MITRAL VALVE MECHANICS

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Published by Linköping University Electronic Press
Linköping University Library
Linköping Sweden

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ISBN: 978-91-7685-952-0

DOI: 10.3384/book.diva-117057

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THIS BOOK IS DEDICATED TO
OUR PARENTS
OUR TEACHERS
OUR COLLEAGUES
BUT ABOVE ALL
TO
OUR FAMILIES
JUDY, ANNE, AND NEIL III INGELS
-AND-
ANNA, MARKUS, AND OSKAR KARLSSON

INTRODUCTION

The goal of this book is to develop a working hypothesis for mitral valve function in the beating heart. We have been studying the 4-D dynamics of the heart using biplane radiography of surgically implanted radiopaque markers for the past forty years,¹ with emphasis on the mitral and aortic valves during the past 20 years,²⁻¹⁶ and dense leaflet and annular marker arrays during the past several years.¹⁷⁻²⁷ Data from the control runs in these studies comprise the substrate for this book.

The data files described in the Appendices and provided in the Repository are the most important parts of this book. We present our interpretations of these data in the following chapters, but our interpretations may be wrong. It is our hope that readers will challenge and/or build on these ideas, all the while using (and constrained by) these data.

We wish to make this material freely available and shareable, thus, it can be accessed directly by clicking on the [MITRAL VALVE MECHANICS](#) footer at bottom of each page. Readers should feel free to download this material, use it in any way they wish, and distribute it to anyone who might be interested in this subject.

In this brief introduction, we cannot individually recognize and thank each of the many individuals who have participated in these studies. This would require another book. Instead, we recognize them by listing some of their authored publications below, with each publication acknowledging and thanking the supporting individuals for that study. Without the superb interdisciplinary skills and almost miraculous collaborative efforts of all these individuals in conducting these intricate studies, these data would not exist.

Three individuals, however, have devoted more than 30 years to these studies and we must thank them individually; D. Craig Miller, in whose Stanford Laboratories these studies were conducted and without whom none of this would have been possible; George Daughters, who was crucially and fully engaged in all aspects of this work; and Carol Mead, who performed an invaluable role in both data acquisition and analysis.

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CHAPTER 01 ANATOMY AND MARKER SITES

Figure 1.1 is a view from a 3-D rendering of systolic geometry for the left ventricle, mitral valve, and aortic valve, computed as a composite from two experiments involving precise measurement of 83 marker sites. The methods used to obtain this 3-D dataset, including the full dataset file, are outlined in Appendix B. Note that in this systolic rendering, the aortic valve is open and the mitral valve is closed.

Figure 1.2 is an enlarged view from the 3-D rendering of diastolic geometry using the composite technique described in Appendix B and used to produce Figure 1.1. The Figure caption and labels define the nomenclature that will be used in this book to describe the left ventricle, mitral valve, and aortic valve. Note that in this diastolic rendering, the aortic valve is closed and the mitral valve is open.

Figures 1.3 and 1.4 show the numbered sites where radiopaque markers were located in the left ventricle, mitral annulus, papillary muscles, and mitral anterior and posterior leaflets for the six hearts H1-H6 (see Appendix A).

Figure 1.3 Numbered left ventricular and mitral annular marker sites. APM=Anterior Papillary Muscle Tip; PPM=Posterior Papillary Muscle Tip. Marker #29 at the Left Fibrous Trigone, Marker #24 at the Right Fibrous Trigone, Marker #22 at the Annular "Saddlehorn", Marker #18 at the Lateral Annulus, Marker #16 at the Anterior Commissure, Marker #20 at the Posterior Commissure.

Figure 1.4 Numbered anterior mitral leaflet marker sites. Marker 37 is at central posterior leaflet scallop edge.

CHAPTER 02 FIBROUS MITRAL ANNULUS

A fibrous collagen wedge, pointing toward the left ventricle, separates the mitral valve and left atrium from the aortic valve. The portion of this wedge between the mitral and aortic valves is known as the aortic mitral curtain or the intervalvular fibrous curtain. The fibrous mitral annulus (Figure 2.1), at the point of this wedge, serves as the hinge for the anterior mitral leaflet. In our studies, seven markers are spaced along this hinge (Figure 2.2), from the left fibrous trigone (LFT, Marker#29), through Markers #15 and #30, to the annular “saddlehorn” (SH, Marker #22), then on through Markers #23 and #21, to the right fibrous trigone (RFT, Marker#24).

The length of the fibrous mitral annulus for the six hearts (Figure 2.3), obtained by summing the length of segments D2915, D1530, D3022, D2223, D2321, and D2124, ranged from 28 to 39 mm and this length varied from 6 to 10% during the cardiac cycle. Fibrous mitral annular length was minimum during diastole, rose steadily during ejection, then fell abruptly immediately after mitral valve opening, in concert with LV contraction, not LV pressure.

The fibrous mitral annular angle for the six hearts (Figure 2.3), defined from the LFT (Marker #29) to the SH (Marker #22) to the RFT (Marker #24), *i.e.*, $\theta_{29-22-24}$, ranged from 116 to 145°, and varied from 7 to

Figure 2.1. Diagram of the mitral valve and its neighbors, viewed from the left atrium. A fibrous curtain of variable length separates the aortic and mitral annuli. From the Cardiovascular Research and Training Center, Cardiac Imaging Research Lab, University of Washington, Seattle, Washington. Figure drawn by Starr Kaplan.

Figure 2.2 Fibrous Mitral Annulus (red), the hinge region for the anterior mitral leaflet (gray), as delineated by radiopaque markers from the left fibrous trigone (LFT, Marker#29), through Markers #15 and #30, to the “Saddlehorn” (SH, Marker #22), through Markers #23 and #21, to the right fibrous trigone (RFT, Marker#24).

11% during the cardiac cycle. The fibrous mitral annular angle was maximum at end diastole, fell abruptly as LVP increased during IVC, continued to fall (but more slowly) during ejection, then increased in a manner similar to LV filling during and after IVR.

Figure 2.3 LFT-SH-RFT Fibrous mitral annular length and angle for hearts H1-H6.

CHAPTER 03 FIBROUS ANNULUS-PAPILLARY TIP-LV RELATIONSHIP

Figure 3.1 illustrates the geometric relationships between the LFT (Marker#29), APT (Marker#31), SH (Marker#22), RFT (Marker#24), and PPT (Marker#33) for diastole (left panel) and systole (right panel).

Figures 3.3a and 3.3b plot, for hearts H1-H6, the distance between the APM tip and the fibrous annulus from the LFT to the SH (D2931, D1531, D3031, D2231), the distance between the PPM tip and the fibrous annulus from the RFT to the SH (D2433, D2133, D2333, D2233), the distance between the papillary tips (D3133), LVP, and identify the time of mitral valve opening (MVO) and closing (MVC).

Note, in Figures 3.3a and 3.3b, that the distances from the APT to the fibrous annulus (D2931, D1531, D3031, and D2231) and the distances from the PPT to the fibrous annulus (D2433, D2133, D2333, D2233) are relatively constant throughout the cardiac cycle, in spite of the wide variation in the distance between the papillary tips (D3133, greatest at end diastole, decreasing during ejection, then increasing during filling).

Table 3.1 quantifies the changes in all these distances throughout the cardiac cycle. The data in this table were obtained by first analyzing 130 consecutive samples for the 3 beats in each individual heart, finding the maximum and minimum values for this dataset in that heart, then computing the percent change for that heart as $100 \times ((\text{max} - \text{min}) / \text{min})$. The maximum change observed for the 6 hearts analyzed is shown as MAX%, the minimum change observed as MIN%, and the mean change for the 6 hearts is MEAN%. As can be seen, even with these very stringent criteria, changes in the distances from the papillary tips to their respective half of

	MAX%	MIN%	MEAN%
D2931	6	3	4
D1531	5	2	4
D3031	6	2	4
D2231	7	3	4
D2433	5	2	3
D2133	5	2	3
D2333	6	2	4
D2233	4	2	3
D3133	32	60	42

Table 3.1 Group MAX%, MIN%, and MEAN% length changes throughout the cardiac cycle for H1-H6.

the fibrous annulus were small, ranging from 2-7%, while the distance between the papillary tips (D3133) ranged from 32-60%.

These nearly constant papillary tip to fibrous annulus distances suggest rather tight coupling between the papillary tips and the fibrous annulus. The material basis for this coupling can be observed anatomically (Figures 3.2a, 3.2b, and 3.2c) as relatively thick, so-called “strut” chordae, emanating from the papillary tips, inserting into the belly of the anterior leaflet, continuing on as somewhat diffuse structures on the ventricular side of the anterior leaflet to insert with the leaflet into the fibrous annulus and chordae from the papillary tips to the trigones. The differences between Figure 3.2a and 3.3b suggest anatomical differences between ovine and human chordae, although both species have chords from the papillary tips to the anterior leaflet belly and from the papillary tips to the trigones that could result in this constant-distance behavior.

Figure 3.2a Ventricular surface of postoperative excised ovine anterior leaflet from one of our studies. Note two prominent chordae from papillary tips that may provide the constant annular-papillary tip distances discussed in this chapter. Note also the radiopaque markers sewn to all aspects of the valve complex, particularly those at the papillary tips and mid-strut chord, allowing assessment of strut chord length changes throughout the cardiac cycle as discussed in Chapter 21. Photo by Eleazar Briones.

Figure 3.2b. Anterior leaflet and papillary muscles. Paramedial (pm), strut (s), and paracommissural (pc) chordae tendineae of the anterior leaflet (AL). APM =anterior papillary muscle; PPM=posterior papillary muscle. From Antunes, MJ, MITRAL VALVE REPAIR, 1989, Verlag R.S. Schulz.

Figure 3.2c Ventricular view of the anterior mitral leaflet showing the typical insertion of chordae tendineae into the free edge and rough zone of the leaflet. From Antunes, MJ, MITRAL VALVE REPAIR, 1989, Verlag R.S. Schulz.

Such relatively constant distances between the papillary tips and the fibrous annulus have potentially important implications. If, to a crude first approximation, we model the fibrous annulus-APT and -PPT connections as chordal threads, capable of supporting tension, but buckling in compression, then the only way to maintain these constant distances is to rotate the papillary tips around axes defined on the fibrous annulus. We define two such axes for each heart in Figures 3.4a, b, and c.

- The first axis, for the APT (#31), has its origin at the SH (#22) and extends through the LFT (#29). A plane 22-29-1 (blue) anchors this axis to the LV apex (#1). Another plane 22-29-31 (red) contains the chordal threads to the APT (#31).
- The second axis, for the PPT (#33), has its origin at the SH (#22) and extends through the RFT (#24). A plane 22-24-1 (green) anchors this axis to the LV apex (#1). Another plane 22-24-33 (red) contains the chordal threads to the PPT (#33).

We further define:

- “pat” as the projection of the APT (#31) on the 22-29-1 plane and “qa” is the point on the 22-29 axis where a normal to this axis passes through the APT (#31).
- α_{31} as the 29-22-pat angle in the 22-29-1 plane.
- β_{31} as the APT angle 31-qa-pat with respect to the 22-29-1 plane, with positive angles toward the lateral annular marker (#18).
- LAC31 as the #22 to qa distance.
- RAC31 as the #qa to APT(#31) distance
- “ppt” as the projection of the PPT (#33) on the 22-24-1 plane and “qp” is the point on the 22-24 axis where a normal to this axis passes through the PPT (#33).
- α_{33} as the 24-22-ppt angle in the 22-24-1 plane.
- β_{33} is the PPT angle 33-qp-ppt with respect to the 22-24-1 plane, with positive angles toward the lateral annular marker (#18).
- LPC33 as the #22 to qp distance.
- RPC33 as the #qp to PPT(#33) distance

Note that LAC31, RAC31, and β_{31} describe the APT (#31) in a cylindrical coordinate system (defined by 22-29-1), and LPC33, RPC33, and β_{33} describe the PPT (#33) in another cylindrical coordinate system (defined by 22-24-1).

An important finding demonstrated in Figures 3.5a and 3.5b is that RAC31 and RPC33, the radial components of their respective cylindrical coordinate systems, are nearly constant. This indicates that the two coordinate systems just constructed (using 22-29-1 and 22-24-1) provide axes of symmetry around which the papillary tips exhibit almost pure rotation. This tends to justify our chordal thread assumption used to derive these coordinate systems. Further, whether or not this assumption is valid, these coordinate systems reduce the very complex papillary tip dynamics in 3D space to simple rotations around anatomically definable LV axes. This is important to allow us to gain a greater understanding of the role of these papillary muscles with respect to the mitral valve within the LV chamber.

We next explore some of the implications of the data in Figures 3.5a and 3.5b, observing that:

- Papillary tip motions can be almost completely characterized as a rotation around their respective trigone axes (β_{31} around 22-29 and β_{33} around 22-24, both plotted in red). This rotation follows LV flow (actually, more properly, EDV), not pressure, becoming increasingly positive during LV filling and increasingly negative during LV ejection.
- The rotation of the papillary tips (β_{31} , β_{33}) is least at mitral valve opening (MVO), but always $> -7^\circ$ (i.e., very near the fibrous annular -LV planes), increases rapidly during diastolic filling to $\geq 0^\circ$ during diastole, and is always positive at mitral valve closure (MVC). This is important and will be discussed in subsequent chapters, but for now we only point out that large, negative β 's would place the papillary tips into LV outflow tract territory.
- Because papillary tip motions can be almost completely characterized as a rotation around their respective trigone axes, and their chordal distances to the fibrous annulus vary so little (without buckling), this implies that the strut chords are always in tension and that this tensile force is exerted:
 - by the anterior papillary muscle in the APT-LFT-SH plane (shown in red in Figures 3.4a, b, and c), directed in the narrow range between the force vectors labeled as F1 and F2 in Figures 3.4a, b, and c, and
 - by the posterior papillary muscle in the PPT-RFT-SH plane (shown in red in Figures 3.4a, b, and c) and directed in the narrow range between the force vectors labeled as F3 and F4 in Figures 3.4a, b, and c.
- We know something about this force. Salisbury, et al.¹, implanted force transducers in series with canine strut chordae and showed that strut chordal force was always tensile throughout the cardiac cycle, with a maximum of 25-75 gm and a minimum during diastole of about 12 gm. Van Rijk-Zwikker et al.² showed that strut chordae remain under tension throughout the cardiac cycle. Nielsen, et al.³, also implanted force transducers in series with ovine strut chordae and showed that maximum force was about 0.5-0.9 N ($\cong$ 50-90 gm), in agreement with Salisbury, et al.¹ It is important to emphasize that these are very small forces, approximately an order of magnitude less than the force produced by systolic pressure on the surface of the anterior leaflet. So, at this point, we have a good estimate of the magnitude of strut-chordal force component and now have a fairly precise estimate of its vector orientation throughout the cardiac cycle, as well.
- Marker #3 is the closest LV marker to the anterior papillary tip marker (#31). Comparing D2203 in Figures 3.5a and 3.5b with D2231 in Figures 3.3a and 3.3b, note that the variation in distance (D2203) throughout the cardiac cycle from marker #3 to the SH (#22) is more than 4 times that of the variation in distance D2231 from the anterior papillary tip (#31). Likewise, Marker #9 is the closest LV marker to the posterior papillary tip marker (#33). Comparing D2209 in Figures 3.5a and 3.5b with D2233 in Figures 3.3a and 3.3b, note that the variation in distance (D2209) throughout the cardiac cycle from marker #9 to the SH (#22) is also more than 4 times that of the variation in distance D2233 from the anterior papillary tip (#33). This strongly suggests that the bodies of the papillary muscles must serve as springs with variable spring constants that couple the large movements of the LV myocardium relative to the SH (#22) to the almost invariant distances of the papillary tips (#31 and #33) from the SH. As the LV fills in diastole and the papillary tips rotate around their trigone hinges and thereby increase their inter-papillary tip distance (D3133, Figures 3.3a and 3.3b), these springs must stretch because D2203 and D2209 increase during filling, but D2231 and D2233 are constant. As the LV empties during systole, the springs must shorten because D2203 and D2209 are gradually shortening (and wall thickness is increasing, as well, throughout systole), but D2231 and D2233 remain constant.

In summary, then, we can liken the papillary tips (#31 and #33) to the tips of chordal “wings” (the red triangles in Figures 3.4a, b, and c) flapping around their attachments to their individual trigonal axes (22-29 and 22-24), with a simple rotation toward the lateral mitral annulus (#18) during LV filling, and a simple rotation away from the lateral mitral annulus (#18) during LV ejection. Each wingtip is attached to a continuously stretched papillary spring anchored at one end in the LV wall and pulling to maintain tension in the strut chordae at the other, thereby maintaining the papillary tips at a constant distance from the central fibrous annulus saddlehorn (#22) as the LV myocardium stretches and contracts throughout the cardiac cycle. The criteria leading to these dynamics set rather stringent limits on the location of the papillary muscle tips within the LV chamber. This could have implications with regard to fetal heart development.

But what are these struts doing? Their weak tension, along with their orientation, just about precludes any role for these struts as important factors in generating LV pressure, reducing LV dimensions to aid ejection, or holding the anterior leaflet steady against high systolic pressures. We begin to address this question in the next chapter.

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CHAPTER 04 ANTERIOR LEAFLET TRAMPOLINES

In Chapter 03 we asked what the anterior and posterior strut complexes were doing. In this chapter, we explore one of their likely functions. In future chapters, we examine additional functions.

A trampoline is a device that stretches a material taut with forces from peripheral radial springs. Here, we suggest that one of the functions of the anterior and posterior strut complexes is to stretch two anterior leaflet regions into a specific taut configuration at a specific time in the cardiac cycle.

Figure 4.1 displays data from a representative beat from heart H1 to illustrate these two regions (contained within the red outlines superimposed on the anterior (ANTERIOR) and posterior (POSTERIOR) halves of the anterior leaflet) and the time interval (from the onset of rapid left ventricular pressure rise (LVPO, top row) to the time of mitral valve closure (MVC, bottom row)). Leaflet color coding shows the displacements (mm) above (red) or below (blue) the planes defined by the Saddlehorn (#22), LFT (#29), and APT (#31) for the ANTERIOR half of the leaflet (left column), and the Saddlehorn (#22), RFT (#24), and PPT (#33) for the POSTERIOR half of the leaflet (right column). Note that, in spite of the much greater displacements of the leaflet edges, the anterior leaflet regions associated with the strut chordae (approximated by the areas contained within the red line boundaries) are maintained within roughly ± 1 mm of these respective planes immediately before the onset of rapid left ventricular pressure rise.

Figures 4.2a, b, and c show these same data for representative beats from hearts H1-H6 at the times of LV peak inflow (top row), onset of rapid LVP rise (second row), mitral valve closure (third row), and LV peak outflow (bottom row). As in Figure 4.1, in these hearts the two regions associated with their respective strut chordae are very little displaced from these respective chordal planes at the onset of rapid LVP rise and mitral valve closure.

These findings lead us to suggest that the strut chords, coupled with their trigone regions, serve to provide sufficient traction to guide these two regions of the anterior leaflet into prescribed geometric configurations immediately prior to the onset of the rapid LVP rise at the beginning of each beat.

Recall that Salisbury et al.¹ showed that this traction is about 12 grams (0.12N) during diastole, with the struts never slacking. While this force is so small as to seem almost negligible, it is sufficient to pull these regions of the leaflet into these specific positions during diastasis when there are few other forces on the anterior leaflet; LVP is low, the valve is open (with nearly the same pressure on both anterior leaflet faces), and LV inflow is almost zero. The idea of such an “equilibrium” diastolic leaflet position associated with chordal traction is not new. It has been a classic subject of investigation, as summarized many years ago by Binkley et al.² What is new here is the idea that this traction sets the geometry of specific regions of the anterior leaflet into a specific geometric configuration just before the valve closes.

What is the significance of guiding these regions into this specific geometry? We explore an answer to this question in the next two chapters.

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Figure 4.2c. Data from hearts H5 (left two columns) and H6 (right two columns). Anterior leaflet displacement (mm) above (yellow-red) or below (green-blue) planes defined by the saddlehorn marker (#22), LFT marker (#29), and APT (#31) for the Anterior half of the leaflet (first and third columns), and the saddlehorn marker (#22), RFT marker (#24), and PPT (#33) for the Posterior half of the leaflet (second and fourth columns). Black lines represent a first approximation of strut chord force vectors from the trigone region to the papillary tips (APT on the left, PPT on the right). Top row=time of peak LV inflow; second row=onset of rapid LV pressure rise; third row=time of mitral valve closure; bottom row=time of LV peak outflow.

CHAPTER 05 ANTERIOR LEAFLET MOBILITY

In Chapter 04 we explored the displacements of the two anterior leaflet regions near the trigones associated with the APT-LFT-SH and PPT-RFT-SH planes and found that, at ED, these regions are nearly contained within these planes. In this chapter, we pull back and look at displacements throughout the cardiac cycle of the entire anterior leaflet, this time with respect to a plane formed by the saddlehorn and the two papillary tips (i.e. APT-SH-PPT).

These displacements were quantified by defining, for each frame in each heart, an APT-SH-PPT (#31-#22-#33) plane containing the X-Y basis vectors in a Euclidian reference system with positive Z defined toward the left atrium and negative Z toward the LV. For each beat, a mid-systolic frame (fs) was defined, and the Z-coordinate of each marker ($Z(m,fs)$) obtained for that frame (this was not a critical time-choice because the leaflet marker Z-coordinates were virtually unchanging throughout systole). During the following diastole, the frame (fd) containing the maximum excursion of the central meridional edge marker (#38) was identified and the Z-coordinate of each marker ($Z(m,fd)$) obtained for that frame. The total displacement for each marker during LV filling was then computed as $\Delta Z(m) = Z(m,fs) - Z(m,fd)$, which was positive if the displacement of that marker was towards the left atrium and negative if the displacement of that marker was towards the left ventricle during LV filling.

Figure 5.1 maps these total displacements for the six hearts (H1-H6). As expected, the leaflet edge is highly mobile, with displacements of up to 15mm during opening. What is new here, however, is the demonstration that the annular half of the leaflet has severely restricted mobility, with excursions of only a few mm throughout the entire cardiac cycle. The picture that emerges is that of a quite immobile anterior leaflet hinge region, with a highly mobile edge that is responsible for most of the leaflet opening motion. This was previously demonstrated for the central anterior leaflet meridian in Karlsson, et al.¹, but is shown here to hold for the entire leaflet.

Figures 5.2A-F illustrates this leaflet motion for 8 time-points from diastole to systole for each heart H1-H6, as viewed edge-on from the LFT to the RFT. Leaflet edge mobility is seen to be in sharp contrast to the almost immobile annular region of the anterior leaflet.

Interestingly, the leaflet annular region between the two strut trampolines seems just as immobile as the trampoline regions throughout the cardiac cycle. We explore some implications of this finding in the next chapter.

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CHAPTER 06 ANTERIOR LEAFLET CURVATURES

Anterior leaflet circumferential and radial curvatures were quantified in the six hearts as described in Appendix C. In brief, for each frame a best-fit plane was fit to all the anterior leaflet markers, including the trigonal hinge markers. Coordinate X-Y basis vectors were established in this plane and radial curvature was defined from the radius of a circle passing through the X-Z coordinates of radial marker triplets in this coordinate system (roughly perpendicular to the line connecting the LFT-RFT markers) and circumferential curvature defined from the radius of the circle passing through the Y-Z coordinates of circumferential marker triplets (roughly parallel to the line connecting the LFT-RFT markers). As defined in this fashion, positive curvature was concave to the LV, negative curvature was convex to the LV.

Figures 6.1A and 6.1B plot these radial and circumferential anterior leaflet curvatures for all beats in hearts (H1-H6). Note that when the mitral valve is closed:

- The circumferential trigone leaflet hinge (markers #29-#22-#24), circumferential leaflet belly (markers #50-#41-#53), and radial leaflet central edge (#40-#39-#38) always have concave curvature to the LV, and
- The central radial leaflet annulus (markers #22-#41-#40) and radial belly (#41-#40-#39) always have convex curvature to the LV.

Figure 6.2 illustrates these regions with consistent curvature in the closed valve as gray lines superimposed on the systolic geometry of the anterior leaflet of heart H3.

We think that this is an important function of the strut chordae; *e.g.* to set the annular half of the anterior leaflet into a specific initial 3D geometric configuration (stiff hyperbolic paraboloid “saddle” shape, radially convex, circumferentially concave to the LV) at the time of the initial systolic increase of LVP. Why is this so important?

In our finite element studies of the anterior leaflet,¹ we found that if our initial condition for the shape of the anterior leaflet was flat or prolapsed (both circumferentially and radially concave to the LV), then the onset of left ventricular pressure loading produced both radial and circumferential tension and the leaflet tended to “balloon” into the left atrium. If, however, we started with the anterior leaflet in a “saddle” shape (radially convex, circumferentially concave to the LV), then the onset of left ventricular pressure loading on the ventricular surface of the leaflet produced an offsetting combination of radial compression and circumferential tension that dramatically decreased load-induced leaflet deformation. Architects have recognized this property of hyperbolic paraboloids for many years. This shape was recently utilized in the roof design for the Velodrome for the 2012 London Olympics. Levine *et al.*² have also invoked this shape in their classic study of the mitral annulus.

What we describe here, however, is considerably different than the boundary conditions involved in architectural roof design and has almost nothing to do with the mitral annulus. The anterior leaflet isn’t a complete saddle shape. As can be appreciated in Figure 6.2, only the leaflet annular and belly regions assume this shape, the leaflet edge does not.

Thus, what we propose is that the curved stiff region between the trigones sets the circumferential concavity of the anterior leaflet at and near the hinge, while supporting the leaflet region between the saddlehorn and the trigones much like a drumhead. Immediately before the onset of left ventricular pressure rise, the strut “trampolines” pull the leaflet on either side to extend this circumferential leaflet concavity further out into the leaflet, while simultaneously acting to pull the leaflet belly against the

drumhead region, thereby extending the radial convexity of the leaflet further out into the belly region. The annular leaflet region between the “trampolines”, although not directly supported by the strut chordae, is tensed by the opposing forces directed toward the APT and PPT. Thus, roughly, the annular half of the anterior leaflet is formed by the very small forces in the strut chords into a taut “saddle” shape at the beginning of every beat. The thickened region near the hinge in Figures 3.2A, B, and C may serve as an anatomical base for this stiff structure; it has the proper shape and has multiple strut chord insertions.

This proposal regarding the function of the strut chords finds support in the second-order chord cutting experiments of Rodriguez et al.³ When they divided the major strut chords, the compound radial curvature of the anterior leaflet shape during systole was preserved, but the circumferential curvature was altered, and in some cases, even reversed.

At the onset of left ventricular pressure increase at the beginning of each beat, with a proper saddle shape, these annular and belly regions lock into position as a nearly-rigid body during systole. This rigid section of the anterior leaflet serves to anchor one side of the more mobile leaflet edge regions that are supported at their edges, at least in part, by primary chords.

We will have much more to say about the systolic rigidity of the anterior leaflet in later chapters, even demonstrating a burst of extra leaflet stiffness that occurs during IVC in addition to the very stiff *in vivo* leaflet material properties. But we'll close this chapter with a homely example illustrating the type of rigidity we are invoking for the annular half of the anterior leaflet.

Figure 6.3 shows an inverted water pitcher, with its saddle-shaped pouring lip which we here take as an analog of the annular half of the anterior mitral leaflet. Note that if pressure (LVP) is applied to the undersurface of the lip, this compresses the belly of the lip (COMPRESSION), while tending to rotate the lip about its base (the “TRIGONE REGION”) and thereby put the edges of the lip in tension (TENSION). Not illustrated is the circumferential tension, normal to the compression arrows, that will be created by the LVP loading. The reason that the lip holds its shape under load, cantilevered into space, is that its stiff spout is anchored to a solid support, the pitcher itself, against which these tensile and compressive forces can act. We suggest that the rigid trigone region provides a similar solid support for the stiff annular half of the anterior leaflet. The strut chords, however, must draw the anterior leaflet into this hyperbolic paraboloid configuration just at the beginning of left ventricular pressure rise in order to insure that the anterior leaflet, less than 2 mm thick, can withstand the full pressures generated by the left ventricular cardiac muscle that is more than 5 times this thickness, without the leaflet becoming, essentially, an aneurysm.

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Figure 6.3. Illustration of a cantilevered structure mimicking the geometry of the annular portion of the anterior leaflet.

CHAPTER 07 ANTERIOR LEAFLET CHORDAL SAFETY NET

In Chapters 03-06 we provided evidence that one function of the strut chords was to set the annular half of the anterior leaflet into a specific initial 3D geometric configuration (stiff hyperbolic paraboloid “saddle” shape, radially convex, circumferentially concave to the LV) at the time of the initial systolic increase of LVP, after which the leaflet becomes locked into this rigid 3D configuration by LVP loading throughout the rest of systole. In this chapter, we provide evidence for another important role for the strut chordae, namely, to prevent the anterior mitral leaflet, particularly its leading edge, from encroaching beyond a certain point into the LV outflow tract during LV filling.

Figure 7.1 displays the distance between the anterior leaflet edge markers #38, #43, #44, #45, and #46 and a plane formed by the marker triplets APT-SH-PPT (#31-#22-#33) during a representative cardiac cycle for each of the six hearts (H1-H6). If, by definition, we arbitrarily consider the APT-SH-PPT plane as a divider between the LV inflow and outflow tracts, then if the distance from this plane to an edge marker is positive, this edge site will be considered in the LV inflow region; if negative, the site will be considered in the LV outflow region.

If the anterior leaflet edge regions were to protrude sufficiently into the LV outflow region at the beginning of each beat, then the rapidly rising LVP could (catastrophically) drive the anterior leaflet toward the LV septum (toward valve opening), rather than away from the LV septum (toward valve closure). This is the basis for the systolic anterior motion (SAM) complication that can follow mitral valve repair operations.

Figure 7.1 shows that in hearts H1-H6 the leaflet edges are driven briefly as much as 10 mm into the outflow tract region (so-defined) by the rapid flow accompanying maximum early LV filling. As such early filling wanes, however, the leaflet edges tend to drift back into the inflow region, driven perhaps by vortices behind the leaflets and/or other flow fields, as well as the continuous small pull on the leaflet belly by the strut chords bringing the leaflet back toward closure. Any subsequent A-wave filling pulse will drive the leaflet edges back towards (and sometimes into) the outflow tract region.

Table 7.1 shows the position of each edge marker for the frame corresponding to the onset of LV rapid pressure rise for the beats shown in Figure 7.1. Note that the mean distance was uniformly positive,

TABLE 7.1	EDGE MARKER DISTANCE (mm) TO APT-SH-PPT PLANE AT LVP ONSET				
HEART	Z38	Z43	Z44	Z45	Z46
H1	7.2	1.1	2.4	6.2	4.3
H2	3.5	2.7	3.4	5.1	2.3
H3	0.7	0.6	-0.3	2.0	-0.9
H4	0.6	0.8	1.4	0.7	-1.6
H5	2.8	4.6	6.3	1.9	0.0
H6	0.6	0.5	1.3	0.9	-2.7
HIGH	7.2	4.6	6.3	6.2	4.3
LOW	0.6	0.5	-0.3	0.7	-2.7
MEAN	2.6	1.7	2.4	2.8	0.2

with only 4 of 30 regions dipping a few mm into the outflow region at this time. The greatest excursion into the outflow tract was -2.7 mm by H6 marker #46, although H3 dipped briefly into outflow tract

territory during IVC, at the onset of LV rapid pressure rise. Thus, the physical network of taut strut chords, along with the prevailing flow patterns inside the LV, appear to provide conditions that assure that the anterior leaflet edges remain in the inflow region, thus will swing towards closure when left ventricular pressure begins to increase at the beginning of each beat, with the resulting trace regurgitant flow driving the edges on toward the closed position.

We ascribe the bulk of this safety net function to the secondary (strut) chordae, rather than the primary (edge) chordae because of the data in Figure 7.2 showing the distances 3143, 3144, 3345, and 3346 between the APT marker (#31) and two anterior leaflet edge markers (#43 and #44), and the PPT marker (#33) and two anterior leaflet edge markers (#45 and #46) during a representative cardiac cycle in hearts H1-H6. Because these distances are spanned by edge chordae radiating from the papillary tips to the anterior leaflet edge either directly and/or as branches from strut chordae, we refer to them here as “chord lengths”. Note that such chord lengths are not reduced significantly as left ventricular pressure drops from high systolic values to low diastolic values during IVR, strongly suggesting that such chordae, are stretched very little by maximum systolic LVP. Thus, rather than shortening as LVP falls during isovolumic relaxation, they would buckle, unlike the strut chords that have been shown to be in continuous (albeit small) tension.

If the opening leaflet swung open widely during diastole and its excursion was to be limited by the primary chordae, we would expect to see the chord lengths in Figure 7.2 (after buckling at MVO) rapidly re-lengthen during rapid filling back to their systolic lengths. This is illustrated schematically in Figure 7.3, where an initially taut edge chord (red, dashed) from a papillary tip (PT) to an anterior leaflet edge (S) during systole, buckles at diastolic anterior leaflet edge position D1 (blue, dashed), then re-lengthens to its systolic length if the anterior leaflet edge continues opening to position D2 where its excursion is limited by the re-lengthened chord (green, dashed). We see such re-lengthening behavior in only one region, 3144, in one heart, H3, and even this only partially, as this chord does not achieve its full systolic length during diastole. Thus, as only 1 of 24 sites in these 6 hearts exhibited behavior that could be ascribed only partly to primary edge chordae, we conclude that the important safety net keeping the anterior leaflet edges out of the outflow tract during diastole involves the strut chordae, not the buckled primary edge chordae.

Further evidence as to why the primary chordae almost certainly do not limit anterior leaflet edge excursion can be seen in Figures 5.2A-F. Note, in these figures, that the widely open anterior leaflet becomes almost planar, with the APT and PPT sites nearly lying in this plane. For the primary chords to limit anterior leaflet edge excursion, anterior leaflet rotation (clockwise in Figures 5.2A-F) would have to be much greater than we have observed in these experiments. Referring to Figure 7.3, we typically see the anterior leaflet edge suspended in a line between the SH and the PT, as in D1, virtually never see the anterior leaflet edge continue to open to position D2, *i.e.*, widely into the outflow tract, where its excursion would be limited by primary chords. That is not to say that the primary chords never limit anterior leaflet edge excursions, only that this is not their normal role...but they could be counted on to serve this role in possibly extreme conditions.

CHAPTER 08 ANTERIOR LEAFLET SHAPES

Figures 8.1A-F display the anterior leaflet shape in each of the six hearts (H1-H6) during six key times during a representative cardiac cycle in each heart: T1 at the time of peak LV diastolic inflow; T2 at the onset of LVP increase preceding IVC; T3 at MV closing; T4 at the time of peak LV systolic outflow; T5 as MV is just beginning to open; and T6 a few frames after T5 at a time of maximum leaflet opening shape change.

Computational details are given in Appendix C, however, briefly, for each frame, a best-fit plane to all the anterior leaflet markers was defined, then this plane was clamped to an Euclidian X-Y plane, with +Z upward toward the left atrium, allowing visualization of leaflet shape independent of leaflet rotation. With this display, rotation of the anterior leaflet with respect to the mitral annulus (denoted by filled large symbols) is observed solely as rotation of the annulus with respect to the fixed leaflet plane.

A line from the saddlehorn (Marker #22, red fill, black border) to the LV apex (Marker #1) is shown (thick black line) along with three edge chordae and one strut chord (thin black lines) for each half (anterior and posterior) of the anterior leaflet. A (green) line is drawn from the lateral annulus (Marker #18) to the central posterior leaflet edge (Marker #37) to allow visualization of valve opening and closing.

Figure 8.2 displays the view along the Z-axis (from the left atrium toward the left ventricle) with the best-fit anterior leaflet plane clamped to the X-Y axes for hearts H1-H6 during peak left ventricular systolic pressure. The color coding (colorbar to the right of each figure) shows the regional elevation (mm) above (red) or below (blue) this best-fit anterior leaflet plane. Also shown are the mitral annulus as viewed from this perspective and estimates of chordae from the anterior leaflet to the left and right papillary muscle tips. The left fibrous trigone is identified as Marker #29, the right fibrous trigone as Marker #24, the Saddlehorn (Marker #22) is just above the label, the central leaflet meridian is identified as Marker #38, and the central lateral mitral annulus as Marker #18.

Note that, during systole, the anterior leaflet takes on a hyperbolic paraboloid (saddle) shape that is important for leaflet stiffness. During diastole, the anterior leaflet flattens considerably and its free edge takes on very complex shapes. In the next few chapters we use this construct to examine the stability of anterior leaflet geometry during systole with the valve closed.

CHAPTER 09 ANTERIOR LEAFLET SYSTOLIC SHAPE INVARIANCE

Leaflet shape change in each heart was quantified by fitting (as described in Appendix C) a best-fit plane to all anterior leaflet markers for each frame (f) in the three consecutive beats studied. The distance (Z) from each anterior leaflet marker (m) to this plane in each frame $Z(f,m)$ was then obtained. A systolic average, $Z_{avg}(m)$, was then obtained for each leaflet marker using all frames from mitral valve closing (MVC) to opening (MVO) for all three beats. For each frame, and each marker, the difference $Z(f,m) - Z_{avg}(m)$ was then computed and squared. The square root of the mean of these differences for all markers was then obtained for each frame as $Z_{rms}(f)$.

Figure 9.1 plots $Z_{rms}(f)$ vs. Frame for the three consecutive beats in each of the six hearts (H1-H6) studied. Note that the full range of the ordinate is 0 - 1 mm in each graph. As expected, Z_{rms} during diastole is off this scale because the systolic shape of the anterior leaflet in the closed valve is far different than its shape in the open valve. Figure 9.1 shows that the systolic shape of the leaflet is remarkably constant throughout systole in each beat and exhibits remarkable beat-to-beat repeatability.

Table 9.1, tabulated from the data displayed in Figure 9.1, quantifies this systolic leaflet shape invariance and repeatability. For each heart (H1-H6) and each beat (B1-B3) the Z_{rms} values were obtained from frames MVC+1 (just after valve closure), MVO-1 (just before valve opening), and minimum systolic Z_{rms} (Z_{rms} MIN). Note that:

- Z_{rms} MIN had a mean three-beat value of 0.1 mm (this is just at the resolution of our measurement system) with a total range for the three beats of 0.1 - 0.2 mm. Thus, anterior leaflet shape is highly repeatable from beat-to-beat.
- Z_{rms} at MVC+1 had a mean three-beat value of 0.4 mm, with a total range of 0.3-0.5mm. Thus, the leaflet shape is within a few tenths of a millimeter (rms) of its systolic shape when the mitral valve has just closed, but before the aortic valve opens. This is the case over a wide range of pressures just after closure, from 46 to 83 mmHg, with a mean of 69 mmHg.
- Z_{rms} at MVO-1 had a mean three-beat value of 0.4 mm, with a total range of 0.2-0.5mm. Thus, leaflet shape is within a few tenths of a millimeter (rms) of its systolic shape when the mitral valve is just about to open after aortic valve closure. This is the case over a wide range of pressures just before opening, from 11 to 29 mmHg, with a mean of 22 mmHg.

Thus, the shape of the anterior leaflet appears to be virtually constant from aortic valve opening and throughout left ventricular ejection. Because the anterior leaflet is an important component of the LV outflow tract, this invariant shape will be important for efficient outflow patterns, as demonstrated by the computational fluid dynamic studies of Stevanella, *et al.*¹

One surprising feature of this near-invariance of anterior leaflet shape is that it is maintained throughout isovolumic relaxation until just before mitral valve opening. As shown in Figure 9.1 and Table 9.1, the mean systolic Z_{rms} is the same (0.4 mm) at just after mitral valve closing with a mean LVP of 69 mmHg as just before mitral valve opening at mean LVP of 22 mmHg. Thus, anterior leaflet shape changes very little over a wide range of left ventricular pressures. This suggests that systolic leaflet shape is achieved when LVP exceeds a fairly small threshold and doesn't change much as long as LVP continues to exceed this threshold, even though the left ventricle is undergoing considerable geometric changes during ejection, *e.g.* the distance between the papillary tips is changing by 30-60% (see Table 3.1). As will be seen in later chapters, the mitral annular dimensions also change considerably during isovolumic relaxation, but anterior leaflet shape holds virtually constant. It appears then, at least in

these six beating hearts, that the shape of the anterior leaflet in the closed valve is virtually independent of the dynamics of the mitral annulus, papillary muscles, and the left ventricular myocardium.

Figures 9.2A-F and 9.3 show the regional distribution of the Z-differences from the Z-values at maximum left ventricular pressures for selected frames from a representative beat in each of the six hearts, along with the LVP and FLOW data during that beat. Very small dimensional changes are displayed: the entire color coded region ranges from -1 mm below the values at LVPmax to +1 mm above these values. Note that:

- At the onset of LVP increase, the saddlehorn (SH) region is below (toward the LV chamber) its position at LVPmax, but about 30 msec later, at the time of mitral valve closure, it increases to within a few tenths of a millimeter from its systolic position and holds this position, not only throughout ejection, but throughout the pressure drop during almost all of IVR.
- At the onset of LVP increase, the trigones (LFT, RFT) are above (toward the left atrium) their positions at LVPmax, but about 50 msec later, roughly at the time of aortic valve opening, they decrease to within a few tenths of a millimeter from their systolic positions and hold these positions, throughout the bulk of ejection, rising again toward the left atrium as LVP falls during IVR in hearts H1 and H2, but virtually unchanging during the fall of LVP during IVR in hearts H3-H6. Thus, the trigones appear to be driven toward their systolic position by LVP during IVC, but a more complex set of factors drives them back to their diastolic positions during IVR. In any event, they assume their diastolic positions within 17 msec after mitral valve opening (MVO).
- At the onset of LVP increase, the leaflet belly is typically below (toward the LV) its position at LVPmax. During ejection, the leaflet belly tends to prolapsed very slightly (a few tenths of a millimeter) and continuously toward the left atrium, with the greatest change occurring in the last half of ejection. This is not a simple function of left ventricular pressure, however, because it occurs whether LVP is rising (H1-H3) or falling (H4-H6) during end ejection. It is possible that this reflects the time-varying loading conditions on the leaflet as the ventricle empties. It is additionally possible that this reflects the time-varying reduction in leaflet stiffness throughout systole that is discussed in Chapter 29.
- At the onset of LVP increase, the left leaflet edge (Marker #43) is typically within one millimeter of its position at LVP max, but after 30 msec it achieves a position within <0.5 mm of its position at LVPmax and holds this sub-millimeter position throughout ejection and during the full reduction of LVP during IVR.
- At the onset of LVP increase, the right leaflet edge (Marker #46) is within three millimeters of its position at LVP max, but within 30 msec thereafter it achieves a position within <0.8 mm of its position at LVPmax and holds this sub-millimeter position throughout ejection and during the full reduction of LVP during IVR.
- At the onset of LVP increase, the central, unsupported leaflet edge (Marker #38) is within three millimeters of its position at LVP max, but within 30 msec thereafter it achieves a position within <0.9 mm of its position at LVPmax and holds a sub-millimeter position throughout ejection and during the full reduction of LVP during IVR.

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Table 9.1 HEART	BEAT	FRAME	FRAME	Zrms(mm)	Zrms(mm)	Zrms(mm)	LVP(mmHg)	LVP(mmHg)
		MVC+1	MVO-1	MVC+1	MIN	MVO-1	MVC+1	MVO-1
H1	B1	22	40	0.38	0.19	0.45	83	28
	B2	58	76	0.37	0.19	0.47	82	28
	B3	94	112	0.35	0.18	0.48	82	23
H2	B1	24	41	0.54	0.19	0.43	68	24
	B2	60	77	0.49	0.2	0.45	70	23
	B3	96	113	0.47	0.2	0.46	72	22
H3	B1	30	51	0.28	0.1	0.33	74	19
	B2	78	99	0.31	0.12	0.33	73	21
	B3	126	147	0.34	0.12	0.27	72	23
H4	B1	17	37	0.38	0.1	0.21	55	29
	B2	60	80	0.3	0.1	0.21	76	19
	B3	102	122	0.31	0.11	0.21	75	19
H5	B1	23	44	0.35	0.09	0.24	46	29
	B2	63	84	0.29	0.11	0.29	57	24
	B3	102	123	0.28	0.12	0.2	48	28
H6	B1	18	42	0.3	0.13	0.46	70	11
	B2	63	87	0.28	0.1	0.44	70	11
	B3	108	132	0.28	0.11	0.41	70	11
MIN	mm			0.3	0.1	0.2	46	11
MAX	mm			0.5	0.2	0.5	83	29
MEAN	mm			0.4	0.1	0.4	69	22

Figure 9.1 H1-H6 anterior leaflet Zrms. LVP=Left Ventricular Pressure; MVC=Mitral Valve Closure; MVO=Mitral Valve Opening.

Figure 9.2C. H3 (nam18r03) representative beat. Color map (key, lower right) of difference (mm) in anterior leaflet Z-values for selected frames from Z-values at maximum left ventricular pressure (LVPmax). LVP=Left Ventricular Pressure; MVC=Mitral Valve Closure frame; MVO=Mitral Valve Opening frame; FLOW=Left Ventricular (LV) inflow. LVPmax at Frame=85. Red dots at LFT=Left Fibrous Trigone (Marker #29), SH=Annular "Saddlehorn" (Marker #22), and RFT=Right Fibrous Trigone (Marker #24). View from left atrium, normal to best-fit anterior leaflet plane in each frame. Scale: 10 mm bar under frame 97 figure.

Figure 9.3 H1-H6 Anterior leaflet Zrms values (mm) for selected leaflet regions during beats corresponding to Figures 9.2A-F. LVP(dashed black)=Left Ventricular Pressure/50 (mmHg); Z29 (Marker#29, Cyan)=LFT; Z22(Marker #22, yellow)=Annular Saddlehorn; Z24(Marker #24,blue)=RFT; Z40 (Marker#40, black)=Leaflet Belly; Z43(Marker #43, magenta)=Leaflet edge near LFT; Z38 (Marker #38, red)=Mid-Leaflet Edge; Z46(Marker #46, green)=Leaflet edge near RFT.

CHAPTER 10 ANTERIOR LEAFLET AREA

Anterior leaflet area was calculated using the Matlab algorithm given in Appendix C. For each frame in each heart, this algorithm fits a surface to all the anterior leaflet markers shown in Figure 1.2, tiles this surface with a fine mesh of rectangular elements with dimensions dx by dy , computes the area of each element as $dx \cdot dy$, then sums all these areas to arrive at the total leaflet surface area. Tests of this algorithm showed that it is capable of measuring the surface area of a half sphere to within 1%.

Figure 10.1 shows the anterior leaflet areas for each frame throughout three consecutive cardiac cycles in each of the six hearts. Note, in Figure 10.1, that:

- In each heart, leaflet area vs. time (frame) morphology is virtually identical from beat-to-beat. This suggests very little biological and computational randomness for this variable. The data in Table 10.1 support this point.
- Leaflet areas change very little during the entire time the mitral valve is closed. This is of particular interest because LVP changes considerably during IVR, but leaflet area remains relatively unaffected. Table 10.1 quantifies this change from the MVC+1 frame to the MVO-1 frame. During this interval, mean LVP falls from 69 to 22 mmHg, yet mean leaflet area changes only -1%. Further, this area change ranges from -7% to +4% in these six hearts, decreasing in some hearts, increasing in others. This is not the behavior of a simple tense elastic membrane responding to changes in pressure loading. These small area changes also set limits on leaflet strains, a subject that will be explored in the next chapter.
- The small leaflet area change during ejection is consistent with the concept, emphasized in previous chapters, that the anterior leaflet serves as a stable structural boundary for the LV outflow tract throughout systole.
- As will be discussed in a subsequent chapter, the dynamics of anterior leaflet area are not correlated with the dynamics of mitral annular area through the cardiac cycle, showing, once again, the independence of the anterior leaflet from other components of the mitral valvular complex.
- Finally, computing leaflet area during diastole is subject to considerable noise. We know the coordinates of the leaflet markers to within roughly 0.1 mm through the cardiac cycle, and hold the best-fit leaflet plane in a constant position in each frame, yet Figure 10.1 still demonstrates that the leaflet area calculation is very noisy during diastole. The reason this is such a noisy calculation during diastole is that the local curvature of the leaflet becomes so great (the leaflet even folds back on itself during some diastolic excursions) that it becomes impossible to define leaflet area with the markers spaced as they are in this study. If our arrays employed thousands of markers, perhaps much of this steep curvature could be measured, but even then it would be difficult to fit a spatial curve to regions that were folding back on themselves. It is important to understand how noisy the measurement of leaflet area is in diastole, because this is a measurement that is studied in a clinical context. Unlike diastole, however, leaflet shape is quite stable during systole and thus is thus amenable to reasonably accurate and reproducible area measurement.

TABLE 10.1 HEART	BEAT	FRAME F1 MVC+1	FRAME F2 MVO-1	AREA A1 AT F1 (mm ²)	AREA A2 AT F2 (mm ²)	% CHANGE 100*(A2-A1) /A1	LVP AT F1 mmHg	LVP AT F2 mmHg
H1	B1	22	40	625	601	-4	83	28
nac03r04	B2	58	76	625	593	-5	82	28
	B3	94	112	623	599	-4	82	23
H2	B1	24	41	510	490	-4	68	24
nam14r01	B2	60	77	519	487	-6	70	23
	B3	96	113	521	483	-7	72	22
H3	B1	30	51	610	599	-2	74	19
nam18r03	B2	78	99	619	602	-3	73	21
	B3	126	147	617	600	-3	72	23
H4	B1	17	37	483	488	1	55	29
nsa12r01	B2	60	80	482	489	1	76	19
	B3	102	122	486	493	1	75	19
H5	B1	23	44	592	583	-2	46	29
nac09r03	B2	63	84	587	590	1	57	24
	B3	102	123	591	583	-1	48	28
H6	B1	18	42	780	811	4	70	11
nas07r03	B2	63	87	779	809	4	70	11
	B3	108	132	780	809	4	70	11
LOW				482	483	-7	46	11
HIGH				780	811	4	83	29
MEAN				602	595	-1	69	22
MEDIAN				601	592	-2	71	23

CHAPTER 11 ANTERIOR LEAFLET STRAINS

In Chapter 10, we found that while the mitral valve was closed, anterior leaflet surface area was constant to within a few percent over a wide range of left ventricular pressures. In this chapter, we attempt to better understand the underlying basis for this very small systolic area change.

Stevanella *et al.*¹ analyzed anterior leaflet strains by finite element analysis in three ovine hearts that had the same marker array as six hearts (H1-H6) studied in this book. Five time-points (Figure 11.1) were identified during the time the mitral valve was closed: t_1 , mitral valve closure; t_2 , end IVC; t_3 , LVPmax; t_4 , the time when LVP mostly closely matched LVP at t_2 ; and t_5 , the sample immediately preceding mitral valve opening.

The undeformed reference frame for this analysis was taken at t_5 , as at this time the trans-leaflet pressure is both defined and minimum as can be seen by the nearly equal left ventricular and left atrial pressures at t_5 in Figure 11.1.

The results of this analysis are shown in Figures 11.2. A key finding of this study was that radial surface strains are largely *compressive* with increasing LVP (see Figure 11.2 right block where these small compressive strains are highlighted in black), while circumferential surface strains are largely tensile (note the absence of the black compressive zones in the left block of Figure 11.2). These compressive/tensile strains are mostly expected, given the fact that much of the anterior leaflet radial curvature is convex to the LV in the closed valve, thus compresses as LVP increases, while much of the circumferential curvature is concave to this chamber, thus stretches with LVP increase.

This strain pattern is consistent with the nearly constant anterior leaflet area shown over this same time interval in Chapter 10. If radial surface dimensions decrease and circumferential surface dimensions increase as LVP increases, then surface area, the product of these two dimensions will change less than if both radial and circumferential strains were of the same sign. In this regard, tensile circumferential strains were on the order of 1% in the annular and belly region of the leaflet, while radial strains were on the order of -0.2% in these regions. Again, these small (and offsetting) strains are consistent with a constant leaflet area in the closed valve. Further, they are consistent with the concept of an anterior leaflet that is very stiff throughout systole, remaining at nearly constant shape in the face of widely varying hemodynamic variables, as demonstrated in Chapter 9.

¹ Stevanella M, Krishnamurthy G, Votta E, Swanson JC, Redaelli A, Ingels NB, Jr. Mitral leaflet modeling: Importance of in vivo shape and material properties. *J Biomech.* 2011;44(12):2229-2235.

CHAPTER 12 MITRAL LV RELATIONSHIP

Figures 12.1-12.6 show the geometric relationships between the left ventricle and the mitral valve components for hearts H1-H6. The view is from the right fibrous trigone towards the left fibrous trigone, *i.e.*, from the posterior wall of the LV towards the anterior wall. The best fit anterior leaflet plane is clamped to the X-Y axis for both the top frame (maximum LV inflow) and the bottom frame (maximum left ventricular pressure). LV markers #1-4 and # 8-13 are subepicardial; septal markers #5-7 are endocardial. The outflow tract is at lower right in each figure.

Figure 12.5. LV-mitral valve relationship for heart H5. Top frame=Peak LV Inflow; Bottom Frame=LVPmax. View: from RFT to LFT. Best-fit anterior leaflet plane clamped to X-Y axis. Longitudinal Lateral (top)-Septal (bottom) LV (red); Longitudinal Anterior-Posterior LV (blue). Chordae from Anterior and Posterior Papillary tips (black). Central Posterior Leaflet (green). Mitral Annulus (black). Anterior Mitral Leaflet (color coded from blue, below, to red, above, best fit leaflet plane). Marker Sites (filled black circles). LV Basal, Equatorial, Apical cross-sections (black hoops). Outflow Tract, lower right. Scale in mm.

Figure 12.6. LV-mitral valve relationship for heart H6. Top frame=Peak LV Inflow; Bottom Frame=LVPmax. View: from RFT to LFT. Best-fit anterior leaflet plane clamped to X-Y axis. Longitudinal Lateral (top)-Septal (bottom) LV (red); Longitudinal Anterior-Posterior LV (blue). Chordae from Anterior and Posterior Papillary tips (black). Central Posterior Leaflet (green). Mitral Annulus (black). Anterior Mitral Leaflet (color coded from blue, below, to red, above, best fit leaflet plane). Marker Sites (filled black circles). LV Basal, Equatorial, Apical cross-sections (black hoops). Outflow Tract, lower right. Scale in mm.

CHAPTER 13 ANTERIOR LEAFLET LV POSITION

In Chapter 9 we showed that anterior mitral leaflet shape is maintained with sub-millimeter precision while the mitral valve is closed. In this chapter we assess the variability of the 3-D position of this rigid leaflet within the left ventricular chamber throughout ventricular ejection.

The Euclidian coordinate system employed for this assessment placed, for each frame (f), the saddlehorn marker (#22) at the origin, the LV apical marker (#1) on the $-z$ axis, and the lateral annular marker (#18) in the x - z plane. A three-beat systolic mean x -coordinate ($Xmean(m)$) for each leaflet marker ($m=15, 21-24, 29, 30, 38-53$) was obtained using all frames from LV outflow onset to LV outflow end for the three sequential beats. A three-beat systolic mean y -coordinate ($Ymean(m)$) and z -coordinate ($Zmean(m)$) for each leaflet marker were obtained in similar fashion. For each frame, and each marker, the distance

$$D(f, m) = \sqrt{(x(f, m) - Xmean(m))^2 + (y(f, m) - Ymean(m))^2 + (z(f, m) - Zmean(m))^2}$$

was obtained. The mean value of all leaflet distances for each frame was then computed as

$$Dmean(f) = \frac{1}{23} \sum_{m=1}^{23} D(f, m)$$

Figure 13.1 plots $Dmean(f)$ vs. frame for the six hearts H1-H6. The times of mitral valve closure, LV ejection onset, LV ejection maximum flow, and LV ejection end are identified in each graph. Note that the ordinate of each graph ranges from 0 to 1.2 mm.

Examination of the six graphs shows that leaflet position within the left ventricular chamber for each heart exhibits sub-millimeter reproducibility throughout ejection in each beat and from beat-to-beat for three sequential beats. Table 13.1 quantifies this reproducibility, with only one heart (H3) displaying a variation of 1.1 mm at one instant (outflow onset), while this heart at other instants, as well as the other hearts at all instants exhibited sub-millimeter 3D positional stability within the LV chamber.

Thus, we can now conclude that, not only does the anterior mitral leaflet maintain a rigid shape in the closed mitral valve, but this rigid shape is maintained in a fixed position in the left ventricular chamber throughout ejection, in spite of the fact that the papillary muscles are moving continuously inward over this interval. This is likely to be important to LV outflow, as the anterior mitral leaflet sets an important boundary for the LV outflow tract.¹

1. Dimasi A, Cattarinuzzi, E., Stevanella, M., Conti, C.A., Votta, E., Maffessanti, F., Ingels, N.B.Jr, Redaelli, A. Influence of mitral valve anterior leaflet in vivo shape on left ventricular ejection. *CARDIOVASCULAR ENGINEERING AND TECHNOLOGY*. 2012;3:388-401

TABLE 13.1 HEART	BEAT	LV OUTFLOW ONSET FRAME	LV OUTFLOW MAX FRAME	LV OUTFLOW END FRAME	DMEAN (mm) OUTFLOW ONSET	DMEAN (mm) OUTFLOW MAX	DMEAN (mm) OUTFLOW END
H1	1	22	25	36	0.8	0.3	0.8
nac03r04	2	58	61	72	0.6	0.4	0.7
	3	94	97	108	0.8	0.4	0.8
H2	1	24	27	37	0.8	0.4	0.8
nam14r01	2	60	63	73	0.8	0.3	0.8
	3	96	99	108	0.8	0.4	0.7
H3	1	29	31	47	1.1	0.8	0.7
nam18r03	2	77	79	96	1.1	0.8	0.7
	3	126	128	144	1	0.7	0.7
H4	1	18	21	34	0.6	0.4	0.6
nsa12r01	2	61	63	76	0.5	0.4	0.4
	3	103	105	118	0.5	0.3	0.5
H5	1	24	31	42	0.8	0.2	0.4
nac09r03	2	64	69	81	0.6	0.2	0.4
	3	103	109	121	0.7	0.2	0.4
H6	1	19	22	35	0.7	0.4	0.4
nas07r03	2	64	69	80	0.6	0.2	0.4
	3	109	112	125	0.6	0.3	0.4
MIN					0.5	0.2	0.4
MAX					1.1	0.8	0.8
MEAN					0.7	0.4	0.6
MEDIAN					0.8	0.4	0.7

CHAPTER 14 ANNULAR SIZE VARIATION

In Appendix C we described the methods used to derive the best-fit planes to the annular and anterior leaflet markers. In this chapter, we visualize the valve along the Z-axis for the six hearts H1-H6, looking from the left atrium toward the left ventricle, clamping the best-fit annular plane to the X-Y axis. All scales are in mm.

Figures 14.1A and 14.1B show two time-samples during the cardiac cycle, the left panel at minimum annular area (during systole), the right panel at maximum LV inflow (during diastole) with the mitral annulus clamped to the X-Y axis. In these figures, the red symbols with black borders show annular marker positions with a cubic spline (thick black curved line) connecting these markers to delineate the mitral annular border. The larger black symbols show anterior leaflet edge marker positions, with lines connecting these markers to delineate the anterior leaflet border. Smaller black symbols show marker positions on the marker belly. A green line, drawn from lateral annular marker #18 to posterior leaflet edge marker #37 indicates the position of the central meridian of the posterior leaflet P2 scallop. Thin black lines, representing chordal connections, radiate from the anterior papillary tip (Marker #31, on the left) to the anterior edge and belly of the anterior leaflet and from the posterior papillary tip (Marker #33, on the right) to the posterior edge and belly of the anterior leaflet. A heavy black line is drawn from the septal annular marker (#22) at the top of each figure downward to the left ventricular apex (Marker #1, not shown). Anterior leaflet color coding maps the Z-coordinate of leaflet regions as being above or below (mm) the best-fit annular plane that is clamped to the X-Y axis. Color coding in the left (minimum annular area) panels is dark red (+3 to +4mm); red (+1mm); yellow (-1mm); green (-2mm); turquoise (-3mm); blue (-5mm); and dark blue (-6 to -9mm). Color coding in the right (maximum inflow) panels is dark red (+3 to +4mm); red (-1mm); yellow (-4mm); green (-6mm); turquoise (-10mm); blue (-14mm); and dark blue (-15 to -20mm).

At no time during the cardiac cycle does the edge or belly of the anterior leaflet bulge above the annular plane. The only portion of the anterior leaflet above this annular plane is the “drumhead” hinge region supported rather tightly by the rigid trigone collagen skeleton.

Note that the mitral annulus exhibits a large variation in size during the cardiac cycle and these dimensional changes occur rather uniformly throughout the entire contractile (non-trigonal) portion of the annulus. Note also that during maximum inflow (right panels) the anterior leaflet does not open completely, but presents a surface to partially deflect left ventricular inflow away from the outflow tract.

Figure 8.2 in Chapter 08 visualizes the gap that must be filled by the posterior leaflet scallops from the mitral annulus to the anterior leaflet edge in the closed valve.

CHAPTER 15 ANNULAR AND ANTERIOR LEAFLET AREA AND PERIMETER

Figure 15.1 shows mitral annular and anterior leaflet areas throughout sequential cardiac cycles for hearts H1-H6. The mitral annular area displayed in these figures is the projected annular area in the X-Y plane with the best-fit annular plane clamped to the X-Y axis for each frame. It is calculated as the sum of all the triangular areas from adjacent annular marker projections to the projection of the annular midpoint in that frame.

Note that annular area, greatest in diastole, begins to fall in all hearts well before the onset of left ventricular pressure rise and valve closure. This pre-systolic event is well-known and discussed in some detail in the next chapter. Here, we only mention that it results from annular contraction triggered by atrial excitation.

During systole, annular area may increase (H5, H6), decrease (H3, H4), or remain nearly unchanged (H1, H2). Tsakiris et al.¹ showed, long ago, that annular area excursions throughout systole depend on specific hemodynamic conditions. In the next chapter we explore some of the balance-of-force mechanisms that may underlie this finding.

Annular area begins to increase well before mitral valve opening. In these six hearts, annular area started to increase an average of 67 ms (range 17-100 ms) before mitral valve opening, as left ventricular pressure is falling rapidly during isovolumic relaxation. We also discuss some of the mechanisms likely to underlie this phenomenon in the next chapter.

Appendix C provides the algorithm used to compute anterior leaflet area for each frame. In all six hearts, as shown in Chapter 10, anterior leaflet area was found to be constant to within a few percent throughout ejection. That leaflet 3D geometry is rather constant during ejection (as we have shown in previous chapters) makes this measurement possible and perhaps reasonably reliable throughout ejection, provided we are not missing too many regions of unmeasured curvature with our sparse marker arrays. If leaflet geometry is not constant, as is true anytime the valve is open throughout diastole, leaflet area is almost impossibly difficult to measure at the present time. This can be seen as the reproducible, but very noisy leaflet area computation during diastole, at a time when external forces are highly unlikely to be changing leaflet area in the open valve. To measure leaflet area reliably throughout diastole will require measuring many hundreds of specific points on the leaflet surface with a 3D resolution of about 0.1 mm at each site. Any studies of leaflet stretching or growth involving leaflet area measurements during diastole in the beating heart must be treated with the utmost skepticism. The noisy area measurements observed during diastole in all six hearts in this study certainly reflect leaflet shape change, far more than leaflet area change, as the leaflet cracks like a whip, doubles back on itself, and flips curvatures on a ms time scale. The problem of diastolic leaflet area measurement is not unlike measuring the surface area of a flag waving and cracking in a stiff breeze blowing in random directions.

Note that leaflet and annular area time-histories are not correlated. This highlights an important fact, namely that the mitral annulus and anterior leaflet are almost completely uncoupled. The only place they are coupled is at the trigone hinge, and this hinge is almost unmoving. This independence of leaflet and annulus mechanics almost dooms attempts to link leaflet stresses or strains to annular shape and motion.

¹ Tsakiris AG, Von Bernuth G, Rastelli GC, Bourgeois MJ, Titus JL, Wood EH. Size and motion of the mitral valve annulus in anesthetized intact dogs. *J Appl Physiol.* 1971;30(5):611-618.

Figure 15.2 shows annular trigone perimeters, annular contractile region perimeters, and anterior leaflet edge perimeters for hearts H1-H6. Trigone-trigone annular perimeters (Markers #29-15-39-22-23-21-24 path) are almost invariant, as are anterior leaflet edge perimeters (Markers #29-42-43-44-38-45-46-47-24 path). Annular contractile perimeters (Markers #29-16-28-17-27-18-26-18-25-20-24 path), in contrast, are quite mobile, increasing in length from systole to diastole by some 12-19% with the same timing (described above) as mitral annular area change. Once again, note that variations in annular contractile perimeters and anterior leaflet edge perimeters are uncorrelated, further emphasizing the disconnect between the mitral annulus and the anterior mitral leaflet.

Figure 15.3 compares the length-variations throughout the cardiac cycle of 16 regions around the mitral annular perimeter. The markers defining these regions are numbered in Figure 15.4 and the annular regions defined by these markers in Table 15.1. In each heart, 3D marker coordinate data were used to compute regional lengths between each adjacent pair of annular markers around the annular perimeter. The three-beat mean and standard deviation for the length of each region was obtained, then the coefficient of variation (standard deviation divided by the mean) computed.

As can be seen in Figure 15.3, regional annular length changes displayed two peaks, a sharp peak for regions 3 and 4 in all hearts, and a more diffuse peak for regions 7 and 8. The annular location of the first peak, surrounding Marker #17, is shown in red in Figure 15.4; the second, surrounding Marker 19 in blue. We will discuss these regions further in future chapters, but will only indicate here that the first (red) region is close to the interface between posterior leaflet P1 and P2 scallops and the second (blue) region near the interface between posterior leaflet P2 and P3 scallops. The dynamics of these interface regions likely play a role in the peak length changes in these regions. Note the relatively lower length changes of regions 10-16 and 1, comprising the entire annulus from Marker #20 counterclockwise to Marker #16, strongly suggesting the influence of the relatively immobile trigone region. Note also the relatively lower length changes in regions 5 and 6, on either side of Marker #18, possibly reflecting the fact that this region includes the central meridian of the central posterior leaflet scallop.

Table 15.1																
REGION	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
MARKERS (FROM-TO)	29-16	16-28	28-17	17-27	27-18	18-26	26-19	19-25	25-20	20-24	24-21	21-23	23-22	22-30	30-15	15-29

MITRAL BOOK CHAPTER 16 LV-MITRAL ANNULAR COUPLING

The mitral leaflets hinges define the mitral annulus, thus changes in mitral annular dimensions impact leaflet opening, closing, and coaptation. At least six forces influence mitral annular dimensions, including left ventricular pressure, left atrial pressure, left heart blood flow, left atrial contraction, left ventricular contraction, and mitral chordae. In this chapter we postulate a working hypothesis concerning the impact of these forces on mitral annular dimensions throughout the cardiac cycle.

We begin by comparing, in Figure 16.1, the mitral annular septal-lateral dimension (distance between markers #22 and #18 (2218SLA) with the septal-lateral left ventricular basal dimension (distance between markers #07 and #13 (0713SLLV) for the six hearts (H1-H6). In Figure 16.1 we also compare the commissure-commissure dimension of the mitral annulus (the distance between markers #16 and #20 (1620CCA) and the anterior-posterior dimension of the left ventricle (the distance between markers #04 and #10). As can be seen, 1620CCA changes very little throughout the cardiac cycle, in spite of the much greater changes in the LV basal dimension 0410CCLV. Thus the annulus and the LV basal myocardium do not seem to be tightly coupled in the commissure-commissure direction. We next note that the changes in 2218SLA and 0713SLLV also suggest a near-independence of the annulus and LV basal myocardium in the septal-lateral direction, as well.

We know that the basal LV myocardium is in direct continuity with the mitral annulus, but this attachment must be very complex for the mechanics of the basal LV and mitral annulus to be so nearly independent. At this point we take a closer look at the junction between the left atrium, mitral annulus, and left ventricle. Fortunately, we have an excellent histological preparation of this atrioventricular

region, Figure 16.2, adapted from the excellent text by Antunes M.J. *Mitral Valve Repair* 1989, Page18, Figure 2.5, Verlag R.S. Schulz. In this micrograph, what appears to be a collagen tether (blue stain, red arrow) links the left atrial muscular wall (LAW), the left ventricular myocardial wall (LVW), and the posterior mitral leaflet (PL). A specialized basal myocardial region (red star, rough reddish surface) appears to provide a possible tendon-like attachment of this collagen tether to the basal LVW.

Many markers would be needed to fully describe the mechanics of this complex junctional region, but we have two markers (#18, #13, Figure 16.2) in good position to allow us to approximate these mechanics in the septal-lateral direction (we will discuss 13' later in this chapter). In the following analysis, we refer to the mitral annular "saddlehorn" as the location of marker #22, and compare the actual saddlehorn-lateral annular dimension (2218SLA) with the saddlehorn-lateral LV dimension (2213SHLV, Figure 16.1). If we assume the 3D displacement of marker #13 to be a reasonable surrogate for the LVW basal region marked by the red star in Figure 16.2, the distance 2213SLLV-2218SLA allows discussion of a hypothesized mechanism in terms of the variable stretch of a nonlinear collagen spring tether (red arrow) between #18 and the red star LVW region throughout the cardiac cycle.

Figure 16.3 displays the saddlehorn-lateral left ventricular dimension (D2213) as the fluctuation of the top of the black floating bar graph, the saddlehorn-lateral mitral annular dimension (D2218) as the fluctuation of the bottom of the black floating bar graph, the putative tether spring length (D2213-D2218) in green; and left ventricular pressure in red. D2213 (black floating bar graph top) behaves as expected, with a gradual reduction in this dimension as the LV empties during ventricular systole and a two-stage increase as the LV experiences E-wave and A-wave filling. D2218 (bar graph bottom) also behaves as expected, with a low fairly steady value during systole, followed by an increase at mitral valve opening, followed by a diastolic bounce between E-wave and A-wave filling, then a pre- and early-systolic reduction at mitral valve closure.

Although these are expected behaviors, they reflect a complex interaction between several time-dependent forces. Below, we postulate one way this interaction might play out:

- During EJECTION, the LV dimension (D2213) is continuously reduced as the stiff contracting myocardium contracts and blood flows out of the left ventricular chamber. During this period, the lateral mitral annulus continues to be pulled inward by left ventricular pressure acting on the ventricular surface of the posterior leaflets that are concave to the LV, an inward pull that is

Figure 16.2 Histological preparation of the atrioventricular junction showing a tendon-like structure (red arrow) linking the posterior mitral valve leaflet (PL), the left atrial wall (LAW), and ventricular wall (LVW). A specialized region (red star) may provide a tendon-like attachment to the basal LVW. Adapted from Antunes M.J. *Mitral Valve Repair* 1989, Page18, Figure 2.5, Verlag R.S. Schulz

limited in part by the interaction between the posterior leaflet pressing against the fixed, nearly rigid anterior leaflet and tension in the tether spring. As a result, the tether spring (green curve, Figure 16.3), maximally stretched at the onset of systole, is continuously shortening back toward its minimum length.

- During ISOVOLUMIC RELAXATION, D2213 holds rather steady, as the LV myocardial contraction and stiffness begin to wane, but D2218 begins to rise as LVP falls and the left ventricular pressure against the concave posterior leaflet wanes. This increase in D2218 is aided by residual tension in the tether spring. Depending on the interplay between the LVP and tether spring forces, in some hearts D2218 increases throughout IVR, in others, the D2218 increase is more sudden as LVP approaches its opening value. With increasing D2218, the posterior leaflet hinge region pulls away from the fixed anterior leaflet, flattening the posterior leaflet, although the anterior and posterior leaflets edges are still in contact and the valve hasn't opened yet.
- At MITRAL VALVE OPENING, left ventricular pressure falls to or below left atrial pressure, the anterior and posterior leaflets are forced open by this pressure gradient, and blood begins to flow rapidly from the left atrium into the left ventricle. This flow (along with some residual papillary muscle tension) forces both the anterior and posterior leaflets outward and, on the posterior leaflet, this force pushes the mitral annular hinge #18 region further away from the saddlehorn (#22), a push that is supplemented by a complimentary pull on the #18 region by the residual stretch in the LV tether spring which is immobile at this time on its ventricular myocardial end. Thus, just at the time of peak LV inflow, the mitral annulus is pushed (by the posterior leaflet) and pulled (by the tether spring) into its most widely open configuration, which has the desirable effect of allowing maximum inflow area for rapid early filling.
- IMMEDIATELY AFTER MITRAL VALVE OPENING, the tether spring is shortest and storing the least energy, which allows the now relatively-flaccid LV myocardium basal region to begin to expand without having to overcome significant tether spring force.
- During E-WAVE FILLING INCREASE, D2213 and D2218 both increase rapidly, thus the tether spring is stretched, but not maximally. This spring force, however, acts through the D2213 increase resulting from LV volume increase, and this force, along with the force resulting from the flow against the anterior face of the posterior leaflet continues to push the annulus open even more widely.
- During E-WAVE FILLING DECREASE, D2213 continues to increase, driven outward by the filling-driven LV volume increase which would tend to drag the mitral annulus outward *via* tension in the tether spring, but there isn't much tension in this spring because collagen is very compliant at low stretch. The waning LV inflow, however, exerts less outward force on the open posterior leaflets, thus this drop in outward force, coupled with the weak tether outward-directed force, allows the lateral mitral annulus to move slightly back toward the saddlehorn (#22).
- During A-WAVE FILLING INCREASE, the left atrial muscle has just been excited as reflected in the ECG p-wave and begins contracting, which tends to pull the lateral annulus toward the saddlehorn (#22). But this inward-directed force is offset by the outward directed force of the A-wave flow against the atrial side of the posterior leaflets. The tether spring is still not fully stretched, but its LV myocardial end is continuing to move away from the saddlehorn (#22), driven by LV filling, thus it also contributes to the small outward movement of the annulus and the annulus enlarges slightly.
- During E-WAVE FILLING DECREASE, the left atrial muscle is still actively contracting, which acts to pull the annulus toward the saddlehorn (#22). Further, the decrease in E-wave flow decreases the force on the atrial side of the open posterior leaflets, diminishing the outward force on the annulus. The atrial contraction thus overcomes this flow force and the annulus begins to

contract. The LV myocardial position, however, is now nearly constant (LV diastasis), thus annular contraction abruptly begins a rapid increase in the length of the tether spring, but this outward-directed spring force is no match for the contracting atrial muscle and the annulus continues to contract. Another possible annular contractile mechanism relates to the swinging toward closure of the posterior leaflets at this time, associated with LV flow patterns, with this ensuing leaflet rotation moving the junction (marker #18) closer to the saddlehorn (#22).

- At LEFT VENTRICULAR PRESSURE ONSET, the atrial muscle is still contracting which continues to force the annulus toward contraction. A small regurgitant flow from LV to LA as LVP rises also drives the leaflets rapidly toward closure. This backflow force, acting on the ventricular side of the posterior leaflets, acts to further contract the annulus, even though the valve isn't yet closed. Opposing this is the tether force acting to pull the annulus open toward its LV myocardial end that is fixed in position. But this tether force is insufficient to overcome the backflow force on the posterior leaflet coupled with atrial muscle contraction, thus the annulus continues to contract.
- At MITRAL VALVE CLOSURE, the atrial muscle is still contracting. The backflow force against the posterior leaflet is now replaced by a much greater force due to the greatly increased LVP acting on the ventricular side of the posterior leaflet. The tether spring is maximally stretched, but its pull toward opening is no match for atrial contraction combined with the LVP force against the posterior leaflet, thus the mitral annulus continues to contract.
- At END ISOVOLUMIC CONTRACTION, the atrial muscle is still contracting. Full systolic LVP now acts on the ventricular side of the posterior leaflets. Although the tether spring is maximally stretched, its tendency to pull the annulus open is overwhelmed by the atrial muscle contraction and, even more importantly, the larger LVP forces on the ventricular surface of the posterior leaflets that maintain the annulus at near-minimum size.
- At EJECTION ONSET, the atrial muscle continues to contract and LVP continues to drive the posterior leaflets toward closure, thereby maintaining near-minimum annular size. Although the tether spring is still maximally stretched, it still cannot drive the annulus outward. The potential energy stored in the tether spring may be employed to aid ejection and the cycle just described is repeated in the next beat, 100,000 times per day.

The length of the postulated tether spring from the LV base (Marker #13) to the posterior leaflet hinge (Marker #18) for hearts H1-H6 is indirectly characterized in Figure 16.3, as it is expressed as the difference D2213-D2218, where Marker #13 is considerably below the mitral annular plane in these hearts. Fortunately, an additional cohort of six hearts (F3, F4, F5, F7, F8, F9, see Appendix F), with similar markers, was available for analysis, with Marker #13 placed considerably closer to the mitral annular plane (nearly at the red star in Figure 16.2). The PowerPoint animations in Appendix F demonstrate the 3-D location of Marker #13 relative to the mitral annulus throughout the cardiac cycle. As a result, the tether length can be more directly estimated in these hearts simply from D1318 or D1326, whichever marker pair exhibits the least minimum dimension. This result is shown in Figure 16.4, which looks very similar to Figure 16.3. Thus, the indirect and semi-direct estimates of tether behavior appear to agree.

Two hearts in the F-series, F10 and F11 (see Appendix F animations), however, had particularly interesting Marker #13 locations, as it turned out that this marker had been placed in the junctional ring tissue surrounding the mitral annulus (roughly at site 13' in Figure 16.2). As can be seen in Figure 16.5, with this location of Marker #13, D2213' *increases* during systole and *decreases* during diastole, in concert with *left atrial* emptying and filling, just the opposite of D2213 that *decreases* during systole and *increases* during diastole, in concert with *left ventricular* emptying and filling. As a result, an additional potential tether is revealed, connecting the fibrous skeleton and the posterior leaflet hinge, as

schematically illustrated as spring S2 in Figure 16.6. This tether operates in opposite fashion (stretching during ventricular systole, shortening during ventricular diastole as shown in Figure 16.5) from the LV-posterior leaflet tether S1 (shortening during ventricular systole, stretching during ventricular diastole as shown in Figure 16.4), although both stay in tension throughout the cardiac cycle. This additional S2 tether can presumably act to help restrain the posterior leaflet hinge from moving too far inward during ventricular systole, as the leaflet is driven inward by the force of LVP on its concave ventricular surface.

The junctional region shown in Figures 16.2 and 16.6 is quite complex. The tissue labeled “Junctional Ring” in Figure 16.6 was once thought to consist of a fibrous skeleton surrounding the mitral valve, but detailed histological studies of human hearts by Angelini, *et al.*¹ showed that, although this was sometimes seen, it was the exception, with most hearts displaying a mixture of segments in which the left atrium, left ventricle, and posterior leaflets were inserted into a cord or simply met. Figures 1 and 3 of Angelini, *et al.*¹ are particularly helpful in illustrating this point. While the “Junctional Ring” tissue in Figure 16.6 must have some fibrous tissue capable of supporting forces associated with LA, LV, and leaflet dynamics, there is also a considerable amount of adipose tissue in this region; a region that must exhibit high electrical impedance such that atrial excitation does not break through to directly excite the LV basal myocardium with each beat.

We will have more to say regarding the balance of forces acting on the posterior leaflet hinge regions in Chapter 19 when we discuss the chordal attachments from the papillary muscles to the posterior leaflet hinges.

Interestingly, the LVP forces on the LV side of the posterior leaflets (arrows, Figure 16.6) are fully capable of creating and maintaining the reduced annular dimensions throughout ventricular systole, as demonstrated by Swanson *et al.*² who showed, *via* LV pacing, that such annular dimension reductions still occur and are maintained throughout left ventricular systolic beats not preceded by p-waves.

¹ Angelini A, Ho SY, Anderson RH, Davies MJ, Becker AE. A histological study of the atrioventricular junction in hearts with normal and prolapsed leaflets of the mitral valve. *Br Heart J*. 1988;59:712-716

² Swanson JC, Krishnamurthy G, Kvitting JP, Miller DC, Ingels NB, Jr. Electromechanical coupling between the atria and mitral valve. *Am J Physiol Heart Circ Physiol*. 2011;300:H1267-1273

Figure 16.4 Directly measured LV-“hinge spring lengths” for F3, F4, F5, F7, F8, F9. LVP=left ventricular pressure (mmHg). D2213=distance (mm) from saddlehorn marker (#22) to lateral LV subepicardial marker (#13). D2218, D2226=distance (mm) from saddlehorn marker (#22) to lateral mitral annular markers (#18 or #22). D1318, D1326 (“hinge spring length”)=distance (mm) from lateral LV subepicardial marker (#13) to lateral mitral annular markers (#18 or #26). Valve opening and closing frames identified by filled LVP symbols.

CHAPTER 17 MITRAL ANNULAR FLEXION

Itoh *et al.*¹ have pointed out that the mitral annulus can be considered as a hinged structure, with the hinge located roughly along a line between the left (Marker #29, LFT) and right (Marker #24, RFT) fibrous trigones. This hinge, separating the contractile and non-contractile portions of the annulus, can be seen in Figures 17.1 and 17.2 (see captions for the views displayed in these figures). Although the studies described here were conducted in different hearts and employed a different geometric approach to data analysis than those of Itoh *et al.*, the findings described here are consistent with theirs and should be considered as an extension of their findings which should be consulted for a very thorough discussion of this topic.

Figure 17.3 shows the changes in two angles, Φ_{X2218} and Φ_{225418} , during sequential cardiac cycles in hearts H1-H6. Φ_{X2218} is a tilt of the mitral annulus with respect to a reference system fixed within the left ventricular chamber. This angle is clearly influenced primarily by left ventricular myocardial contraction, ejection, and filling, not left ventricular pressure. Carlhall *et al.*² have shown how annular displacements of this sort contribute significantly to left ventricular filling and ejection. Figure 17.2 shows how this angle is greater in systole than diastole, supporting this view. In contrast, Φ_{225418} appears to not be significantly influenced by ejection and filling, but primarily by left ventricular pressure. Φ_{225418} , maximum at end diastole, falls precipitously with the rapid left ventricular pressure increase associated with IVC. Figure 17.2 shows that this rapid reduction in Φ_{225418} is produced by a displacement of site 54 (midpoint of the line from LFT #29 to RFT #24) to the left and down, presumably drawn to the left and down by elastic coupling to structures attached to the left and right fibrous trigones. Such displacement may serve to provide continuous tension in the contractile portion of the mitral annulus; much as pulling on the reins of a horse provides tension in the reins and tightens the bit. Note that in the discussion of Figure 2.5 it was pointed out that fibrous mitral annular length was minimum during diastole, rose steadily during ejection, then fell abruptly immediately after mitral valve opening, in concert with LV contraction, not LV pressure. This is consistent with the concept that the LFT and RFT are also being pulled apically by myocardial contraction. This appears analogous to the behavior of Φ_{X2218} , possibly reflecting a saddlehorn (Marker #22) held in place by left ventricular pressure and its aortic attachment, while outlying regions (Lateral Annular Marker #18, LFT Marker #29, and RFT Marker #24) are pulled down (apically) away from it. Also in the discussion of Figure 2.5 it was pointed out that the LFT-SH-RFT angle, maximum at end diastole, fell abruptly as LV myocardial contraction began, much like the LVP-induced behavior of Φ_{225418} during early systole. This suggests that this movement of LFT and RFT sites to the left and down, as in Figure 17.2, happens almost instantly as LVP starts to rise, without initially stretching the non-contractile annulus, which is likely to be important to help bring the lateral mitral annulus (with its attached posterior leaflets) toward the anterior mitral leaflet to facilitate valve closure. Then, once closure is accomplished, this early systolic LFT and RFT translation force is augmented by forces associated with myocardial shortening as ejection proceeds and helps maintain valve closure.

¹ Itoh A, Ennis DB, Bothe W, Swanson JC, Krishnamurthy G, Nguyen TC, Ingels NB, Jr., Miller DC. Mitral annular hinge motion contribution to changes in mitral septal-lateral dimension and annular area. *J Thorac Cardiovasc Surg.* 2009;138(5):1090-1099.

² Carlhall C, Kindberg K, Wigstrom L, Daughters GT, Miller DC, Karlsson M, Ingels NB, Jr. Contribution of mitral annular dynamics to LV diastolic filling with alteration in preload and inotropic state. *Am J Physiol Heart Circ Physiol.* 2007;293(3):H1473-1479.

Figure 17.1 Mitral annulus silhouette at ED for hearts H1-H6. Dimensions in mm. Cubic spline (blue) through non-contractile annulus Markers #29 (left fibrous trigone)-15-30-22 ("saddlehorn")-24-21-24 (right fibrous trigone). Cubic spline (red) through contractile annulus Markers #29 (left fibrous trigone)-16 (anterior commissure)-28-17-27-18 (lateral annulus)-26-19-25-20 (posterior commissure)-24 (right fibrous trigone). Marker #22 at origin (0,0,0), Z-axis from #22 to #01 (left ventricular apex), Marker #18 in X-Z plane. Site 54 at midpoint of 29-24 line segment.

Figure 17.2 Annular flexion triangles (vertices 22-54-18) during diastole (blue) and systole (red) for hearts H1-H6. View is from Marker #29 (left fibrous trigone) to #24 (right fibrous trigone) with Marker #22 at origin. Left and right fibrous trigones overlap at open circles.

Jensen *et al.*³ have provided important information regarding such potential systolic forces acting on the mitral annulus. They sewed a flat annuloplasty ring (instrumented with strain gages to measure bending forces about the saddlehorn, left and right commissures, and lateral annulus) to the mitral annulus in the beating porcine heart and found that systolic torques tended to bend the annulus from a flat configuration in diastole to the curved configuration shown by the dashed line in Figure 17.4.

Their finding, illustrated in Figure 17.4 is consistent with the findings of our marker studies shown in Figures 17.1-17.3, provided that we include the dynamics of the basal endocardial LV septal Marker #7 (shown in Figure 17.5) that is coupled to the LFT and RFT.

With this inclusion, our provisional explanation for this aspect of annular mechanics is:

- The saddlehorn region (Marker #22) is firmly attached to the main body of the collagen “skeleton” of the heart and further constrained by its attachment to the rather rigid aorta that is always subjected to at least diastolic arterial pressure. Thus the saddlehorn region is quite immobile relative to other annular regions.

³ Jensen MO, Jensen H, Nielsen SL, Smerup M, Johansen P, Yoganathan AP, Nygaard H, Hasenkam JM. What forces act on a flat rigid mitral annuloplasty ring? *J Heart Valve Dis.* 2008;17(3):267-275; discussion 275.

- Unlike the saddlehorn, however, the LFT and RFT regions are not as rigidly bound to the stiff collagen skeleton and continuously pressurized aorta; they are at the outer extremities of the collagen skeleton and exposed to the full range of LV pressure fluctuations in the outflow tract.
- The LV pressure rise and LV volume shifts during IVC dilates the outflow tract,⁴ increasing the distance between Markers #22 and #07, and increasing the tension in the outflow tract connections to the LFT (from Marker #07 to #29) and RFT (from Marker #07 to #24).
- This dilation and tension pulls the LFT and RFT laterally towards the interventricular septum and down towards LV apex, rotating and translating them both around the essentially fixed saddlehorn. This can be seen in the correlations between Φ_{225418} and (D2207-D2407) and (D2207-D2907) during systole in Figure 17.6 and the behavior of D2207, D2907, and D2407 during IVC in the summary Figure 17.7. Note that while both the LFT and RFT displace during IVC, the displacement of the RFT is typically considerably greater than that of the LFT, perhaps reflecting the left-right asymmetry of the attachments to the collagen skeleton and myocardium of these trigonal regions as can be seen in Figure 1.3. Figure 17.8 illustrates schematically how aortic root expansion is coupled to trigone displacements during IVC. As discussed in Chapter 22, both the magnitude and change of total left and right papillary forces are very small during IVC, thus chordal force is unlikely to underly these LFT and RFT displacements during IVC.
- The outflow tract dilation and tension appear to be the primary forces underlying the rotations of the LFT and RFT around the saddlehorn; the strut chords do not appear to participate meaningfully in these displacements as can be seen in the poor correlations between Φ_{225418} and (D2233-D2433) and (D2231-D2931 Φ) during systole in Figure 17.6.
- As indicated earlier in this chapter, these displacements of the LFT and RFT as LVP increases during IVC initially help pull the annulus toward the septum, thereby facilitating valve closure, these displacements are then firmly held throughout systole to provide continuous annular tension and help maintain leaflet coaptation.
- An additional force, from myocardial contraction as ejection proceeds, pulls the LFT and RFT toward the left ventricular apex and interventricular septum, while left ventricular pressure and aortic attachment hold the saddlehorn in a relatively fixed position, thereby increasing the tension in the LFT-SH-RFT collagen band and buttressing the effects of outflow tract dilation acting along almost the same force vectors.

A theme that we introduce here and attempt to support additionally in other chapters is that the annulus should not be considered as a continuous entity, rather as two interconnected almost independent parts. This is tacitly assumed in the terminology in this field when reference is made to the “contractile” portion of the annulus, as differentiated from the “non-contractile” portions of the annulus. The “non-contractile” portion of the annulus (which could be considered basically as an extension of the aorta into the LV) provides the fairly rigid hinge for the anterior leaflet, but has almost no connections to the posterior leaflets. The “contractile” portion of the annulus is tightly associated with the posterior leaflet hinges, but almost completely independent of the anterior leaflet. These two annular regions interact, of course, at the LFT and RFT regions, but the influence of trigonal region displacements seems likely to dwarf the influence of the contractile region displacements on trigonal region displacement. Considering these two annular regions as almost separate entities could have important implications in our understanding of valve physiology, and, importantly, potential approaches to valve repair and tissue engineering.

⁴ Rodriguez F, Green GR, Dagum P, Nistal JF, Harrington KB, Daughters GT, Ingels NB, Miller DC. Left ventricular volume shifts and aortic root expansion during isovolumic contraction. *Journal of Heart Valve Disease*. 2006;15:465-473.

Figure 17.5 Same views as H4 in Figure 17.1 during diastole (top) and systole (bottom), but with the addition of the basal endocardial LV septal Marker #7 coupled to the LFT (#29) and RFT (#24).

Figure 17.6 Mitral annular angle and flexion for hearts H1-H6. LVP=Left Ventricular Pressure; MVC=Mitral Valve Closure; MVO=Mitral Valve Opening; $\Phi 225418$ =Angle 22-54-18; Dxyy=distance (mm) from Marker xx to yy.

CHAPTER 18 ANNULAR&LEAFLET SHAPE AND PLANARITY

Annular shape change in each heart was quantified by fitting (as described in Appendix C) a best-fit plane to all annulus markers (#15-#30) for each frame (f) during the three consecutive beats studied. The distance (Z) from each annulus marker (m) to this plane in each frame $Z(f,m)$ was then obtained and the standard deviation of $Z(f,m)$ computed for that frame as $Z_{sd}(f)$. This process was repeated for just the contractile annulus markers (#16-#20; #24-#29). A systolic average, $Z_{avg}(m)$, was then obtained for all annulus markers using all frames from mitral valve closing (MVC) to opening (MVO) for all three beats. For each frame, and each marker, the difference $Z(f,m)-Z_{avg}(m)$ was then computed and squared. The square root of the mean of these differences for all markers was then obtained for each frame as $Z_{rms}(f)$.

Figure 18.1 plots $Z_{rms}(f)$ vs. Frame for the three consecutive beats studied in each of the six hearts (H1-H6). Note that the full range of the ordinate is 0 - 1 mm in each graph. At the beginning of each beat, the mitral annulus is rapidly driven towards its mean systolic shape by the increase in LVP during IVC, starting immediately with the rapid LVP increase, continuing during and after mitral valve closure, and reaching a minimum in mid-to-late systole. Figure 18.1 shows that the shape of both the mitral annulus and the anterior leaflet (previously shown in Figure 9.1) are remarkably constant throughout systole in each beat and both exhibit sub-millimeter beat-to-beat repeatability. Annular shape begins to be driven back towards its diastolic value as LVP falls during the last half of IVR but before mitral valve opening. During systole, annular shape is dictated principally by LV pressure, not LV volume. During diastole, annular shape is dictated principally by LV volume, not LV pressure.

Figure 18.2 shows that the complete mitral annulus (trigone region plus contractile annulus) increasingly flattens throughout diastole, reaching its flattest configuration at the onset of the LVP increase at the beginning of each beat. It immediately becomes more curved in concert with the rising LVP during IVC, reaching its maximum curvature in mid-to-late systole then begins to flatten again in mid-to-late IVR as LVP falls. The contractile annulus, however, is much flatter than the complete mitral annulus and exhibits less curvature change throughout the cardiac cycle. This behavior is consistent with the concepts discussed in Chapter 17, where the annulus is described as consisting of two (nearly) independent parts, a fairly rigid trigone region hinged at an acute angle to an almost flat contractile region. The change in complete annulus flatness throughout the cardiac cycle is thus seen to be brought about primarily by the relative rotation of the contractile annular plane with respect to a trigone annular plane.

Note, in Figure 18.2, that complete mitral annular and anterior leaflet dynamics exhibit similar time-courses during IVC and IVR, but these dynamics are poorly correlated during filling and ejection. This emphasizes a point to be made repeatedly in this book; that the mitral annulus and anterior leaflet are almost independent entities, joined only at the trigonal hinge region around which both the annulus and anterior leaflet rotate.

CHAPTER 19 HINGE CHORDAE

Each posterior leaflet annular radiopaque marker was surgically placed under direct observation at the posterior leaflet hinge points, where tissues associated with the left atrium and left ventricle meet the base of the leaflets. In this book, we define the mitral annulus as the locus of these hinge points, as did Angelini, *et al.*¹

In Chapter 16 we introduced the concept of a time-varying force balance between atrial contractile and fibrous tissue pulling these posterior leaflet hinges inward towards the valve center and elastic elements from both the LV basal myocardium (S1, Figure 19.1) and junctional ring (S2, Figure 19.1) pulling them outward, away from the valve center.

If these were the only forces acting on the hinges, however, this would not substantially limit their displacements in the LV long axis direction (*i.e.*, parallel to the line between Markers #22 and #1) particularly when left ventricular systolic pressure acted on the closed valve. As shown in Figure 17.3, however, the angle Φ_{2218} of annular Marker #18 with respect to this LV long axis is insensitive to changes in LVP during IVC. Thus, hinge displacements in the LV long axis direction seem indeed limited, even with large increases in LVP.

Limiting such hinge displacement is likely to be one important function of chordae from each papillary muscle tip to its adjacent half of the mitral annulus.

Figure 19.1 schematically illustrates the relationship between markers in the LV basal subepicardium (#13), junctional ring (13*), anterior and posterior papillary muscle tips (#31, #33) and bases (#32, #34). The papillary muscle tips are connected by chordae (red) to a posterior leaflet hinge (#18 or #26) as well as chordae (blue) to a posterior leaflet edge (#37). Chordae have many names in the literature, but henceforth in this book (for clarity) we will refer only to “strut chordae” (already defined), “hinge chordae”, and “edge chordae”. Hinge chordae attach to the hinge or to the belly of the posterior leaflet sufficiently near the hinge to have a major effect on the displacement of the annulus. There are actually two types of hinge chordae; both illustrated in Figure 19.1. The one shown in red connects the hinges to

Figure 19.1 Marker site schematic. See definitions in accompanying text.

¹ Angelini A, Ho SY, Anderson RH, Davies MJ, Becker AE. A histological study of the atrioventricular junction in hearts with normal and prolapsed leaflets of the mitral valve. *Br Heart J.* 1988;59(6):712-716.

the papillary muscle tips and thus is capable of conveying papillary muscle forces to the hinge regions. The one shown in blue (dashed, the “tertiary chordae” described by Lam, Ranganathan, *et al.*²) connects the hinges to LV endocardial trabeculations. These chordae may serve to prevent the hinge regions from excessive displacements toward the left atrium.

Figure 19.2 shows the relevant hinge chordae markers for hearts H1-H6 and F1-F9 and illustrates (with blue, red, magenta, and green lines) the inter-marker distances computed (dxxyy, where xx is one marker and yy is another, *e.g.* d3118 is the distance between Markers #31 and #18).

Figures 19.3 A, B, and C illustrate the key finding in this chapter that the distances from each papillary tip to sites on the associated half of the mitral annulus are roughly constant throughout the cardiac cycle. This chordal behavior, consistent with that reported by Dagum *et al.*³, and others, requires papillary muscle shortening during systole and lengthening during diastole, as reported by Rayhill *et al.*⁴ and estimated by the lower curves in each graph, required to compensate for the parallel LV long-axis dimensional changes exhibited by the upper curves in each graph. The papillary muscle length changes displayed in Figures 19.3A, B, and C are only rough estimates, however, because the myocardial and annular marker pairs (*e.g.* #3 and #29, #9 and #24) are only roughly in line with the papillary muscle long axis. Papillary muscle length changes will be dealt with more accurately in Chapter 21 using data from the F-series of hearts where the papillary tip and base were specifically delineated with markers, allowing papillary muscle lengths to be determined more precisely.

Figure 19.2 Distances analyzed for hearts H1-H6 and F1-F9. From anterior LV subepicardial equator (#3, blue) and anterior papillary tip (#31, red) to anterior mitral annular markers (#29, 16, 28, 17, 27, 18) and from posterior LV subepicardial equator (#9, green) and posterior papillary tip (#33, magenta) to posterior mitral annular markers (#24, 20, 25, 19, 26, 18).

In Figures 3.5 A and B, we showed that the papillary tips rotate about their respective trigone axes throughout the cardiac cycle, and in Chapter 17 that the mitral annulus also rotates about a similar trigone axis. The data in Figures 19.3 A, B, and C show that these rotations are tightly coupled by rather stiff chordal connections. Indeed, Tables 19.1 A and B show, using very conservative criteria and data from both the H1-H6 and F1-F9 series, that the chordal networks between the papillary tips and their respective annular connections change length no more than 15% throughout the cardiac cycle;

² Lam JH, Ranganathan N, Wigle ED, Silver MD. Morphology of the human mitral valve. I. Chordae tendineae: a new classification. *Circulation*. 1970;41(3):449-458; Ranganathan N, Lam JH, Wigle ED, Silver MD. Morphology of the human mitral valve. II. The valve leaflets. *Circulation*. 1970;41(3):459-467.

³ Dagum P, Timek TA, Green GR, Lai D, Daughters GT, Liang DH, Hayase M, Ingels NB, Jr., Miller DC. Coordinate-free analysis of mitral valve dynamics in normal and ischemic hearts. *Circulation*. 2000;102(19 Suppl 3):III62-69.

⁴ Rayhill SC, Daughters GT, Castro LJ, Niczyporuk MA, Moon MR, Ingels NB, Jr., Stadius ML, Derby GC, Bolger AF, Miller DC. Dynamics of normal and ischemic canine papillary muscles. *Circ Res*. 1994;74(6):1179-1187.

generally, much less than this, in the 4-8% range. The multiple chords from each papillary tip help stabilize the position of the tip with respect to the saddlehorn-lateral annulus axis.

Tables 19.1 A and B also show that the distance from each papillary tip to the anterior leaflet edge on the associated side can change length by up to 36%, typically 7-21%, depending on location. This is consistent with the findings in Chapter 07, where evidence was provided that edge chords buckle during diastole, unlike strut chords and (now) hinge chords that remain relatively taut.

So what do these hinge chords do?

- Hinge chord coupling maintains constant 3-D mitral valve geometry as LV dimensions change throughout the cardiac cycle and in response to varying hemodynamic demands. This is somewhat like a parachutist swinging in all directions during a descent, yet maintaining a constant relationship to the overhead canopy.
- The constant 3-D mitral valve geometry provides for precise leaflet edge positioning at the moment of valve closure for sub-mm reproducible valve sealing with minimal closing regurgitation.
- The constant positioning of the papillary tips allows the strut chordae to help set the precise anterior leaflet complex geometry at the moment of closure required for the leaflet to respond to left ventricular systolic pressure with limited stress, strain, and shape change, as discussed in Chapter 06.
- The constant papillary tip positions relative to the annulus help provide limits on the anterior leaflet safety net (as discussed in Chapter 07) to prevent an abnormally large swing of the anterior leaflet into the outflow tract during diastole.
- That the papillary tips are maintained at their systolic positions with respect to the annulus throughout the cardiac cycle provides for minimal closing shock on edge chords at the moment of closure when LVP first hits the valve. Edge chords do not have to stretch much when LVP hits the valve because they are already virtually at their systolic length when they just become taut at the moment of closure. This helps prevent the leaflet edges from slamming together with every valve closure and provides consistent and precise coaptation geometry.
- Chordae from each papillary tip radiate to both the anterior and posterior leaflet edges. Holding the papillary tips to constant (and possibly optimal) positions may minimize force components during valve closure that would tend drive the leaflet edges past each other, beyond their closure positions.⁵
- The constant annular-papillary tip geometric support provided by the hinge chordae allows the leaflet edge chords to buckle during diastole, as discussed in Chapter 07. Such slack leaflet edge chords during diastole will reduce restrictions on the leaflet opening swing leading to large valve opening area to help maximize filling and filling rates.
- Forces in the hinge chords appear to provide some left ventricular pumping assist, as reviewed by Askov, *et al.*⁵
- The hinge chords share the total papillary muscle tension with the leaflet edge chords, thereby reducing the tension imposed during systole on the leaflet edge chords. This has been studied by Askov, *et al.*⁶ and will be explored in Chapter 21.

⁵ But the presence of multiple papillary heads will require further study of this possibility.

⁶ Askov JB, Høge JL, Jensen MO, Nygaard H, Hasenkam JM, Nielsen SL. Significance of force transfer in mitral valve-left ventricular interaction: in vivo assessment. *J Thorac Cardiovasc Surg.* 2013;145(6):1635-1641, 1641 e1631.

HEART	D3129	D3116	D3128	D3117	D3127	D3118	D3142	D3143	D3144
H1	3	3	7	8	10	9	3	7	14
H2	5	6	10	12	8	9	7	18	21
H3	6	6	7	9	8	6	5	13	21
H4	5	5	5	6	6	6	5	11	14
H5	3	4	6	6	6	7	4	21	10
H6	3	3	3	6	5	6	2	11	12
F1	5	7	5	4	5	6	7	18	11
F2	2	3	6	8	8	12	11	10	18
F3	4	4	6	6	5	7	5	8	23
F4	3	6	3	4	4	4	4	7	14
F5	5	6	6	6	6	8	8	18	14
F6	3	4	5	7	8	9	7	19	12
F7	5	6	5	5	7	8	17	22	21
F8	6	4	6	8	8	9	13	26	26
F9	4	4	4	6	6	5	14	29	25
MEAN	4	5	6	7	7	7	7	16	17
SD	1	1	2	2	2	2	4	7	5
MAX	6	7	10	12	10	12	17	29	26
MIN	2	3	3	4	4	4	2	7	10

TABLE 19.1A Percent change for hearts H1-H6 and F1-F9 from the largest (Dmax) to the smallest (Dmin) values measured from each anterior papillary muscle tip (#31) throughout 3 complete cardiac cycles expressed as $100 \times (D_{\max} - D_{\min}) / D_{\max}$ and rounded to the nearest percent. Distances D3129, d3116, d3128, d3117, d3127, and d3118 are from the anterior papillary tip to the anterior half of the mitral annulus. Distances D3142, D3143, and D3144 are from the anterior papillary tip to the anterior half of the anterior mitral leaflet.

HEART	D3324	D3320	D3325	D3319	D3326	D3318	D3347	D3346	D3345
H1	3	3	6	7	5	4	9	20	18
H2	3	4	12	14	14	15	8	21	22
H3	3	4	4	6	9	8	10	22	20
H4	4	3	6	8	11	10	3	27	28
H5	3	4	6	10	8	6	11	16	17
H6	2	3	6	10	8	7	3	14	15
F1	5	6	8	7	6	4	10	20	11
F2	3	5	8	7	9	9	7	13	14
F3	7	9	10	9	7	6	10	26	36
F4	2	3	4	4	6	5	10	16	18
F5	6	6	9	10	9	6	15	20	20
F6	4	5	6	7	7	6	8	21	19
F7	2	3	4	5	8	5	14	24	16
F8	3	4	6	8	10	10	23	35	16
F9	3	4	5	6	7	7	14	14	16
MEAN	4	4	7	8	8	7	10	21	19
SD	1	2	2	2	2	3	5	6	6
MAX	7	9	12	14	14	15	23	35	36
MIN	2	3	4	4	5	4	3	13	11

TABLE 19.1B Percent change for hearts H1-H6 and F1-F9 from the largest (Dmax) to the smallest (Dmin) values measured from each posterior papillary muscle tip (#33) throughout 3 complete cardiac cycles expressed as $100 \times (D_{\max} - D_{\min}) / D_{\max}$ and rounded to the nearest percent. Distances D3324, d3320, d3325, d3319, d3326, and d3318 are from the posterior papillary tip to the posterior half of the mitral annulus. Distances D3347, D3346, and D3345 are from the posterior papillary tip to the posterior half of the anterior mitral leaflet.

CHAPTER 20 PAPILLARY VECTORS

In Chapter 19 we estimated the length changes of the papillary muscles from papillary tip and adjacent subepicardial ventricular markers. In this chapter (and the next) we analyze papillary mechanics for the F-series of experiments (See Appendix F), where papillary tip and base markers were placed inside the ventricle under direct visualization during cardiopulmonary bypass, allowing better measurement of papillary muscle lengths. In these hearts (F1-F11) the anterior papillary tip was assigned Marker #31, its base #32; the posterior papillary tip #33, its base #34. Muscle fibers are aligned along the long axes of papillary muscles, thus papillary muscle contractile force is exerted primarily along these axes. In this chapter, because the papillary muscle tips are connected via hinge chordae to the mitral annulus, we explore the orientation of these axes with respect to sites around the mitral annulus.

Figure 20.1 illustrates how these orientations were quantified. For each sample frame, angles θ (in 3-space) were computed between vectors from each annular marker (AM_i) to the tip (#31) and base (#32) of the anterior papillary muscle and from the tip (#33) and base (#34) of the posterior papillary muscle. Clearly, the closer θ is to 0° , the closer the long axis of a papillary muscle (red line in Figure 20.1) is directed towards that particular AM_i site.

Figures 20.2 A, B, and C show the behavior of these angles through 3 complete cardiac cycles in each of the hearts (F1-F11) for both the anterior and posterior papillary muscles. Note that minimum directions can be discerned, having $\theta < 10^\circ$ that vary little throughout the cardiac cycle.

Figure 20.3 graphically illustrates a distribution on a mitral annulus schematic of one site exhibiting minimum angle and minimum variation for each heart (this is not unique - other histograms can be drawn). Note, in this illustration, the posterior-anterior asymmetry with the long axis of the posterior papillary muscle directed almost exclusively toward sites (blue) between the saddlehorn (#22) and right fibrous trigone (#24) and the long axis of the anterior papillary muscle is directed primarily toward sites (red) near the left fibrous trigone (#29) and anterior commissure (#16). Papillary muscle force, of course, will be distributed among all chords on that respective half of the valve, but the greatest force component would be expected to be in line with this long axis. This analysis, of course, is only a first approximation as it assumes papillary muscle linearity and will be increasingly in error to the extent that each papillary muscle curves between its tip and base.

In Chapter 03 we found that the papillary tips swing around their respective trigonal axes within the left ventricle throughout the cardiac cycle, but In Chapter 19 we showed that the lengths of the annular (hinge) chordae were nearly constant throughout the cycle. Thus, although the annular-papillary tip complex rotates as a whole within the ventricle, the papillary tips maintain a constant geometric relationship with respect to the mitral annulus during both systole and diastole. Figures 20.3A-F illustrate this relatively fixed geometric relationship in each of the hearts F1-F11 by clamping, in each frame of each heart, the best-fit annular plane to the X-Y axis, setting the origin at the projection of the annular saddlehorn marker (#22) on the best-fit annular plane in that frame, and constraining the projection of the lateral annular marker (#18) on this best-fit annular plane to the X-Z plane in that frame, then creating a point cloud by superimposing annular and papillary tip marker 3-D positions throughout three consecutive cardiac cycles at 60 frames/second. These graphs show that papillary tip positions with respect to the mitral annulus are maintained constant to within a few millimeters in three-dimensional space throughout the entire cardiac cycle. In many respects, the papillary tips can be considered as suspended, parachute-like, below an annular “canopy” by rather stiff chordal “suspension lines”, while the papillary bases accommodate left ventricular wall motion with papillary muscle length changes.

Figure 20.2B. Left ventricular pressure (LVP/4) and angles related to the anterior papillary muscle (left column) and posterior papillary muscle (right column) for hearts F5-F8. Papanglexxyzz is the angle formed by the papillary tip (xx), the mitral annular site (yy), and the papillary base (zz).

CHAPTER 21 PAPILLARY FORCES

In Chapter 19 we showed that the distance from each half of the mitral annulus to its associated papillary tip (anterior, posterior) was roughly constant throughout the cardiac cycle and that papillary length changes (contraction during systole and stretch during diastole) were associated with this invariance. In Chapter 20 we showed that the long axis of the posterior papillary muscle is aligned with the region near the right fibrous trigone and the anterior papillary muscle is aligned with the region near the anterior commissure. Because papillary muscle fibers are roughly parallel to this long axis, it is likely that this is the principle direction of force development for each papillary muscle. In this chapter, we combine the geometric data from our hearts F1-F11 (see Appendix F) with direct measurements of papillary and chordal forces by Salisbury *et al.*¹, Nielsen *et al.*², and Askov *et al.*³, to offer a general proposal concerning the role of these forces in the valvular-ventricular complex. Our speculation is based on the simplifying assumption of a single anterior and single posterior papillary muscle, recognizing that the actual situation, with multiple papillary tips, will be considerably more complex.

Figure 21.1 schematically depicts the relationship of a selection of the markers in the F1-F11 series as viewed from the anterior toward the posterior commissure. The nomenclature for this figure has been provided in Chapter 19. The papillary basal markers (#32, 34) in the F-Series, as depicted in Figure 21.1, were sewn directly to each papillary base during the pump run.

Figures 21.2A and B identify the marker locations for the F1-F11 hearts. These are the same locations and marker numbers as in hearts H1-H6, but four additional markers were added in the F-series, one at the endocardial base of each papillary muscle (#32 anterior, #34 posterior) and one at the mid-point of each strut chord associated with the anterior leaflet (#35 anterior, #36 posterior).

Figures 21.3A-F plot inter-marker distances for three consecutive beats in each of the F1-F11 hearts. Distance d3738 between the central edges of the anterior and posterior leaflets was used to establish the time of valve opening and closing. Distances d3144 between the anterior papillary tip and an anterior leaflet anterior edge marker, and d3345 between the posterior papillary tip and an anterior leaflet posterior edge marker, suggest a small buckling of leaflet edge chords during the E-wave, as already noted and discussed in Chapter 7.

¹ Salisbury PF, Cross CE, Rieben PA. Chorda tendinea tension. *Am J Physiol.* 1963;205:385-392.

² Nielsen SL, Timek TA, Green GR, Dagum P, Daughters GT, Hasenkam JM, Bolger AF, Ingels NB, Miller DC. Influence of anterior mitral leaflet second-order chordae tendineae on left ventricular systolic function. *Circulation.* 2003;108(4):486-491.

³ Askov JB, Hønge JL, Jensen MO, Nygaard H, Hasenkam JM, Nielsen SL. Significance of force transfer in mitral valve-left ventricular interaction: in vivo assessment. *J Thorac Cardiovasc Surg.* 2013;145(6):1635-1641, 1641 e1631.

Note, in Figures 21.3A-F, the small variation in distance throughout the cardiac cycle from the anterior papillary tip to markers on the anterior half of the mitral annulus (d2231, d3129, d3116, d3118) and the posterior papillary tip to markers on the posterior half of the mitral annulus (d2233, d3324, d3320, d3318). These findings from F1-F11 are consistent with those from H1-H6 (illustrated in Figures 19.3A-C), incorporated into Tables 19.1A-B, as well as those from H1-H6 that provided the basis for the trigonal coordinate system described in Chapter 3. Note also that the strut chords exhibit near-zero strains throughout the cardiac cycle, as evidenced by the virtually unchanging values of d2231, d3135, d2233,

Figure 21.2A Anterior-side lengths analyzed for hearts F1-F11. From anterior papillary tip marker (#31) to: anterior mitral annular markers (#29, 16, 28, 17, 27, 18, blue); to edge markers on the anterior half of the anterior leaflet (#29, 42, 43, 44, 38, red); and to the anterior papillary basal marker (#32). Marker #37 (open circle) shows marker location on the edge of the central posterior leaflet scallop in this closed valve. Unlabeled vertical line at lower right displays posterior papillary tip and base markers for reference.

Figure 21.2B Posterior-side lengths analyzed for hearts F1-F11. From posterior papillary tip marker (#33) to: posterior mitral annular markers (#24, 20, 25, 19, 26, 18, blue); to edge markers on the posterior half of the anterior leaflet (#24, 47, 46, 45, 38, red); and to posterior papillary basal marker (#34). Marker #37 (open circle) shows marker location on the edge of the central posterior leaflet scallop in this closed valve. Unlabeled vertical line at lower left delineates anterior papillary tip and base markers for reference.

and d3336 in Figures 21.3A-F. This strongly suggests that the strut chords are either quite stiff, experiencing little force, or both. Salisbury *et al.*¹ found that strut chords were always in tension, with

values up to 0.15N in diastole and 1N in mid-systole. Nielsen *et al.*² found that strut chord tension was near zero during IVC and end IVR, with a maximum of 0.7N in mid-systole. These are very small forces.

As previously described by Rayhill *et al.*⁴ and Marzilli *et al.*⁵, these directly-measured papillary muscle lengths (d3132 and d3334 in Figures 21.3A-F) exhibit length changes that are virtually identical to left ventricular volume — shortening during systole and lengthening during diastole, with little length change during IVR and (particularly) almost none during IVC. Percent shortening values for the F1-F11 papillary muscles are shown in Table 21.1

This relative invariance of chordal lengths during IVC, particularly no abrupt increase in these directly-measured hinge chord lengths as left ventricular pressure rises, leads to a potentially important conclusion. Askov *et al.*³ directly measured anterior and posterior papillary muscle force with a gauge inserted in series with each papillary muscle tip and found very little papillary force development during IVC. At end-IVC, however, the valve is closed and the leaflets are experiencing near-maximum left ventricular systolic pressure, thus one would predict that both chordal stretch and papillary force would be near-maximum at end IVC — but they aren't. Askov *et al.*³ found that papillary force isn't maximum until near mid-systole, about 150 ms after LV excitation, with a rise-time similar to that observed by Holmes *et al.*⁶ in isolated rabbit ventricular papillary muscle at 37°C.

HEART	D3132	D3334
F1	19	18
F2	17	14
F3	13	18
F4	13	17
F5	19	17
F6	14	11
F7	20	16
F8	19	20
F9	12	16
F10	21	21
F11	12	12
MEAN	16	16
SD	3	3
MAX	21	21
MIN	12	11

*Table 21.1 Papillary Shortening
100*(dmax-dmin)/dmax (%)*

Cronin *et al.*⁷ have written: “It has been generally assumed that the papillary muscles are activated very early in the cardiac cycle so that during the sudden rise in pressure associated with isovolumic contraction, the papillary muscles are thought to be already in a state of increased tension and prepared to support the forces acting upon the atrioventricular valves. Careful examination of the simultaneous recordings of force and pressure development do not support this reasoning. Rather, it is clearly evident that intraventricular pressure frequently rises considerably in advance of the development of increased tension in the papillary muscle”. So, how can this be? A provisional (and rather startling) conclusion is that the leaflets in the closed valve are nearly self-supporting, without requiring significant tension in the chordae to maintain their closed configuration. In support of this notion, direct measurements by Nielsen *et al.*⁸ have shown that leaflet edge chords exhibit a maximum tension of about 0.3N, even less than the strut chords maximum tension of about 0.7N, both being very small forces. Also in support of this notion, Guo *et al.*⁹ found that “ablation of the posterior papillary muscle of the left ventricle by

⁴ Rayhill SC, Daughters GT, Castro LJ, Niczyporuk MA, Moon MR, Ingels NB, Jr., Stadius ML, Derby GC, Bolger AF, Miller DC. Dynamics of normal and ischemic canine papillary muscles. *Circ Res.* 1994;74(6):1179-1187.

⁵ Marzilli M, Sabbah HN, Goldstein S, Stein PD. Assessment of papillary muscle function in the intact heart. *Circulation.* 1985;71(5):1017-1022.

⁶ Holmes JW, Hunlich M, Hasenfuss G. Energetics of the Frank-Starling effect in rabbit myocardium: economy and efficiency depend on muscle length. *Am J Physiol Heart Circ Physiol.* 2002;283(1):H324-330.

⁷ Cronin R, Armour JA, Randall WC. Function of the in-situ papillary muscle in the canine left ventricle. *Circ Res.* 1969;25(1):67-75.

⁸ Nielsen SL, Hansen SB, Nielsen KO, Nygaard H, Paulsen PK, Hasenkam JM. Imbalanced chordal force distribution causes acute ischemic mitral regurgitation: Mechanistic insights from chordae tendineae force measurements in pigs. *J Thorac Cardiovasc Surg.* 2005;129(3):525-531.

⁹ Guo LS, Zhou X, Li YH, Cai J, Wei DM, Shi L, Yang G, Armoundas AA, Yang XC. Alcohol ablation at the posterior papillary muscle prevents ventricular fibrillation in swine without affecting mitral valve function. *Europace.* 2010;12(12):1781-1786.

injection of dehydrated alcohol results in no new or worsening mitral regurgitation". So, papillary muscle contraction may not be essential to hold the leaflet edges in their closed configuration. But how could these leaflets be self-supporting in the closed valve? In the next several chapters we develop a hypothesis addressing this question, but will simply note here that aortic valves placed upside down in the mitral position are clinically employed as mitral valve replacements – and these replacement valves can close and support left ventricular systolic pressure without chordal support.

So if the mitral valve leaflets in the closed valve are nearly self supporting, requiring almost no chordal tension to remain closed, what is the role of the force of about 6N measured by Askov *et al.*³ during ejection in each papillary muscle? We propose (as did Askov *et al.*³) that this force is applied to the mitral annulus throughout systole primarily to contribute to LV ejection, a proposal that finds support in both basic studies¹⁰ and the finding, originally by Lillehei *et al.*¹¹ but validated many times since, that clinical outcomes are improved by chordal preservation during mitral valve replacement. The importance of this 12N (2x6N) papillary muscle force measured by Askov *et al.*³ can be put into perspective. Considering that left ventricular systolic pressure is total left ventricular force divided by total left ventricular chamber area, a rough calculation shows that total left ventricular force during ejection is about 120N (90mmHg x 100 cm²). Thus the 12N from the two papillary muscles contributes about 10% to total left ventricular force, a small, but non-negligible, quantity, considering that it is applied to about 100,000 beats each day.

In summary, then, we propose that the papillary tips are held in a precise and relatively fixed geometric relationship to the mitral annulus throughout the cardiac cycle by stiff chordae subjected to rather small forces. This fixed geometric relationship allows the leaflets to close gently during IVC, with almost no tension in the chordae or their associated papillary muscle, with leaflet shape and position established at the moment of closure in very nearly the geometry that will be maintained throughout systole. Subsequent papillary force development later in systole, transmitted through the hinge chords, contributes about 10% to the total force of contraction, particularly in mid-to-late systole.

If this is the case, simple papillary passive elasticity, without the need for active papillary force development, could suffice for proper mitral valve leaflet opening and closing. The chords, attached to the papillary tips, serve to position and shape the leaflets during valve closure, not to forcibly hold them in position throughout systole. The leaflets, once closed, are virtually self-supporting. Because papillary force is so small at the instant of valve closure, the rigid annulus/leaflet structure must be held in place in the LV by its direct attachment to the myocardium *via* the S1 spring in Figure 21.1 and tertiary chords (dashed blue in Figure 21.1). Subsequent papillary force development, applied to the annulus, helps pump blood.

Askov *et al.*³ suggested that this chordal arrangement "...allows a significant load [to be] transferred through the basal chordae and distributed toward the mitral annulus without pulling the leaflets apart in an apical direction." But Askov *et al.*³ found continued papillary force development throughout IVR, and both Rayhill *et al.*⁴ and Marzilli *et al.*⁵ found that papillary muscle shortening also continues throughout IVR. This late papillary force and shortening, potentially supplementing the primary opening force associated with the reversal in the LVP/LA pressure gradient, may well play an active role to aid quick and reliable valve opening at end IVR.

¹⁰ Rodriguez F, Langer F, Harrington KB, Tibayan FA, Zasio MK, Cheng A, Liang D, Daughters GT, Covell JW, Criscione JC, Ingels NB, Miller DC. Importance of mitral valve second-order chordae for left ventricular geometry, wall thickening mechanics, and global systolic function. *Circulation*. 2004;110(11 Suppl 1):II115-122.

¹¹ Lillehei CW, Levy MJ, Bonnabeau RC, Jr. Mitral Valve Replacement with Preservation of Papillary Muscles and Chordae Tendineae. *J Thorac Cardiovasc Surg*. 1964;47:532-543.

Figure 21.3E. LVP and inter-marker distances for hearts F9 (top) and F10(bottom). Anterior papillary tip (#31) to anterior mitral annulus (d3129, d3116, d3118). Anterior papillary tip (#31) to anterior half of the anterior mitral leaflet (d3144). Anterior papillary tip (#31) to anterior papillary base (d3132). Posterior papillary tip (#33) to posterior mitral annulus (d3324, d3320, d3318). Posterior papillary tip (#33) to posterior half of the anterior mitral leaflet (d3345). Posterior papillary tip (#33) to posterior papillary base (d3334). Anterior strut chord half-length (d3135). Posterior strut chord half-length (d3336). Saddlehorn (#22) to APT (d2231) and PPT (d2233). Anterior-posterior leaflet edge-edge distance (d3738).

CHAPTER 22 PAPILLARY CHIMERA

This chapter analyzes papillary muscle mechanics for a mythical “PORVINE” heart created by superimposing PORcine and oVINE data. Porcine data were obtained from the LVP and papillary force curves in Figure 3 of Askov *et al.*¹, digitized and interpolated with a cubic spline function. Ovine data are from our F10 heart, selected solely because the F10 LVP waveform was very similar to the LVP curve shown in Askov *et al.*¹ Systolic duration was roughly matched by assigning a sampling interval of 15 ms to the ovine data, rather than the actual sampling interval of 16.67 ms. The porcine data were then sampled at these same 15 ms intervals. The resulting LVP, papillary force, and papillary length curves are shown in Figure 22.1, with magnitudes scaled or translated, as necessary, to fit the <0-9> ordinate. Additional ovine data, with time- but no magnitude-scaling, are shown in Figures 22.2, 22.5, and 22.6. Figure 22.7 shows the original data used to construct Figure 22.1.

This PORVINE construction had two purposes. The first was to emphasize a point made in Chapter 21, namely, that at the moment of mitral valve closure, with near-maximum LVP pressing on the closed leaflets, the chordae experience very little force, about 8% and 1%, respectively, of the maximum force developed in mid-systole by the anterior and posterior papillary muscles. Note, in Figure 22.1, that MVC is at 120 ms, but F_{ant} is <1.5N and F_{post} is <0.5N at this time. This supports the concept that the mitral valve leaflets in the closed valve are nearly self-supporting, without requiring major chordal/papillary forces to maintain valve closure.

The second reason for this PORVINE construction was a crude attempt to understand the behavior of papillary force-length loops in the beating heart. Figures 22.3 and 22.4 show these resulting loops for the anterior and posterior papillary muscles, respectively.

In Chapter 21, we showed (Table 21.1) that papillary muscle shortening in the F1-11 hearts ranged from 11-21%. By chance, heart F10, the one picked solely for its LVP wave-shape and analyzed in this chapter, exhibited 21% shortening in both papillary muscles. These values are large, but less than the values up to 30% measured by Grimm *et al.*² using radiopaque marker pairs in tranquilized canines.

Slack sarcomere length in cardiac muscle is 1.9 μ m. Wu *et al.*³ found that the giant protein titin is the primary contributor to passive tension of cardiac muscle and that sarcomere lengths in cardiac muscle are limited by both collagen and titin to about 2.4 μ m (below the 2.5 μ m length where collagen is damaged). This suggests that the 21% papillary shortening in F10 is associated with sarcomeres operating over their full range of lengths ($100 \times (2.4 - 1.9) / 2.4$) and such proposed sarcomere lengths are shown at the top of Figures 22.3 and 22.4, assuming that maximum papillary length is associated with maximum (*i.e.*, 2.4 μ m) sarcomere length. Rodriguez *et al.*⁴ found that cardiac muscle sarcomeres in beating hearts can shorten from 2.4 μ m down to as much as 1.7 μ m (29%), but Wu *et al.*³ find that, below slack length, titin compression restores sarcomere lengths back to 1.9 μ m.

¹ Askov JB, Hønge JL, Jensen MO, Nygaard H, Hasenkam JM, Nielsen SL. Significance of force transfer in mitral valve-left ventricular interaction: in vivo assessment. *J Thorac Cardiovasc Surg.* 2013;145(6):1635-1641, 1641 e1631.

² Grimm AF, Lendrum BL, Lin HL. Papillary muscle shortening in the intact dog; a cinderadiographic study of tranquilized dogs in the upright position. *Circ Res.* 1975;36(1):49-57.

³ Wu Y, Cazorla O, Labeit D, Labeit S, Granzier H. Changes in titin and collagen underlie diastolic stiffness diversity of cardiac muscle. *J Mol Cell Cardiol.* 2000;32(12):2151-2162.

⁴ Rodriguez EK, Hunter WC, Royce MJ, Leppo MK, Douglas AS, Weisman HF. A method to reconstruct myocardial sarcomere lengths and orientations at transmural sites in beating canine hearts. *Am J Physiol.* 1992;263(1 Pt 2):H293-306.

Figure 22.1 "PORVINE" data. Porcine left ventricular pressure (LVP/10) and anterior (Fant) and posterior (Fpost) papillary muscle force. Ovine left ventricular pressure (F10, LVP/10) and anterior (Lant) and posterior (Lpost) papillary muscle length. MVC= valve closure. MVO=valve opening.

Figure 22.2 Ovine F10 data. LVP=left ventricular pressure; AOP=aortic pressure; LAP=left atrial pressure; LVV=left ventricular volume; Dmmnn=distance (length) between Markers mm and nn.

CHAPTER 23 POSTERIOR MITRAL LEAFLET ANATOMY AND MARKER SITES

In previous chapters we have studied hearts with 23 anterior leaflet markers but only a single marker on the free edge of the central posterior leaflet. In this and the next several chapters we conduct a more complete study of the dynamics of the posterior leaflet(s) employing datasets from hearts with 9 markers on the posterior leaflet edges and 10 markers on the anterior leaflet. These datasets and animations arising from them are given in Appendix E.

We begin by examining the anatomy of the posterior mitral leaflet(s) as shown in Figures 23.1 and 23.2, both adapted from Antunes' excellent text MITRAL VALVE REPAIR.

Figure 23.1 illustrates the chordal attachments of the posterior leaflet(s) to the papillary muscles as well as the connection between the posterior and anterior leaflets. As viewed in this unrolled fashion, it is tempting to describe all the mitral valve leaflets as one large connected leaflet structure, and in many ways this is correct. But, as we have already documented, and will document further, the anterior and posterior leaflet(s) exhibit quite distinct behavior and the reason that we use parentheses in the term “posterior leaflet(s)” is that, in many ways, various portions of the posterior leaflet also exhibit quite distinct dynamics. This is not a new observation, as distinct regions of the posterior leaflet (P1, P2, and P3) have long been identified.

Figure 23.2 is a closer view of the posterior leaflet. It should be noted that P1 is nearest the anterior commissure, P2 is the central posterior leaflet scallop, and P3 is located nearest the posterior commissure. Note also that the central meridian of P2 is relatively free of chordal attachments, but is supported on either side by chordal attachments from the anterior and posterior papillary muscles. This is similar to the chordal support of the central meridian of the anterior leaflet and allows the central portion of these leaflets to be supported, without placing chordal obstructions in the primary outflow pathway for left ventricular ejection.

Figure 23.2 Posterior leaflet anatomy with posterior leaflet regions (P1, P2, P3) identified. Adapted from Antunes M.J. *Mitral Valve Repair* 1989, Page22, Figure 2.12, Verlag R.S. Schulz.

Figure 23.3, a repeat of Figure E.1 in Appendix E, shows the markers arrays used in the study of posterior leaflet dynamics. Markers #15, 22, and 21 are trigonal, Marker #16 is at the anterior commissure, Marker #20 at the posterior commissure, Markers #17, 18, and 19 are on the contractile portion of the mitral annulus, Markers #1, 4, 7, 10, and 13 are on the anterior leaflet edge, Marker #2 is on the anterior commissural leaflet of the posterior leaflet complex, Marker #14 is on the posterior commissural leaflet of the posterior leaflet complex, Markers #3, 5, and 6 are at the P1-P2 boundary, Marker #8 is on the central meridional edge of the P2 scallop of the posterior leaflet, Markers #9, 11, and 12 are at the P2-P3 boundary, Markers #26, 27, and 28 are on the anterior papillary muscle tip, Marker #29 is the point of insertion of the strut chord from anterior papillary muscle tip Marker #26 to the anterior leaflet, and Markers #23, 24, and 25 are on the posterior papillary muscle tip, with Marker #30 at the point of insertion of the strut chord from the posterior papillary muscle tip Marker #23 to the anterior leaflet.

CHAPTER 24 POSTERIOR LEAFLET OPEN

Figure 24.1 repeats, for reference purposes, the marker locations shown and described in Chapter 23.

We begin by examining the maximum extent of posterior leaflet opening relative to the mitral annulus. To view this, in each sample frame we performed a translation to place Marker #22 at the origin, perform 2 rotations to place Marker #18 on the x-axis, then performed a final rotation to place anterior commissure Marker #16 into the x-y plane. This placed the mitral annulus into the x-y plane (to very close approximation) at each sample time. We then view the resulting mitral valve geometry along the z-axis, looking from the left atrium toward the left ventricle. Appendix E provides frame-by-frame animations showing the geometry of the mitral valve as described by three-dimensional cubic splines passing through connected marker locations during a representative beat (from maximum LVP in one beat to maximum LVP in the following beat) for the hearts studied in this fashion.

Figures 24.2, 24.3, and 24.4 show three views of the mitral complex during the frame in the animation exhibiting maximum posterior leaflet opening (greatest posterior leaflet perimeter) for hearts

COM07R04, COM02R02, and COM06R01. In each figure, the lower left panel plots left ventricular pressure (LVP, mmHg) in blue, the distance between anterior and posterior leaflet edge markers (D78,

mm) in green, the annular perimeter (AP, mm) in red, and the posterior leaflet perimeter (LP, mm) in teal. Perimeters were assessed in each frame by summing the distances in 3-space between adjacent markers for that frame. An open circle is placed at the time-frame (in Figure 24.2, Frame 35) when the geometric data in the other three panels are visualized. These three panels illustrate mitral valve geometry in three orthographic views: the upper right panel viewing the valve from the left atrium to the left ventricle, the upper left panel from the posterior commissure toward the anterior commissure, and the lower right panel from the septum toward the lateral mitral annulus. The red dot in each of these panels is the saddlehorn Marker #22, the black dot is the lateral mitral annular Marker #18, and the green dot is the anterior commissure Marker #16. The dashed lines represent the strut chords from the anterior papillary tip (Marker #26) to its insertion into the anterior leaflet (Marker #29) and from the posterior papillary tip (Marker #23) to its insertion into the anterior leaflet (Marker #30). The red spline shows the anterior leaflet edge (connecting Markers #1-4-7-10-13), the blue spline shows the posterior leaflet edge (connecting Markers #1-2-3-5-6-8-9-11-12-14-13) and the black spline shows the mitral annulus (connecting Markers #22-15-16-17-18-19-20-21-22).

Note that:

1. The maximum posterior leaflet opening silhouette is virtually identical to the annular silhouette (upper right panel in each figure). Thus, flow from the left atrium into the left ventricle would not be expected to encounter significant restriction associated with a narrowed opening due to the posterior leaflet.
2. The strut chordae hold the basal half of the anterior leaflet out of the left ventricular outflow tract (upper right panel in each figure), so this portion of the anterior leaflet will slightly impede LV inflow.
3. Anterior leaflet opening takes place primarily at the leaflet edge (upper left panel in each figure).
4. The posterior leaflet perimeter varies to a much greater extent throughout the cardiac cycle than the annular perimeter (lower left panel in each figure). The posterior leaflet perimeter in these hearts ranged from 51 to 90 mm during the cardiac cycle with a mean change of 32 mm; the mitral annular perimeter ranged from 88 to 114 mm, with a mean change of 13 mm; and the anterior leaflet perimeter (shown in the next chapter) ranged from 27 to 38 mm with a mean change of only 7 mm.
5. It is almost impossible to assess the geometry of the leaflet edges from any single view, even if that view is derived from 3-D data. Several simultaneous views are required to understand the very complex geometry of these leaflets in three-dimensional space.

CHAPTER 25 POSTERIOR LEAFLET CLOSED

In Chapter 24 we noted that the posterior leaflet edge perimeter changes by a mean value of 32 mm throughout the cardiac cycle, while the mitral annular perimeter changes by 13 mm and the anterior leaflet perimeter by only 7 mm. This suggests the possibility that the posterior leaflet may play a disproportionate role in mitral valve opening and closing. In this chapter, we begin to explore this possibility.

Figure 25.1 repeats, for reference purposes, the marker locations shown and described in Chapter 23. Data and animations for this chapter are in Appendix E.

Figures 25.2, 25.3, and 25.4 show the leaflet, annular, and papillary geometry associated with the closed valves whose maximally open geometry was shown in Chapter 24, Figures 24.2, 24.3, and 24.4.

Figure 25.3 Three dimensional view of the mitral complex during maximum posterior leaflet closing for COM06R01

Figure 25.4 Three dimensional view of the mitral complex during maximum posterior leaflet closing for COM02R02.

As can be seen in the upper right panels of each figure, clearly the posterior leaflet in the closed valve has not only considerably reduced the perimeter of its free edge from its open state, but this edge has now approximated some of the scalloped geometric features shown in Figure 23.2.

Figures 25.6, 25.6, and 25.7 show the nature of this transition in greater detail. The upper left panel in each of these figures displays left ventricular pressure (LVP, mmHg) and leaflet separation D0708 (SEPARATION, mm) during a multiple-beat sequence. The upper middle panel shows the corresponding annular perimeter (ANNULUS), posterior leaflet edge perimeter (POSTERIOR LEAFLET), and anterior leaflet edge perimeter (ANTERIOR LEAFLET), all in mm, for these beats. Note the much greater dimensional changes of the edge of the posterior leaflet relative to the edge of the anterior leaflet throughout the cardiac cycles. The remaining 9 panels show the distance (mm) between adjacent markers on the posterior leaflet edge during these beats, starting from the anterior commissure (D0102) and ending with the posterior commissure (D1413). While each heart exhibits its own pattern of posterior leaflet edge segmental dynamics, in each heart, D0506 and D0911 exhibit consistently large excursions, suggesting that these regions contribute importantly to the opening and closing dynamics of the posterior leaflet in all three hearts. In the next chapter, we further explore the behavior of the posterior leaflet regions near these regions (*i.e.*, near Markers #5, 6, 9, and 11).

Figure 25.6 Posterior leaflet edge segmental lengths for COM06R01. See text for details.

Figure 25.7 Posterior leaflet edge segmental lengths for COM02R02. See text for details.

CHAPTER 26 POSTERIOR LEAFLET PLEATS AND SCALLOPS

In Chapter 25 we noted that the posterior leaflet regions in the vicinity of Markers #5 and 6 and #9 and 11 were undergoing consistently large dimensional changes with valve opening and closing in each of the three hearts studied, and thus might be considered as prime candidates for the large changes of the posterior leaflet perimeter throughout the cardiac cycle. In this chapter we explore the kinematics of these regions in greater detail. Again, we provide Figure 26.1 as a reference for marker placement in these studies.

Markers #5 and 6 are near the P1-P2 junction. Figure 26.2A illustrates the relative position of the markers in this region in the widely open valve and Figure 26.2B their position in the closed valve. Figures 26.2A and B are two frames from an animated sequence provided in Appendix E for a complete cardiac cycle in heart COM07R04.

In Figures 26.2A and B, Marker #17 is identified with a filled black symbol, Marker #3 with a filled blue symbol, Marker #5 with a filled green symbol, Marker #6 with a filled red symbol, and Marker #4 (at the nearby anterior leaflet edge) with a black-bordered yellow symbol. The continuous black curve is a cubic spline through the annular markers, the red curve is a cubic spline through the anterior leaflet edge markers, and the blue curve is a cubic spline through adjacent posterior leaflet edge markers as shown in Figure 26.1. The triangle bounded by Markers #5-6-17 is filled in red and the triangle bounded by Markers #3-5-17 is filled in blue. All features of the 4 panels in each figure are as described in Chapter 24; Figures 26.2A and B are a closer study of the specific P1-P2 region of the posterior leaflet.

Figure 26.1 Marker location schematic. See Chapter 23 text for marker locations.

Markers #9 and 11 are near the P2-P3 junction. Figure 26.3A illustrates the relative position of the markers in this region in the widely open valve and Figure 26.3B their position in the closed valve. Figures 26.3A and B are also two frames from an animated sequence provided in Appendix E for one complete cardiac cycle in heart COM07R04.

In Figures 26.3A and B, Marker #19 is identified with a filled black symbol, Marker #9 with a filled blue symbol, Marker #11 with a filled green symbol, Marker #12 with a filled red symbol, and Marker #10 (at the nearby anterior leaflet edge) with a black-bordered yellow symbol. Again, the continuous black curve is a cubic spline through the annular markers, the red curve is a cubic spline through the anterior leaflet edge markers, and the blue curve is a cubic spline through adjacent posterior leaflet edge markers as shown in Figure 26.1. The triangle bounded by Markers #11-12-19 is filled in red and the triangle bounded by Markers #9-11-19 is filled in blue. All features of the 4 panels in each figure are as described in Chapter 24; Figures 26.3A and B are a closer study of the specific P2-P3 region of the posterior leaflet.

Animations from two other hearts, COM02R02 and COM06R01, are also provided in Appendix E.

These four figures strongly suggest that the P1-P2 and P2-P3 junctions are capable, almost entirely, of providing the large change in posterior leaflet perimeter needed to open the valve widely during left ventricular filling and close it tightly during ejection. In many respects, these regions provide junctions similar to pleats, commonly used to gather a wide piece of fabric to a narrower circumference. In this case, these posterior leaflet pleats are greatly flattened during diastole and gathered tightly during systole.

Note that these data provide only a rough idea of pleat geometry because our widely-spaced markers were placed in flaccid hearts under cardiopulmonary bypass without precise knowledge of pleat geometry. Although dozens more markers would be needed to precisely characterize each pleat, these data allow an improved understanding of a possibly important mechanism employed to allow large changes in the mitral orifice throughout the cardiac cycle.

Along with potential chordal guidance, the scalloped geometry of the P1, P2, and P3 regions of the posterior leaflet may be important to assure that the pleats fold and unfold in an appropriate manner with each beat. The greater surface area at mid-scallop would allow greater force to be exerted from LV pressure gradients during IVC at mid-scallop than at the pleats, thereby preventing a potentially disastrous inversion of pleat geometry that would impede valve closure.

Figure 26.2A COM07R04 posterior leaflet P1-P2 pleat geometry in open valve. See text for details.

Figure 26.2B COM07R04 posterior leaflet P1-P2 pleat geometry in closed valve. See text for details.

Although the changing dimensions of the P1-P2 and P2-P3 regional pleats may dominate the perimeter expansion and contraction of the posterior leaflet during the cardiac cycle, the data shown in Figures 25.5, 25.6, and 25.7 suggest that a number of other sites (highlighted in red in these Figures) may also be folding and unfolding to provide additional perimeter changes. Again, a future study with much greater spatial resolution than the present study would be needed to elucidate the importance of these additional folds. The severe folds at the commissural scallops adjoining the left and right fibrous trigones are of considerable interest in this regard.

Finally, it should be recognized that any folded pleats in the closed valve will be pressed tightly together by systolic left ventricular pressure acting on their outer (ventricular) surfaces (*i.e.* the outer surfaces of both the red and blue triangles in Figures 26.2B and 26.3B). This provides a rib-like structure that may help stiffen the posterior leaflet to help the valve resist systolic deformation.

Figure 26.3A COM07R04 posterior leaflet P2-P3 pleat geometry in open valve. See text for details.

Figure 26.3B COM07R04 posterior leaflet P2-P3 pleat geometry in closed valve. See text for details.

CHAPTER 27 COAPTATION

In Chapter 26 we identified two major pleats at the P1/P2 and P2/P3 junctions of the posterior leaflet, characterized their kinematics throughout the cardiac cycle, and approximated their surfaces with two filled (red and blue) triangular surfaces. These triangles, however, are only intended as a visualization device; we know that the actual pleats in the closed valve would bow inward toward one another as systolic left ventricular pressure acts on their outer ventricular surfaces to press their convex faces tightly together. We cannot appreciate such curvature in these studies, however, because of the limited spatial resolution of our sparse marker arrays.

In an attempt to better visualize the actual 3D shape of the valve leaflets, we developed a whole-valve model based on the anatomical dissection shown in Figure 2.3 in Antunes' text *MITRAL VALVE REPAIR*, previously presented as our Figure 23.1. We enlarged and printed this figure, then cut along its perimeter, *i.e.*, the dotted lines in Figure 27.1. This cutout was then used as a template on a sheet of aluminum foil, which was cut to this shape. Because this anatomical specimen is an unrolled mitral valve, we re-rolled the foil to join the left and right-most regions. We found that this 3D restoration process required, at minimum, four folds to allow leaflet coaptation in the model. After the model was completed and photographed, it was unrolled to reveal the folds as identified by the gray-shaded regions (1-4) in Figure 27.1.

Figure 27.2 shows the resulting model as viewed from the left atrium. The fold between the anterior leaflet and P1 is identified as shaded region #3 in Figure 27.1, the fold between P1 and P2 by #2 in this figure, the fold between P2 and P3, by #1, and the fold between P3 and the anterior leaflet by #4. The model in Figure 27.2 appears to be a reasonable approximation of the mitral valve, which is not entirely surprising as it is anatomically-based. Our knowledge of the compound curvature of the anterior leaflet was required to fit the compound-curved anterior leaflet into the model. Although the radial curvature of the posterior leaflet edge must be concave to the left ventricle to allow coaptation with the anterior leaflet edge, the analysis in Chapter #41 shows that the radial curvature of the posterior leaflet belly is just as likely to be flat or convex as concave to the left ventricle, so posterior leaflet shape is also quite complex.

An interesting outcome of this 3D modeling process, besides suggesting the nature of the folds and leaflet curvatures required for coaptation in this curved geometry, is illustrated in Figure 27.3, showing the P2-P3 pleat from Figure 27.2 as viewed from the left ventricle. Note that, in order to prevent regurgitation, three convex surfaces in this pleat region must be pressed tightly together by systolic LVP; P2, P3, and the adjacent region of the anterior leaflet. We encounter this same mechanism for tightly sealing the aortic valve. Thus, one could say that the mitral valve can be viewed as two inverted aortic valves. Note that for most of the mitral valve coaptation regions, only two convex surfaces must be pressed into a fluid-tight seal, but for these critical pleated regions, required by the demands of 3D geometry, three forces must act to form a tight seal. It seems likely that the most vulnerable regurgitation sites would be at these pleat regions that require a more complex leaflet geometric interaction than the other regions of the coapting leaflets.

In the previous chapter, we mentioned that the pleats might geometrically stiffen the posterior leaflet against deformation due to left ventricular pressure. Figure 27.3 allows appreciation of how this might come about, with a potentially stiff rib being created by LVP acting on the P2/P3 fold.

Figure 27.3 Left ventricular surface of the Figure 27.2 P2-P3 junction.

CHAPTER 28 ANTERIOR LEAFLET INDEPENDENCE

This chapter discusses the PULL STUDY that was designed to assess the impact of posterior leaflet coaptation pressure on anterior leaflet edge geometry in the closed valve. Figure 28.1 shows the marker locations and coordinate system used in this study. Table 28.1 identifies the datasets associated with the CONTROL and PULL runs for the three technically-satisfactory experiments analyzed (Appendix P provides these datasets). Figure 28.2 illustrates the protocol schematically.

Mitral regurgitation was trace or none during the CONTROL runs (slack suture) as assessed by Doppler Echocardiography. The posterior leaflet suture was then pulled (as illustrated in Figure 28.2) to create sustained moderate-severe regurgitation during the PULL runs.

TABLE 28.1	CONTROL	PULL
	pul08r23pre.1E	pul08r24pull.1E
	pul13r01pre-2frames.1E	pul13r05pull.1E
	pul14r01pre.1E	pul14r02pull-2frames.1E

The results for the three hearts analyzed are shown in Figures 28.3-28.5 and Tables 28.2 and 28.3.

The top panel in each of the Figures 28.3-28.5 shows the X, Y, and Z edge-marker coordinates and left ventricular pressure data for the three beats analyzed in each run for each heart. The bottom panel in each figure shows one of these beats with an expanded time-scale.

Table 28.2, derived from these data, shows that the end systolic position of each of the anterior and posterior leaflet edge markers was remarkably constant from beat-to-beat, varying only several tenths of a millimeter during the 3-beats of the CONTROL runs.

Table 28.3 shows the results of the PULL study, with the posterior leaflet edge markers being displaced by the suture pull by several millimeters at end-systole, while the anterior leaflet edge markers were displaced by only about 1 millimeter or less at this time. Figures 28.3-5 show that these very small displacements of the anterior leaflet edge, when posterior leaflet coaptation pressure was removed, were not just present at end systole, but characterized the entire time from end-IVC to end-IVR. Further, anterior leaflet edge position was virtually unchanged by changes in LVP, as demonstrated by the large change in LVP between the control and pull runs in Figure 28.5, and the fact that anterior leaflet edge position is also virtually invariant as pressure drops during IVR from peak systolic LVP to low end-IVR values in each heart.

Thus the position of the anterior leaflet edge, once established at end IVC, shows high beat-to-beat reproducibility and is virtually independent of changes in left ventricular pressure, the changing geometry of the LV throughout ejection and isovolumic relaxation, and the pressure of the coapting posterior leaflets in the closed valve. These data are consistent with the results discussed in Chapter 13 obtained from other hearts (H1-H6). This anterior leaflet edge position invariance strongly suggests that anterior leaflet shape is optimized to maintain the systolic geometry of the leaflet under widely varying conditions, and this shape was discussed in Chapters 8 and 9. But leaflet material properties are also involved, as the anterior leaflet supports extensive radial compression, as demonstrated in Chapter 11.

In the next chapter, we will provide further information about the very complex material properties of the anterior leaflet.

Figure 28.4. Heart PUL14. Marker X-coordinate (red), Y-coordinate (green), Z-coordinate (blue), LVP/4 (black). CONTROL (solid lines). PULL (dashed lines). Top panel, 3 beats; bottom panel, enlarged time-scale single beat from the top panel.

TABLE 28.2 DIFFERENCE IN X,Y,AND Z-VALUES (ES,MAX-MIN, mm) FOR CONTROL 3 BEATS

HEART	X#23	X#24	X#25	X#28	X#26	X#27
PUL08R23	0.1	0.2	0.3	0.1	0.1	0.2
PUL13R01	0.1	0.2	0.2	0.2	0.3	0.2
PUL14R01	0.1	0.1	0.3	0.2	0.7	0.2
X MEAN	0.1	0.2	0.3	0.1	0.3	0.2
HEART	Y#23	Y#24	Y#25	Y#28	Y#26	Y#27
PUL08R23	0.1	0.2	0.4	0.2	0.2	0.4
PUL13R01	0.2	0.4	0.3	0.3	0.2	0.3
PUL14R01	0.3	0.1	0.4	0.3	0.5	0.2
Y MEAN	0.3	0.3	0.3	0.3	0.3	0.2
HEART	Z#23	Z#24	Z#25	Z#28	Z#26	Z#27
PUL08R23	0.3	0.5	0.3	0.6	0.2	0.2
PUL13R01	0.2	0.2	0.1	0.2	0.1	0.3
PUL14R01	0.4	0.4	0.3	0.3	0.3	0.5
Z MEAN	0.3	0.4	0.3	0.4	0.2	0.4
HEART	D#23	D#24	D#25	D#28	D#26	D#27
PUL08R23	0.3	0.5	0.6	0.7	0.4	0.5
PUL13R01	0.3	0.5	0.3	0.4	0.3	0.4
PUL14R01	0.5	0.4	0.6	0.4	0.9	0.6
3D MEAN	0.4	0.5	0.5	0.5	0.5	0.5

TABLE 28.3 DIFFERENCE IN X,Y,AND Z-VALUES (ES,3-BEAT MEANS, mm) CONTROL TO PULL

HEART	X#23	X#24	X#25	X#28	X#26	X#27
PUL08R23_24	-0.1	-0.2	-0.2	5.1	1.4	-0.2
PUL13R01_05	0.9	0.8	0.9	3.6	1.1	2.4
PUL14R01_02	1.0	1.3	1.0	5.9	1.9	1.0
X MEAN	0.6	0.6	0.5	4.8	1.5	1.1
HEART	Y#23	Y#24	Y#25	Y#28	Y#26	Y#27
PUL08R23_24	-0.7	-0.5	-0.8	-5.6	-1.8	-1.1
PUL13R01_05	-0.1	-0.1	0.0	0.2	0.6	-1.9
PUL14R01_02	-0.5	-0.3	-0.4	0.1	2.9	-1.0
Y MEAN	-0.8	-0.6	-0.7	-2.1	0.2	-1.6
HEART	Z#23	Z#24	Z#25	Z#28	Z#26	Z#27
PUL08R23_24	0.2	-0.1	0.4	1.6	0.6	2.3
PUL13R01_05	0.6	0.5	0.2	0.4	-0.3	0.4
PUL14R01_02	-0.1	0.0	-0.1	-0.4	0.3	0.2
Z MEAN	0.2	0.1	0.2	0.6	0.2	1.0
HEART	D#23	D#24	D#25	D#28	D#26	D#27
PUL08R23_24	0.7	0.6	0.9	7.7	2.3	2.6
PUL13R01_05	1.1	0.9	0.9	3.6	1.3	3.1
PUL14R01_02	1.1	1.3	1.0	5.9	3.5	1.4
3D MEAN	1.0	0.9	0.9	5.8	2.4	2.4

CHAPTER 29 ANTERIOR LEAFLET STIFFNESS

In Chapters 09 and 13 we showed that the anterior leaflet in the closed valve maintains a nearly invariant shape and position in the ventricle as the leaflet is subjected to the large and variable trans-leaflet pressures in the beating heart. This implies that the leaflets must be quite stiff—and this stiffness depends on leaflet shape, boundary conditions, and elastic moduli.

The elastic modulus of a region of a leaflet in a given direction at a given stress-strain level is defined as the slope of the stress-strain curve of that region in that direction at that stress-strain point. Figure 29.1 shows the radial and circumferential stress-strain curves and moduli obtained at two specific points on each curve in the classic study of May-Newman and Yin¹ of the belly region of whole, excised, flattened, preconditioned porcine leaflets subjected to equibiaxial stretches. Note that the anterior leaflet belly is very compliant for strains up to about 0.15, but becomes 40X-100X stiffer above this “transitional” point; that posterior leaflets are very compliant for larger strains (up to about 0.30); and that circumferential stiffness is greater than radial stiffness for both anterior and posterior leaflets.

Figure 29.1 Stress-strain curves (adapted from Figure 6 of May-Newman and Yin¹) for excised anterior and posterior porcine leaflets. Tables show mean PRE- and POST-transitional elastic moduli in the circumferential (CIRC) and radial (RAD) directions for ANTERIOR(Left Table) and POSTERIOR(Right Table) leaflets. Anterior CIRC (solid blue) and RAD (solid red). Posterior CIRC (dashed blue) and RAD (dashed green).

In our studies, we employed inverse finite element analysis to derive the circumferential and radial elastic moduli of the ovine leaflet *in vivo*, in each region and each instant, given the instantaneous leaflet geometry and boundary conditions from our marker studies. Figure 29.2, from Krishnamurthy, *et al.*³, shows the miniature radiopaque markers sewn to the anterior leaflet and annulus. Figure 29.3 specifies the marker numbers and the orientation of the circumferential and radial axes used in this analysis.

In our experiments, left ventricular pressure (LVP), left atrial pressure (LAP), and the 3D coordinates of the anterior and posterior papillary tip markers and each of the anterior leaflet markers shown in Figures 29.2 and 29.3 were recorded every 16.67ms throughout several sequential heartbeats. We were thus able to quantify the change in LVP and LAP on each side of the leaflet in the closed valve during a given time interval and associate that change in trans-leaflet pressure with leaflet deformation measured during this interval.

Inverse finite element analysis, described by Krishnamurthy, *et al.*,³ was used to associate such changes in pressure with leaflet deformation. A computer model of the leaflet was first developed using the 3D coordinates of the markers shown in Figures 29.2 and 29.3. This model incorporated regional leaflet thickness values and assigned strut chords from the papillary tip markers to their insertion points in the leaflet belly. The model was then subjected to LVP and LAP measured at time T1 and again at time T2 and leaflet displacements over this same time interval from T1 to T2 was predicted for initial estimates of radial (E_{rad}) and circumferential (E_{circ}) moduli. The computer-predicted displacements were then compared with the actual measured displacements and this information used to improve the E_{rad} and E_{circ} estimates for the next computer iteration. This process was repeated until the E_{rad} and E_{circ} values stabilized at values producing a specified minimum difference between the measured and predicted leaflet displacements. These final E_{rad} and E_{circ} values are those reported in this chapter.

Applying this technique to data from 17 hearts (control run datasets provided in Appendix F), Krishnamurthy, *et al.*³ found that the elastic moduli of the ovine anterior leaflet during IVR (T1 at end-IVR, assumed as the minimum-stress reference state; T2 at IVR onset) were $E_{circ} = 43 \pm 18 \text{ N/mm}^2$ and $E_{rad} = 11 \pm 3 \text{ N/mm}^2$, respectively; thus the ovine anterior leaflet *in vivo* was found to be anisotropic, roughly 4x stiffer in the circumferential than radial direction. With these values, the computer model predicted the anterior leaflet shape at T2 with group mean residuals of $0.4 \pm 0.2 \text{ mm}$ (mean $\pm$ SD, range 0.2-0.7 mm). These small residuals suggest that the anterior leaflet material is remarkably homogeneous during IVR, because a single type of finite element with constant moduli, applied throughout the leaflet and modified only by regional leaflet geometry, allowed a very close fit to very complex leaflet displacements. Further, this stiff leaflet, exhibiting small leaflet displacements, appeared to be operating over a very limited range of strains for a wide range of trans-leaflet pressures, as pointed out in Chapter 11.

These E_{circ} and E_{rad} values from beating hearts were considerably greater than *post*-transitional values from excised leaflets (E_{circ} 5-12X greater, E_{rad} 2-55X greater) and several orders of magnitude greater than *pre*-transitional moduli from such leaflets. Although Krishnamurthy, *et al.*³ found that leaflet stiffness was quite sensitive to leaflet thickness (as expected), large variations in the elastic moduli assumed for the strut chords inserted at correct anatomical positions into the anterior leaflet belly had only negligibly small effects on the computed circumferential and radial moduli. Thus it appears, as discussed previously in this book, that the strut chords have only a minor role in supporting the leaflet belly against systolic pressures.

Our next series of experiments tested whether leaflet stiffness was greater during isovolumic contraction (IVC), at the beginning of each beat, than during isovolumic relaxation (IVR), at the end of that same beat. These experiments were motivated by the work of Cooper, *et al.*⁴ who demonstrated the presence of atrial muscle in the anterior leaflet, Sonnenblick, *et al.*⁵ who showed that isolated anterior leaflets exhibited active contraction in response to electrical stimulation, and Curtis and Priola⁶ who demonstrated that the leaflets were electrically excited at the beginning of each beat. Itoh, *et al.*⁷ found that this was indeed the case, with both circumferential and radial moduli being from 50-70% greater during IVC than during IVR ($C > R$, Figure 29.4). Thus the anterior leaflet experiences a stiffness “twitch” at the beginning of each beat; a twitch that is abolished by β -blockade with esmolol ($C = R$, ESML, Figure 29.4). Such a twitch may stiffen the leaflet to absorb the shock of the rapidly rising LVP at the beginning of each beat.

Because Marron, *et al.*⁸ had shown that the anterior leaflet is richly innervated and Curtis and Priola⁶ showed that anterior leaflet motion could be influenced by neural stimulation, our next experiment was performed to determine whether leaflet stiffness *in vivo* could be altered by neural stimulation. Itoh, *et al.*⁷ found that sub-threshold pulse stimulation of the saddlehorn region (near Marker #22) at 320 min⁻¹ left all other measured cardiac variables unchanged (by design), but nearly *doubled* both circumferential and radial moduli (STIM, Figure 29.4). Note that neural stimulation had no effect on the leaflet stiffness twitch (C>R, Figure 29.4), unlike β -blockade. Subsequent work by Swanson *et al.*⁹ showed that both circumferential and radial moduli could also be reduced by central vagal stimulation. These findings suggest the possibility of both local and central control of leaflet stiffness, a speculation strengthened by the known presence of sensory nerves in the leaflet that might be reporting leaflet stretch.

We next examined the regional stiffening of the leaflet, motivated by the knowledge that muscle fibers are present almost exclusively in the annular half of the leaflet. Krishnamurthy *et al.*¹⁰ partitioned the leaflet as shown in Figure 29.5.

Figure 29.5 Heterogeneous FEA model. ANNULUS (green); BELLY (magenta); EDGE (blue).

Figure 29.4 Anterior leaflet circumferential (top) and radial (bottom) moduli (group mean $\pm$ SD) for esmolol (ESML) and sub-threshold electrical pulse stimulation (STIM) interventions. C=IVC modulus; R=IVR modulus. ESML control (CTRL, solid blue, red); ESML (crosshatched blue, red). STIM control (CTRL, solid black, green); STIM (crosshatched black, green)

As shown in Figure 29.6, Krishnamurthy *et al.*¹⁰ found that both CTRL E_{circ} and CTRL E_{rad} were quite similar in the three leaflet regions (ANNULUS, BELLY, EDGE), but β -blockade (ESML) completely abolished the IVC twitch stiffening in the ANNULUS region, partially in the BELLY region, but not in the EDGE region. Because leaflet muscle is similarly distributed, most dense in the ANNULUS, sparse in the BELLY, and none in the EDGE, this strongly suggested that the leaflet twitch arises from stimulation of these fibers by atrial excitation at the beginning of every beat, with β -blockade eliminating the twitch stiffening of these fibers. Once again, and consistent with earlier results, β -blockade had no effect on IVR stiffness.

The extra IVC stiffness (relative to IVR stiffness) in the EDGE region remains an unresolved issue. It is not due to leaflet muscle fibers in this region, because they are not present. Further, this extra stiffness is not affected by β -blockade, once again reducing the probability of muscle fiber involvement. It is also unaffected by neural stimulation. As discussed in Krishnamurthy *et al.*¹⁰, this could relate to geometric stiffening due to edge curvature change during coaptation, but this will require further study. The stiffness support provided to the anterior leaflet edge by contact with the posterior leaflet edges during coaptation also has not been fully explored, although anterior leaflet edge markers do reflect the effect of this interaction.

Figure 29.7 Four systolic time intervals (Δt_1 , Δt_2 , Δt_3 , Δt_4) analyzed in Krishnamurthy *et al.*². IVC=isovolumic contraction; MID=mid systole; IVR=isovolumic relaxation; LVP=left ventricular pressure; LAP=left atrial pressure.

Figure 29.6 Group mean anterior leaflet circumferential (top) and radial (bottom) moduli, control (CTRL) vs. esmolol (ESML) intervention, for the three leaflet regions (ANNULUS, BELLY, EDGE) defined in Figure 29.5. IVR moduli (blue); IVC moduli for same beat (red).

If the leaflet stiffening twitch is due to slips of atrial muscle fibers in the anterior leaflet, then leaflet stiffening should drop to near-IVR values in the latter half of ventricular systole. To test this possibility, Krishnamurthy *et al.*² measured anterior leaflet E_{circ} and E_{rad} for the four time intervals shown in Figure 29.7.

As postulated, Krishnamurthy *et al.*² found that leaflet stiffness moduli, both E_{circ} and E_{rad} , fell rapidly from IVC values to near-IVR values after mid-systole, adding further evidence that the early systolic stiffness twitch arises from transient contraction of excited muscle fibers in the leaflet that relax in late systole.

If the leaflet stiffness twitch arises from leaflet muscle fibers excited from atrial depolarization, then this twitch stiffening should be abolished in ventricular beats not preceded by atrial excitation. In order to test this postulate, Swanson *et al.*¹¹ utilized high-septal left ventricular pacing to create ventricular beats that were not preceded by atrial depolarization. Figure 29.8 from this study (control run datasets provided in Appendix A) demonstrates that the leaflet stiffening twitch requires atrial excitation. Without such excitation, early systolic twitch stiffening is abolished in the annular region and attenuated in the leaflet belly. Note the similarity of these results to those after β -blockade (Figure 29.6), suggesting that leaflet muscle contraction, the basis of the early systolic stiffening twitch, requires excitation from atrial depolarization as well as intact β -receptors.

Further analysis by Swanson *et al.*¹¹ of these CTRL and NAC data during the four time intervals defined in Figure 29.7 showed that total leaflet stiffness (Figure 29.9, red bars) is the sum of the leaflet early systolic stiffening twitch and a constant, steady-state baseline leaflet “tone” (Figure 29.9, blue bars) throughout systole.

If total leaflet stiffness is the sum of leaflet twitch plus leaflet tone, the question arises “do leaflet twitch and tone arise from a single mechanism with multiple responses, or multiple mechanisms with independent responses?” Swanson *et al.*¹² studied this by first blocking leaflet β -receptors with systemic esmolol, then stimulating leaflet nerves with sub-threshold (320 min^{-1}) current pulses to the saddlehorn region (Marker #22, Figure 29.3). The results, shown in Figure 29.10, show that even when anterior leaflet myocyte contraction was

blocked by β -blockade, neural stimulation stiffened all regions of the leaflet during both IVC and IVR. This demonstrated that there are at least two contractile systems in the leaflet; one being the leaflet cardiac muscle, involving a β -dependent pathway, others via a β -independent pathway, likely involving valvular interstitial cells and/or smooth muscle cells.

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CHAPTER 30 ACTIVE ANTERIOR LEAFLET

Mitral valve leaflets have long been considered as passive flaps. The findings described in Chapter 29 suggest otherwise, but the possibility that the large stiffness of the anterior leaflet arises simply from leaflet residual strains that place passive leaflet elastic elements into the post-translational nonlinear region of their stress-strain curves must be considered. In the nonlinear stress-strain curves obtained by May-Newman and Yin¹ from excised mitral leaflets (Figure 29.1) this requires residual stretch of roughly 15% or more for the anterior leaflet.

For many reasons, we do not think that the behavior of hyperelastic (nonlinear) passive leaflet elements, with stress-strain relations such as those in Figure 29.1, can accommodate the findings in Chapter 29. One of these involves the leaflet stiffness response to neural stimulation; the STIM experiment of Itoh *et al.*², as discussed in Chapter 29.

Because the saddlehorn stimulation (near Marker #22) was, by design, sub-threshold in intensity and too rapid for the heart to follow, the STIM pulses did not alter left ventricular hemodynamics (Figure 30.1) or mitral annular dimensions (Figure 30.2), but they nearly doubled both circumferential stiffness (Figure 30.3) and radial stiffness (Figure 30.4) throughout the entire anterior leaflet. While this alone strongly suggests active behavior (characteristic of contractile tissues), the maximal principal strain response to STIM poses an additional problem for any attempt to explain this result by invoking passive nonlinear elastic elements stretched into the post-translational region. Note that maximal principal strain (Figure 30.5) was reduced by almost half with STIM. In Figure 29.1, passive stiffness is only increased if stretch is increased. With the STIM experiment, however, stiffness was nearly doubled with a reduction in strain by nearly half. This is typical behavior of active tissues, such as muscles, but incompatible with passive soft tissues having hyperelastic stress-strain curves similar to those displayed in Figure 29.1.

Further, Krishnamurthy *et al.*³ computed circumferential and radial moduli during 4 time-intervals during isovolumic relaxation for 3 beats in each of 8 hearts. Each time interval was analyzed independently, thus the results represented 192 separate, independent inverse finite element solutions, with no requirement for the combined time-steps to exhibit linear behavior. But the linearity of the stress-strain curve for each beat, characterized by the correlation coefficient (r^2) associated with a linear regression analysis of each curve, was 0.995 ± 0.003 (SD) for the circumferential curves and 0.994 ± 0.003 (SD) for the radial curves. While this linear behavior is at odds with post-translational elasticity of passive biological tissues (which is highly nonlinear as shown in Figure 29.1), and thus does not support the concept of passive hyperelastic leaflet tissue, it is even more remarkable because it strongly suggests that *leaflet stiffness is insensitive to pressure and time-invariant during isovolumic relaxation*. This is consistent with the virtually invariant anterior leaflet shape during IVR discussed in Chapter 9 and the nearly invariant anterior leaflet area during IVR discussed in Chapter 10. In many ways, then, the anterior leaflet is behaving much like a canvas sail that can bend to its near-final shape in a light breeze, yet hold this shape, with very little displacement or surface strain, in a gale. This behavior may contribute to the remarkable ability of this thin membrane-like anterior leaflet to withstand the high systolic pressures generated by the millions of contractile cells in the ~1cm-thick left ventricular myocardium without buckling.

¹ May-Newman K, Yin FC. Biaxial mechanical behavior of excised porcine mitral valve leaflets. *Am J Physiol*. 1995;269(4 Pt 2):H1319-1327.

² Itoh A, Krishnamurthy G, Swanson JC, Ennis DB, Bothe W, Kuhl E, Karlsson M, Davis LR, Miller DC, Ingels NB, Jr. Active stiffening of mitral valve leaflets in the beating heart. *Am J Physiol Heart Circ Physiol*. 2009;296(6):H1766-1773.

³ Krishnamurthy G, Itoh A, Bothe W, Swanson JC, Kuhl E, Karlsson M, Craig Miller D, Ingels NB, Jr. Stress-strain behavior of mitral valve leaflets in the beating ovine heart. *J Biomech*. 2009;42(12):1909-1916.

Figure 30.1 STIM experiment group mean ($\pm$ SD) left ventricular hemodynamic parameters CTRL (before) and STIM (during) sub-threshold 320 min⁻¹ saddlehorn electrical pulse stimulation (N=7).

Figure 30.2 STIM experiment group mean ($\pm$ SD) mitral annular dimensional parameters CTRL (before) and STIM (during) sub-threshold 320 min⁻¹ saddlehorn electrical pulse stimulation. (N=7).

Figure 30.3 Individual and group mean ($\pm$ SD) circumferential anterior leaflet moduli, CTRL (before) and STIM (during) sub-threshold 320 min⁻¹ saddlehorn electrical pulse stimulation. (N=7).

Figure 30.4 Individual and group mean ($\pm$ SD) radial anterior leaflet moduli, CTRL (before) and STIM (during) sub-threshold 320 min⁻¹ saddlehorn electrical pulse stimulation. (N=7).

CHAPTER 31 VALVULAR INTERSTITIAL CELLS

The stiffening “twitch” of the annular half of the anterior mitral leaflet at the beginning of each beat likely arises from P-wave-stimulated, β -dependent, neurally-insensitive myocytes located in this region. The source of the ubiquitous, β -independent, neurally-sensitive, steady-state stiffness “tone” of the entire anterior leaflet is less clear, but may involve contractile Valvular Interstitial Cells (VICs) bound to leaflet collagen by $\alpha 2\beta 1$ integrins, as discussed by Stephens *et al.*¹

Figure 31.1, by Dr. Julia Swanson, schematically shows actin-containing VIC extensions binding to collagen fibers via $\alpha 2\beta 1$ integrin and linking proteins.

Figure 31.2 schematically illustrates some of the results from Stephens *et al.*¹

- TOP: KCL induces contractile force in VICs that is transmitted to collagen via integrin binding and results in the development of leaflet contractile force.
- MIDDLE: VIC/Collagen binding is prevented by $\alpha 2\beta 1$ integrin antibody, resulting in uncoupling KCL-induced VIC contractile force from leaflet contractile force.
- BOTTOM: Cytochalasin prevents KCL-induced VIC contraction and thus leaflet contractile force, in spite of $\alpha 2\beta 1$ integrin binding of VICs and collagen.

Figure 31.1 Schematic by Julia Swanson showing actin-containing VIC extensions binding to collagen fibers via $\alpha 2\beta 1$ integrin and linking proteins.

Figure 31.2 VIC-Collagen-Integrin interaction schematics. See text.

¹ Stephens EH, Durst CA, Swanson JC, Grande-Allen KJ, Ingels NB, Jr., Miller DC. Functional coupling of valvular interstitial cells and collagen in the mitral leaflet. *Cellular and Molecular Bioengineering*. 2010;3(4):428-437.

CHAPTER 32 ANTERIOR LEAFLET PERFUSION

The anterior leaflet contains both sensory and motor nerves, striated and smooth muscle, VICs, and other metabolizing cell types, thus it is not surprising that blood vessels have been found in the leaflet body and chordae, although such findings have sometimes stirred controversy. Swanson *et al.*¹ employed selective injections of fluorescein dye into the left anterior descending and circumflex coronary arteries of ovine hearts excised immediately after heparinization and cardioplegic arrest to assess potential leaflet perfusion patterns associated with such vessels.

Figure 32.1, a typical finding from the study of Swanson *et al.*¹, shows vessels extending and branching into the leaflet from regions near the anterior commissure. Figure 32.2 shows endocardial vessels leading up to chordae as one potential source of such perfusion.

From these studies, Swanson *et al.*¹ concluded that the myocyte-containing annular half of the anterior leaflet had a rich vascular supply arising from the mid- and distal left circumflex coronary artery, entering the leaflet near the trigones, particularly near the commissures. Additional leaflet perfusion may also be provided by both strut and, possibly, edge chordae.

Figure 32.1. A prominent vessel extending down into the leaflet near the anterior commissure.

¹ Swanson JC, Davis LR, Arata K, Briones EP, Bothe W, Itoh A, Ingels NB, Miller DC. Characterization of mitral valve anterior leaflet perfusion patterns. *J Heart Valve Dis.* 2009;18(5):488-495.

Figure 32.2 shows endocardial vessels leading up to chordae.

CHAPTER 33 LEAFLET ANGLES AND SEPARATION

In this chapter we explore the opening and closing behavior of the anterior and posterior leaflets whose hinge regions define the mitral annulus.

Figure 33.1 defines the leaflet edge-edge separation distance (D3738) and anterior ($\Phi 182238$) and posterior ($\Phi 221837$) leaflet edge angles with respect to the mitral annulus that will be examined in this chapter. Figure 33.2 displays the time history of these variables throughout three cardiac cycles for hearts H1-H6 (data in Appendix A).

During ejection, the anterior leaflet maintains a virtually unchanging angular relationship to the mitral annulus in all hearts, while the posterior leaflet angle may be relatively constant (in H1, H2, and H4) or decrease (in H3, H5, and H6) as ejection proceeds.

During left ventricular relaxation, the onset of rapid anterior and posterior leaflet opening rotations (onset of increases in $\Phi 182238$ and $\Phi 221837$) occurs within ± 17 ms of mitral valve opening as defined by the time of the abrupt increase of leaflet edge-edge separation, *i.e.* D3738 increase. The most likely candidate triggering leaflet opening is simply the trans-leaflet pressure gradient associated with the reduction in left ventricular pressure below left atrial pressure at the end of isovolumic LV relaxation.

During diastole, the effect of early (E-wave) and late (A-wave) flow from the left atrium into the left ventricle in sequentially pulsing the leaflet edges apart is always in evidence, but to various degrees in each heart. The posterior leaflet opens more widely (greater angle with respect to the annulus) than the anterior leaflet in all hearts, suggesting that it offers less resistance to left ventricular inflow than the anterior leaflet.

Valve closure is complex. The interval from the onset of the rapid systolic rise of LVP to mitral valve closure (defined as a stable minimum of D3738) is seen to range from 17-83ms. In these hearts, both the anterior and posterior leaflet edges begin well-defined abrupt rotations towards closure (onset of reductions in $\Phi 182238$ and $\Phi 221837$) as early as 33ms before or as late as 33ms after the onset of the rapid systolic rise of LVP. Thus, although the rapid rise of LVP would always be expected to force valve closure (a fail-safe mechanism), something other than simply the onset of the rapid systolic rise of LVP is also capable of abruptly triggering the rotation of both leaflet edges towards closure and this mechanism exhibits variable trigger timing with respect to IVC onset. Further, the time of onset of the abrupt rotations toward closure of both the anterior and posterior leaflets is highly-correlated in these hearts (0.93), suggesting that a common mechanism is acting to initiate the movement of both leaflets towards closure. Local LV regional flow patterns acting in concert on the leaflets with waning A-wave flow in the space between the leaflets is a likely candidate for this mechanism. Some flow-related issues will be explored in the next chapter.

Figure 33.2 Anterior and posterior leaflet edge-edge separation and angles with respect to the mitral annulus for hearts H1-H6 (data in Appendix A). LVP=left ventricular pressure; MVO=mitral valve opening; MVC=mitral valve closure; PML=posterior mitral leaflet; AML=anterior mitral leaflet; $\Phi 221837$ =posterior leaflet angle subtended by markers #22-18-37; $\Phi 182238$ =anterior leaflet angle subtended by markers #18-22-38; D3738=separation distance (mm, left ordinate) between central meridional anterior and posterior leaflet edges.

CHAPTER 34 LEFT VENTRICULAR FLOW

In Chapter 05 we studied the relationship of anterior leaflet shape to left ventricular pressure and flow from mid-diastole through mid-systole for hearts H1-H6 (data in Appendix A), finding that the anterior leaflet edge was highly mobile, in contrast to the almost immobile annular third of the leaflet. In this chapter we examine the relationship of anterior and posterior leaflet edge mobility to left ventricular inflow (quantified as described in Appendix C) and pressure.

Figure 34.1 shows that the E- and A-wave inflow patterns are highly reproducible from beat-to-beat in hearts H1-H6, although they exhibit significant differences from heart-to-heart. Note that initial LV inflow occurs slightly before mitral valve opening (*i.e.* leaflet separation). This results from leaflet shape changes as LVP falls to low values immediately before valve opening. Because the anterior leaflet is so stiff, the elastic change in posterior leaflet geometry is likely to be a prime candidate for this volume change.

Figure 34.2 displays single beats from Figure 34.1 on an expanded scale, with inclusion of leaflet edge central meridian angles with respect to the annulus. Table 34.1 gives the regurgitant volumes associated with mitral valve closure for each beat in each heart. Some preliminary comments regarding these results:

- H1 has very little inflow in the last third of diastole, yet both anterior and posterior leaflet edges are at their closed positions. A brief atrial systole kicks the leaflets open a bit (very little), so closure driven by the initial LVP increase doesn't have far to go. It is noteworthy that even though the leaflets are almost at their closed positions when LVP starts to rise, closing regurgitation is a large 6.9ml, 18% of SV, seemingly very inefficient.
- H2 has good E- and A-wave filling, each of which kick the leaflets open, but regurgitation starts early, before the onset of LVP increase, so the leaflets are half-closed before the LVP increase shuts them for good. Closing regurgitation is a large 3ml, 12% of SV. While flow and leaflet excursions are tightly coupled during the E-wave, during the A-wave, leaflet excursion is significantly delayed behind flow.
- H3 has almost no inflow for most of the last half of diastole and both anterior and posterior leaflet edges stay at their closed positions all this time. A very late atrial systole with almost no inflow kicks the leaflets wide open, but the early systolic LVP increase abruptly swings them back shut with 2.9ml closing regurgitation, 8% of SV. While flow and leaflet excursions are tightly coupled during the E-wave, leaflet excursion is delayed behind flow quite a bit during the A-wave.
- H4 has normal-looking E- and A-waves. The leaflets open widely and are only about half-way back toward their closed position when they are sealed by the rising LVP. Closing regurgitation is essentially zero. This may be the most normal beat analyzed of all these 6 hearts studied.
- H5 has a strong E-wave, but, although the A-wave kicks the leaflets open some, this is not accompanied by a burst of filling. This casts some doubt on the concept that leaflet opening motions are completely dictated by filling bursts....perhaps they are also driven by atrial excitation contracting atrial muscle fibers in the annular portion of the anterior and posterior leaflets that swings them towards opening? (This may be occurring in H3 as well...almost no filling burst with A-wave excitation, but a big kick opening for the leaflets). H5 closing regurgitation is only 0.4 ml, less than 2% of SV, a very efficient closure.
- H6 exhibits normal-looking E- and A-wave patterns. Both anterior and posterior leaflets are rapidly shut, however, by the rising LVP at the onset of systole. While flow and leaflet excursions

are tightly coupled during the E-wave, leaflet excursion is delayed behind flow quite a bit during the A-wave. Closing regurgitation is 2.1ml, 8% of SV.

In all these six hearts, although E-wave inflow kicks both the anterior and posterior leaflets toward open positions, they swing back towards their closed positions as early filling wanes. This could result from at least two forces acting on the leaflets. The collapse of the lowered pressure in the inflow stream from the Bernoulli Effect may tend to push the leaflets back towards closed positions. Perhaps even more important might be the strut chord forces tending to gently close the leaflets at all times. The vortices shed behind the leaflets are possible factors, but they may be too brief to have a major effect driving the leaflets toward closure.

Being in a nearly closed position as LVP just starts to rise does not seem to confer an advantage toward efficient closing as measured by closing regurgitation. H1 and H2 are in nearly closed positions at the onset of LVP increase, but exhibit large (seemingly inefficient) closing regurgitation.

Besides the pressure of inflowing blood, A-wave-induced leaflet opening may involve atrial muscle contraction in the annular portion of the anterior and posterior leaflets. H3 and H5 exhibited late diastolic leaflet opening, with little or no E-wave flow. This may relate to the phenomenon measured by Curtis and Priola¹, as well as the early-systolic anterior leaflet stiffening “twitch” discussed in Chapter 29.

¹ Curtis MB, Priola DV. Mechanical properties of the canine mitral valve: effects of autonomic stimulation. *Am J Physiol.* 1992;262(1 Pt 2):H56-62.

HEART	BEAT	LVPonset	MVC	Δ LVV	SV	HR	CO	Δ LVVavg	REGURG
		FRAME	FRAME	ml	ml	B/M	L/M	ml	%SV
H1	B1	19	21	-6.9	38.5	100	3.9	-6.9	18
	B2	55	57	-7.1					
	B3	91	93	-6.6					
H2	B1	21	23	-3.2	24.3	100	2.4	-3	12
	B2	57	59	-3					
	B3	93	95	-2.8					
H3	B1	24	29	-3.2	36.2	74	2.7	-2.9	8
	B2	72	77	-2.7					
	B3	121	125	-2.8					
H4	B1	15	16	-0.2	24.1	86	2.1	0.1	0.3
	B2	57	59	0.1					
	B3	99	101	0.3					
H5	B1	20	22	-0.9	23.1	91	2.1	-0.4	1.6
	B2	60	62	0.2					
	B3	99	101	-0.5					
H6	B1	14	17	-2.4	26.7	80	2.1	-2.1	8
	B2	59	62	-2.1					
	B3	104	107	-1.9					

Table 34.1. Regurgitant volume associated with mitral valve closure for 3 sequential beats in hearts H1-H6. LVPonset=time of initial increase of left ventricular pressure (sampling rate= 60 frames/sec); MVC=time of mitral valve closure; Δ LVV=change in left ventricular volume from LVPonset to MVC; SV=left ventricular stroke volume; HR=heart rate; CO=cardiac output (SV*HR); Δ LVVavg=3-beat average of regurgitant volume for each heart; REGURG=average regurgitant volume expressed as a percentage of SV for each heart.

CHAPTER 35 CLOSURE AND ANIMATIONS

Figures 35.1-35.6 display mitral valve annular and leaflet geometry snapshots from the animations provided in Appendix D for specific instants associated with left ventricular inflow and pressure from peak diastolic inflow through valve closure and early left ventricular systole for hearts H1-H6 (data in Appendix A).

Appendix D provides the frame-by-frame animations of these same data throughout a complete cardiac cycle for each heart from two viewpoints: side views from the right fibrous trigone towards the left fibrous trigone; top views from the left atrium towards the left ventricle. For each view, the current instant in the cardiac cycle is identified by the black symbol on the left ventricular pressure curve (gray). The marker positions at that instant are connected by lines, with the mitral annulus in blue, anterior leaflet edge in red, and lateral LV epicardium merging into the central meridian of the P2 posterior leaflet scallop in green (side view) and lateral annular marker to central P2 posterior leaflet edge marker in green (top view). The color-coded dots in each frame show the previous locations of each marker throughout the cardiac cycle. The top view also shows the left ventricular basal marker positions at each instant (large black symbols), with anterior LV at left, posterior LV at right, lateral LV at bottom, and septum at top.

Figure 35.3 Mitral valve annular and leaflet geometry (TOP) during specific instants (COLOR CODED) associated with (BOTTOM) left ventricular inflow (FLOW, dashed) and left ventricular pressure (LVP) during valve closure for heart H3. Maximum inflow (purple); onset of systolic LVP rise (green); leaflet closure (blue). TOP: Marker #22=annular saddlehorn; #16=left fibrous trigone; #24=right fibrous trigone; #13=lateral basal left ventricular epicardium.

CHAPTER 36 COAPTATION REPEATABILITY AND RIGIDITY

Competent mitral valve closure requires tight coaptation of the edge surfaces of the anterior and posterior leaflets. This chapter explores the precision with which specific sites on these surfaces are geometrically aligned at the beginning of each beat (repeatability) and the precision with which this alignment is maintained throughout left ventricular ejection (rigidity).

Figure 36.1 repeats, for reference purposes, the marker array for the ovine COM-series discussed in Chapters 23-27 (see also the COM data and animations in Appendix E). The 5 markers on the anterior leaflet edge and the 9 opposing posterior leaflet edge markers allow 3-D measurements every 16.7 ms of geometric leaflet edge alignments at the beginning of each beat as well as throughout left ventricular ejection for each beat.

Figures 36.2-36.7 display the distances between apposed leaflet edge markers throughout three cardiac cycles in each of 6 COM hearts. Visual inspection of the top panel in each figure suggests that edge-edge geometric relationships are highly repeatable from beat to beat, as well as throughout each beat, but a further analysis was conducted to quantify these relationships.

Figure 36.1 COM-series marker array. See Chapter 23 text for marker locations.

If $D_{xxyy}(f)$ is the distance between markers xx and yy in frame f , and $D_{xxyysysavg}$ is the average distance between these markers in the closed valve for all three beats, combined, then the difference between these quantities, $D_{xxyydev}(f) = D_{xxyy}(f) - D_{xxyysysavg}$ is the deviation of the distance between markers xx and yy for each frame from their 3-beat systolic average. The lower middle panel in Figures 36.2-36.7 illustrates all $D_{xxyydev}(f)$ on an expanded scale for one beat from the upper panel in each heart. Again, these graphs suggest that edge-edge geometric relationships are highly repeatable from beat to beat, as well as during each beat, but Table 36.1 (below), showing the standard deviation (mm) for each $D_{xxyydev}(f)$ during the time the valve was closed for all three beats combined, further quantifies this conclusion.

HEART	D0403	D0405	D0406	D00706	D0708	D0709	D1009	D1011	D1012
C-1	0.6	0.6	0.9	1.0	0.6	1.8	0.5	0.6	0.6
C-2	0.2	0.4	0.2	0.2	0.3	0.6	0.3	0.4	0.2
C-3	0.3	0.3	0.3	0.5	0.7	0.9	0.5	0.4	0.1
C-4	0.6	0.5	0.5	0.9	0.8	1.6	0.6	0.4	0.2
C-5	0.3	0.4	0.5	0.3	0.3	0.4	0.3	0.3	0.6
C-6	0.2	0.2	0.3	0.2	0.3	0.2	0.4	0.3	0.3
MEDIAN	0.3	0.4	0.4	0.4	0.5	0.7	0.4	0.4	0.3
MAX	0.6	0.6	0.9	1.0	0.8	1.8	0.6	0.6	0.6
MIN	0.2	0.2	0.2	0.2	0.3	0.2	0.3	0.3	0.1

Thus, in this study, these sites on the leaflet edges were reproducibly aligned at the beginning of each beat with mm (and typically sub-mm) precision and this alignment precision was preserved, as though the coaptation region was nearly-rigid, in the closed valve for the duration of each beat.

Figures 36.8-36.13, again utilizing data from hearts C1-C6 (Appendix E), further demonstrate this coaptation repeatability and rigidity in the closed valve. In each frame of each heart, a best-fit annular plane was obtained from Markers #15-22, the projection of Marker #22 was translated to the origin, the projection of Marker #18 was rotated to lie on the minus X-axis, and the best-fit annular plane was rotated to coincide with the X-Y plane. In this orientation, the posterior leaflet P1 scallop had a positive Y-coordinate and the left ventricular aspect of the valve a negative Z-coordinate.

Note, in Figures 36.8-36.13, the tightly superimposed curves indicating, not only positional stability during ejection and during large reductions in left ventricular pressure during isovolumic relaxation, but that these valve components returned to the *same* positions in each of the three sequential beats. We interpret this positional stability as reflecting the importance of all chordae in guiding the exact positions of all portions of the leaflet at the moment of closure, with subsequent rigidity attributable to additional aspects of valve geometry and mechanics discussed in Chapters 9, 10, 11, 13, 22, 29, and 41.

Figure 36.2 Top panel: Inter-marker distances (e.g., D0403=Distance from marker #04 to #03) with scaled left ventricular pressure (LVP/3, for timing) for C1 COM07R04. Frame rate=60sec⁻¹ Lower left panel: Marker locations, mm scales. Lower middle panel: One-beat example of the deviation (mm) from the systolic mean for each inter-marker distance (LVP/10 for timing). Lower right panel: Color-code for inter-marker distances.

Figure 36.3 Top panel: Inter-marker distances (e.g., D0403=Distance from marker #04 to #03) with scaled left ventricular pressure (LVP/3, for timing) for C2 COM06R01. Frame rate=60sec⁻¹ Lower left panel: Marker locations, mm scales. Lower middle panel: One-beat example of the deviation (mm) from the systolic mean for each inter-marker distance (LVP/10 for timing). Lower right panel: Color-code for inter-marker distances.

Figure 36.4 Top panel: Inter-marker distances (e.g., D0403=Distance from marker #04 to #03) with scaled left ventricular pressure (LVP/3, for timing) for C3 COM02R02. Frame rate=60sec⁻¹. Lower left panel: Marker locations, mm scales. Lower middle panel: One-beat example of the deviation (mm) from the systolic mean for each inter-marker distance (LVP/10 for timing). Lower right panel: Color-code for inter-marker distances.

Figure 36.5 Top panel: Inter-marker distances (e.g., D0403=Distance from marker #04 to #03) with scaled left ventricular pressure (LVP/3, for timing) for C4 COM01R04. Frame rate=60sec⁻¹. Lower left panel: Marker locations, mm scales. Lower middle panel: One-beat example of the deviation (mm) from the systolic mean for each inter-marker distance (LVP/10 for timing). Lower right panel: Color-code for inter-marker distances.

Figure 36.6 Top panel: Inter-marker distances (e.g., D0403=Distance from marker #04 to #03) with scaled left ventricular pressure (LVP/3, for timing) for C5 COM03R04. Frame rate=60sec⁻¹ Lower left panel: Marker locations, mm scales. Lower middle panel: One-beat example of the deviation (mm) from the systolic mean for each inter-marker distance (LVP/10 for timing). Lower right panel: Color-code for inter-marker distances.

Figure 36.7 Top panel: Inter-marker distances (e.g., D0403=Distance from marker #04 to #03) with scaled left ventricular pressure (LVP/3, for timing) for C6 COM04R01. Frame rate=60sec⁻¹ Lower left panel: Marker locations, mm scales. Lower middle panel: One-beat example of the deviation (mm) from the systolic mean for each inter-marker distance (LVP/10 for timing). Lower right panel: Color-code for inter-marker distances.

Figure 36.8 Heart C1. Upper left panel: View from LA to LV of cubic splines through annular markers (#15-22, outer black perimeter), posterior P1 edge (#2,3,5), P2 edge (#5,6,8,9,11), P3 edge (#11,12,14), and anterior leaflet edge (#2,1,4,7,10,13,14) superimposed for all LVP times identified by red symbols in the lower left panel. Right panel: 3D view of curves in upper left panel. See text.

Figure 36.9 Heart C2. Upper left panel: View from LA to LV of cubic splines through annular markers (#15-22, outer black perimeter), posterior P1 edge (#2,3,5), P2 edge (#5,6,8,9,11), P3 edge (#11,12,14), and anterior leaflet edge (#2,1,4,7,10,13,14) superimposed for all LVP times identified by red symbols in the lower left panel. Right panel: 3D view of curves in upper left panel. See text.

Figure 36.12 Heart C5. Upper left panel: View from LA to LV of cubic splines through annular markers (#15-22, outer black perimeter), posterior P1 edge (#2,3,5), P2 edge (#5,6,8,9,11), P3 edge (#11,12,14), and anterior leaflet edge (#2,1,4,7,10,13,14) superimposed for all LVP times identified by red symbols in the lower left panel. Right panel: 3D view of curves in upper left panel. See text.

Figure 36.13 Heart C6. Upper left panel: View from LA to LV of cubic splines through annular markers (#15-22, outer black perimeter), posterior P1 edge (#2,3,5), P2 edge (#5,6,8,9,11), P3 edge (#11,12,14), and anterior leaflet edge (#2,1,4,7,10,13,14) superimposed for all LVP times identified by red symbols in the lower left panel. Right panel: 3D view of curves in upper left panel. See text.

CHAPTER 37 FOUR BALLOONS

In this chapter, we metaphorically characterize the mitral leaflets as segments of four inflated balloons pressed together on the ventricular side of the mitral annulus in such a geometric configuration as to preclude their crowding through the mitral annulus into the left atrium. The greater the inflation pressure (LVP), the more firmly the balloon interfaces press together, the more impossible it becomes to crowd this assemblage through the annulus. This concept, visualized schematically in Figures 37.1 and 37.2, makes the closed valve almost self supporting, requiring very little chordal force to maintain its closed configuration. The resulting stiffness of this

Figure 37.2. Mitral valve geometry as viewed from the left atrium (top panel) and LFT to RFT (bottom panel). ANT=anterior leaflet; P1,2,3= posterior leaflets P1, P2, P3. Arrows represent left ventricular pressure pressing on balloon interfaces.

Figure 37.1. Four balloon mitral valve analogy. ANT=anterior leaflet balloon; P1,2,3=posterior leaflet P1, P2, P3 scallop balloons. Mitral annulus (black) and anterior leaflet (color coded) from ovine data.

assemblage could contribute significantly to the remarkable ability of these very thin leaflets to withstand the large systolic pressures generated by the contractile forces from the thick-walled left ventricular myocardium.

The contact regions of the balloons exhibit three geometric configurations: folding near the annulus; 2-curve coaptation further from the annulus (in the 5 regions where 2 balloons intersect); and 3-curve coaptation further still from the annulus (in the 2 leaflet regions where 3 balloons intersect). Figure 37.3 illustrates a hypothetical sequence of folding, 2-curve coaptation, and 3-curve coaptation accompanying valve closure for a hypothetical P2-P3 region model. Experimental data supporting this sequence is provided in Chapters 24, 25, and 26 and Appendix E).

The three-dimensional geometry of the mitral leaflets in the closed valve is difficult to describe with two-dimensional media, such as this page. As suggested in Chapter 27, however, the best way to visualize

this geometry is to create a wrap-around model based on actual leaflet anatomy such as that shown in Figure 27.1. Figures 37.4-37.9 are photographs of such a model from six angles. Note that the fold-regions produced from the wide inter-scallop regions in the actual anatomic dissections are more pronounced than those produced in the relatively narrow “V-shaped” inter-scallop region in the hypothetical model shown in Figure 37.3.

These pronounced inter-scallop folds (e.g. like those produced at the dashed line in Figure 37.3A and labeled as F1-F4 in Figures 37.4-37.9, with F1 and F4 being commissural folds) could serve a number of important functions:

- They would allow the valve to open widely (as shown in Chapter 24), yet not offer significant resistance to leaflet rotation toward closure by the almost negligibly small diastolic pressure gradients following the E-wave. This would allow rapid but gentle closure at the moment LVP began to increase.
- They would prevent leakage between adjacent leaflets near the annulus when the valve was closed.

- Left ventricular systolic pressure on each side of each fold would help prevent mitral annular regional perimeter expansion during systole of the P1-P2 and P2-P3 annular interface (possibly accounting for the findings in Figure 15.3). Such annular expansion would be further resisted by translation of the left and right fibrous trigones towards the left ventricular septum driven by expansion of outflow tract by left ventricular pressure increase that further tenses the annulus, as discussed in Chapter 17. Annular expansion throughout systole would also be resisted by the inward forces associated with left ventricular systolic pressure acting on the ventricular surfaces of the posterior leaflets, as discussed in Chapter 16. During isovolumic relaxation, the decreasing left ventricular pressure would reduce all three of these forces, drawing the annulus inwards and thereby allowing annular expansion in preparation for rapid early diastolic filling.
- They would help align and position adjacent leaflet coapting surfaces precisely at the moment of valve closure.
- They would help prevent shear of adjacent leaflets from unequal forces acting on the leaflets in the closed valve.
- They would provide a rigid skeleton-like scaffold in each region to help minimize leaflet displacement in response to systolic left ventricular pressure.

All the data and analysis in this book point to the fact that initial leaflet geometry at the moment of valve closure is crucial to systolic valve mechanics. If the initial geometric conditions are set properly at this moment (*i.e.*, the complex anterior leaflet curvatures are set precisely and all leaflet edges are positioned precisely with respect to one another and the LV chamber at this time), the resulting leaflet assemblage is nearly self-supporting, becoming nearly a rigid body whose geometry is virtually independent of subsequent flow and pressure throughout systole. This concept is supported by the small papillary forces measured at the moment of valve closure, as discussed in Chapters 21 and 22, and the beat-to-beat repeatability and leaflet systolic positional stability discussed in Chapters 9, 13 and 18. Such initial leaflet shape and positioning is achieved by positioning the papillary tips at precise 3D locations at the moment of valve closure, as discussed in Chapters 3, 4, and 19, with all the chordae distributed from these tips to the many leaflet attachment sites having exactly the right lengths to place the leaflet edges to within a millimeter of their closed positions at the moment of closure, as discussed in Chapter 13. In this view, the papillary muscles and chordae act primarily to keep the anterior leaflet out of the outflow tract during diastole and to gently and precisely position the leaflets into a precise geometric configuration at the moment of closure; exerting only about 10% of ejection force during the last half of systole, as described in Chapter 22. As left ventricular pressure just begins to rise during the ECG R-wave, the slightest regurgitant pressure gradients will force the large-area anterior leaflet and P1, P2, and P3 scallops inward relative to the smaller areas exposed in the clefts between these leaflet regions, thereby assuring proper folding geometry, similar to the sequence shown in Figure 37.3. The precise initial positioning associated with all of these mechanisms also prevents the leaflet from colliding forcefully at the beginning of each beat, allowing gentle closing mechanics that spares both valve and blood components from damage.

Frictional interactions between the “rough zones” in the coaptation regions at the edges of the anterior, P1, P2, and P3 leaflets (*e.g.*, C1-C5 in Figures 37.4-37.9) lock the leaflet edges in place, thereby preventing the leaflet “balloons” from slipping past each another toward the left atrium. The folds and coaptation regions (F1-F4 and C1-C5, respectively, Figures 37.4-37.9) also form a structurally rigid supporting “skeleton” that resists displacement of the assembly towards the annulus. The higher the left ventricular pressure, the more these regions press together, and the stiffer and more extensive this structural support becomes, thereby further resisting the tendency of the leaflet assembly to displace towards the mitral annulus as LVP increases.

The shape and stiffness of the anterior leaflet allows its annular half to be virtually self-supporting, as discussed in Chapters 6, 8, 9, and 10, as well as allowing the anterior leaflet to support the radial compression (relative to its end-IVR geometry) associated with coaptation, as discussed in Chapter 11. The extra “twitch” stiffening of the annular half of the anterior leaflet, associated with atrial excitation (discussed in Chapter 29) helps maintain the self-supporting saddle-shape of this leaflet region during the sudden left ventricular pressure increase at the beginning of each beat. These additional factors help resist the tendency of the leaflet assembly to displace towards the annulus with increasing left ventricular pressure. The saddle-shape of the annular half of the anterior leaflet is also important to smooth left ventricular outflow, as described in Chapter 13.

Spreading coaptation over a large surface “rough zone” contact area reduces crushing forces below the threshold required to damage blood cells that may be trapped in the coaptation region, thus preventing blood cell damage, yet maintaining tight closure. Microscopic spaces distributed throughout the rough zone contact areas may also allow protected regions where the blood components would not be subjected to crushing forces associated with leaflet coaptation.

Near the trigones, the commissural folds (F1 and F4 in Figures 37.4-37.9) have a more restricted opening angle than F2 and F3 during LV filling. This is because F1 and F4 are at the vertices of the angle between the annular and anterior leaflet planes (see Chapter 8), allowing only limited space in that region for opening. In contrast, the posterior leaflet folds, F2 and F3, far from these vertices, exhibit opening angles of nearly 180° during diastolic filling as shown in Chapter 24. Such limited opening near the vertices, illustrated in Chapter 5, may also contribute to the limited opening of the annular half of the anterior leaflet.

The very wide opening of the posterior leaflets has flow consequences. This opening would squeeze almost all the blood out from behind them because they nearly contact the LV endocardium. This blood would flow in the same direction as, and contributes to, central LV inflow. When the posterior leaflets close again, a fresh charge of blood would enter this space; a mechanism that could prevent stasis behind the posterior leaflets. In contrast, the anterior leaflet, when maximally open, leaves a large space behind itself in the outflow tract. Indeed, the anterior leaflet region near the annulus is like a drumhead, supported by the stiff trigone regions, which guides diastolic inflow away from the LV outflow tract. Even the anterior edge region is prevented from entering too far into the outflow tract by the strut chordae. As a result, the anterior leaflet may be thought of as a flow-guiding boundary for both LV inflow and outflow, while the posterior leaflets serve the primary role of offering a minimum impediment to LV inflow during filling, then closing against the anterior leaflet to prevent regurgitation, but having a lesser impact on flow during ejection.

Figure 37.4. View from Left Atrium towards Left Ventricle. SH=Saddlehorn; LFT=Left Fibrous Trigone; RFT=Right Fibrous Trigone; LAT=Lateral annulus; ANT=Anterior Leaflet; P1,2,3= Posterior Leaflet Scallop; F1,2,3,4=Fold; C1,2,3=Two-Curve Coaptation Sites; C4,5=Three-Curve Coaptation Sites

Figure 37.5. View from Lateral Annulus towards Annular Saddlehorn. SH=Saddlehorn; LFT=Left Fibrous Trigone; RFT=Right Fibrous Trigone; LAT=Lateral annulus; ANT=Anterior Leaflet; P1,2,3= Posterior Leaflet Scallop; F1,2,3,4=Fold; C1,2,3=Two-Curve Coaptation Sites; C4,5=Three-Curve Coaptation Sites

Figure 37.6. View from Left Ventricle towards Left Atrium. SH=Saddlehorn; LFT=Left Fibrous Trigone; RFT=Right Fibrous Trigone; LAT=Lateral annulus; ANT=Anterior Leaflet; P1,2, = Posterior Leaflet Scallops; F1,2,3,4=Folds; C1,2,3=Two-Curve Coaptation Sites; C4,5=Three-Curve Coaptation Sites

Figure 37.7. View from Left Ventricle towards Left Atrium. SH=Saddlehorn; LFT=Left Fibrous Trigone; RFT=Right Fibrous Trigone; LAT=Lateral annulus; ANT=Anterior Leaflet; P2= Posterior Leaflet Scallop; F1,2,3,4=Folds; C1,2,3=Two-Curve Coaptation Sites; C4,5=Three-Curve Coaptation Sites

Figure 37.8. View from Left Fibrous Trigone towards Right Fibrous Trigone . SH=Saddlehorn; LFT=Left Fibrous Trigone; RFT=Right Fibrous Trigone; ANT=Anterior Leaflet; P1= Posterior Leaflet Scallop; F1,2,4=Fold; C1,2,3=Two-Curve Coaptation Sites; C4,5=Three-Curve Coaptation Sites

Figure 37.9. View from Annular Saddlehorn towards Lateral Annulus. SH=Saddlehorn; LFT=Left Fibrous Trigone; RFT=Right Fibrous Trigone; ANT=Anterior Leaflet; F1, 4=Fold; C1,2,3=Two-Curve Coaptation Sites; C4,5=Three-Curve Coaptation Sites

CHAPTER 38 THE COMMISSURES

The anterior commissure is the junctional region between the anterior leaflet and the P1 scallop of the posterior leaflet (Markers 1, 2, 3, and 16 in Figure 38.1; fold 3 in Figure 27.1). Figures 38.2 and 38.3 show individual frames from an animation of anterior commissure data during a representative heartbeat in COM07R04 with the valve closed, and open, respectively.

The posterior commissure is the junctional region between the anterior leaflet and the P3 scallop of the posterior leaflet (Markers 12, 13, 14, and 20 in Figure 38.1; fold 4 in Figure 27.1). Figures 38.4 and 38.5 show individual frames from an animation of posterior commissure data during the same heartbeat in COM07R04 with the valve closed, and open, respectively.

The commissure membranes allow the anterior leaflet and the P1 posterior scallop, as well as the anterior leaflet and the P3 posterior scallop, to swing freely around nearly orthogonal hinge axes in response to the very small internal LV pressure gradients when the valve is open, yet fold to form precise, rigid, tight seals between the anterior leaflet and the P1 posterior scallop and the anterior leaflet and the P3 posterior scallop as the rising LVP compresses each fold at the instant of valve closure and thereafter throughout systole.

Chapters 24, 25, and 26 provide additional illustrations of posterior leaflet folding at the P1/P2 and P2/P3 posterior leaflet junctions during this heartbeat. Appendix E provides the full animations of all dynamics throughout this heartbeat.

Figure 38.2 COM07R04 anterior commissure closed valve. Three views at Frame 53 identified on LVP (blue) and D78 (green) curves in lower left panel. Marker numbers in upper left panel refer to markers identified in Figure 38.1. Anterior leaflet blue. Anterior (P1) leaflet red. See animation in Appendix E.

Figure 38.3 COM07R04 anterior commissure open valve. Three views at Frame 35 identified on LVP (blue) and D78 (green) curves in lower left panel. Markers identified in Figures 38.1 and 38.2. Anterior leaflet blue. Posterior (P1) leaflet red. See animation in Appendix E.

Figure 38.4 COM07R04 posterior commissure closed valve. Three views at Frame 53 identified on LVP (blue) and D78 (green) curves in lower left panel. Marker numbers in upper left panel refer to markers identified in Figure 38.1. Anterior leaflet cyan and blue. Posterior P3 leaflet red. See animation in Appendix E.

COM07R04 LVP(b) D78(g) APP-E coaptationcom27.m

Figure 38.5 COM07R04 posterior commissure open valve. Three views at Frame 35 identified on LVP (blue) and D78 (green) curves in lower left panel. Markers identified in Figures 38.1 and 38.4. Anterior leaflet cyan and blue. Posterior (P3) leaflet red. See animation in Appendix E.

CHAPTER 39 SUSPENDERS, BELT

In Chapter 36 we noted that the anterior leaflet edge is roughly fixed in position throughout systole and in Chapter 28 that this edge position is almost independent of its interaction with the posterior leaflet. This suggests that effective coaptation requires the posterior leaflet to conform tightly to the edge of the stiff anterior leaflet. In this chapter, again employing the data in Appendix E, we suggest that the posterior leaflet folds are important for this task.

Figure 39.1 schematically illustrates the marker-delineated perimeters analyzed in this chapter: the anterior leaflet perimeter by Markers #2, 1, 4, 7, 10, 13, and 14; the posterior leaflet scallop perimeter (without folding) by #2, 3, 5, 6, 8, 9, 11, 12, and 14; the posterior leaflet perimeter (with folding) by #2, 3, 6, 8, 9, 12, and 14; the annular perimeter (LFT to RFT) by #15, 16, 17, 18, 19, 20, and 21; and the annular perimeter (ACOM to PCOM) by #16, 17, 18, 19, and 20.

Figures 39.2-39.5 show three views of these perimeters in the open and closed valve for four hearts in the COM series (Appendix E). Color-coded sites are annular saddlehorn (#22, cyan), left fibrous trigone (#15, open black circle), right fibrous trigone (#21, open blue circle), anterior commissure for annulus (#16, yellow) and leaflets (#2, green), and posterior commissure for annulus (#20, magenta) and leaflets (#14, red)

Figure 39.1 Schematic illustration of numbered markers delineating the mitral annulus (gray), anterior leaflet perimeter (green), and posterior leaflet perimeter (red). Dashed red lines illustrate the effect of posterior leaflet folding on posterior leaflet perimeter reduction.

Figures 39.6-39.9 show the associated perimeter lengths (obtained by numerical integration along cubic splines through the marker coordinates) for three beats in the four COM hearts analyzed. Although it was impossible to predict at the time of surgery where to place the markers so as to completely capture posterior leaflet folding dynamics, Figures 39.6-39.9 illustrate that posterior leaflet folding during closure, by reducing the distance between markers #3 and 6 at the P1/P2 junction, and markers #9 and 12 at the P2/P3 junction, allows a greater tightening of the posterior leaflet perimeter “belt” around the anterior leaflet perimeter. The unfolding of these regions during diastole allows almost the full scallop perimeter to be displayed, thereby opening the posterior portion of the valve at least as widely as the annular perimeter from LFT to RFT, allowing rapid inflow with minimum interference from the posterior leaflets. In contrast, as can be seen in Figures 39.2-39.5, the anterior leaflet basal portion does not open as widely, thereby preventing the direct diastolic inflow stream from entering the outflow tract, which could result in the inefficient collision of two flow streams in the left ventricle.

The reason that this chapter is named “Suspenders” and “Belt” is that at the instant of valve closure the 3-D geometry of the leaflets is first established by the chordae (the “Suspenders”) and then the posterior leaflet folds are forced toward one another and toward the anterior leaflet by LVP, which tightens the posterior leaflet perimeter (the “Belt”) against the anterior leaflet. The higher the left ventricular pressure, the greater the stiffness of the anterior leaflet (via the interplay between compression and tension in the saddle-shaped anterior leaflet, see Chapters 29 and 30) and the more forcefully the posterior leaflet “belt” is tightened about the stiff anterior leaflet perimeter (see additional discussion of these concepts in Chapters 26, 27, and 37).

Figure 39.6 Mitral annular (LFT to RFT, dashed black; ACOM to PCOM, solid black), anterior leaflet (green), and posterior leaflet (with folding, solid red; without folding, dashed red) perimeters vs. left ventricular pressure (LVP, blue) for H1 COM07R04.

Figure 39.7 Mitral annular (LFT to RFT, dashed black; ACOM to PCOM, solid black), anterior leaflet (green), and posterior leaflet (with folding, solid red; without folding, dashed red) perimeters vs. left ventricular pressure (LVP, blue) for H2 COM06R01.

Figure 39.8 Mitral annular (LFT to RFT, dashed black; ACOM to PCOM, solid black), anterior leaflet (green), and posterior leaflet (with folding, solid red; without folding, dashed red) perimeters vs. left ventricular pressure (LVP, blue) for H3 COM02R02.

Figure 39.9 Mitral annular (LFT to RFT, dashed black; ACOM to PCOM, solid black), anterior leaflet (green), and posterior leaflet (with folding, solid red; without folding, dashed red) perimeters vs. left ventricular pressure (LVP, blue) for H6 COM04R01.

CHAPTER 40 LEAFLET TENT

The concept of the closed mitral valve forming a tent-like structure is well-known in the literature. The mitral annulus forms the “floor” of the tent and the leaflets form the tent “walls” that extend from the annulus into the LV. In this chapter we build on this concept, utilizing concepts developed from our findings in earlier chapters based on 4-D marker data.

In Chapter 39 we suggested that, during valve closure, the posterior leaflet folds at the P1/P2 and P2/P3 junctions (and, possibly, additional sites, as well) roll the adjacent scallops toward one another as LVP increases and that this increasingly tightens the posterior leaflet perimeter “belt” around the edge of the stiff anterior leaflet. Further, in Chapter 36 we showed that the fold and coaptation regions between the anterior and posterior leaflets are quite rigid, and in Chapter 22 we interpreted the experimental data of Askov *et al.*¹ as suggesting that the closed valve is nearly self-supporting, requiring very little chordal force to remain closed.

Figure 40.1, showing two views of the valve from heart H3 (Appendix D), illustrates one possibility as to how the valve could be nearly self-supporting. In the closed valve, the stiff fold and coaptation regions (red) form a tent-like structure (Figure 40.2) that can self-maintain valve geometry without requiring chordal support as systolic LVP presses on the leaflet surfaces (Figure 40.3).

In this view, systolic LVP has the following effects during and after valve closure (relevant chapters in parentheses):

1. LVP acts on posterior leaflet surfaces to force the annulus inwards (Chapter 16).
2. LVP-driven outflow tract expansion pulls trigone attachments toward the septum, increasing annular tension (Chapter 17).
3. LVP stiffens the saddle-shaped anterior leaflet *via* radial compression and circumferential expansion (Chapters 29 and 30).
4. LVP tightens the posterior leaflet coaptation “belt” around anterior leaflet by squeezing posterior leaflet folds (Chapter 39).
5. LVP produces stiff fold and coaptation “tent” support members that prevent leaflet eversion through the annulus.
6. LVP presses leaflet edge rough zones gently together (no blood component damage), but with sufficient force and height (‘h’) to prevent regurgitation.

The primary role of the chordae in this view is to set the precise leaflet 3-D geometry at the initial instant of valve closure at the beginning of each beat. If this precise initial leaflet 3-D geometry is set properly, the valve becomes almost self-supporting as LVP presses on its leaflet surfaces (drawing the annulus inwards and the posterior scallops against the stiff anterior leaflet) as well as creating internal load-bearing rigid leaflet coaptation regions and folds.

¹ Askov JB, Hønge JL, Jensen MO, Nygaard H, Hasenkam JM, Nielsen SL. Significance of force transfer in mitral valve-left ventricular interaction: in vivo assessment. *J Thorac Cardiovasc Surg.* 2013;145(6):1635-1641, 1641 e1631.

Figure 40.2 Correspondence, in the closed valve, between folding/coaptation regions in Figure 40.1 and the structural components of a Eureka "Timberline" tent.

Figure 40.3 Schematic illustration of the effect of left ventricular systolic pressure (LVP) on the outer posterior P1 and P2 leaflet surfaces of the tent, relative to the low left atrial pressure (LAP) inside the tent.

CHAPTER 41 P2 SHAPE AND TERTIARY CHORDS

This chapter tests the hypothesis that the central belly of the P2 posterior leaflet deforms as an unsupported elastic membrane subjected to left ventricular pressure in the closed valve. This hypothesis produces at least three marker-testable predictions: first, that radial leaflet curvature is concave to the left ventricle throughout ejection; second, that this curvature changes very little during the nearly constant systolic pressure during ejection; and third, that this curvature flattens as LVP falls precipitously during isovolumic relaxation.

Data from 14 hearts in the DOS and SOD series, provided in Appendix S, were used to test these predictions. In each frame, a vector (V1822) was constructed from the lateral annular marker (#18) to the annular saddlehorn marker (#22), another from the lateral annular marker (#18) to the P2 belly marker (V1828 in SOD; #V1836 in DOS), and a third from the lateral annular marker (#18) to the P2 edge marker (V1827 in SOD; V1835 in DOS). P2 edge angle (Φ_{edge} , plotted in blue in Figures 41.2A, B, and C) was defined as the angle between V1822 and V1827 in SOD or between V1822 and V1835 in DOS. P2 belly angle (Φ_{belly} , plotted in red in Figures 41.2A, B, and C) was defined as the angle between V1822 and V1828 in SOD or between V1822 and V1836 in DOS. P2 radial curvature was concave to the LV if $\Phi_{\text{belly}} < \Phi_{\text{edge}}$, convex to the LV if $\Phi_{\text{belly}} > \Phi_{\text{edge}}$, and flat if $\Phi_{\text{belly}} = \Phi_{\text{edge}}$.

The findings in Figures 41.2A, B, and C do not consistently support any of these three predictions. Although P2 radial curvature during ejection was concave to the LV in 7 hearts (S1, S2, S7, S9, D1, D2, and D3), it was convex to the LV in 5 hearts (S3, S5, S6, S10, and D5), and flat in 2 hearts (S4 and D4). P2 radial curvature drifted lower throughout ejection in 10 hearts (S2, S3, S4, S5, S6, S7, S9, S10, D2, and D3), stayed roughly constant in 3 hearts (S1, D1, and D4), and increased in one heart (D5). Of the 14 hearts, only two, S1 and S9, exhibited the hypothesized concave radial curvature to the LV during ejection and flattened (as evidenced by a reduction in $\Phi_{\text{edge}} - \Phi_{\text{belly}}$) as LVP fell during IVR. Thus it seems highly unlikely that the central belly of the P2 posterior leaflet is an unsupported elastic membrane in the closed valve. But if the posterior leaflet belly is not a straightforward collagen-like (hyper)elastic membrane, then what?

We suggest that this posterior leaflet behavior is more consistent with that expected if the leaflet belly had chordal support. We further suggest that this supporting role could be well served by the tertiary chordae described by Lam, *et al.*¹ from the LV endocardial trabeculae to the posterior leaflet. If the tertiary chordae support the posterior leaflet bellies, this would offer an explanation as to why Φ_{belly} in most of the hearts tended to stay relatively constant or drifted somewhat downward as ejection proceeds. This could then be a function of LV long axis shortening, plotted as D1810 in Figures 41.2A, B, and C that could release the posterior leaflet belly to displace closer to the annular plane during ejection. We do not think that the support chordae likely originate from the papillary muscle tips because the leaflet belly positions are established during IVC and Askov, *et al.*² have shown that total papillary force is very small at this time.

¹ Lam JH, Ranganathan N, Wigle ED, Silver MD. Morphology of the human mitral valve. I. Chordae tendineae: a new classification. *Circulation*. 1970;41(3):449-458.

² Askov JB, Hønge JL, Jensen MO, Nygaard H, Hasenkam JM, Nielsen SL. Significance of force transfer in mitral valve-left ventricular interaction: in vivo assessment. *J Thorac Cardiovasc Surg*. 2013;145(6):1635-1641, 1641 e1631.

In Chapter 19 we drew a schematic (Figure 19.1), consistent with the data analyzed to that point, to describe the relationship between the mitral annulus, LA, LV, and edge and hinge chordae originating from the papillary muscles, as well as our conception as to where the tertiary chordae might be acting. In Figure 41.1 we upgrade this schematic to now include the possibility of tertiary chordae not only acting at the mitral annular hinge regions of the posterior leaflets, but acting to support the posterior leaflet belly, as well.

With this concept, mitral valve closing would involve swinging the posterior leaflet towards closure, having the posterior leaflet belly stopped before complete closure by tertiary chordal tethering, then further rotation of the remaining posterior leaflet edge would complete coaptation with the anterior leaflet edge.

Figure 41.2A P2 Φ belly (red), Φ edge (blue), left ventricular pressure (LVP, mm, black), LV lateral long-axis length from Marker #18 to Marker #10 (D1810, green) for hearts S1-S6. P2 is convex to the LV during ejection if Φ belly > Φ edge (red curve above blue curve), concave during ejection if Φ belly < Φ edge (blue curve above red curve), and flat if Φ belly = Φ edge (red and blue curves roughly superimposed) during ejection.

Figure 41.2B P2 Φ_{belly} (red), Φ_{edge} (blue), left ventricular pressure (LVP, mm, black), LV lateral long-axis length from Marker #18 to Marker #10 (D1810, green) for hearts S7, S9, S10, and D1-D3. P2 is convex to the LV during ejection if $\Phi_{belly} > \Phi_{edge}$ (red curve above blue curve), concave during ejection if $\Phi_{belly} < \Phi_{edge}$ (blue curve above red curve), and flat if $\Phi_{belly} = \Phi_{edge}$ (red and blue curves roughly superimposed) during ejection.

CHAPTER 42 LEFT ATRIAL FLOW

Throughout left ventricular systole, with the mitral valve closed, pulmonary venous flow fills the left atrium, presumably stretching and storing potential energy in the left atrial walls. During early diastole, immediately following mitral valve opening, this potential energy is presumably available to assist rapid (E-wave) filling. Later in diastole, ECG P-wave activation triggers left atrial contraction that actively drives additional (A-wave) LV filling. When the mitral valve is open, however, there is nothing to prevent pulmonary venous flow from directly entering the left ventricle, with the left atrium acting only as a conduit. In this chapter we attempt to estimate the relative proportion of left ventricular filling that can be ascribed to the potential energy stored in the left atrial walls and left atrial contraction in relation to left ventricular filling that can be attributed to direct conduit flow.

Six hearts in the SOD series of experiments (see Appendix S) had markers suitable to estimate, via space-filling tetrahedral (as illustrated in Figure 42.1), simultaneous left atrial and left ventricular volumes. As discussed in Appendix C, we have previously shown that, although absolute volumes obtained in this fashion have considerable error, their time-derivatives are well correlated with chamber flows (largely because of the constant-volume property of contracting muscle). If, at any instant in diastole, we know the change in left atrial volume, we know the maximum flow that can be delivered to the left ventricle by the release of the potential energy in the left atrial wall. The difference between this flow and the total flow into the left ventricle at this instant yields an estimate of the flow that must arise from the pulmonary veins, with the left atrium acting as a conduit.

Figure 42.2A, B, and C show the results of these calculations in SOD hearts S1, S2, S3, S7, S9, and S10. In these sheep hearts, at least, under these (immediate postoperative) conditions, the left atrium played a very minor role in either E-wave or A-wave left ventricular filling. By far, the dominant role in LV filling was played by the direct conduit function of the left atrium as a straightforward connector between the pulmonary veins and the left ventricle.

As this is a side issue in this mitral valve book, we will not explore these results further at this time. With the data available in Appendix S, however, perhaps others can perform additional work to further this analysis.

Figure 42.1 Space-filling tetrahedral for volume calculations in SOD heart S2. See definitions in Appendix S.

CHAPTER 43 THE NORMAL VALVE-CONCEPT SUMMARIES

The following are brief summaries of concepts underlying normal mitral valve mechanics that we find most compatible with the currently available data. Chapters developing and supporting these concepts are identified at the end of each summary.

FIBROUS ANNULUS

At the onset of each beat, immediately before valve closure, increasing LVP dilates the LV outflow tract which abruptly displaces the left and right fibrous trigones laterally towards the interventricular septum and down towards the LV apex (decreasing the fibrous annulus angle (LFT-SH-RFT)). These displacements produce tension in the contractile portion of the mitral annulus; much as pulling on the reins of a horse provides tension in the reins and tightens the bit. As ejection proceeds, myocardial contraction (not LVP) pulls the trigones further in these directions. CHAPTERS 02, 17

PAPILLARY TIPS

Papillary tips rotate around their respective trigone axes throughout the cardiac cycle, thereby maintaining their positions constant with respect to the mitral annulus to within a few millimeters in three-dimensional space throughout the entire cardiac cycle. In many respects, the papillary tips can be considered as suspended, parachute-like, below an annular “canopy” by rather stiff chordal “suspension lines”, while the papillary bases accommodate left ventricular wall motion *via* papillary muscle length changes. Papillary tip positional constancy is needed to properly set the initial geometric conditions for the leaflets (*i.e.*, shape, position) at the instant of valve closure, thereby allowing the valve to be nearly self-supporting. CHAPTERS 03, 19, 20

ANTERIOR LEAFLET STRUT CHORDAE

Anterior strut chordae are always in tension and remain at roughly constant length. During diastole, they prevent the anterior mitral leaflet, particularly its leading edge, from encroaching beyond a certain point into the LV outflow tract. At the moment of valve closure, they help set the annular half of the anterior leaflet into a specific initial 3D geometric configuration (stiff hyperbolic paraboloid “saddle” shape, radially convex, circumferentially concave to the LV), after which the leaflet becomes locked into this rigid 3D configuration by LVP loading throughout the rest of systole and IVR. CHAPTERS 03, 04, 06, 07, 19, 21

ANTERIOR LEAFLET MOBILITY

Anterior leaflet opening takes place primarily at the leaflet edge; the annular half of the leaflet has severely restricted mobility. CHAPTERS 05, 24

ANTERIOR LEAFLET SHAPE

The annular two-thirds of the anterior leaflet is set in a hyperbolic paraboloid “saddle” shape (radially convex, circumferentially concave to the LV; not associated with annular shape) at the moment of valve closure. Subsequent loading of this structure produces an offsetting combination of radial compression and circumferential tension that dramatically decreases load-induced anterior leaflet deformation. Anterior mitral leaflet shape is maintained with sub-millimeter precision the entire time the mitral valve is closed, in spite of changing LVP. The anterior leaflet behaves much like a canvas sail that can bend to its near-final shape in a light breeze, yet hold this shape, with very little displacement or surface strain, in a gale. Because the anterior leaflet is an important component of the LV outflow tract, this invariant shape is important for efficient outflow patterns. During diastole, the anterior leaflet flattens considerably and its free edge takes on very complex shapes, including sometimes folding back on itself. CHAPTERS 06, 08, 09, 11, 18, 30

ANTERIOR LEAFLET STIFFNESS

The anterior mitral leaflet owes its systolic stiffness to both its shape and highly active material properties. In the closed valve, its saddle shape provides radial leaflet compression and circumferential leaflet tension that offset to minimize deformation with pressure loading. In response to A-wave excitation, cardiac myocytes in the annular half of the leaflet provide a stiffening twitch at the beginning of each ventricular systole. This stiffness-twitch is abolished by beta-blockade, but insensitive to neural stimulation. The bulk of steady-state leaflet stiffness is provided by contractile cells (likely VICs, cross-linking collagen throughout the leaflet), insensitive to beta-blockade, but responding to neural stimulation with rapid increases or decreases of overall leaflet stiffness. The stiffness of this leaflet may be under reflex and/or central control, providing leaflet stiffness changes to maintain appropriate outflow-tract geometry under widely-varying hemodynamic conditions. CHAPTERS 11, 29, 30, 31, 37

ANTERIOR LEAFLET LV POSITION

The position of the anterior leaflet edge in the LV, once established at end IVC, exhibits unchanging 3D positional stability throughout ejection in each beat as well as sub-millimeter reproducibility from beat-to-beat. Its 3D position is virtually independent of changes in left ventricular pressure, the changing geometry of the LV throughout ejection and isovolumic relaxation, and pressure from coapting posterior leaflets in the closed valve. CHAPTERS 13, 28

ANTERIOR LEAFLET AREA

Anterior leaflet surface area is constant to within a few percent over the wide range of left ventricular pressures from mitral valve closure to end IVR. CHAPTER 10

ANTERIOR LEAFLET PERFUSION

The myocyte-containing annular half of the anterior leaflet has a rich vascular supply arising from the mid- and distal left circumflex coronary artery, entering the leaflet near the trigones, particularly near the commissures. Additional leaflet perfusion is possibly provided through both strut and edge chordae. CHAPTER 32

ANNULAR SIZE VARIATION

The mitral annulus exhibits a large variation in size during the cardiac cycle and these dimensional changes occur rather uniformly throughout the entire contractile (non-trigonal) portion. Annular area, greatest in diastole, begins to fall, driven by annular contraction (triggered by atrial excitation) well before the onset of left ventricular pressure rise and valve closure. Systolic pressure on the LV side of the posterior leaflets is fully capable of creating and maintaining the reduced annular dimensions throughout ventricular systole. Annular area begins to increase during isovolumic relaxation, as left ventricular pressure is falling rapidly, well before mitral valve opening. CHAPTERS 14, 15, 16, 24

LV-ANNULAR COUPLING

The contractile mitral annulus and the LV basal myocardium are elastically tethered but their movements are out of phase, with the connecting tethers shortening during ventricular systole and stretching during ventricular diastole. CHAPTER 16

ANNULAR SHAPE AND FLEXION

The mitral annulus is a hinged structure, with the hinge (separating the contractile and non-contractile portions of the annulus) located roughly along a line between the left and right fibrous trigones. At the beginning of each beat, the mitral annulus is rapidly driven towards its mean systolic shape by the increase in LVP during IVC, starting immediately with the rapid LVP increase, continuing during and after mitral valve closure, and reaching a minimum in mid-to-late systole. Mitral annular shape is constant throughout systole in each beat and exhibits

sub-millimeter beat-to-beat repeatability. Annular shape begins to be driven back towards its diastolic value as LVP falls during the last half of IVR but before mitral valve opening. During systole, annular shape is dictated principally by LV pressure, not LV volume. During diastole, annular shape is dictated principally by LV volume, not LV pressure. The complete mitral annulus (trigone region plus contractile annulus) increasingly flattens throughout diastole, reaching its flattest configuration at the onset of the LVP increase at the beginning of each beat. It immediately becomes more curved in concert with the rising LVP during IVC, reaching its maximum curvature in mid-to-late systole then begins to flatten again in mid-to-late IVR as LVP falls. The contractile annulus, however, is much flatter than the complete mitral annulus and exhibits less curvature change throughout the cardiac cycle. CHAPTERS 17, 18

HINGE CHORDAE

Chordae from the papillary tips to the mitral annulus (leaflet hinge sites) maintain constant 3-D mitral valve geometry as LV dimensions change throughout the cardiac cycle. This constant geometry provides precise leaflet shape and edge positioning at the moment of valve closure and positions strut chordae to prevent diastolic anterior leaflet incursions into the outflow tract. Papillary forces, transmitted through the hinge chordae, limit annular displacement towards the left atrium (along with tertiary chordae) and help pump blood, particularly in the last half of systole. If precise leaflet 3-D geometry at the instant of valve closure is set properly, the valve becomes almost self-supporting as LVP presses on its leaflet surfaces (drawing the annulus inwards and the posterior scallops against the stiff anterior leaflet) as well as creating internal load-bearing rigid leaflet coaptation regions and folds. CHAPTERS 19, 40

PAPILLARY FORCE AND CONTRACTION

The long axis of the posterior papillary muscle is aligned with the region near the right fibrous trigone and the anterior papillary muscle is aligned with the region near the anterior commissure. As papillary muscle fibers are aligned with the papillary long axis, the greatest force generation will be in this direction. The papillary tips are held in a precise and relatively fixed 3D geometric relationship to the mitral annulus throughout the cardiac cycle by stiff chordae subjected to rather small forces. This fixed geometric relationship allows the leaflets to close gently during IVC (with almost no tension in the chordae or their associated papillary muscle), with leaflet shape and position established at the moment of closure in very nearly the geometry that will be maintained throughout systole. At the moment of mitral valve closure, with near-maximum LVP pressing on the closed leaflets, the chordae experience very little force, about 8% and 1%, respectively, of the maximum force developed in mid-systole by the anterior and posterior papillary muscles. This supports the concept that the mitral valve leaflets in the closed valve are nearly self-supporting, without requiring major chordal/papillary forces to maintain valve closure. Papillary force development, transmitted through the hinge chords, contributes about 10% to the total force of contraction, particularly in mid-to-late systole. Papillary muscles can shorten up to 30% and shortening continues throughout IVR. Such late papillary force and shortening, potentially supplementing the primary opening force associated with the reversal in the LVP/LA pressure gradient, may well play an active role to aid quick and reliable valve opening at end IVR. CHAPTERS 20, 21, 22

POSTERIOR LEAFLETS

The maximum posterior leaflet edge opening silhouette is virtually identical to the annular silhouette as viewed from LA to LV. Thus, flow from the left atrium into the left ventricle does not encounter significant restriction associated with a narrowed opening due to the posterior leaflet. The P1-P2 and P2-P3 junctions are capable, almost entirely, of providing the large change in posterior leaflet perimeter needed to open the valve widely during left ventricular filling and close it tightly during ejection. In many respects, these regions provide junctions similar to pleats used to gather a wide piece of fabric to a narrower circumference. Posterior leaflet pleats are greatly flattened during diastole and gathered tightly during systole. Folded pleats in the closed valve are pressed tightly together by systolic left ventricular pressure acting on their outer (ventricular) surfaces,

helping to align and position adjacent leaflet coapting surfaces precisely at the moment of valve closure and providing a rib-like structure that helps stiffen the posterior leaflet to resist systolic deformation. The posterior leaflet belly has tertiary chordal support. The very wide opening of the posterior leaflets has flow consequences. Such opening squeezes most of the blood out from behind these leaflets because they nearly contact the LV endocardium. This “squeezed” blood flows in the same direction as, and contributes to, central LV inflow. When the posterior leaflets close again, a fresh charge of blood enters this space, preventing stasis behind the leaflets. In contrast, the anterior leaflet, when maximally open, leaves a large space behind itself in the outflow tract. Indeed, the anterior leaflet region near the annulus is like a drumhead, supported by the stiff trigone regions, which guides diastolic inflow away from the LV outflow tract. Even the anterior edge region is prevented from entering too far into the outflow tract by the strut chordae. As a result, the anterior leaflet can be thought of as a flow-guiding boundary for both LV inflow and outflow, while the posterior leaflets serve the primary role of offering a minimum impediment to LV inflow during filling, then closing against the anterior leaflet to prevent regurgitation, but having a lesser impact on flow during ejection. CHAPTERS 24, 25, 26, 27, 37, 39, 41

COAPTATION

The contact regions of the anterior and posterior leaflets exhibit three geometric configurations: folding near the annulus; 2-curve coaptation in 5 regions further from the annulus; and 3-curve coaptation (similar to the aortic valve) in 2 regions further still from the annulus. Specific sites on the leaflet edges are reproducibly aligned at the beginning of each beat with mm (and typically sub-mm) precision and this alignment precision is preserved (rigid coaptation region) in the closed valve for the duration of each beat. At the instant of valve closure, the 3-D geometry of the leaflets is first established by the chordae, then the posterior leaflet folds are forced toward one another and toward the anterior leaflet by LVP which tightens the posterior leaflet perimeter against the anterior leaflet. The higher the left ventricular pressure, the greater the stiffness of the anterior leaflet (via the interplay between compression and tension in the saddle-shaped anterior leaflet) and the more forcefully the posterior leaflet perimeter is tightened about the stiff anterior leaflet perimeter. Spreading coaptation over a large surface “rough zone” contact area reduces crushing forces below the threshold required to damage blood cells trapped in the coaptation region, thereby preventing blood cell damage, yet maintaining tight closure. Microscopic spaces distributed throughout the rough zone contact areas could allow protected regions where the blood cells are not subjected to crushing forces associated with leaflet coaptation. Frictional interactions between the “rough zones” in the coaptation regions at the edges of the anterior, P1, P2, and P3 leaflets lock the leaflet edges in place, thereby preventing the leaflets from slipping past each another toward the left atrium. The folds and coaptation regions in the closed valve form a structurally rigid supporting “skeleton” that resists displacement of the assembly towards the annulus. The higher the left ventricular pressure, the more these regions press together, the stiffer and more extensive this structural support becomes, thereby further resisting the tendency of the leaflet assembly to displace towards the mitral annulus as LVP increases. CHAPTERS 26, 27, 28, 29, 30, 36, 37, 39

FLOW

Initial LV inflow occurs slightly before mitral valve opening (*i.e.* leaflet separation). This results from leaflet shape changes as LVP falls to low values immediately before valve opening. Because the anterior leaflet is so stiff, the elastic change in posterior leaflet geometry is a prime candidate for this volume change. Although E-wave inflow kicks both the anterior and posterior leaflets toward open positions, they swing back towards their closed positions as early filling wanes. This could result from at least two forces acting on the leaflets. The collapse of the lowered pressure in the inflow stream from the Bernoulli Effect may tend to pull the leaflets back towards closed positions. Perhaps even more important might be the strut chord forces tending to gently close the leaflets at all times. The vortices shed behind the leaflets are possible factors, but they may be too brief to have a major effect driving the leaflets toward closure. Regurgitation volume associated with valve closure ranges from 0-18% of SV. Being in a nearly closed position as LVP just starts to rise does not seem to confer an

advantage toward efficient closing as measured by closing regurgitation. Some valves are in nearly closed positions at the onset of LVP increase, but exhibit large (seemingly inefficient) closing regurgitation. Energy storage in the left atrial wall plays a very minor role in either E-wave or A-wave left ventricular filling. By far, the dominant role in LV filling is played by the direct conduit function of the left atrium as a straightforward connector between the pulmonary veins, the atrial reservoir, and the left ventricle. CHAPTERS 34, 37, 41

COMMISSURES

The anterior and posterior commissure membranes allow the anterior leaflet and the P1 posterior scallop, as well as the anterior leaflet and the P3 posterior scallop, to swing freely around nearly orthogonal hinge axes in response to the very small internal LV pressure gradients when the valve is open, yet fold to form precise, rigid, tight seals between the anterior leaflet and the P1 posterior scallop and the anterior leaflet and the P3 posterior scallop as the rising LVP compresses each fold at the instant of valve closure and thereafter throughout systole. They provide part of the rigid “skeleton” support for the leaflets in the closed valve. CHAPTER 38

MITRAL “SKELETON”

In the closed valve, the stiff fold and coaptation regions form a skeletal, tent-like support structure that helps maintain valve geometry without requiring chordal support as systolic LVP presses on the leaflet surfaces. CHAPTERS 22, 39, 40

OVERVIEW

Initial leaflet geometry at the moment of valve closure is crucial to systolic valve mechanics. If the initial geometric conditions are set properly at this moment (*i.e.*, the complex anterior leaflet curvatures are set precisely and all leaflet edges are positioned precisely with respect to one another in the LV chamber at this time), the resulting leaflet assemblage is nearly self-supporting, becoming nearly a rigid body whose geometry is virtually independent of subsequent flow and pressure throughout systole. This concept is supported by the small papillary forces measured at the moment of valve closure, as discussed in Chapters 21 and 22, and the beat-to-beat repeatability and leaflet systolic positional stability discussed in Chapters 9, 13 and 18. Such initial leaflet shape and positioning is achieved by positioning the papillary tips at precise 3D locations at the moment of valve closure, as discussed in Chapters 3, 4, and 19, with all the chordae distributed from these tips to the many leaflet attachment sites having exactly the right lengths to place the leaflet edges to within a millimeter of their closed positions at the moment of closure, as discussed in Chapter 13. In this view, the papillary muscles and chordae act primarily to keep the anterior leaflet out of the outflow tract during diastole and to gently and precisely position the leaflets into a precise geometric configuration at the moment of closure; exerting about 10% of ejection force during the last half of systole, as described in Chapter 22. As left ventricular pressure just begins to rise during the ECG R-wave, the slightest regurgitant pressure gradients force the large-area anterior leaflet and P1, P2, and P3 scallops inward relative to the smaller areas exposed in the clefts between these leaflet regions, thereby assuring proper folding geometry, similar to the sequence shown in Chapter 37. The precise initial positioning associated with all of these mechanisms also prevents the leaflet from colliding forcefully at the beginning of each beat, allowing gentle closing mechanics that spares both valve and blood components from damage.

APPENDIX A. MARKER SITES AND DATAFILE COLUMNS

Datafiles (provided in this Appendix) associated with the six heart (H1-H6) study are:

HEART	CONTROL STUDY	
	FILE1	FILE2
H1	NAC03R04.1EC	NAC03R04.1IC
H2	NAM14R01.1EC	NAM14R01.1IC
H3	NAM18R03.1EC	NAM18R03.1IC
H4	NSA12R01.1EC	NSA12R01.1IC
H5	NAC09R03.1EC	NAC09R03.1IC
H6	NAS07R03.1EC	NAS07R03.1IC

- Each datafile has (if the parameter was successfully recorded)
 - Electrocardiogram (mV) in Column 4
 - Left Ventricular Pressure (mmHg) in Column 5
 - Left Atrial Pressure (mmHg) in Column 6
 - Aortic Pressure (mmHg) in Column 7
 - In addition, *.1EC datafiles have (See Figure A.1)
 - Marker#1 x, y, z lab coordinates (cm) in Columns 11, 12, 13
 - Marker#2 x, y, z lab coordinates (cm) in Columns 14, 15, 16
 - ...
 - Marker#13 x, y, z lab coordinates (cm) in Columns 47, 48, 49
 - Marker#14 is not used, placeholders in Columns 50, 51, 52
 - Marker#15 x, y, z lab coordinates (cm) in Columns 53, 54, 55
 - ...
 - Marker#31 x, y, z lab coordinates (cm) in Columns 101, 102, 103
 - Marker#32 is not used, placeholders in Columns 104, 105, 106
 - Marker#33 x, y, z lab coordinates (cm) in Columns 107, 108, 109
 - In addition, *.1IC datafiles have (as Markers#34, 35, 36 were not used) (See Figure A.1)
 - Marker#37 x, y, z lab coordinates (cm) in Columns 20, 21, 22
 - Marker#38 x, y, z lab coordinates (cm) in Columns 23, 24, 25
 - ...
 - Marker#53 x, y, z lab coordinates (cm) in Columns 68, 69, 70 (#53 is the last marker)
 - Each datafile row is a single sample time, with sampling occurring 60 times/sec (i.e. every 16.67msec). Row numbers correspond in 1EC and 1IC datafiles.
 - Marker numbers were assigned so as to retain backward compatibility with previous marker studies.

MARKER LOCATIONS: LEFT VENTRICULAR, MITRAL ANNULAR, AND PAPILLARY MUSCLES

LEFT VENTRICULAR (LV) MARKERS

- LV Apex (Marker#1)
- LV Anterior Subepicardium, apical plane (Marker#2), equatorial plane (Marker#3), basal plane (Marker#4), inserted before the pump run
- LV Septal Subendocardium, apical plane (Marker#5), equatorial plane (Marker#6), basal plane (Marker#7), inserted during the pump run
- LV Posterior Subepicardium, apical plane (Marker#8), equatorial plane (Marker#9), basal plane (Marker#10), inserted before the pump run
- LV Lateral Subepicardium, apical plane (Marker#11), equatorial plane (Marker#12), basal plane (Marker#13), inserted before the pump run

MITRAL ANNULUS (ALL MARKERS PLACED AT DIRECTLY OBSERVED LEAFLET “HINGE” LOCATIONS DURING THE PUMP RUN)

- Trigone Region
 - Left Fibrous Trigone(LFT) (Marker #29)
 - “Saddlehorn” (SH) (Marker#22)
 - Right Fibrous Trigone (RFT) (Marker #24)
 - LFT to SH (Markers#15,30)
 - SH to RFT (Markers#23,21)
- Contractile Annulus
 - Anterior Commissure (AC) (Marker#16)
 - Lateral Annulus (Marker#18)
 - Posterior Commissure (PC) (Marker#20)
 - AC to Lateral Annulus (Markers#28,17,27)
 - Lateral Annulus to PC (Markers#26,19,25)
- PAPILLARY MUSCLES (INSERTED DURING THE PUMP RUN)
 - Anterior Papillary Muscle Tip (Marker#31)
 - Posterior Papillary Muscle Tip (Marker#33)

MARKER LOCATIONS: LEAFLETS

- ANTERIOR LEAFLET
 - Trigone Region (See Figure 01) is the Anterior Leaflet Hinge Region
 - Leaflet Edge (markers sewn to atrial side of leaflet)
 - Central Edge (Marker#38)
 - LFT to Central Edge (Markers#42,43,44)
 - Central Edge to RFT (Markers#45,46,47)
 - Central Meridian from Central Edge to SH (Markers#39,40,41)
 - Left Belly (Markers#48,50,51)
 - Right Belly (Markers#49,52,53)
- POSTERIOR LEAFLET
 - Only one marker (Marker#37) sewn to the central meridian edge of the central scallop for timing of valve opening and closing

APPENDIX B. NAC-MAD COMPOSITE DATASET

Here, we describe an attempt to model, as accurately as possible in 3-D space, the geometric relationship between the various components of the left ventricle, the mitral valve, and the aortic valve during systole and diastole.

Datasets from two hearts were combined to develop this model:

- The first dataset was from a mitral valve study (nac09r03.1eg and nac09r03.1ig, datasets provided in this Appendix), with diastole defined at Frame 50 and systole at Frame 76.
- The second dataset was from an aortic valve study (MAD09R01.1E, dataset provided in this Appendix), with maximum diastole defined at Frame 50 and systole at Frame 42.

A Euclidian coordinate system was defined, with x-axis positive to the right, z-axis positive up, and y-axis positive into the plane of the paper.

Coordinate data from the diastolic mitral valve dataset sample (Frame 50) were first translated to place the annular “saddlehorn” Marker#22 (see Figure B.1) at the origin, then two rotations were performed to place the left ventricular apex (Marker#1) onto the negative z-axis. A final rotation was performed to place the lateral annulus (Marker#18) in the x-z plane. This process was repeated for the systolic mitral valve dataset sample (Frame 76).

Coordinate data from the diastolic aortic valve dataset sample (Frame 50) were first translated to place the annular “saddlehorn” Marker#23 (see Figure B.1) at the origin, then two rotations were performed to place the left ventricular apex (Marker#1) onto the negative z-axis. A further rotation was performed to place the lateral annulus (Marker#18) in the x-z plane. This process was repeated for the systolic aortic valve dataset sample (Frame 42).

The two datasets were then merged, resulting in two 3-D datasets (one for diastole, the other for systole) that could be viewed from any angle, such as that displayed as Figures 1.1 and 1.2 in Chapter 01. These datasets

- COMPOSITE_NAC09R03_MAD09R01_DIASTOLIC_DATASET.dat
- COMPOSITE_NAC09R03_MAD09R01_SYSTOLIC_DATASET.dat

are provided in this Appendix. Figure B.1 associates the column numbers in the merged datasets with the marker coordinates (*e.g.*, the x-coordinate of nac Marker#24 is in column 70, its y-coordinate in column 71, and its z-coordinate in column 72; the x-coordinate of MAD Marker#16 is in column 205, its y-coordinate in column 206, and its z-coordinate in column 207, *etc.*).

APPENDIX C: COMPUTATIONAL DETAILS

BEST-FIT ANTERIOR LEAFLET AND ANNULAR PLANE CLAMP

- ECG, LVP, AoP, and marker x, y, z coordinate data were loaded into a MATLAB program from the pairs of files (*such as nac03r04.1ec and nac03r04.1ic*).
- Marker coordinates were indexed as $x(f, m)$, $y(f, m)$, and $z(f, m)$, where frame $f = 1, 2, \dots$ is the sampling instant (the same as the datafile row numbers at the sampling rate of 60 frames/second) and marker numbers $m = 1, 2, \dots$ are as identified as in Figures 1.1 and 1.2.
- A right-hand orthogonal coordinate reference system was defined with the positive x-axis pointing to the right on the page, positive y-axis pointing into the page, and positive z-axis pointing up.
- All marker x, y, z data were then rotated such that the x-coordinate of the leaflet edge marker#18 was always positive in this coordinate system for all frames.
- For each frame, f , a best-fit leaflet plane of the form

$$L(1) * x + L(2) * y + L(3) = z$$

was then found from

$$L = (M' M)^{-1} (M' F),$$

where

$$M = \begin{bmatrix} x(f, 15) & y(f, 15) & 1 \\ x(f, 21) & y(f, 21) & 1 \\ \vdots & \vdots & \vdots \\ x(f, 53) & y(f, 53) & 1 \end{bmatrix},$$

(*i.e.*, using all the anterior leaflet markers #15, 21-24, 29, 30, 38-53 shown in Figure 1.2),

and

$$F = \begin{bmatrix} z(f, 15) \\ z(f, 21) \\ \vdots \\ z(f, 53) \end{bmatrix}.$$

The coordinates x_p, y_p, z_p , of the projection of each heart marker, m , for this frame, f , on this plane was then found as

$$x_p(f, m) = x(f, m) + L(1) * K,$$

$$yp(f, m) = y(f, m) + L(2) * K ,$$

and

$$zp(f, m) = z(f, m) - K ,$$

where

$$K = \frac{-L(3) - L(1) * x(f, m) - L(2) * y(f, m) + z(f, m)}{L(1)^2 + L(2)^2 + 1} .$$

- The coordinates of all heart markers were then translated to locate $xp(f, 22)$, $yp(f, 22)$, and $zp(f, 22)$ at the reference system origin (0,0,0) in each frame, yielding the un-projected coordinates $xt(f, m)$, $yt(f, m)$, and $zt(f, m)$, and projected coordinates $xpt(f, m)$, $ypt(f, m)$, and $zpt(f, m)$.
- A rotation $r1$ was then performed around the z-axis to place the projected coordinates of marker #38 into the x-z plane for each frame, yielding un-projected coordinates $xtr1(f, m)$, $ytr1(f, m)$, and $ztr1(f, m)$, and projected coordinates $xptr1(f, m)$, $yptr1(f, m)$, and $zptr1(f, m)$.
- A second rotation $r2$ was then performed around the y-axis to place the projected coordinates of marker #38 onto the x-axis for each frame, yielding un-projected coordinates $xtr1r2(f, m)$, $ytr1r2(f, m)$, and $ztr1r2(f, m)$, and projected coordinates $xptr1r2(f, m)$, $yptr1r2(f, m)$, and $zptr1r2(f, m)$.
- A final rotation $r3$ was then performed around the x-axis to place marker #29 into the x-y plane for each frame, yielding un-projected coordinates $xtr1r2r3(f, m)$, $ytr1r2r3(f, m)$, and $ztr1r2r3(f, m)$, and projected coordinates $xptr1r2r3(f, m)$, $yptr1r2r3(f, m)$, and $zptr1r2r3(f, m)$, these latter projected points all now clamped into the x-y plane for each frame, resulting in a “LEAFLET CLAMP”.

This same procedure was followed to find the best-fit plane to the mitral annular markers shown in Figure 1.1 (*i.e.*, Markers #15-30) and clamp this plane to the x-y axis, resulting in an “ANNULAR CLAMP”.

LEFT VENTRICULAR VOLUME AND FLOW

The volume, VOL, contained within a tetrahedron with vertices, P1 (x1, y1, z1) , P2 (x2, y2, z2) , P3 (x3, y3, z3), and P4 (x4, y4, z4), is

$$VOL = \frac{1}{6} ABS \begin{vmatrix} x1 & y1 & z1 \\ x2 & y2 & z1 \\ x3 & y3 & z3 \\ x4 & y4 & z4 \end{vmatrix}.$$

Left ventricular volume, LVV(*f*), for every frame, (*f*), was computed as the sum of the VOL's of 20 LV-space-filling tetrahedra, (T1, T2, ..., T20), with vertices (P1, P2, P3, P4) at the coordinates of the markers M#nn (as shown in Figures 1.1 and 1.2) during that frame:

TETRAHEDRON	P1	P2	P3	P4
T1	M#01	M#02	M#05	M#08
T2	M#01	M#02	M#08	M#11
T3	M#03	M#05	M#02	M#08
T4	M#03	M#05	M#08	M#06
T5	M#03	M#06	M#08	M#09
T6	M#03	M#02	M#08	M#11
T7	M#08	M#03	M#11	M#12
T8	M#08	M#03	M#09	M#12
T9	M#03	M#04	M#09	M#06
T10	M#04	M#06	M#09	M#07
T11	M#04	M#07	M#09	M#10
T12	M#03	M#04	M#09	M#12
T13	M#04	M#09	M#12	M#13
T14	M#04	M#09	M#10	M#13
T15	M#04	M#16	M#10	M#07
T16	M#07	M#10	M#16	M#22
T17	M#10	M#16	M#22	M#20
T18	M#10	M#13	M#16	M#04
T19	M#10	M#13	M#18	M#16
T20	M#10	M#16	M#18	M#20

Using magnetic flowmeters, we have previously determined¹ that, while this LVV significantly overestimates chamber volume, because it yields the sum of LV myocardial volume and blood volume, the *change in LVV* is a reliable indicator of blood flow into and out of the LV chamber.

FLOW (ml/sec), at the time of each frame, *f*, was then found as

$$FLOW(f) = 30 * (LVV(f + 1) - LVV(f - 1)).$$

This flow equation is used is because, unlike a simple change in volume from adjacent frames, which yields the flow at the *midpoint* in time between these frames, this estimates the flow at the instant of each frame by averaging the flows calculated from the volume changes during the intervals immediately before and immediately after that frame.

VECTOR LENGTHS AND ANGLES

Given three points, P1 (x1, y1, z1), P2 (x2, y2, z2), and P3 (x3, y3, z3), defined by any three markers, construct row vectors

$$V21 = (x1 - x2, y1 - y2, z1 - z2),$$

and

$$V23 = (x3 - x2, y3 - y2, z3 - z2).$$

The distance from P1 to P2 is

$$D21 = \sqrt{V21 \cdot V21'},$$

the distance from P2 to P3 is

$$D23 = \sqrt{V23 \cdot V23'},$$

and the angle $\angle P1P2P3$ is

$$\angle P1P2P3 = \cos^{-1}((V21 \cdot V23')/(D21 * D23)).$$

With the best-fit leaflet plane clamped to the x-y plane, the ROLL, PITCH, and YAW of the LV long axis (from Marker#22 to Marker#01) with respect to this plane are found from

$$ROLL = \tan^{-1}(ztr1r2r3/xtr1r2r3),$$

$$PITCH = \tan^{-1}(ztr1r2r3/ytr1r2r3),$$

and

$$YAW = \tan^{-1}(ytr1r2r3/xtr1r2r3).$$

RADIUS OF CURVATURE

Given 3 non co-linear points, P1 (x1,y1) , P2 (x2,y2), and P3 (x3,y3) in a plane, the radius, ROC, of the circle containing these points is centered at X0 and Y0, where

$$X0 = \frac{((x1^2+y1^2)-(x2^2+y2^2))(y2-y3)-((x2^2+y2^2)-(x3^2+y3^2))(y1-y2)}{2((x1-x2)(y2-y3)-(y1-y2)(x2-x3))},$$

$$Y0 = \frac{((x1^2+y1^2)-(x2^2+y2^2))(x2-x3)-((x2^2+y2^2)-(x3^2+y3^2))(x1-x2)}{2((y1-y2)(x2-x3)-(x1-x2)(y2-y3))}, \text{ and}$$

$$ROC = \sqrt{(x1 - X0)^2 + (y1 - Y0)^2}.$$

By definition

$$CURVATURE \equiv ROC^{-1}.$$

In this study, with the best-fit leaflet plane clamped to the x-y plane as previously described, then

- For RADIAL leaflet curvature, the generic x-axis above is defined to be the leaflet x-axis, and the generic y-axis above is defined to be the leaflet z-axis.
- For CIRCUMFERENTIAL leaflet curvature, the generic x-axis above is defined to be the leaflet y-axis, and the generic y-axis above is defined to be the leaflet z-axis.

Under these constraints, if the generic (y2-Y0) > 0, then CURVATURE is positive (*i.e.*, concave to the LV), otherwise CURVATURE is negative (*i.e.*, convex to the LV).

LEAFLET SURFACE AREA

Leaflet surface area for each frame is obtained from the coordinates of the leaflet markers for that frame, using a MATLAB algorithm developed by Richard Brown and published on the Web¹. *We discovered an error in this code, conveyed the correction to Dr. Brown, and the corrected code is now available on the web, as below.* Basically, this algorithm fits a surface to all the anterior leaflet markers shown in Figure 1.2, tiles this surface with a fine mesh of rectangular elements with dimensions dx by dy, computes the area of each element as dx*dy, then sums all these areas to arrive at the total surface area.

In MATLAB, this algorithm is

```
%Calculate the area of the anterior leaflet
for frame=1:totalframes;
xxx(frame,:)=[xtr1r2r3(frame,15) xtr1r2r3(frame,21:24)
xtr1r2r3(frame,29:30) xtr1r2r3(frame,38:53)];
```

¹<http://www.mathworks.co.uk/matlabcentral/answers/35501>

```

    yyy(frame,:)=[ytrlr2r3(frame,15) ytrlr2r3(frame,21:24)
ytrlr2r3(frame,29:30) ytrlr2r3(frame,38:53)];
    zzz(frame,:)=[ztrlr2r3(frame,15) ztrlr2r3(frame,21:24)
ztrlr2r3(frame,29:30) ztrlr2r3(frame,38:53)];
    end
    xxxmin=min(min(xxx(:,:)));xxxmax=max(max(xxx(:,:)));xxxminmax=xxxmax-
xxxmin;
    yyymin=min(min(yyy(:,:)));yyymax=max(max(yyy(:,:)));yyyminmax=yyymax-
yyymin;
    finescale=500;
    dx=xxxminmax/finescale;% x-axis calibration
    dy=yyyminmax/finescale;% y-axis calibration

    for frame=1:totalframes;
    xxxlin = linspace(xxxmin,xxxmax,finescale);
    yyylin = linspace(yyymin,yyymax,finescale);
    [XXX,YYY] = meshgrid(xxxlin,yyylin);
    ZZZ = griddata(xxx(frame,:),yyy(frame,:),zzz(frame,:),XXX,YYY, 'cubic');
    [m, n] = size(ZZZ);
    areas = 0.5*sqrt((dx*dy)^2 + (dx*(ZZZ(1:m-1,2:n) - ZZZ(1:m-1,1:n-1))).^2 +
... (dy*(ZZZ(2:m,1:n-1) - ZZZ(1:m-1,1:n-1))).^2) + ...
    0.5*sqrt((dx*dy)^2 + (dx*(ZZZ(1:m-1,2:n) - ZZZ(2:m,2:n))).^2 + ...
    (dy*(ZZZ(2:m,1:n-1) - ZZZ(2:m,2:n))).^2);
    surfacearea(frame) = nansum(areas(:));
    end

```

1 Comment

[Richard Brown](#) about 22 hours ago

[Link](#)

[Flag](#)

I've just had it pointed out to me that there is a small mistake in this code. Assuming that x corresponds to columns, and y to rows, then the first two lines (but not the second two lines) of the areas calculation hasdx and dy backwards. I've fixed it in my original answer below.

Corrected code as of 7/15/2013 is

```

[m, n] = size(Z);
areas = 0.5*sqrt((dx*dy)^2 + (dy*(Z(1:m-1,2:n) - Z(1:m-1,1:n-1))).^2 + ...
    (dx*(Z(2:m,1:n-1) - Z(1:m-1,1:n-1))).^2) + ...
    0.5*sqrt((dx*dy)^2 + (dx*(Z(1:m-1,2:n) - Z(2:m,2:n))).^2 + ...
    (dy*(Z(2:m,1:n-1) - Z(2:m,2:n))).^2)
surfaceArea = sum(areas(:))

```

edit: Jul 15, 2013 There was a mistake, and dx and dy were backwards in the first two lines of the code. The code has been corrected now.

REFERENCES

1. Moon MR, DeAnda A, Jr., Daughters GT, 2nd, Ingels NB, Jr., Miller DC. Experimental evaluation of different chordal preservation methods during mitral valve replacement. *Ann Thorac Surg*. 1994;58(4):931-943; discussion 943-934.

APPENDIX D MITRAL VALVE ANIMATIONS

The PowerPoint mitral valve animations in this Appendix can be accessed by double-clicking the filenames. Both side view (LEFT PANEL, looking from posterior to anterior) and top view (RIGHT PANEL, looking from base to apex) are provided. All graphs have Marker #22 at the origin, Marker #1 on the Z-axis, and Marker #18 in the X-Z plane. The animations can be stepped forward with the right arrow and backwards with the left arrow with time-steps of 16.67 ms. The left ventricular pressure associated with each time step is indicated by the black dot on the LVP curve imbedded in the graph. Hit Escape to exit each animation. The H1-H6 datasets are located in Appendix A.

APPENDIX E COM STUDIES

Figure E.1 shows the markers arrays used in the COM study of posterior leaflet dynamics. The COM DATAFILES folder contains files from 6 control runs: com01r04.1E, com02r02.1E, com03r04.1E, com04r01.1E, com06r01.1E, and com07r04.1E. Frame Rate = 60 frames/sec (16.667 msec/frame); Each

Row in the Datasets is a frame; ECG Voltage is in Dataset Column 4; LVP in Column 5; Marker #1X(cm) is in Column 11, #1Y(cm) in Column 12, #1Z(cm) in Column 13; Marker #2X(cm) is in Column 14, #2Y(cm) in Column 15, #2Z(cm) in Column 16; ETC., ETC.

Markers #15, 22, and 21 are trigonal, Marker #16 is at the anterior commissure, Marker #20 at the posterior commissure, Markers #17, 18, and 19 are on the contractile portion of the mitral annulus, Markers #1, 4, 7, 10, and 13 are on the anterior leaflet edge, Marker #2 is on the anterior commissural leaflet of the posterior leaflet complex, Marker #14 is on the posterior commissural leaflet of the posterior leaflet complex, Markers #3, 5, and 6 are at the P1-P2 boundary, Marker #8 is on the central meridional edge of the P2 scallop of the posterior leaflet, Markers #9, 11, and 12 are at the P2-P3 boundary, Markers #26, 27,

and 28 are on the anterior papillary muscle tip, Marker #29 is the point of insertion of the strut chord from anterior papillary muscle tip Marker #26 to the anterior leaflet, and Markers #23, 24, and 25 are on the posterior papillary muscle tip, with Marker #30 at the point of insertion of the strut chord from the posterior papillary muscle tip Marker #23 to the anterior leaflet.

Figure E.1 COM study marker locations. See text for anatomical descriptions.

Various PowerPoint animations are provided in this Appendix to illustrate leaflet movements, shapes, and folding patterns in 3D space relative to timing points on the left ventricular pressure curve.

APPENDIX F FLAP STUDIES

Hearts F1-F11 were studied. Datafiles (provided in this Appendix) associated with each study are:

HEART	CONTROL STUDY	
	FILE1	FILE2
F1	fee17r04.1E	fee17r04.1i
F2	fee18r03.1E	fee18r03.1i
F3	fes19r02.1E	fes19r02.1i
F4	fes21r03.1E	fes21r03.1i
F5	fes22r01.1E	fes22r01.1i
F6	fes23r05.1E	fes23r05.1i
F7	fes24r05.1E	fes24r05.1i
F8	fes25r02.1E	fes25r02.1i
F9	fes26r04.1E	fes26r04.1i
F10	fes06r01.1E	fes06r01.1i
F11	fes15r03.1E	fes15r03.1i

- Each datafile has (if the parameter was successfully recorded)
 - Electrocardiogram (mV) in Column 4
 - Left Ventricular Pressure (mmHg) in Column 5
 - Left Atrial Pressure (mmHg) in Column 6
 - Aortic Pressure (mmHg) in Column 7
 - In addition, *.1E datafiles have (See Figure F.1)
 - Marker#1 x, y, z lab coordinates (cm) in Columns 11, 12, 13
 - Marker#2 x, y, z lab coordinates (cm) in Columns 14, 15, 16
 - ...
 - Marker#13 x, y, z lab coordinates (cm) in Columns 47, 48, 49
 - Marker#14 is not used, placeholders in Columns 50, 51, 52
 - Marker#15 x, y, z lab coordinates (cm) in Columns 53, 54, 55
 - ...
 - Marker#31 x, y, z lab coordinates (cm) in Columns 101, 102, 103
 - Marker#32 x, y, z lab coordinates (cm) in Columns 104, 105, 106
 - Marker#33 x, y, z lab coordinates (cm) in Columns 107, 108, 109
 - Marker#34 x, y, z lab coordinates (cm) in Columns 110, 111, 112
 - Marker#35 x, y, z lab coordinates (cm) in Columns 113, 114, 115
 - Marker#36 x, y, z lab coordinates (cm) in Columns 116, 117, 118
 - *.1i datafiles have (See Figure F.1)
 - Marker#37 x, y, z lab coordinates (cm) in Columns 11, 12, 13
 - Marker#38 x, y, z lab coordinates (cm) in Columns 14, 15, 16
 - ...
 - Marker#53 x, y, z lab coordinates (cm) in Columns 59 60 61
(#53 is the last marker)
 - Each datafile row is a single sample time, with sampling occurring 60 times/sec (i.e. every 16.67msec). Row numbers correspond in 1E and 1i datafiles.
 - Marker numbers were assigned so as to retain backward compatibility with previous marker studies.

FLAP MARKER LOCATIONS: LEFT VENTRICULAR, MITRAL ANNULAR, MITRAL LEAFLET, AND PAPILLARY MUSCLES

LEFT VENTRICULAR (LV) MARKERS

- LV Apex (Marker#1)
- LV Anterior Subepicardium, apical plane (Marker#2), equatorial plane (Marker#3), basal plane (Marker#4), inserted before the pump run
- LV Septal Subendocardium, apical plane (Marker#5), equatorial plane (Marker#6), basal plane (Marker#7), inserted during the pump run
- LV Posterior Subepicardium, apical plane (Marker#8), equatorial plane (Marker#9), basal plane (Marker#10), inserted before the pump run
- LV Lateral Subepicardium, apical plane (Marker#11), equatorial plane (Marker#12), basal plane (Marker#13), inserted before the pump run

MITRAL ANNULUS (ALL MARKERS PLACED AT DIRECTLY OBSERVED LEAFLET “HINGE” LOCATIONS DURING THE PUMP RUN)

- Trigone Region
 - Left Fibrous Trigone(LFT) (Marker #29)
 - “Saddlehorn” (SH) (Marker#22)
 - Right Fibrous Trigone (RFT) (Marker #24)
 - LFT to SH (Markers#15,30)
 - SH to RFT (Markers#23,21)
- Contractile Annulus
 - Anterior Commissure (AC) (Marker#16)
 - Lateral Annulus (Marker#18)
 - Posterior Commissure (PC) (Marker#20)
 - AC to Lateral Annulus (Markers#28,17,27)
 - Lateral Annulus to PC (Markers#26,19,25)
- PAPILLARY MUSCLES (INSERTED DURING THE PUMP RUN)
 - Anterior Papillary Muscle Tip (Marker#31)
 - Anterior Papillary Muscle Base (Marker#32)
 - Posterior Papillary Muscle Tip (Marker#33)
 - Posterior Papillary Muscle Base (Marker#34)
- STRUT CHORDAE MIDPOINTS
 - Anterior Strut (Marker #35)
 - Posterior Strut (Marker #36)

MARKER LOCATIONS: LEAFLETS

- ANTERIOR LEAFLET
 - Trigone Region (See Figure 01) is the Anterior Leaflet Hinge Region
 - Leaflet Edge (markers sewn to atrial side of leaflet)
 - Central Edge (Marker#38)
 - LFT to Central Edge (Markers#42,43,44)
 - Central Edge to RFT (Markers#45,46,47)
 - Central Meridian from Central Edge to SH (Markers#39,40,41)
 - Left Belly (Markers#48,50,51)
 - Right Belly (Markers#49,52,53)
- POSTERIOR LEAFLET
 - Only one marker (Marker#37) sewn to the central meridian edge of the central scallop for timing of valve opening and closing

APPENDIX P PULL STUDY MARKERS, DATASETS, PROTOCOL SCHEMATIC

The PULL STUDY (see results in Chapter 28) was designed to assess the effect of posterior leaflet pressure on anterior leaflet edge geometry in the closed valve. Figure P1 shows the marker array and coordinate system used in this study.

Table P1 shows the datasets associated with the CONTROL and PULL runs for the three hearts analyzed in Chapter 28.

TABLE P1	CONTROL	PULL
	pul08r23pre.1E	pul08r24pull.1E
	pul13r01pre-2frames.1E	pul13r05pull.1E
	pul14r01pre.1E	pul14r02pull-2frames.1E

Figure P2 schematically illustrates the PULL protocol.

APPENDIX S SOD AND DOS STUDIES

Table S.1 defines the SOD marker anatomical locations and Figures S.1 and S.2 illustrate these locations in two views of S2 sod04r02. Table S.2 defines the DOS marker anatomical locations and Figure S.3 illustrates these locations in D5 dos21r01. Table S.3 defines the markers delineating the space-filling tetrahedral for volume calculations. Figures S.4A-F display these tetrahedral within the left atrium and left ventricle of SOD hearts S1, S2, S3, S7, S9, and S10.

Frame Rate = 60 frames/sec (16.667 msec/frame)

Each Row in the Datasets is a frame.

ECG Voltage is in Dataset Column 4; LVP in Column #5;

Marker #1X(cm) is in Column 11, #1Y(cm) in Column 12, #1Z(cm) in Column 13;

Marker #2X(cm) is in Column 14, #2Y(cm) in Column 15, #2Z(cm) in Column 16;

ETC., ETC.

TABLE S.1 SOD MARKER ANATOMICAL LOCATIONS	MARKER #'s
Apex	1
Anterior LV Subepicardium	2,3
Septal LV Subepicardium	4,5
High Septal Endocardium	6
Posterior LV Subepicardium	7,8
Lateral LV Subepicardium	9,10
Posterior Papillary Tip	11
Posterior Papillary Base	12
Anterior Papillary Tip	13
Anterior Papillary Base	14
Mitral Annular Septal	22
Mitral Annular Anterior Commissure	16
Mitral Annular Midpoint Between #22 and #16	15
Mitral Annular Lateral	18
Mitral Annular Midpoint Between #16 and #18	17
Mitral Annular Posterior Commissure	20
Mitral Annular Midpoint Between #18 and #20	19
Mitral Annular Midpoint Between #20 and #22	21
Anterior Leaflet Radial Meridian (Annulus to Edge)	23,24,25,26
Posterior (P2) Leaflet Radial Meridian (Annulus to Edge)	28,27
Anterior Leaflet A1 Edge (Paired with #30)	29
Posterior Leaflet P1 Scallop Edge (Paired with #29)	30
Anterior Leaflet P3 Edge (Paired with #32)	31
Posterior Leaflet P3 Scallop Edge (Paired with #31)	32
Septal Left Atrium	33
Posterior Left Atrium	34
Lateral Left Atrium	35
Anterior Left Atrium	36
Apex Left Atrium	37

Figure S.2 S2 sod04r02 marker locations, view [-78 -11] animatesod04.m

TABLE S.2 DOS MARKER ANATOMICAL LOCATIONS	MARKER #'s
Apex	1
Anterior LV Subepicardium	2,3
Septal LV Subepicardium	5,6
High Septal Endocardium	7
Posterior LV Subepicardium	12,13
Lateral LV Subepicardium	9,10
Posterior Papillary Tip	23
Posterior Papillary Base	24
Anterior Papillary Tip	25
Anterior Papillary Base	26
Mitral Annular Septal	22
Mitral Annular Anterior Commissure	16
Mitral Annular Midpoint Between #22 and #16	15
Mitral Annular Lateral	18
Mitral Annular Midpoint Between #16 and #18	17
Mitral Annular Posterior Commissure	20
Mitral Annular Midpoint Between #18 and #20	19
Mitral Annular Midpoint Between #20 and #22	21
Anterior Leaflet Radial Meridian (Annulus to Edge)	31,32,33,34
Posterior (P2) Leaflet Radial Meridian (Annulus to Edge)	36,35
Anterior LV subendocardium (Paired with #3)	28
Septal LV subendocardium (Paired with #6)	27
Posterior LV subendocardium (Paired with #13)	30
Lateral LV subendocardium (Paired with #10)	29
Septal Left Atrium	8
Posterior Left Atrium	14
Lateral Left Atrium	11
Anterior Left Atrium	4

All datasets in Appendix S have markers suitable for the analysis in Chapter 41, but some have missing markers that could affect other analyses. All markers are present in D1 (dos09r01.1e), D3 (dos12r01.1e), and D5 (dos21r01.1e); some are missing in D2 (dos11r01.1e) and D4 (dos18r01.1e). All markers are present in S1 (sod03r02.1E), S2 (sod04r02.1E), S3 (sod07r01.1E), S7 (sod11r02.1E), S9 (sod12r01.1E), and S10 (sod13r02.1E); some are missing in S4 (sod08r04.1E), S5 (sod09r02.1E), and S6 (sod10r02.1E).

SOD LV TETRAHEDRON	P1	P2	P3	P4
T1	M#1	M#2	M#7	M#9
T2	M#1	M#2	M#4	M#7
T3	M#5	M#2	M#4	M#7
T4	M#5	M#2	M#3	M#7
T5	M#5	M#8	M#3	M#7
T6	M#10	M#8	M#3	M#7
T7	M#10	M#2	M#3	M#7
T8	M#10	M#2	M#9	M#7
T9	M#3	M#5	M#6	M#8
T10	M#6	M#15	M#21	M#22
T11	M#3	M#6	M#15	M#21
T12	M#3	M#6	M#20	M#21
T13	M#3	M#6	M#8	M#20
T14	M#15	M#20	M#21	M#22
T15	M#3	M#20	M#10	M#15
T16	M#3	M#8	M#10	M#20
T17	M#15	M#19	M#10	M#20
T18	M#15	M#19	M#10	M#18
T19	M#15	M#17	M#10	M#18
T20	M#15	M#17	M#10	M#16
T21	M#15	M#16	M#10	M#3
T22	M#19	M#20	M#10	M#8
SOD ATRIAL TETRAHEDRON	P1	P2	P3	P4
T1	M#21	M#22	M#20	M#33
T2	M#15	M#22	M#20	M#33
T3	M#15	M#19	M#20	M#33
T4	M#15	M#19	M#18	M#33
T5	M#15	M#17	M#18	M#33
T6	M#15	M#17	M#16	M#33
T7	M#19	M#20	M#34	M#33
T8	M#19	M#18	M#34	M#33
T9	M#17	M#18	M#34	M#33
T10	M#17	M#18	M#34	M#35
T11	M#17	M#33	M#34	M#35
T12	M#17	M#33	M#36	M#35
T13	M#17	M#33	M#36	M#16
T14	M#15	M#33	M#36	M#16
T15	M#19	M#34	M#35	M#18
T16	M#37	M#33	M#36	M#34
T17	M#37	M#35	M#36	M#34

Table S.3 Marker-defined space-filling tetrahedral points for S1, S2, S3, S7, s9, s10.

Figure S.4A S1 space-filling tetrahedra

Figure S.4B S2 space-filling tetrahedra

Figure S.4C S3 space-filling tetrahedra

Figure S.4D S7 space-filling tetrahedra