral valvular function [16, 17, 18, 19, 20, 21]. Most of these models utilized MV geometries obtained either by parametric modeling, by image reconstruction of markers placed on the valvular apparatus, or from excised valve specimens. More recently, MV modeling strategies have been transitioning to morphologically realistic patient-specific MV modeling utilizing real-time 3D imaging data [22, 23, 24]. However, one of the obstacles limiting patient-specific modeling has been the inability to accurately represent the complex chordal structure of the native valve. Moreover, certain experimental research studies, such as our previous study of forces exerted on the chordae from papillary muscles [25], cannot be used for validation of computational simulations that use simplified chordal structure. While in the experimental settings, such as in-vivo, it has already been attempted to classify the importance of certain chordal groups [26]. Therefore, in addition to providing increased applicability, it is likely more accurate if the full and detailed subject-specific chordal structure is preserved in the model used.

To increase computational efficiency, most current models of the MV also use simplified element types to represent chordae tendineae and leaflet geometry. Models commonly take advantage of the chordal cable-type structure to justify the use of rod elements and the thinness of the leaflets to justify the use of shell elements [19, 27, 28, 29, 30, 31, 32, 33].

Some models do represent the leaflets with 3D elements (e.g. tetrahedral) but often only utilizing a single layer in order to reduce computational time. Furthermore, the detailed 3-D branching nature of the chordae has not been well-represented. These simplifications may limit the accuracy of the computational results. Improved anatomic accuracy is necessary for a thorough investigation of valvular dynamics post-chordal rupture.

We have recently developed and validated an ex vivo MV imaging methodology and associated computational platform, wherein the subject-specific MV geometry can be modeled with an unprecedented level of leaflet and chordal detail [34]. For the first time, secondary and tertiary chordae are incorporated into FSI simulations of MV closure using a detailed finite element model. Using this new simulation capability with an explanted ovine MV, the goal of this study was to understand the sensitivity of this specific geometry to the rupture of any of the 51 possible chordae tendineae rupture points. Following rupture of each chorda in at least one location, valve closure was simulated. The resulting regurgitant orifice area (ROA) was analyzed, along with the change in strain in the subvalvular apparatus.

2. Methods

2.1. Model Development

Fig. 2 shows the pipeline of the entire computational process from imaging the explanted MV through creating the surface mesh, volume mesh, running FSI analysis to post-processing the results.

As shown in Fig. 2, there are five phases that need to be completed in order to reach the computational results of the subject-specific MV with preserved chordal structure. Firstly, the MV must be imaged in order to obtain the raw volume. Secondly, processing must be performed on the volume to create a 3D model. Next, a high quality robust mesh must be generated using this 3D model. Then, the numerical algorithms must be employed to produce solutions, e.g. the closure of the leaflets. And, lastly, the results must be post-processed and analyzed.

Here, acquiring high resolution images of MV geometry is necessary for accurate modeling. However, no existing clinical imaging modality is capable of visualizing the full MV anatomy with adequate spatial or temporal resolution. For this purpose, our extensively validated Georgia Tech Left Heart Simulator (CLHS) is an ideal tool to reproduce realistic geometries of explanted MVs, which can be imaged by micro-computed tomography (μ CT) [35].

Locally sourced ovine MV was first excised, then mounted onto the annulus plate of the pulsatile CLHS. Ultrasound imaging (Philips iE33 xMATRIX, Philips Healthcare, Andover, MA) was used to view valve closure parameters under pulsatile flow. Papillary muscle positions were then adjusted to achieve healthy closure. The chamber was then dismantled from the pulse-duplicator in preparation for μ CT imaging. All imaging was done by an Inveon μ CT Scanner (Siemens Medical Solutions USA, Inc., Malvern, PA) optimized to image soft tissue (80 kV energy, 500 μ A intensity, 650 ms integration time) at 43.29 μ m isotropic voxel resolution.

A novel technique for treating MV specimens in preparation for μ CT scanning was used to obtain an MV image significantly more detailed in chordal structure, accurate in leaflet shape, and close to its physiological diastolic geometry than ever before achieved [34]. The resulting geometry is shown in Fig. 3.

2.2. Computational Model

After μ CT image processing and mesh generation, an FSI approach was used to simulate the opening and closing of the valve. Image acquisition and processing, mesh generation and segmentation, fiber directions calculation and constitutive modeling with the material parameters used are explained in detail in our previous work [20, 34, 36].

Various approaches have been adopted to address the challenge of modeling valve function using FSI. In this study, we adopted an approach based on smoothed particle hydrodynamics (SPH), wherein the fluid is modeled as a collection of discrete particles [37].

Fluid motion and boundary interaction was solved with the IMPETUS Afea SPH Solver[®] (IMPETUS Afea AS, Norway), while large deformation in the solid MV was simultaneously solved with the IMPETUS Afea Solver[®]. Both the solvers use a GPU workstation for parallel processing, thus avoiding the need for a large computer cluster. Parallelization of fully coupled FSI systems for computer clusters is still a challenging and developing field [38]. All solid elements were fully integrated, removing the possibility of hourglass modes and element inversion that plague the classic under-integrated elements.

Both fluid and solid domains, and their interaction, were solved with an explicit integration scheme. All simulations were solved on a standard workstation. Parallel acceleration was achieved with a Tesla K40 GPU with 12 GB of Graphic DDR memory and 2880 CUDA Cores. To confirm that convergence was reached, h-refinement of the finite element mesh was performed and the solution was found to yield the same results.

The fluid particles were confined in a pipe-like rigid structure surrounding the model, and two pistons moved within the pipe at a prescribed velocity (Fig. 4). The nodes at the bottom of the papillary muscles were fixed in all three directions, as well as the nodes on the annular attachment. The MV model consisted of 92,640 tetrahedral elements, and 476,199 fluid particles were used to represent the fluid. The resulting simulated closure of the MV model has been previously validated and showed a strong agreement to the μ CT scan of the closed valve [34]. The resulting simulated forces on the chordae tendineae throughout the cardiac cycle were also validated against experimental data [20]. We have also demonstrated that fully resolved 3D models of the mitral valve require an FSI analysis to correctly load the valve [36]. This fully validated MV model can now be used to analyze various chordae-related pathologies and repair techniques.

The constitutive model for the material properties utilized a three-dimensional splay invariant, based on an approximation of a three-dimensional Gaussian distribution of fibers [39]. The model is defined in terms of the 2nd Piola-Kirchhoff stress, $\mathbf{S}$, as follows

$$\mathbf{S} = \kappa J(J-1)\mathbf{C}^{-1} + \mu J^{-2/3} \mathbf{Dev}[(I - \bar{\mathbf{C}}^{-2})/4] + \sum_{i=1}^n \sigma_i(\lambda_i) J^{-2/3} \mathbf{Dev}[\mathbf{K}_i] + \sum_{i=1}^n \varepsilon(\lambda_i) J^{-2/3} \mathbf{Dev}[\mathbf{K}_i],$$

where J is Jacobian, κ is bulk modulus, σ_i is passive fiber stress-strain rule for the i^{th} (1 or 2) fiber population, ε is active fiber stress-strain rule, $\mathbf{Dev}$ is deviatoric projection operator, and $\mathbf{C}$ is right-Cauchy deformation, and λ_i is dispersed fourth invariant defined as

$$\lambda_i^2 = \text{tr}(\mathbf{K}\bar{\mathbf{C}}),$$

where $\bar{\mathbf{C}}$ is the isochoric part of the right-Cauchy deformation, $\mathbf{K}$ is called the dispersion tensor or anisotropy tensor and is given in global coordinates; note, as $\mathbf{K}$ embodies the concept of dispersion, λ is not a stretch in a classical sense. The matrix $\mathbf{K}$ is governed by splay parameters described in literature [39]. The material parameters and more detailed description of the material model is presented in the previous papers utilizing this model [20, 34, 36].

2.3. Simulating and Assessing Chordal Rupture

The importance of individual chordae tendinae was assessed by simulating ruptures in every possible branch of the chordal tree. This amounted to 51 rupture points (Fig. 5). The ruptures were produced by removing the elements from the volume mesh at half-length of the chorda which usually is the location of its minimum waist. For each ruptured model, the resulting systolic geometry after the closure was compared to the original model (referred to as the ‘healthy’ model) with all chordae preserved. Additionally, strain in the subvalvular apparatus of the MV was evaluated after closure simulations following each chordal rupture.

The impact of chordal rupture on MV closure geometry was assessed as follows. First, the nodes enclosing the coaptation line at full closure were identified in the no rupture, i.e. healthy, control case, Fig. 6(a). Along the coaptation line, coordinates of node n_i are x_i , y_i and z_i . The area, A , of a polygon in the space formed by the nodes of the coaptation line with coordinates vectors $\mathbf{x}$, $\mathbf{y}$ and $\mathbf{z}$ is calculated using a function from a library geom3D called polygonArea3d [40].

Even though zero area would be expected in the case of a healthy and perfectly simulated closure (Fig. 6(a)), small imperfection in the simulation, and especially manual identification of the nodes enclosing the coaptation line lead to a small nonzero value, i.e. 2.13 mm². This area is hereafter referred to as the Coaptation Line Enclosed Area (CLEA). Then, the same nodes were used to compute the enclosed area in the FSI results of each ruptured chorda case, e.g. Fig. 6(b), and all the CLEA values are reported after being offset by 2.13 mm² to compensate for the above mentioned imperfection. Note, in this way, the CLEA represents an approximation of the true ROA. We selected this approach because the alternative approach of directly identifying the ROA would risk significant error, due to the required manual node selection following each rupture simulation.

As explained in a review article by Thavendiranathan et al. [41], the best way to measure the ROA is using 3D techniques. The Fig. 7 demonstrates the different scenarios that can occur

with rupture of a different chorda. Using the most common 2D techniques the ROA would not be accurately captured when the leaflets are on top of each other yet separated allowing the back-flow to happen (Fig. 7(b)). This kind of ROA is referred to, by Thavendiranathan et al., as anatomic ROA. Furthermore, considering that in this model the coaptation zone between the leaflets was small, the nodes manually selected near the coaptation line would always capture the outline of the ROA. Despite our confidence that this node selection leads to accurate ROA, in this work we decided to call it CLEA to avoid misconceptions.

3. Results

Two variables were used to assess the rupture: our approximation of the ROA explained above, and strain values measured in papillary muscle tips. These variables were computed for all 51 simulations and we analyzed the correlation between the diameters of the ruptured chordae and these variables as follows.

3.1. Coaptation Line Enclosed Area

After simulated chordal rupture, CLEA was measured for all 51 cases and summarized in Fig. 9. For example, CLEA of # 9 is 134 mm² (Figs. 6(b) and 8), which is $\approx$ 132 mm² after being offset by 2.13 mm². Each number in Fig. 9 within the three circles (thresholds) represents one chorda and indicates the resulting CLEA. Among all chordae, mean $\pm$ SD CLEA was 38 $\pm$ 40 mm². With CLEA ranging from 1 to 132 mm², it is evident that the impact of chordal rupture on CLEA varies greatly with the specific ruptured chorda.

We hypothesized that CLEA would trend positively with diameter of the ruptured chorda (Fig. 10). Indeed, a statistically significant positive trend was observed ($p < 0.05$); however, the correlation of CLEA to chordal diameter was very weak ($R^2 = 0.1168$). CLEA was observed to differ meaningfully following subclassification of chordae based on chordal segment (trunk or branch), leaflet of insertion (anterior, P2, or P1/P3), or region of insertion (marginal or non-marginal) (Fig. 11). Of note, trunk chordal rupture induced significantly greater CLEA than branch rupture ($p < 0.05$). This suggested that stronger correlations between CLEA and chordal diameter may exist within these subclasses. Results of these investigations are presented in Figs. 12 and 13. It was observed that diameter of the ruptured chorda was a strong predictor of the resulting CLEA, specifically among trunk chordae or chordae inserting into the P2 leaflet. Other subclasses did not reveal significant correlations.

3.2. Strain Values at Papillary Muscle Tips

Finally, the change in strain in the subvalvular apparatus was evaluated after chordal rupture and closure simulations. It can be observed that the mean levels of strain in all chordae are lower when a chorda is ruptured, because the pressure in the left ventricle is also to be lower due to reversed blood flow through the resulting non-zero CLEA. Fig. 15(a) shows the change in mean strain versus the diameter of the ruptured chorda; little to no correlation was observed. However, as shown in Fig. 15(b), strain change did correlate strongly to CLEA. This result is reasonable, given the similarity between CLEA and the ROA, through which left ventricular pressure is relieved.

4. Discussion

The novel modeling platform outlined here combines the use of cutting-edge software, GPU technology, and in vitro imaging methodologies. Fluid-structure interaction modeling using high resolution images of explanted mitral valves enables examination of dynamic phenomena of valve closure, whereas previously used models are only able to interrogate the start and end state of valve closure. Additionally, the distinction of subject specific chordal branching and topology enables an unprecedented look into the mechanics and function of the subject-specific chordal tree in computational simulation. The utility of the platform is demonstrated here by simulating chordal discontinuities (cuts/ruptures) systematically in each chordal segment, and examining the resulting mechanical effects on valve closure. The effect on simulated valve closure resulting from these chordal ruptures was examined; CLEA and strain in PM tips in the resulting closed model were compared with those values observed in the healthy model.

After simulated chordal rupture, CLEA was measured and summarized in Fig. 9. The data in Fig. 9 can be analyzed together with Fig. 5 to find out what type of chorda causes what level of approximated regurgitation. For example, chorda #10 is of large diameter, but its rupture only results in small to moderate regurgitation. As can be seen, in Fig. 5, that particular chorda is reinforced by multiple surrounding smaller chordae that can take over the increased load [42]. Similar observation can be made based on Fig. 10, where the rupture points in chordae #9 and #10 yield very different CLEA values despite of the chorda being of similar thickness.

The CLEA depends not only on the diameter of the ruptured chorda but also on its location and its relationship with surrounding chordae. When examining the relationship of ruptured chorda diameter with CLEA in groups of chordae, significant positive trends were found in the trunk chordae and in those chordae inserting into the P2 segment of the posterior leaflet (Fig. 13). Though general trends were identified, outliers were found within each grouping, illustrating the importance of subject-specific modeling. For example, rupture of some small chordae resulted in significant CLEA after closure.

On the other hand, some ruptures did not lead to significant change to closure geometry. In these cases, heightened strain on neighboring chordae was observed, as they took on the load-bearing function lost by the ruptured chord. Such phenotypes, though not acutely problematic, could promote chronic disease states via subsequent chordal ruptures, valvular/ventricular remodeling, or some combination thereof. In other cases, the rupture prompted significant increases in CLEA. This type of response is more representative of acute disease, where the patient experiences sudden regurgitation, pulmonary hypertension, and edema leading to acute morbidity.

In quantifying strain in the subvalvular apparatus, it was observed that with a larger CLEA, pressure buildup inside the left ventricle was reduced, and the peak loads exerted on the chordae tendinae were smaller. Though chordal rupture is often a pathological event, chordal cutting during valve repair is sometimes used to relieve leaflet tethering and enhance valve closure [43]. However, we have shown here that the removal of chordae without change to

the CLEA will increase the strain in the subvalvular apparatus by distributing the same load over fewer chordal supports. This may lead to additional unintended chordal rupture following the therapeutic procedure.

Of course, certain limitations exist in the methodology used in the study. First, the imaging and modeling components of the platform are labor intensive, and only currently suitable for long term investigation within the research environment. Translation of the platform to clinical usage is distant. Also, though significant improvements have been made in sample preparation for μ CT imaging, some details in the chordal structure remain indiscernible, namely in the commissures of the MV. Another limitation is the use of idealized, cylindrical geometry representing the left ventricle. Future work will seek to reproduce the left ventricular geometry within the simulation platform, first with rigid and then with moving walls. By simulating the MV function within a left ventricle geometry, we can understand the impact of MV disease and repair on ventricular filling and function. Also, we have not used the experimental set-up to directly validate the regurgitation related to the rupture of some of the chordae. Even though the validation would not be difficult, chordal rupture is non-reversible, so it is impossible to validate for any more than one rupture. We have made the assumption that a simulation that yields a validated closure of a healthy MV will also accurately model simulated pathologies. And, more subject-specific valves are to be simulated to draw statistically stronger conclusions. However, even with these limitations in mind, one can draw two main points from this work; 1) even small chordae with small diameter can cause large ROA, and 2) only certain subclassifications have a strong correlation of ROA to chordal diameter.

As chordal rupture is both pathological and palliative, the results illustrate the importance of understanding the positive and negative effects on valve closure. In the pathological case, this work gives insight into acute valve behavior following chordal rupture, and may lead to a better understanding of mechanisms underlying chronic remodeling following these events. In the palliative case, future work will look into the chordal cutting procedure as a method of alleviating leaflet tethering after ischemic left ventricular remodeling and mitral regurgitation. A mechanistic understanding of the load redistribution and mitral regurgitation following this procedure could assist surgeons in planning the procedure and deciding the appropriate chordal cutting strategy for optimal surgical results. This platform is useful not only for chordal rupture modeling; in fact, with new methods for interventional simulation under development, many different types of valve repair operations can be simulated. Results have the potential to inform mechanistic outcomes of these different procedures at an unprecedented level of detail.

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References

1. Grinberg AR, Finkielman JD, Pineiro D, Festa H, Cazenave C. Rupture of mitral chorda tendinae following blunt chest trauma. Clin Cardiol. 1998; 21:300–301. [PubMed: 9580528]

2. Portugese S, Amital H, Tenenbaum A, Bar-Dayana Y, Levy Y, Afek A, Shemesh J, Shoenfeld Y. Clinical characteristics of ruptured chordae tendineae in hospitalized patients: primary tear versus infective endocarditis. *Clin Cardiol.* 1998; 21(11):813–816. [PubMed: 9825193]
3. Anderson Y, Wilson N, Nicholson R, Finucane K. Fulminant mitral regurgitation due to ruptured chordae tendineae in acute rheumatic fever. *J. Paediatr. Child Health.* 2008; 44(3):134–137. [PubMed: 17854408]
4. Kaymaz C, Ozdemir N, Ozkan M. Differentiating clinical and echocardiographic characteristics of chordal rupture detected in patients with rheumatic mitral valve disease and floppy mitral valve: impact of the infective endocarditis on chordal rupture. *Eur J Echocardiogr.* 2005; 6(2):117. [PubMed: 15760688]
5. Gabbay U, Yosefy C. The underlying causes of chordae tendinae rupture: a systematic review. *Int J Cardiol.* 2010; 143(2):113–118. [PubMed: 20207434]
6. Grenadier E, Alpan G, Palant A. The prevalence of ruptured chordae tendineae in the mitral valve prolapse syndrome. *Am. Heart J.* 1983; 105(4):603–610. [PubMed: 6837414]
7. Nkomo VT, Gardin JM, Skelton TN, Gottdiener JS, Scott CG, Sarano ME. Burden of valvular heart diseases: a population-based study. *The Lancet.* 2006 Sep; 368(9540):1005–1011.
8. Kunzelman KS, Cochran RP, Chuong CJ, Ring WS, Verier ED, Eberhart RC. Finite element analysis of the mitral valve. *J Heart Valve Dis.* 1993; 2:326–340. [PubMed: 8269128]
9. Kunzelman KS, Cochran RP, Chuong CJ, Ring WS, Verier ED, Eberhart RC. Finite element analysis of mitral valve pathology. *J Long Term Eff Med Implants.* 1993; 3:161–179.
10. Kunzelman KS, Reimink MS, Cochran RP. Annular dilatation increases stress in the mitral valve and delays coaptation: A finite element computer model. *Cardiovasc Surg.* 1997; 5:427–434. [PubMed: 9350801]
11. Kunzelman KS, Reimink MS, Cochran RP. Flexible versus rigid ring annuloplasty for mitral valve annular dilation: A finite element model. *J Heart Valve Dis.* 1998; 7:108–116. [PubMed: 9502148]
12. Cochran RP, Kunzelman KS. Effect of papillary muscle position on mitral valve function: relationship to mitral homografts. *Annals of Thoracic Surgery.* 1998; 66(Suppl):S155–S161. [PubMed: 9930439]
13. Reimink MS, Kunzelman KS, Verier ED, Cochran RP. The effect of anterior chordal replacement on mitral valve function and stresses. *ASAIO Transactions.* 1995; 41:M754–M762.
14. Kunzelman KS, Reimink MS, Verier ED, Cochran RP. Replacement of mitral valve posterior chordae tendineae with expanded polytetrafluoroethylene suture: A finite element study. *J Card Surg.* 1996; 11:136–145. [PubMed: 8811408]
15. Reimink MS, Kunzelman KS, Cochran RP. The effect of chordal replacement suture length on function and stresses in repaired mitral valves: A finite element study. *J Heart Valve Dis.* 1996; 5:365–375. [PubMed: 8858500]
16. Einstein DR, Reinhall PG, Kunzelman KS, Cochran RP. Nonlinear finite element analysis of the mitral valve. *J Heart Valve Dis.* 2005; 3:376–385.
17. Einstein DR, Kunzelman KS, Reinhall PG, Nicosia MA, Cochran RP. The relationship of normal and abnormal microstructural proliferation to the mitral valve closure sound. *Transactions of the ASME.* 2005; 127:134–147.
18. Kunzelman KS, Einstein DR, Cochran RP. Fluid-structure interaction models of the mitral valve: function in normal and pathological states. *Phil. Trans. R. Soc. B.* 2007; 362:1393–1406. [PubMed: 17581809]
19. Einstein DR, DelPin F, Jiao X, Kuprat AP, Carson JP, Kunzelman KS, Cochran RP, Guccione JM, Ratcliffe MB. Fluid-structure interactions of the mitral valve and left heart: Comprehensive strategies, past, present, and future. *International Journal for Numerical Methods in Biomedical Engineering.* 2010; 26(3–4):348–380.
20. Toma M, Jensen MO, Einstein DR, Yoganathan AP, Cochran RP, Kunzelman KS. Fluid-structure interaction analysis of papillary muscle forces using a comprehensive mitral valve model with 3D chordal structure. *Ann Biomed Eng.* 2016 Apr; 44(4):942–953. [PubMed: 26183963]
21. Chandran KB, Kim H. Computational mitral valve evaluation and potential clinical applications. *Ann Biomed Eng.* 2014 Aug 19. [Epub ahead of print].

22. Pouch AM, Yushkevich PA, Jackson BM, Jassaa AS, Vergnat M, Gorman JH, Gorman RC, Sehgal CM. Development of a semi-automated method for mitral valve modeling with medial axis representation using 3d ultrasound. *Med. Phys.* 2012; 39(2):933–950. [PubMed: 22320803]
23. Votta E, Caiani EG, Veronesi F, Soncini M, Motevecchi FM, Redaelli A. Mitral valve finite-element modelling from ultrasound data: a pilot study for a new approach to understand mitral function and clinical scenarios. *Philos. Trans. Ser., A.* 2008; 366(1879):3411–3434.
24. Votta E, Le TB, Stevanella M, Fusini L, Caiani EG, Redaelli A, Sotiropoulos F. Toward patient-specific simulations of cardiac valves: state-of-the-art and future directions. *J. Biomech.* 2013; 46(2):217–228. [PubMed: 23174421]
25. Jensen MO, Fontaine AA, Yoganathan AP. Improved in vitro quantification of the force exerted by the papillary muscle on the left ventricular wall: Three-dimensional force vector measurement system. *Annals of Biomedical Engineering.* 2001; 29:406–412. [PubMed: 11400721]
26. Jimenez JH, Soerensen DD, He Z, Ritchie J, Yoganathan AP. Mitral valve function and chordal force distribution using a flexible annulus model: An in vitro study. *Annals of Biomedical Engineering.* 2005 May; 33(5):557–566. [PubMed: 15981857]
27. Rim Y, Laing ST, McPherson DD, Kim H. Mitral valve repair using ePTFE sutures for ruptured mitral chordae tendineae: A computational simulation study. *Annals of Biomedical Engineering.* 2014; 42(1):139–148. [PubMed: 24072489]
28. Mansi T, Voigt I, Georgescu B, Zheng X, Mengue EA, Hackl M, Ionasec R, Noack T, Seeburger J, Comaniciu D. An integrated framework for finite-element modeling of mitral valve biomechanics from medical images: Application to mitralclip intervention planning. *Medical Image Analysis.* 2012; 16:1330–1346. [PubMed: 22766456]
29. Schievano S, Kunzelman KS, Nicosia MA, Cochran RP, Einstein DR, Khambadkone S, Bonhoeffer P. Percutaneous mitral valve dilatation: Single balloon versus double balloon. a finite element study. *Journal of Heart Valve Disease.* 2009; 18:28–34. [PubMed: 19301550]
30. Wenk JF, Zhang Z, Cheng G, Malhotra D, Bolton GA, Burger M, Suzuki T, Saloner DA, Wallace AW, Guccione JM, Ratcliffe MB. First finite element model of the left ventricle with mitral valve: Insights into ischemic mitral regurgitation. *Annals of Thoracic Surgery.* 2010; 89(5):1546–1554. [PubMed: 20417775]
31. Maisano F, Redaelli A, Soncini M, Votta E, Arcobasso L, Alfieri O. An annular prosthesis for the treatment of functional mitral regurgitation: Finite element model analysis of a dog bone-shaped ring prosthesis. *Annals of Thoracic Surgery.* 2005; 79(4):1268–1275. [PubMed: 15797061]
32. Stevanella M, Maffessanti F, Conti CA, Votta E, Arnoldi A, Lombardi M, Parodi O, Caiani EG, Redaelli A. Mitral valve patient-specific finite element modeling from cardiac MRI: Application to an annuloplasty procedure. *Cardiovascular Engineering and Technology.* 2011; 2(2):66–76.
33. Lau KD, Diaz V, Scambler P, Burriesci G. Mitral valve dynamics in structural and fluid-structure interaction models. *Medical Engineering & Physics.* 2010; 32:1057–1064. [PubMed: 20702128]
34. Toma M, Bloodworth IV CH, Einstein DR, Pierce EL, Cochran RP, Yoganathan AP, Kunzelman KS. High resolution subject-specific mitral valve imaging and modeling: Experimental & computational models. *Biomechanics and Modeling in Mechanobiology.* 2016 [Epub ahead of print].
35. Rabbah J-P, Saikrishnan N, Yoganathan AP. A novel left heart simulator for the multi-modality characterization of native mitral valve geometry and fluid mechanics. *Annals of Biomedical Engineering.* 2013; 41(2):305–315. [PubMed: 22965640]
36. Toma M, Einstein DR, Bloodworth IV CH, Cochran RP, Yoganathan AP, Kunzelman KS. Fluid-structure interaction and structural analysis using a comprehensive mitral valve model with 3D chordal structure. *Int. J. Numer. Methods in Biomed. Eng.* 2016 [Epub ahead of print].
37. Liu PGR, Liu MB. Smoothed Particle Hydrodynamics: A Meshfree Particle Method. World Scientific Publishing Company. 2003
38. Toma M, Oshima M, Takagi S. Decomposition and parallelization of strongly coupled fluid-structure interaction linear subsystems based on the Q1/P0 discretization. *Computers & Structures.* 2016; 173:84–94.

39. Freed AD, Einstein DR, Vesely I. Invariant formulation for dispersed transverse isotropy in aortic heart valves: an efficient means for modeling fiber splay. *Biomech Model Mechanobiol.* 2005; 4:100–117. [PubMed: 16133588]
40. Amberg, B., Romdhani, S., Vetter, T. Optimal step nonrigid icp algorithms for surface registration; *Computer Vision and Pattern Recognition, 2007. CVPR'07. IEEE Conference on.* IEEE; 2007. p. 1-8.
41. Thavendiranathan P, Phelan D, Collier P, Thomas JD, Flamm SD, Marwick TH. Quantitative assessment of mitral regurgitation: How best to do it. *JACC: CARDIOVASCULAR IMAGING CME.* 2012; 5(11):1161–1175.
42. McCarthy PM. A chain is only as strong as its weakest link. *The Journal of Thoracic and Cardiovascular Surgery.* 2016 [Epub ahead of print].
43. Messas E, Guerrero JL, Handschumacher MD, Conrad C, Chow C-M, Sullivan S, Yoganathan AP, Levine RA. Chordal cutting: A new therapeutic approach for ischemic mitral regurgitation. *Circulation.* 2001; 104:1958–1963. [PubMed: 11602501]

Figure 1.
Primary chorda attached to the edge of the mitral valve leaflet and secondary chorda attached to the belly of the mitral valve leaflet. Tertiary chordae do not extend from the leaflets.

Figure 2.

Pipeline of the computational process from a medical imaging technique (micro-computed tomography, i.e. μ CT) to post-processing the results in order to investigate the anatomy and physiology of the mitral valve.

Figure 3.
The detailed MV model extracted from DICOM μ CT images with all chords preserved.

Figure 4.

The fluid particles are confined in a pipe-like rigid structure surrounding the MV model. Prescribed velocity boundary conditions are applied to the open ends via the use of moving pistons in z-direction.

Figure 5.

Ruptured chordae tendinae numbering, i.e. the locations where the elements are removed from the mesh in individual chordae in order to obtain a representation of its rupture. A given number can appear more than once if the chord rupture place is visible in more than one view presented.

Figure 6.

Coaptation line is found by drawing a line on atrial faces of the coaptation zone in fully closed configuration, 2.13 mm² (a) and then the same line, i.e. connecting the same nodes on the mesh, is used to compute the approximation of ROA for the ruptured chorda, e.g. #9, 134 mm² (b).

Figure 7.

Depending on which chorda is ruptured, different kind of prolapse can occur, i.e. (a) the leaflets are separated with clear ROA visible even with traditional 2D techniques, (b) the leaflets are on top of each other but allowing the back-flow anyway which cannot be captured by 2D techniques, or (c) even with ruptured chorda there is no regurgitation to observe. This schematic demonstrates the importance of 3D measurements to capture the ROA accurately.

Figure 8.

The anatomic ROA/CLEA for rupture # 9 calculated using the nodes enclosing the coaptation line in the control, i.e. healthy, case (blue nodes in the figure). It can be seen that the leaflets are on top of each other yet separated allowing the back-flow to happen (Fig. 7(b)).

Figure 9.

CLEA resulting from cutting the chordae in 51 places, e.g. for chorda # 9 Fig. 6(b) after being offset by Fig. 6(a) = 132 mm², in logarithmic scale. The green (dot-dashed) lines represent cuts that resulted in no significant change, i.e. up to 3 mm², blue (dotted) lines represent the cuts where moderate change occurred, i.e. up to 20 mm², and the red (dashed) lines belong to the chordae where their rupture resulted in significant enlargement of the orifice area, i.e. > 20 mm².

Figure 10.

CLEA versus diameter of ruptured chordae. A significant, positive trend was found between chorda diameter and CLEA, ($p < 0.05$). Though a significant positive trend was observed, the differences in the two circled measures illustrate the heterogeneity in the measurements. Therefore, we subdivided these into different anatomical groups of chordae.

Figure 11.

Mean±SD for each chordal sub-class [# chordae]. Chordae were classified according to branch type (trunk, branches), leaflet of insertion (anterior, P1/P3, P2), or leaflet insertion region (marginal, non-marginal); *p<0.05.

Figure 12.

Relationship between the diameters of where the rupture occurs and the resulting CLEA grouped by belonging to different types of chordae that can be classified as (a) marginal, (b) non-marginal.

Figure 13.

Relationship between the diameters of where the rupture occurs and the resulting CLEA grouped by belonging to different types of chordae that can be classified as (a) trunk, (b) branches, (c) anterior, (d) P2, (e) P1/P3.

Figure 14.

Strain in the mitral chordae tendinae in the original model with all chordae intact (a) and the model with simulated rupture (b) at the $T=T_{systole}$, rupture of chorda #9 in Fig. 5. Dashed circles denote the locations of the ruptured chordae.

Figure 15.

Change in the strain measured at papillary muscle tips compared to healthy MV with all chordae preserved (a). Negative values of strain change indicate non-zero CLEA. More evident trend can be observed when the strain change is directly compared with the CLEA (b).