Chapter 5

Modeling the macrostructure of the heart: healthy and diseased

5.1 Introduction

One of the common heart diseases is dilated cardiomyopathy (DCM). Dilated cardiomyopathy is associated with a number of pathological signs. The outward symptoms presented by patients with this disease are caused by the reduction in heart function, i.e., a reduced maximal left ventricular ejection fraction. Structurally there is a whole series of events called left ventricular remodeling, the most glaring of which is that the chamber dilates (loosing its normal ellipticity and becoming more spherical in shape), and the walls become thinner. However, it is presently unclear what else is involved in the remodeling, and in general the fact that chamber dilation is easily observed does not imply that this is the most important factor in the reduced functionality of the heart. Particularly, there is no consensus on the significance of myofiber orientation changes: some groups consider it essential [17, 56], while others claim that the only important factor is the change of the ventricle shape [25]. In this chapter we strive to gain some insight into the dominant cause of the functional reduction – whether it is a result of the anatomical shape change or the change in the fiber angle.

Such an insight has a potential to guide the ventricular surgical restorations, such as the DOR procedures, which are commonly used to treat patients with left ventricular remodeling pathologies [70]. Indeed, papers [25, 59, 71] discuss whether the ventricular surgical restoration should aim to primarily address the change in myofiber orientation or to focus on fixing the shape of the ventricle chamber. Of course, the choice between these two strategies depends on how much relative weight is given to the change in chamber shape as opposed to the change in fiber orientation.

It is unsurprising that this issue is difficult to resolve clinically, since it is hard to judge which factor is important – the changes to the shape of the chamber and the orientation of the fibers happen more or less simultaneously. To untangle this conundrum we use computational modeling, which allows us to look at the effects of chamber shape change and fiber orientation change separately.

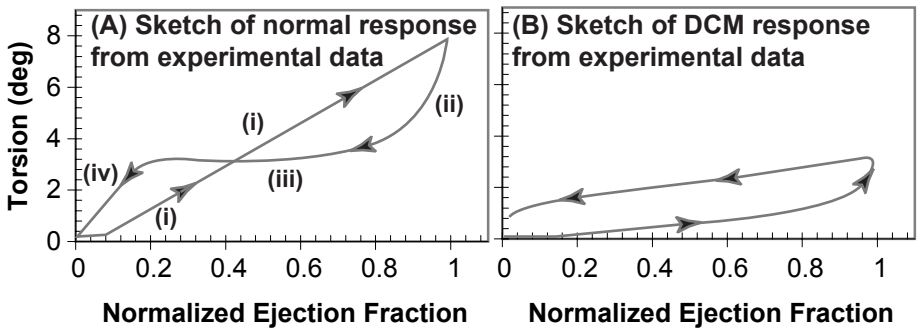

Figure 5.1: Sketches of plots of torsion vs. normalized ejection fraction. The arrows indicate the progression through the loops with time. (A) A schematic sketch showing the physiological torsion for a normal heart adapted from works by Tibayan et al. and Nakai et al. [72, 73]. (i) Systole. (ii) Early diastole - rapid inflow. (iii) Diastasis. (iv) Late diastole or atrial systole. (B) A schematic sketch for a heart with DCM adapted from [73];

To resolve by modeling whether or not the shape change is the leading cause of the reduced maximal ejection fraction we need a diagnostic tool that is independent from visual observations of structural changes. The reduction in ejection fraction alone cannot serve as such an indicator, as it is also reduced in other types of heart disease. Instead, we turn to the observation of the twisting motion of the left ventricle. It has long been observed that the left ventricle rotation changes significantly if the heart is damaged or is being stressed [31, 32, 56]. It was found that the relationship between the twist of the left ventricle and the ejection fraction is very sensitive to damage of heart and in the future might be used as a diagnostic tool [27–29]. During a beat of a healthy heart, the volume of the left ventricle is reduced as it is twisted, after end systole, but before filling starts, the heart untwists isovolumetrically, i.e., without a change in the left ventricular volume. This is best visualized in a parametric plot of the twist vs. the ejection fraction as both of these variables develop in time. In such a plot a healthy response has a characteristic shape with two loops, a schematic of which is shown in figure 5.1A. Some researches associate dilated cardiomyopathy with an initial negative twist [56], however such a characteristic is sometimes found in healthy patients as well [72]. It has been found that in dilated cardiomyopathy, unlike other pathologies, there is only one counterclockwise loop in this relationship [73] (figure 5.1B shows a sketch of this relationship). In other words, the ventricle does not twist as much initially as the healthy heart, and there is no isovolumetric (isochoric) untwisting. We use this characteristic to judge whether the model represents a heart with dilated cardiomyopathy.

The models used in this dissertation are based on the histological and DTMRI evidence that the myocardium can be approximated as a double helical muscle band (as seen in figure 5.2) [21, 23]. A detailed discussion of different characteristics of this model is published elsewhere. In this chapter, our objective is to test whether the change of the shape of the left ventricle or of the fiber orientation is responsible for presenting the dilated cardiomyopathy symptoms. The plan for this chapter is as

follows: After presenting all relevant methodical issues in section 5.2, we describe simulation results in section 5.3. We discuss the finding in section 5.4, starting with the general qualitative description of the importance of the double-loop relationship between twist and ejection fraction. We formulate the main conclusion in section 5.4.3.

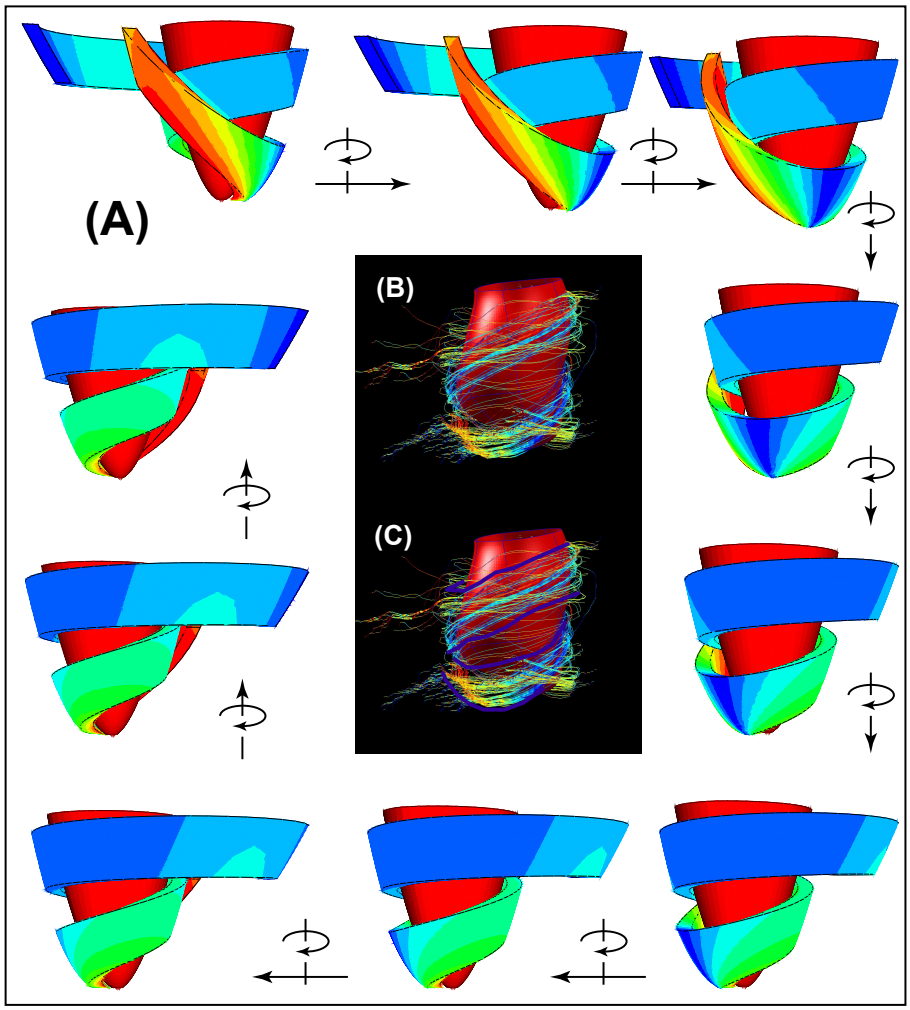

Figure 5.2: (A) The model double helical band is color coded for the fiber angle – blue and red representing circumferential and axial fibers, respectively. The fiber angle was calculated in the same way as in paper by Helm et al. [23]. The red chamber is the left ventricle. The series of snapshots around the perimeter show the model from different view points. (B) DTMRI of the muscle fibers in the myocardium color coded for fiber angle – blue and red representing circumferential and axial fibers, respectively. The red chamber is the left ventricle. The image was given to us by Helm. (C) The DTMRI image with the band outlined in dark blue.

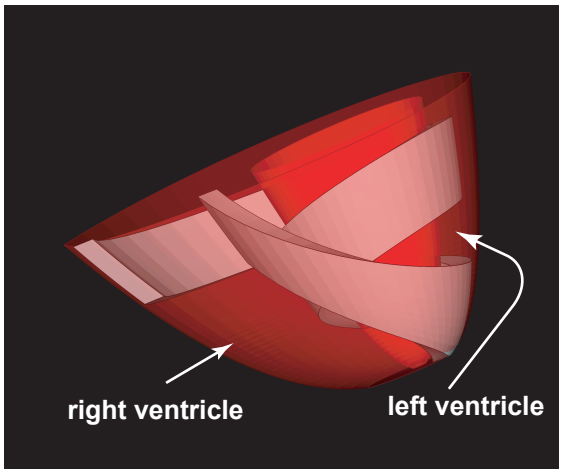

Figure 5.3: The band (grey) inside the heart shell (transparent red) with the left and right ventricles indicated.

5.2 Methods

5.2.1 Geometries of the bands

In order to determine the relative importance of different types of damages in dilated cardiomyopathy we chose a model that approximates the myocardium as a double helical band. Such view of the arrangement of cardiac muscle fibers is supported by both histological and DTMRI data [24]. In this approximation the muscle band starts from the pulmonary aorta, hugs the right ventricle, winds down to the apex, as the descending segment, and then spirals up to the aortic valve as the ascending segment. The exact path of the band in space is dictated by the fiber angle and the shape of the chambers bounded by the band (i.e., the right and left ventricle). The double helical band inside the shell of the myocardium can be found in figure 5.3.

A healthy heart has an elongated shape, that looks like an American football. As a result, the heart is often times modeled as an elongated half-ellipsoid. However, since in this chapter we focus on the function of the left ventricle, we found it more convenient to approximate the shape with a paraboloid. In case of dilated cardiomyopathy the heart is expanded to the point where it looks more spherical than ellipsoidal (i.e., more like a soccer ball than a football). The other change attributed to dilated cardiomyopathy is the change in fiber angle. To test the hypothesis that the change in fiber orientation is the primary factor responsible for the specific characteristics of dilated cardiomyopathy we examine four separate types of models: A model for a healthy heart; models with varying reduction in fiber angle in the region of the apex; models with a dilated left ventricular chamber; a model with other damage introduced to the band.

The normal shape of the left ventricle can be approximated with a paraboloid, with a long axis of 7 cm and the basal radius of 3.5 cm. The normal fiber orientation was taken from histological

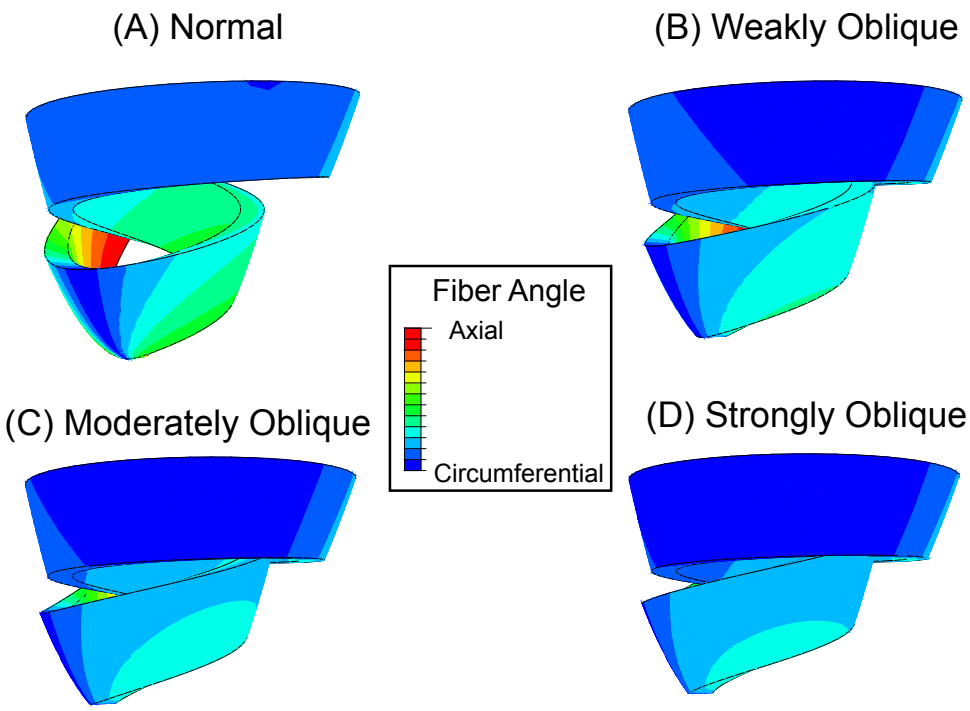

Figure 5.4: The model double helical band is color coded for the fiber angle – blue and red representing circumferential and axial fibers, respectively. The fiber angle was calculated in the same way as in paper by Helm et.al. [23]. (A)"Normal" model with fiber orientation corresponding to physiological. (B)"Weakly Oblique" model showing the fibers close to the apex to be a little more oblique than in the "Normal" case. (C) "Moderately Oblique" model with fibers considerably more oblique in the apical region than would be normal. (D) "Strongly Oblique" model showing the fibers close to the apex region to be almost circumferential. (A different view of these can be found in figure D.3)

data [21]. For ease of comparison we calculated and plotted (figure 5.4) the fiber angle the same way it is calculated from MRI data [23]. The following lists the different models that we describe in this chapter, along with the shorthand names that will be used to refer to these models in the rest of the chapter.

Normal: A case with the normal elongated shape and normally oriented fibers. The band color coded for the fiber angle can be found in Figure 5.4A. The fitted left ventricular volume can be seen in Figure 5.5A. The ratio of the long axis to the basal radius is taken to be around $7cm/3.5cm = 2$.

Weakly Oblique: A case with the normal elongated shape of the left ventricle, but with fibers in the region of the apex made slightly more obliquely oriented than normal. Figure 5.4B shows this band color coded for the fiber angle, and the region closer to the apex has fewer green tones than in the normal case meaning that the fibers here are more oblique than in the normal fiber orientation.

Moderately Oblique: A case with the normal elongated shape of the left ventricle, but with fibers in the region of the apex made more obliquely oriented than normal. Figure 5.4C shows this band color coded for the fiber angle, and the region closer to the apex has more blue coloring than in the "Weakly Oblique" case meaning that the fibers here are even more oblique.

Strongly Oblique: A case with the normal elongated shape of the left ventricle, but with fibers in the region of the apex made very much more obliquely oriented than normal. Figure 5.4D shows this band color coded for the fiber angle, and the region closer to the apex is mainly blue meaning that the fibers here are even more oblique than in the "Moderately Oblique" case.

Moderately Dilated: A case with the heart slightly dilated – meaning that ratio between the long axis and the basal radius was made to be ≈ 1.2, but we still approximate the volume as a paraboloid as shown in figure 5.5B. The fibers in this model are oriented normally.

Strongly Dilated: A case with the heart very dilated – the geometry of the left ventricular chamber was approximated with a section of a sphere as shown in figure Figure 5.5C, as a result the ratio of long axis to the basal radius is ≈ 1. The fibers in this model are oriented normally.

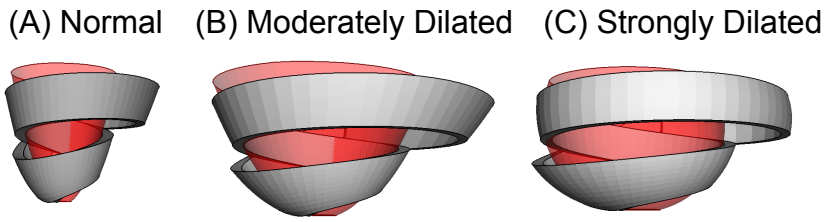

Figure 5.5: The model double helical band (grey) with the fitted left ventricular (LV) volume (red). The long axis dimension in each case is 7 cm. (A)"Normal" model, the LV is approximated with a paraboloid, with the basal radius of ≈ 3.5 cm; (B)"Moderately Dilated" model, the LV is approximated with a paraboloid, with the basal radius of ≈ 6 cm; (C)"Strongly Dilated" model, the LV is approximated with a section of a sphere, with the basal radius of ≈ 7 cm. See different view in figure D.4

Other Damage: A case with normal fiber orientation and a normal shape of the left ventricle, but an outer layer of the band in the region of the apex is made inactive to stimulate other damage that might occur in case of infarction, where part of the myocardium is dead. Figure 5.6 shows the materials used in the "Normal" model and in this model, with the dead material color coded in grey. An additional figure D.6 can be found in the appendix D.

The detailed description of the equations for these bands, along with geometrical constants used in this chapter can be found in appendix C.1.

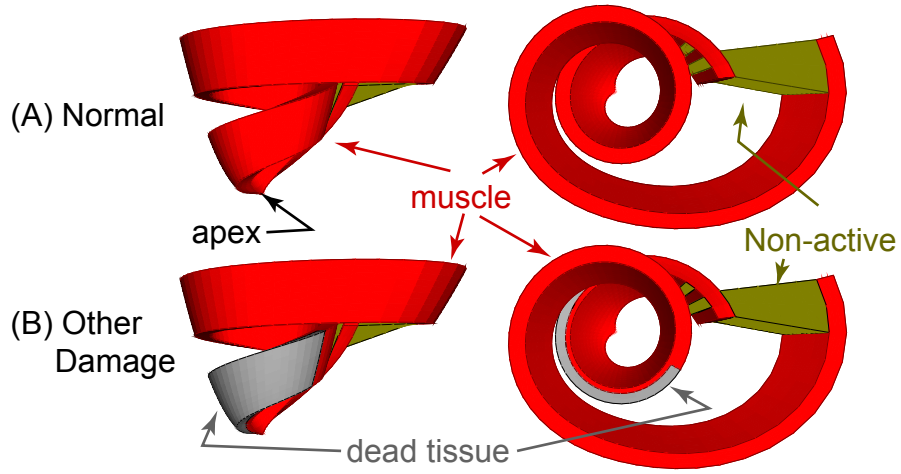

Figure 5.6: The double helical band model color coded for different types of materials used in these simulations: red - muscle, active material; green - non-active, softer, collagen type material; grey - dead tissue with a non-active stiffer material. (A) "Normal" model with no dead tissue from the side view (left) and top view (right). The left panel also shows the location of the apex used to hold the band in the vertical direction. In the horizontal plane the band is constrained by the non-active material. (B) "Other Damage" model showing the dead region near the apex.

5.2.2 Material Properties

The muscle band, which consists of a group of parallel muscle fibers contracts along the direction of the fibers, as each muscle fibers can only contract longitudinally. The fibers cannot contract much over 15% [16], therefore we impose a condition that the band will not exceed this maximum shortening ratio at any point along its length. While it is shortening in the fiber direction the band expands in the other two directions to conserve volume of the material. The whole band can shorten simultaneously, or parts of it can contract independently of each other. That means the muscle cells in different regions of the band can act separately. For simplicity, we assume a linear elastic response as long as the material is not excited. This approximation is appropriate for these simulations because we are not modeling the blood, and therefore we are not considering the pressure forces on the material. The material is incompressible, which ideally would mean that it has the Poisson ratio of $\nu = 0.5$, so we choose the maximal computationally possible Poisson ratio of $\nu = 0.48$. As we do not consider pressure inside the left ventricle, we choose to normalize modulus of each type of material used in these models by the Young's modulus of the muscle.

The double helical band is held together with a non-active material shown in figure 5.6A. The non-active material was chosen to be four times softer then the active material, i.e., the Young's modulus of the non-active material is one fourth of the Young's modulus of the active material.

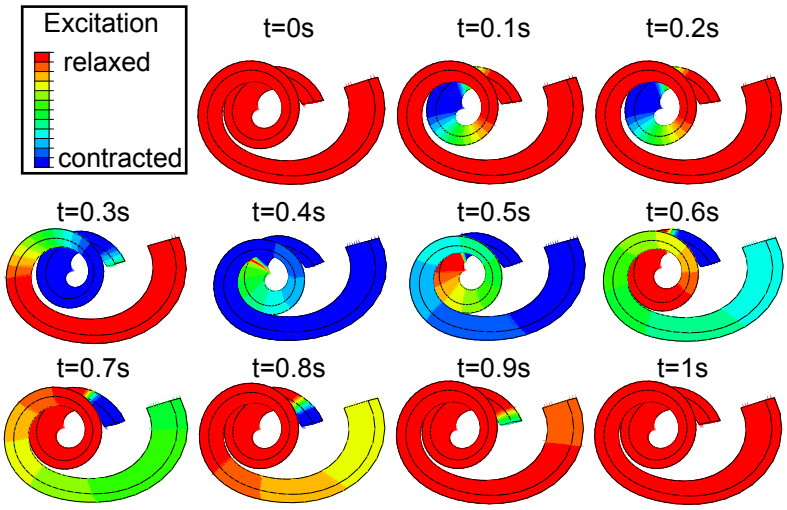

Figure 5.7: Top view of the double helical band model color coded for excitation: red and blue correspond to relaxed and excited, respectively. The material is fully contracted (up to 15% shortening) when it is fully excited (blue). The excitation wave starts at the apex and propagates outwards. The band is completely contracted (end-systole) at $t = 0.38s$. During diastole the relaxation wave front also starts from the apex and travels outward. (See different view in figure D.5.)

5.2.3 Boundary Conditions and Excitation

In order to easily compare the twist in our model to the heart's twist, we wanted to fix the band in space in the same manner as the heart. In the body, the heart's apex does not move up or down, while the base of the heart does not rotate. The band structure is fixed in the horizontal plane by the non-active material, in the same manner as the heart is constrained by the vessels. The lowest point of the double helix is assumed to be the apex, and is constrained in the vertical direction (figure 5.6A).

The excitation scheme was chosen to mimic the Purkinje network that has the excitation start close to the apex and progress outward [15, 56]. Figure 5.7 shows snapshots of the model band at different times during the heartbeat color coded for excitation. For all the different types of contractions the maximal amplitude of enforced stress was adjusted such that at the given Young's modulus of the active material, the resulting strain does not exceed physiological constraints discussed in section 5.2.2.

5.2.4 Computational Methods

To enable spatio-temporal excitation, it is necessary to allow different sections of the bands to contract independently. This creates a complex coupling between local small deformations and huge global shape responses, making it a challenging, but also promising, modeling problem. Another difficulty is that we are considering three dimensional geometries. To combat these problems, we

utilize the idea of finite elements. It is possible, with small quadrilateral elements to build very complicated shapes. The finite element method also breaks down a complex problem of the dynamics of a large system in response to deformation into a set of manageable equations. Since this set is very large, it behooves us to use the computing power available to solve it. We therefore, model these bands using a finite element package, ABAQUS, designed to handle such problems [74]. In the finite element code we use ABAQUS built-in tools to independently "excite" each node, and when the nodes of an element are "excited," the element contracts in the direction of the longitudinal fiber direction.

To model the complicated geometry along with this spatial wave activation we assume elastic equilibrium and utilize the final element package ABAQUS Standard 6.5. We use non-linear analysis with orthotropic elastic material properties.

5.2.5 Data Analysis

The results of the simulations are visualized and analyzed using both ABAQUS CAE 6.5 visualization software, and a code of Fortran and MatLab. The functionality of the left ventricle was judged by calculating the left ventricular volume as a function of time, maximal ejection fraction, torsion (or twist) as a function of time, and the peak rate of filling.

5.2.5.1 Volume and Ejection fraction

The volume of the left ventricle was approximated as the sum of slices of paraboloid for all cases except for "Strongly Dilated," where it was approximated with spherical slices. The ventricle chamber was cut into slices by vertical planes (constant θ) containing the long axis between θ and $\theta + \Delta\theta$, where $\Delta\theta \approx 7.2^\circ$. The calculated volume was normalized over the end diastolic volume (EDV).

The pumping efficiency of the band is measured by calculating the ejection fraction:

$$EF(t) = \frac{V_{end\ diastole} - V(t)}{V_{end\ diastole}}, \tag{5.1}$$

$$EF_{max} = \frac{V_{end\ diastole} - V_{end\ systole}}{V_{end\ diastole}}, \tag{5.2}$$

where, $V(t)$,$V_{end\ diastole}$ and $V_{end\ systole}$ are the volume at time t, end diastolic volume and end systolic volume of the chamber, respectively.

5.2.5.2 Rate of Filling

The peak rate of filling was estimated as the highest slope during early diastole. The period of early diastole was determined to start at the time of the minimum volume (end-systole). Early diastole ends at the start of the diastasis period, where the speed of filling falls sharply.

5.2.5.3 Twist and Torsion

Often times the words twist and torsion are used interchangeably, which makes sense since they measure the same effect. Twist is normally defined as the slope of the linear approximation of the relationship between the angular rotation of the markers and their long axial position [27–29]. Torsion is defined as the average angular rotation of the markers placed at different points along the long axis [73]. However, in some cases the later definition is named twist [72]. While the two values (slope and average) are easily related, one cannot be calculated from the other without additional measurements that are not normally provided in these papers. To be consistent for this chapter we define twist as the slope and torsion as the average of the rotation at different long axis positions. The detailed description of the method used to calculate these quantities can be found in appendix C.2. For this chapter all of the results shown will be of torsion.

5.3 Results

5.3.1 Ejection fraction

For each of the models tested here (Normal, Oblique Fibers, and Dilated Shapes), we calculated the volume of the left ventricle as a function of time. Figure 5.8 shows the change of volume, as percentage of end-diastolic volume, with time for each of the models. The normal case, shown in green, has a physiological response – with a systolic contraction leading to a large stroke volume, i.e., small end-systolic volume, followed by rapid filling, and then a slower filling of the left ventricle. In the cases where the myocardium band is malformed in any way the stroke volume is reduced. The plots show that the more severe the damage introduced into the model the greater the impact on the end-systolic volume. To quantify this we calculated the maximal ejection fraction for each case, the results of the calculations can be found in Table 5.1. The normal model shows a physiological maximal ejection fraction of over 55%. Any kind of introduced damage, be it a change in geometrical shape, a change in fiber angle, or a simulated infarction, reduces maximal ejection fraction. In the cases of progressively more oblique fibers the ejection fraction drops from 46% to 37% as the fiber

Model Type	**Maximum EF**	**Maximal Torsion**	**Peak Rate of Filling**
Normal	58%	8.4°	1.32 (EDV/sec)
Weakly Oblique	46%	7.1°	1.14 (EDV/sec)
Moderately Oblique	40%	6.5°	0.98 (EDV/sec)
Strongly Oblique	37%	5.7°	0.77 (EDV/sec)
Moderately Dilated	46%	4.5°	1.26 (EDV/sec)
Strongly Dilated	33%	2.5°	1.31 (EDV/sec)
Other Damage	52%	4.9°	0.97 (EDV/sec)

Table 5.1: Results for different model types

angle in the apical region is decreased (brown, red, and yellow in the plots of figure 5.8). In the case of a changed overall geometry of the chamber the ejection fraction also decreases from 46% for "Moderately Dilated" shape to 33% in the "Strongly Dilated" model (blue and light blue in the plots of figure 5.8). The "Other Damage" model has the ejection fraction of 52% (grey in the plot of figure 5.8).

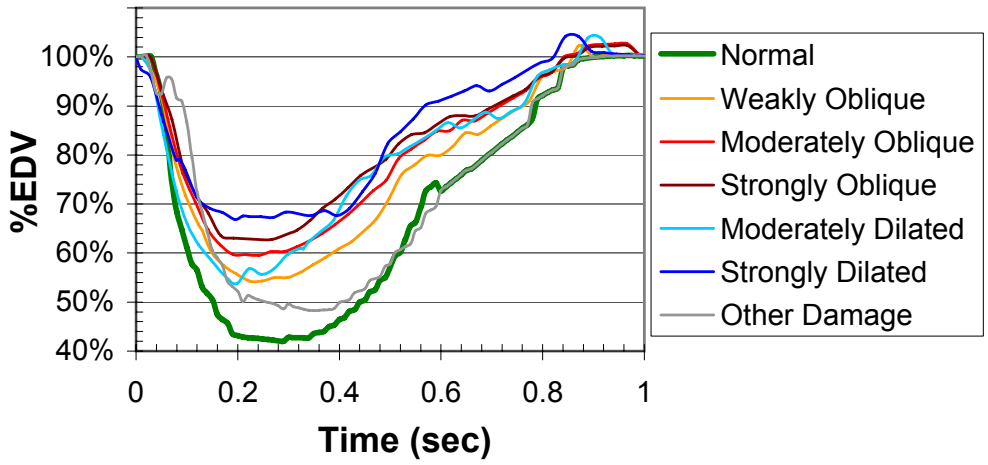

Figure 5.8: Volume of the left ventricle vs. time for each model. The volume is given as a percentage of the initial left ventricular volume, or in other words it is normalized by the end-diastolic volume (EDV). The peak filling rate is calculated from the highest slope during early diastole. Green curve: "Normal" model showing a physiological response with a maximal ejection fraction close to 60% and a rapid early diastolic filling rate. Peak filling rate between $0.4s - 0.55s$. Yellow curve: "Weakly Oblique" model showing a reduced maximum ejection fraction with end-systole at about $t = 0.3s$. Peak filling rate between $0.4s - 0.55s$. Red curve: "Moderately Oblique" model showing a reduced maximal ejection fraction. Peak filling rate is between $0.39s - 0.57s$. Brown curve: "Strongly Oblique" model showing an ejection fraction $< 40\%$. Peak filling rate is between $0.39s - 0.57s$. Blue curve: "Moderately Dilated" model showing a reduced ejection fraction with end-systole volume at $t = 0.2s$. The peak filling rate is between $0.34s - 0.44s$. Dark Blue curve: "Strongly Dilated" model showing the smallest maximal ejection fraction of $\approx 30\%$. Peak filling rate is between $0.4s - 0.55s$. Grey curve: "Other Damage" model showing a change in systolic behavior, but a return to normal during diastole. The peak filling rate is between $0.4s - 0.55s$.

5.3.2 Rate of Filling in the initial diastole period

Figure 5.8 also shows how the rate of filling during the initial diastolic period is affected by damage. In the "Normal" case the change of volume in early diastole is very sharp, which is in agreement with physiological observations. While in some of damaged models it appears to be less than in the normal case, it is hard to judge since the end-systolic volume, and the time at which it is reached, is different for each case. To quantify the observation of the speed of filling we calculated the filling rate. The normal peak filling rate ranges between $1.0 - 3.4$ EDV/sec (where EDV is the end diastolic volume) [75]. Table 5.1 shows the rate of filling for each of the models which was estimated from

early diastole period. The filling rate decreases with the decrease of fiber angle in the apical region, but does not have such a characteristic with the change of shape of the left ventricle. Indeed, in all models except for "Moderately Oblique" fibers and "Strongly Oblique" fibers the rate of filling remains in the normal range.

5.3.3 Torsion of the left ventricle

The torsion was calculated for each of the model cases. Physiologically the maximal torsion in normal cases has been reported between $6° - 9°$ [72, 73]. Table 5.1 shows the maximal torsion for each of the different models. The maximal torsion is within normal range for all the cases, except for the "Moderately Dilated" and "Strongly Dilated" models. Figure 5.9 shows the relationship between the torsion and ejection fraction for each model case. The "Normal," "Moderately Dilated" and "Strongly Dilated" cases show a double looped response while the "Moderately Oblique," and "Strongly Oblique" models present only one counterclockwise loop. In the "Weakly Oblique" model the second loop is partially collapsed. Indeed, the greater the change in fiber angle, the more impact can be seen in the shape of the torsion and ejection fraction relationship. The case of "Other Damage" shows neither a characteristic one loop response nor a normal double loop response (figure 5.9G). The same results calculated as twist can be found in figure D.7.

5.4 Discussion and Conclusion

5.4.1 The importance of the normal double looped response

To gain insight into the meaning of our data let us first consider qualitatively why the relationship between twist and ejection fraction might be indicative of heart damage. If the geometry of the heart is normal in both global geometry and in fiber orientation, the relationship between twist (or torsion) and the normalized ejection fraction has the form of a double looped curve (Figure 5.1A). It is possible to understand in a very robust way that this double loop feature is a signature of efficient pumping.

During the systolic period the heart twists as the muscle is contracted (figure 5.1A(i)). This twist is large enough that it is possible to see with the naked eye in open heart surgeries as well as MRI studies. The material of the heart is elastic, so as soon as the muscle fibers are released from contraction, all of the tissue springs back toward the relaxed state (figure 5.1A(ii)). This produces a very rapid untwisting during the onset of diastole, which lowers the pressure inside the ventricle. In turn, this creates a greater pressure difference between the left ventricle and the atrium allowing for faster initial filling. Once the A-V valve opens the untwisting and refilling of the ventricle (decrease in ejection fraction) happen simultaneously (figure 5.1A(iii)). And lastly, at end diastole the filling

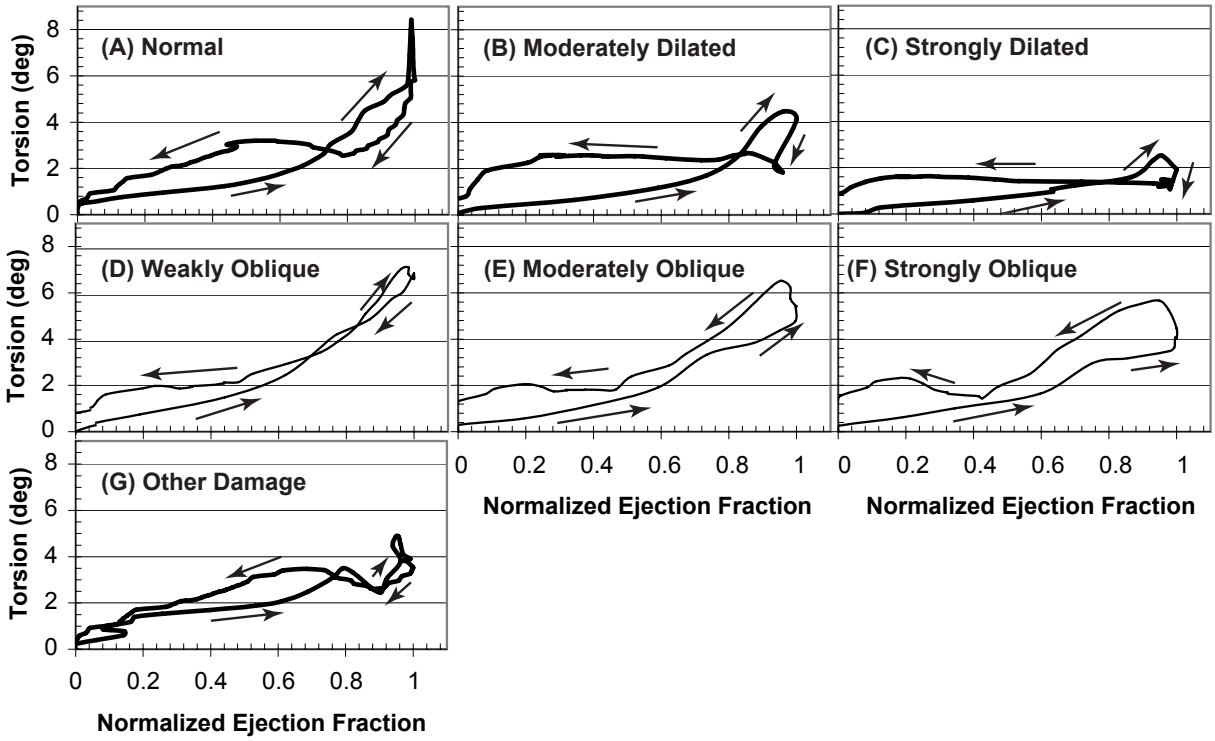

Figure 5.9: Plots of torsion vs. normalized ejection fraction. The arrows indicate the progression through the loops with time. (A) "Normal" model showing a physiological double looped relationship, with a proper maximal value of torsion. (B) "Moderately Dilated" model showing a reduction in maximal value of torsion, but a double loop relationship. (C) "Strongly Dilated" model still has the double looped curve, but a greatly reduced maximal value of torsion. (D) "Weakly Oblique" model showing a collapsed top loop, but no reduction in the maximal value of torsion. (E) "Moderately Oblique" model showing the characteristic to dilated cardiomyopathy (DCM) counterclockwise loop, without a large reduction in maximal value of torsion. (F) "Strongly Oblique" model also showing the characteristic counterclockwise loop with a larger loop than in (E). (G) "Other Damage" model showing randomness in torsion progression close to end-systole.

is much slower, while the untwisting continues (figure 5.1A(iv)).

These characteristics can be used to estimate the slopes of the lines, in a plot of torsion vs. ejection fraction: The slope of the line during early diastole is greater than during systole. During the middle of diastole the slope decreases sharply, and during end diastole it is again greater than that of systole. Figure 5.10 shows a cartoon of the normal torsion and ejection fraction relationship in green. This response, in most cases, is in the form of a double loop. The size of the loops depends on the patient's age and whether or not other damage is present. But what would it mean if only one loop existed?

If the single loop was clockwise, no impact on the rate of filling would be observed, as the initial diastolic untwisting would still be faster then the systolic twisting (dashed green in figure 5.10). However, a counterclockwise loop would imply that the initial untwisting is not rapid enough to effectively assist with filling (in red figure 5.10), indeed the increase in volume would be hindered by

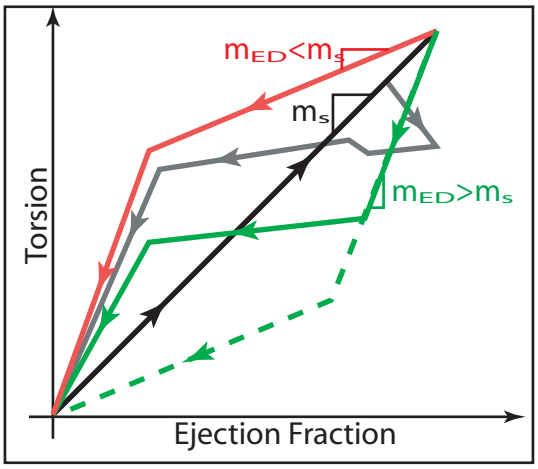

Figure 5.10: Rough schematic drawing of different torsion ejection fraction relationships. The arrows indicate the progression with time. Black line: Systole - with ejection fraction and twisting happening simultaneously. With the slope of the line being m_S. Solid Green lines: Normal classical diastolic progression with early diastolic slope $m_{ED} > m_S$, meaning a fast untwisting. Dashed Green lines: A different possibility for diastole with a rapid early untwist, showing how the bottom loop can take on different sizes or (in this case) disappear all together. Red lines: A diastole progression characteristic of dilated cardiomyopathy with the initial untwisting slower than systolic twist, i.e., the slope of the line $m_{ED} < m_S$. The result is a single counterclockwise loop. Grey lines: Diastolic progression of a case with dead tissue – creating a random response close to end-systole.

the residual twist. As a result the untwisting mechanism is not used effectively to assist refilling. An intermediate case would have the systolic twisting and diastolic untwisting happening at the same rate – which would mean the twist mechanism is not aiding the filling process, but it is also not hindering it.

If the part of the myocardium would become stiffer (as often happens after an infarction due to scarring) the untwisting motion would be unsymmetrical and will depend on the location of the damage. Indeed, the softer tissue would compensate for the stiff portion during the initial contraction, but as the whole structure twists at a maximum the stiffness would impact the dynamics. This would likely affect the relationship between torsion and ejection fraction during maximal twist, disorganizing it. As a result we expect the top loop to loose its symmetry and shape (grey in figure 5.10).

From studies performed on patients it is known that the single counterclockwise loop response, a sketch of which is shown in figure 5.1B, is characteristic of dilated cardiomyopathy [73]. A different type of response occurs for other types of damages [27–29].

5.4.2 Comparing different model results

The double looped response can be reproduced by the “Normal” model that also matches physiological maximal ejection fraction, filling rate, and maximal twist. In this model the myocardium is

defined by a bundle of fibers in the shape of a double helix. The overall shape of the left ventricle is that of an elongated paraboloid, and the fiber orientation in the double helix is consistent with physiological observations. The excitation pattern mimics that of the heart, with the contraction starting near the apex and propagating outwards. The detailed discussion of this model will be published elsewhere. Here, it is important to note that in this model the relationship between torsion (twist) and ejection fraction has the characteristic double looped response (Figure 5.9A). This shows that our model, however simplified, is capable of reproducing the physiological double-looped relationship between torsion and ejection fraction. So does the changes in geometry and fiber orientation affect the response?

As the fiber orientation is changed to be more and more oblique, the rate of filling decreases and the relationship between twist and torsion takes on the form of a counterclockwise single loop and the maximal ejection fraction is reduced. In the case of "Weakly Oblique" model the top loop is collapsed (figure 5.9D), and as the fiber angle is decreased for models "Moderately Oblique" and "Strongly Oblique" there is only one counterclockwise loop present (figures 5.9E and 5.9F). For these models with a change in fiber angle, the maximum torsion is decreased but it is still greater than what is observed in DCM cases (less than 4°).

For the model cases of normal fiber orientation and dilated left ventricle shape the ejection fraction is also decreased. Indeed, our results show that the greater the dilation of the left ventricle the smaller the maximum ejection fraction. However, the rapid filling rate remains within physiological limits and is unrelated to the degree of dilation. Therefore it is not unexpected that the relationship between torsion and ejection fraction remains in the form of the double loop for both the "Moderately Dilated" and "Strongly Dilated" models (figures 5.9B and 5.9C). However, the torsion response is not completely normal, as the maximal torsion is greatly reduced, and is below 4°.

We also took a look at other damage to ensure that the one looped response is characteristic of the change in fiber orientation and not other direct changes to the band. A simulation of a case where a layer of the myocardium is dead (non-active) resulted in greatly reduced maximal ejection fraction and peak filling rate. However, the relationship between torsion and ejection fraction does not take on the form of a single counterclockwise loop (figure 5.9G). Instead, the twisting and untwisting become irregular near maximal values.

5.4.3 Conclusion

The series of models were created to test whether the change of fiber angle or the change of left ventricular shape is the dominant factor in creating the characteristic failing response of dilated cardiomyopathy. In a heart with dilated cardiomyopathy both of these factors are present, but it is important to understand which of them has to be the primary target during the reconstruction surgeries.

We show that only the change in fiber angle produces the characteristic counterclockwise single loop relationship between torsion and ejection fraction. Neither simply dilating the shape of the ventricle nor introducing other damage has such an effect. As we have discussed in section 5.4.1 this relationship can be used to judge the efficiency of the ventricle pumping. Indeed, our results show that unless the fiber angle is fixed the peak rate of filling will remain low, which is detrimental to a patient's exercise capacity [76].

It would be erroneous to assume that fixing the fiber angles alone is sufficient to completely restore the pumping efficiency. Indeed, we show that by dilating the shape of the left ventricle we greatly reduce the maximal ejection fraction as well as the maximal twist. However, our results presented in this chapter demonstrate that the fiber angle is the single predominant determinant of the reduced functionality of the heart, and, therefore, it should be the primary target of surgical procedures directed at ventricle restoration in patients with dilated cardiomyopathy.