Project Number: GRG-1601

A Papillary Muscle Repositioning Device for the Elimination of Mitral Regurgitation

A Major Qualifying Project Report submitted to the faculty of

WORCESTER POLYTECHNIC INSTITUTE

In Partial Fulfillment of the Requirements for the degree of Bachelor of Science

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April 27, 2016

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Acknowledgements

We would like to thank the following members and faculty of Worcester Polytechnic Institute for their assistance in our Major Qualifying Project. Our advisors Professor Glenn Gaudette and John Sullivan. Lisa Wall for all of her assistance during our lab testing. As well as Josh Gershlak and Emily Abbate for their feedback and advice.

Furthermore, we would like to thank Professor Makarov, Omar Younis, and Khashayar Rafatzand for their contributions to our project.

Abstract

Post myocardial infarction can induce mitral regurgitation, which can lead to pulmonary hypertension, atrial fibrillation, and heart failure. Current devices that mitigate this problem put patients on anticoagulants for life or require replacement surgeries approximately every ten years. Our team created a minimally invasive medical device that we believe, based upon our analyses and preliminary results, requires a one-time surgical procedure and cuts down on recovery time. This device is inserted into the papillary muscle where it maneuvers the muscle into a new orientation allowing for proper closure of the leaflets, eliminating mitral regurgitation. Device specifications were determined through experiments and simulations run through SolidWorks and Autodesk ForceEffect. The results of our project suggest that our device could work in vivo and return proper functioning of the heart, but further testing is required.

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I. Introduction

The heart is composed of four valves that control direction of blood flow. The flow is unidirectional through the various chambers of the heart. Oxygenated blood flow from the lungs to the "left" heart, or left ventricle, is controlled by the aortic and mitral valves. Blood flow to the "right" heart, or right atrium, is formed by the pulmonic and tricuspid valves. Between the left ventricular chamber and the aorta is the aortic valve. This aortic valve stops blood from traveling back into the left ventricle after circulation. Between the left atrium and left ventricle is the mitral valve. The mitral valve stops blood from leaking into the left atrium during systole (Mount Sinai, 2005).

The function of the papillary muscle is to prevent prolapse or "ballooning" while the heart is in systole. It allows blood to flow from the atrium into the left ventricle without having reversal of blood flow back into the atrium, causing regurgitation (Mount Sinai, 2005). The papillary muscles contract before the ventricular musculature from impulses received from the moderator band. Because of this, there is a tension applied to the chordae tendineae, which closes the AV valves and limits movement of the bicuspid. The result of this is the prevention of backflow (Hetzer, 2011).

Myocardial infarction (MI), commonly known as heart attacks, is defined as "the irreversible necrosis of heart muscles, only secondary to prolonged ischemia" (Jolly, 2003). According to statistics, half a million Americans suffer from myocardial infarction annually, 1% of which experience papillary muscle rupture post MI and 5% of which contribute to mortality after acute MI (Jolly, 2003).

Papillary Muscle Rupture (PMR) most commonly occurs 2-7 days after the initial infarct; it is believed that the PMR occurs post MI because the preserved contractility exerts increased stress

on the already compromised papillary muscle, ultimately leading to rupture (Grasso, 2014). Papillary muscles maintain valvular competence within the mitral valve. Without proper function of these two muscles, the leaflets cannot close properly, which allows for blood to leak back into the mitral valve each time the left ventricle contracts, and ultimately experience mitral regurgitation (Fradley, 2011). Out of the two papillary muscles within the ventricular wall, the posteromedial papillary muscle is six to twelve times more likely to rupture because it's only source of blood supply is through the posterior descending artery (Jolly, 2003). However, rupture of the anterolateral papillary muscle or both is possible. Complete rupture of both papillary muscles usually results in immediate pulmonary edema, cardiogenic shock, and death. Diagnosis of PMR is found through the use of an echocardiography or right heart catheterization. The holosystolic murmur is essential to listen for when checking for papillary muscle rupture (UCSF, 2004). For a rupture in the posteromedial papillary muscle, the murmur radiates to the left sternal border and may be confused with the murmur of the VSD or aortic stenosis. Anterolateral papillary muscle rupture usually demonstrates a new pansystolic murmur that is audible at the cardiac apex and radiates to the axilla or the base of the heart (Grasso, 2014).

Researchers and businesses are working hard to find solutions to the current problems that arise from myocardial infarction. The current patents and solutions are specific to certain aspects of the papillary muscle and do not encompass a large array of different problems associated with myocardial infarction. Analyzing all current methods of success will help our team to create a solution to the initial client statement.

Project Goal

The project goal is to fix mitral regurgitation when there is papillary muscle displacement in the left ventricle due to myocardial infarction. Our group plans to fix the new orientation of the leaflets due to this change, through the repositioning of the papillary muscle. This will be accomplished through the use of a nitinol cantilever that will be inserted through the outside of the heart. Port access surgery will be the choice of insertion for this device. The repositioning of the papillary muscle will cause the leaflets to close properly in order to eliminate mitral regurgitation.

II. Literature Review

Physiology of Mitral Valve and Papillary Muscles

The heart contains four valves that control the direction of blood flow. Blood flow is unidirectional through the various chambers of the heart. The left ventricle is composed of the aortic and mitral valves. These valves control the flow of oxygen-rich blood from the lungs to the body. The right valve is composed of the pulmonic and tricuspid valves. These valves control the flow of oxygen-depleted blood from the body to the lungs. Between the left ventricular chamber and the aorta is the aortic valve. This aortic valve stops blood from traveling back into the left ventricle after circulation. Between the left atrium and left ventricle is the mitral valve. The mitral valve stops blood from leaking into the left atrium during systole (Mount Sinai, 2005).

There are two left ventricular papillary muscles, the anterolateral and posteromedial papillary muscles, which extend from the left ventricular free wall and attach to the two mitral leaflets (also known as cusps) seen in figure 1. These small myocardial structures have a general thickness similar to that of the left ventricular wall or ventricular septum. The specific location of the papillary muscle various between each person but commonly located "mid one-third of the left ventricular chamber". The two muscles are held firmly to the walls and each other by trabeculae. The anterolateral papillary muscle is slightly longer and narrower than the posteromedial papillary muscle and has a dual blood supply, coming from both the left anterior descending coronary artery and circumflex coronary artery. The posteromedial papillary muscle only has one blood supply, the posterior descending artery. Its sole dependent on the posterior descending artery makes the posteromedial papillary muscle six to twelve times more likely to rupture than the anterolateral papillary muscle (Jolly, 2003).

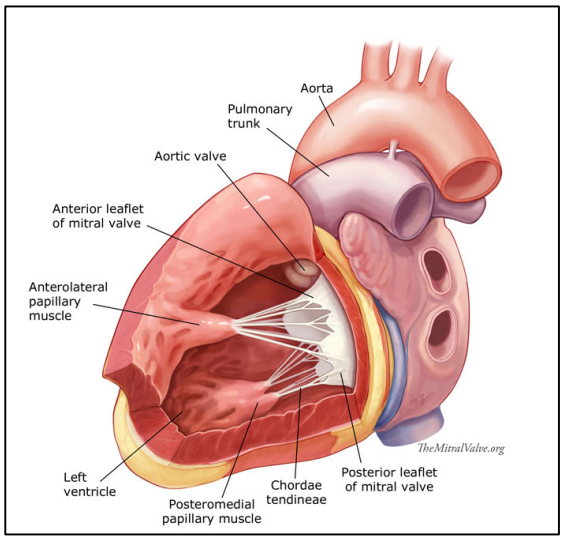


Figure 1: Diagram of the Left Ventricle

The primary responsibility of the papillary muscles is to prevent prolapse, or "ballooning", while the heart is in the systole phase. This means that it will only allow for blood flow to go from the atrium into the left ventricle without reversing back into the ventricle and causing regurgitation (Mount Sinai, 2005). The papillary muscles receive a direct impulse from the moderator band, causing it to contract before the rest of the ventricular musculature. This allows for tension to be applied to the chordae tendineae, thus closing the AV valves and limiting movement of the

bicuspids by placing them in an almost vertical direction, allowing for effective and unstressed closure and ultimately preventing backflow (Hetzer, 2011).

Projecting from each papillary muscle in a fan-shape pattern are several chordae tendineae (Roberts, 1972). These tendineae are composed of 80 % collagen and 20 % elastic fibers, all encased by an elastin mesh about forty micrometers longs and that itself is surrounded by a single layer of endothelial cells (Millington-Sanders, 1998). The wavy arrangement of collagen and surrounding elastic fibers is well suited to handle the cyclical stresses in which the chordae are continuously subjected to. They also act to store and dissipate energy (Dennis, 1986). They are primarily responsible for the end-systolic position of both the anterior and posterior leaflets. During ventricular systole, the low pressure in the atrium causes the AV valves to evert into the atrium; the chordae tendineae, with the help of the papillary muscles, will act as a tethering component and prevent the valves ability the flap back into the atrium and cause regurgitation. In order to function properly, the chordae tendineae must have a high degree of elasticity as well as considerable strength and endurance (Dennis, 1986). The chordae have the ability to bear the weight of the entire heart (Anatomy Expert, 2015). Any type of rupture to one or more tendineae will result in retrograde flow and cause cardiac dysfunction (Anatomy Associates, 2015). On average a papillary muscle will have about twelve chordae tendineae per head, all about 15-20 mm in length and 0.45 mm in diameter (Dennis, 1986). As they rise to meet the mitral valve, they subdivide into different layers: the primary, secondary, and tertiary.

The primary, or marginal, chordae attach to the free margins of the mitral leaflets. Thinner primary chords roles are to maintain leaflet apposition and facilitate valve closure. Failure to do so will result in mitral regurgitation. Secondary, or basal, chordae have the role of maintaining normal left ventricle size and geometry. Improper functioning of these chordae will result in mitral

regurgitation. The thick and long chords of secondary chordae are called strut, stay, or principal chords. They are located at the 4 and 8 o'clock positions on the undersurface of the anterior mitral leaflet. These structures make up the anatomic interface between the musculature of the left ventricle myocardium (at the papillary muscles) and the mitral annulus (at the fibrous trigones), by emerging from the papillary muscles to the dense collagen network of the anterior mitral leaflet, thus allowing for papillary-annular or ventricular-valvular continuity. Loss of tension is transmitted from the PMs to the ventricle epicardial fibers, with which they form a continuous syncytium. Resultant changes in fiber orientation are associated with a measurable decrease in longitudinal strain (Medscaoe, 2015).

The mitral valve is composed of two leaflets. One has a long anterior with a narrow base and the other has a shorter posterior with wider attachments. Within the posterior leaflet there is the lateral, middle, and medial scallop. With the middle being the largest of the three. Carpenter Classification or Duran Classification can be used to classify the leaflet. In Carpenter Classification the scallops of the leaflets are defined as P1 (anterolateral), P2 (middle), and P3 (posteromedial). And the corresponding anterior parts are classified as A1-A3. The next classification method is Duran Classification. This method defines the leaflets by a chordal insertion that is based on the two groups of papillary muscles. The anterior leaflets are divided by the corresponding chordae tendineae crossings from the anterolateral papillary muscle. The same is for the A2 portion of the leaflet that corresponds to the chordae tendineae from the posteromedial papillary muscle. For the posterior leaflet scallops, they are divided into P1 (anterolateral), P2 (posteromedial) and then the middle scallop is divided into PM1 and PM2 by the chordal origins (Shah, 2010).

Papillary Muscle Rupture

Papillary Muscle Rupture (PMR) is a detrimental effect of post-acute to moderate myocardial infarction (MI). In a meta-analysis by Kinn et al, it was found that PMR is the cause for 1-5% of mortality in acute MI. In most cases, PMR occurs in patients with cardiogenic shock post-MI; the earlier stated meta-analysis found about 55% of mortality was due to mitral regurgitation. During myocardial infarction, the left ventricle maintains adequate systolic functioning, allowing shear forces to be exerted on the papillary muscles (Hetzer, 2011). When the muscles undergo rupture, they no longer have the ability to apply tension to the chordae, resulting in an insufficient closing of the mitral leaflets, and ultimately mitral regurgitation.

Papillary Muscle Repair

The two papillary muscles are attached to leaflets of the mitral valve by the chordae tendineae. Because of the attachment of the papillary muscles to the leaflets, if there is rupture, the leaflet can be affected as well (Selder, 2015). Papillary muscle rupture can be repaired in a few different ways. One of the most common is to replace the mitral valve with a prosthetic valve. Another method is mitral valve repair. In this method, the ruptured papillary muscle head is reattached to either the bottom of the papillary muscle or the left ventricle. This can be done with or without using ring annuloplasty (Medscaoe, 2015). Mitral valve prolapse occurs when there is displacement of the superior leaflet tissue into the left atrium and it goes past the mitral annular plane. This could be either flail of the mitral valve or billowing valve with free-edge prolapse. The flail occurs when there is rupture of the chordae. The chordae tendineae snap causing the leaflets to be flail. This flailing causes the leaflets to no longer provide the strength to prevent blood from flowing backwards into the left atrium. The chordae tendineae are prone to rupture, so when this occurs to a large amount of them, the leaflets flail (Ahmed, 2013). Less commonly, when there is

papillary rupture, there will be flail valve prolapse when the mitral valve undergoes myocardial infarction. The billowing valve occurs when there is excess tissue in the leaflet or if there is chordal elongation.

Mitral Valve Repair

There are current surgical procedures that can help repair the mitral valve. Common surgical procedures are leaflet resection. Carpenter developed the technique called quadrangular resection to help treat posterior leaflet prolapse. In this method the prolapsed area is removed from the leaflet and it is repaired by plication of the annulus. After the quadrangular resection has finished an annuloplasty ring is inserted. However, there are issues with this technique, one being due to the addition of an annuloplasty ring, there is accelerated flow and turbulence across the posterior leaflet because stiffness was increased in this region. The geometry and dimensions of the leaflet were altered, as well, by cutting out a certain part. Another procedure that has been used is using polytetrafluoroethylene (PTFE) as neochordae. This will add support to the free edge of the prolapsing area of the leaflet. PTFE loops are placed on the papillary muscle at its fibrous tip. And from there single loops are attached to the posterior leaflet at the prolapsing area. The procedure is finished with the insertion of an annuloplasty ring (Holubec, 2013). Other techniques used for repair are artificial chords, plication, and leaflet reduction.

Fibrin Mircothreads and Regeneration

Fibrin microthreads were developed to act as a scaffold that would organize and align tissues as well as support fibroblast attachment, proliferation, and alignment. The advantage fibrin microthreads has over current scaffolds is the incorporation of fibrin (Murphy, 2008). Fibrin is a substance developed by the body during wound healing, making it much more acceptable to the body than other scaffolding materials. It is much more elastic than current materials and has unique

mechanical strength (Collette, 2015). Fibrin microthreads uses the unique properties of fibrin as a provisional matrix to allow for cells to attach and migrate during wound healing. This matrix decreases the potential for cells to be washed out of their site of implantation. For the case of healing the myocardium after infarction, fibrin microthreads have been inserted in the form of gels for cell delivery. Surgeons are going to be much more inclined to incorporate fibrin microthreads during surgeries because by attaching microthreads to their needles, they now have the ability to deliver stem cells to any location they want within the heart wall (Murphy, 2008).

Stem Cells as a Means of Regeneration

Embryonic stem cells have self-renewing properties that can be very useful for tissue engineering. They can be used for many different tissues including nerves and blood. They are very versatile and can be applied directly to the heart. A group from the Harvard Stem Cell Institute cultured embryonic stem cells that had the ability to contract on their own. These embryonic stem cells could be tested by being incorporating into a decellularized rat heart, to test if heart contraction can be produced (Melton, 2011). The way that this is relevant is that if the team could take the embryonic stem cells that beat, and seed it in the heart, this could lead to function returning to the heart.

The heart is made up of cardiac muscle. This muscle is striated, does not show fatigue, and is separated by intercalated discs. The muscle has a covering that is covered with connective tissue, which helps package the fibers (Georgia, 2015). Cardiac cells are interlocked with strong fibers and bands of actin protein that counter-act with myosin. These cells are to contract in rhythm that allow for the blood to be pumped with power and precision. The pacemaker cells can keep this rhythm going but they can also receive bodily signals that can increase or decrease that rate (Inner Body, 2015). The topic of interest is that cardiac cells were known to not have regenerative

properties. There were some studies that were done that showed that at a smaller rate, some tissue could grow back, however, if it is dead then it could be used as an anchor site.

To go more in depth of the regeneration of the cardiomyocytes, a study was done that took carbon-14 and combined it with DNA to renew cardiac cells in the adult heart. The rate is very minor of <1 percent but it does lead to the idea that if it could be done a little, it could increase, as suggested by the researchers. The many experiments over the years on cardiac stem cells on mice were inconclusive due to the shorter life spans. The reason why they used the carbon-14 was to have a safer way to conduct the tests on humans. The increase in the number of the cardiomyocytes that was postnatal increased based off of the number of the binucleation. The rate of renewal played a role in this as well because the younger cardiomyocytes were more likely to have the replacement happen. This rate of turnover does decrease with age. The end result was some limited functionality returning after the injury to the heart which adds some potential to the process (Bergmann, 2009).

Cell Integration in Scaffolds

Scaffolds have been used as physical supports to guide organization, growth, and differentiation of cells in tissue engineered constructs. They take on the functions of an Extracellular Matrix (ECM) in native tissues. The ideal scaffold will have biological cues such as binding sites for cells, physical cues such as surface topography, a porous structure with interconnectivity for cell migration and for nutrients and metabolites diffusion, controllable degradation mechanisms and rates. Typically scaffolds are composed of natural polymeric materials, synthetic polymers, ceramics, biodegradable polymers, or polymers with adsorbed proteins or immobilized functional groups. However, collagen based scaffolds have shown to have an advantage over these types of materials based on its biocompatibility properties. Collagen can

be used in its native form or as a denatured gelatin. It has grown to be a popular material used in scaffolds due to its abundance in the body, ubiquity, and biocompatibility. They are two forms collagen can take when used as the base material for a scaffold: swollen hydrogels or sparse fibers in a lattice-like organization, cross-linked by various methods but preferably dehydrated cross-linking (Trinity College, 2015). A recent study cultured embryonic and neonatal rat cardiac cells on electro spun tubular collagen scaffolds 15 mm long, 4 mm inner, 5 mm outer diameter. After 3-5 weeks in an HARV bioreactor, the randomized cardiac cells aligned to form sparse synchronously contractile networks, on the inside and outside of the tube (thickness of about 20 micrometers). The cardiac cells displayed registered sarcomeres and randomly distributed gap junctions while the tubular collagen scaffold, based on the results of the stress-strain hysteresis, and exhibited viscoelastic properties which mimicked that of the papillary muscle (Millard, 2011).

Cell Integration in Hydrogels

After myocardial infarction there are a lot of negative occurrences, one being loss of cardio myocytes. Human embryonic stem cells have the ability to differentiate into many different cell types, including cardiomyocytes and vascular cells. There has been an exploration of using biomaterials from decellularized native tissues as cellular or acellular patches and injectable hydrogels. Hydrogels are promising because they resemble the extracellular matrix. They are able to be designed to hold cells and improve the survival of cells and the differentiation and integration into host tissue. In forming hydrogels, aspects of the extracellular matrix have been used in the composition. These have included collagen, gelatin, and even extracts from the extracellular matrix. However, a downfall to using ECM hydrogels is that there is not a definitive characterization of how to form these gels. The Extracellular matrix itself is a very complex structure composed of an independent network of fibrous proteins, proteoglycans, and surrounding

molecules. So producing a hydrogel to include all this aspects will require more studies (Duan, 2011).

According to the studies performed by Duan et al cardiac ECM hydrogels loaded with cardiac progenitors, not containing growth factors, were able to differentiate and mature at a higher rate than collagen hydrogels that were produced with cardiac growth factors. It was also discovered that using a native cardiac tissue matrix mixed with collagen to create a hydrogel helps provide the correct biochemical cues that is important for cardiac regeneration. Collagen type I was used to create this hydrogel due to its protein growth promotion, survival rate of cardiomyocytes, and because there are copious amounts of it in the adult heart. In order to have human embryonic stem cell differentiation into cardiomyoctes, the hydrogel needs to be composed with a high percentage of ECM, around 75%. To test how the embryonic cells reacted to various hydrogels, embryoid bodies were cultured so that their morphilogial changes and distribution of cardiac cell lineages could be calculated. In the hydrogels with ECM around 75%, the embryoid bodies formed a group that allowed them to interact and beat synchronously (Dyan, 2011).

The cells in the 75% ECM hydrogels were able to differentiate and mature, however when growth factors were added to the material, this did not occur. In the studies by Duan et al, they hypothesized that this was due to the bioactive molecules and growth factors that are present in the native cardiac ECM. These factors send the signals for embryoid body differentiation. So, if extra growth factors are added this process is altered. Another hypothesis is the long term affects from the attachment of excess cytokines to the native ECM. This can inhibit cardiac myogenesis, forming of cardiac muscle (Duan, 2011).

Ischemic Left Ventricular Distortion

Ischemic mitral regurgitation is a potential complication of myocardial infarction. It has been shown that ischemic mitral regurgitation can result from left ventricular distortion. Ventricular distortion results in a dyskinetic or akinetic segment of the wall. The dyskinetic region is where the heart contracts at a different time than the rest of the heart and the akinetic region is when the heart does not contract (Trinity College, 2015). This distortion displaces the papillary muscles which causes the mitral leaflets to tether, restricting their closure. There is a lack of therapeutic solutions for left ventricular distortion. The main solution is to perform mitral ring annuloplasty, which reduces mitral annular size so that it is less than the normal systolic dimension, but does not fix ischemic left ventricular tethering of the leaflets (Hung, 2002).

The current solutions to ischemic left ventricular distortion are leaflet tethering, relocating the papillary muscle, surgical plication of the infarcted left ventricle, leaflet augmentation, and placing a patch or discs over the infarct. Another solution is to inject biomaterials into the myocardium. This will be used as a tissue bulking agent, aiding in the repositioning of the papillary muscle. In research performed by Solis et al PVA was the biomaterial used as the bulking agent. This polymer was used because it is biocompatible, bioinert, and can be produced so that it is injectable at 90C but also can form a gel at body temperature. Within 5 minutes an encapsulated gel was formed. Once this PVA hydrogel is injected into the infarcted myocardium there could be possible repositioning of the papillary muscles. This repositioning occurs by tissue displacement and changing of the myocardium so that it bulges less. Because a small amount of PVA was injected, there was not a change in the function or volumes of the left ventricle. There also was no damage to the surrounding myocardial fibers (Solis, 2010).

In current studies there is beginning to be an attempt to solve posterolateral papillary muscle and ventricular wall displacement with the use of hitching sutures. However, this would be added to the current procedure of using an annuloplasty ring. Ischemic mitral regurgitation can be improved if the posteromedial papillary muscle is repositioned. The PA hitch, posteromedial papillary muscle to posteromedial commissure suture, was used in the testing by S.F Marasco et al and pulled the posteromedial papillary muscle up towards the annulus, which relieved some of the tethering on the leaflet. This allowed the free edge of the posterior leaflet to rise and meet the anterior leaflet. An AL hitch was also used, posteromedial papillary muscle to anterolateral commissure suture. This pulled the posteromedial papillary muscle into the middle of the left ventricular cavity which pulled the free edge of the posterior leaflet closer to the coaptation point on the anterior leaflet. This method has more risks because it runs across the mitral valve orifice, which could interfere with the movement of the chordae (Marasco, 2008).

Another test was performed by J. Hung et al were they hypothesized the papillary muscle could be repositioned by placing a Dacron patch containing inflatable balloon over the papillary muscles. This could reverse left ventricular remodeling and reposition the infarcted papillary muscle toward the anterior mitral annulus, in turn reducing leaflet tethering. The procedure was performed by sewing the patch-balloon onto the region of infarction on the myocardium using interrupted sutures. Between the patch and the myocardium was an elongated oval balloon. The degree of balloon inflation and patch placement were determined in situ by echocardiography (Hung, 2002).

The experiment was performed on 10 sheep that mitral regurgitation was induced in. In 3 sheep there was a reduction of mitral regurgitation when the patch was placed. The other 7 required injection of 5 to 15 mL of saline in the balloon. It was shown that in balloon inflation the papillary

muscle shifted anteriorly, causing the bend in the anterior leaflet to be reduced. Also with the placement of this patch the mitral regurgitation volume decreased 0.8 mL/beat (Hung, 2002).

J. Hung et al were able to determine that the placement of this balloon-patch was able to provide direct and reversible control of papillary muscle repositioning. An advantage to this method was that left ventricular systolic function was not compromised and filling pressures were not raised. Further research is needed to be completed on the varying locations and chronicity of ischemia and papillary muscle geometry (Hung, 2002).

Polymer Integration

Polytetrafluoroethylene (PTFE), is a synthetic fluorocarbon polymer commonly used in cardiovascular applications based on its unique properties. It is created by free radical polymerization (Poly Fluro, 2009). Each carbon on the carbon based backbone chain has a fluorine atom attached to it, making it both nonpolar and nonreactive. Being the most electronegative element on the periodic table, the fluorine atoms do not share their electrons with neighboring atoms which results in a low surface free energy and causes the polymer to be "slippery." The low surface free energy and hydrophobicity of the polymer is the reasons why nothing can stick to PTFE (Clough, 2015). Commercially, PTFE may be known as Teflon (Jaganathan, 2014). PTFE has a high density (2.15-2.2 g/cm^3), high molecular weight ($6*10^6$-$10*10^6$), low tensile strength (17-28 MPa), low modulus of elasticity, low surface tension (18.5 ergs/cm^3), and a coefficient of friction of 0.1 (Bhat, 2002). Due to its high melt viscosity, PTFE cannot be injected, molded or melt extruded, so it is typically used in is powdered form where it is sintered at a temperature above 327 degrees Celsius under an applied pressure. This nondegradable polymer has excellent chemical and thermal stability, as well as 100% inertness, which allows for complete biocompatibility, PTFE can be implanted in the body and excellent tissue-material interaction

(Poly Fluro, 2009). Its biocompatibility ratings and temperature stability is much higher than other clinically approved polymers such as PVDF, Epoxy, Polypropylene, Nylon, and Polycarbonate. Typical biomedical applications of PTFE include sutures, pastes, tubes, strands, sheets, vascular grafts, etc. (Poly Fluro, 2009).

Although PTFE has tremendous advantageous for cardiovascular applications, it does have its drawbacks. In most cases, PTFE is considered to have a low wear resistance, but when placed under constant pressure, can undergo rubbing or abrasion resulting in wear particles that can cause chronic inflammatory problems (Poly Fluro, 2009).

In 1958, Bill Gore discovered expanded polytetrafluoroethylene (ePTFE), which is now commercially known as Goretex (Poly Fluro, 2009). This form of PTFE is typically used in external medical devices. The process of creating ePTFE involves heating up unsintered PTFE to a temperature between 350-370 degrees Celsius while it is restrained in a device capable of stretching it at high rates. The polymer may be stretched for a time period ranging from a few seconds to an hour. The higher the stretch rate and temperature, the more uniform of a matrix will be produced. This process is called "amorphous locking". Once the polymer has reached its desired expansion, it is cooled and removed (Poly Fluro, 2009). ePTFE has a higher permeability to gases and liquid then PTFE due to its porous structure, has a crystallinity of 95% (significantly higher than any competing commercial product with unexpanded parts), as well as a higher flex life, improved tensile strength, and maximum service temperature than typical PTFE. Its airflow rate is 2-15,000 mL/cm^2, methanol flow rate 1-10,000 cm^2, water entry pressure of 0-250 psi and a pore size ranging from 0.02-40 micrometers (Poly Fluro, 2009). There are no confirmed reports of allergic reactions to Gore ePTFE to date and studies have tested the product to be non-carcinogenic, non mutagenic, non pyrogenic, and not systemically toxic (Poly Fluro, 2009).

However, thrombus formation have been reported on the surface on ePTFE grafts that have been implanted in vivo (Poly Fluro, 2009).

The use of PTFE sutures to repair mitral regurgitation has shown high success rates in clinical studies. One study used PTFE sutures as chordae reconstruction of the mitral valve after myocardial infarction. This study was performed on a total of seven patients, three of which suffered from prolapse of the anterior leaflet, two from posterior leaflet, and two who ended in hospitalized death due papillary muscle dysfunction. A total of five out of seven patients ended in successful chordal reconstruction through the use of PTFE sutures (Poly Fluro, 2009).

Another study tried similar techniques to repair mitral valve after myocardial infarction by focusing on the reconstruction of the chordae tendineae with ePTFE sutures. There was a total of 22 patients involved in this study, all having gone through moderate-to-severe MI with prolapse of posterior leaflets. Each patient underwent mitral valve repair which involved the reconstruction of artificial chordae with ePTFE sutures without leaflet resection. The final results showed two failures, both of which having to receive reoperation, nonexistent mitral regurgitation in 6 patients, trivial regurgitation in 10 patients and mild regurgitation in 4 patients. The systolic and diastolic dimensions of the left ventricle decreased significantly as well ($p<0.01$). The PTFE sutures exhibited similar flexibility to that of natural chordae. Overall, the results of the study supported the hypothesis that PTFE sutures preserved favorable relationships among leaflet tissues, chordae, and the papillary muscle. The most important factor considered throughout this study was accurately determining the proper length of the reconstructed chordae. It is important to maintain a predetermined distance between the apex and mitral annulus so the natural geometry of the left ventricle is maintained during operation. In most cases, the suture was tied at the leaflet level where the opposite leaflet was stretched (Tomita, 2004).

In very few studies has PTFE sutures resulted in failure or major drawbacks. Kobayashi and associates (Kobayashi, 1996), found that within a year, their artificial PTFE chordae tendineae became covered by a host fibrosa which resulted in thickening and stiffening and ultimately mitral valve dysfunction. One study reported calcification in an experimentally isolated PTFE chordae, but otherwise has not been reported in any other cases (Tomita, 2004).

As the interest of PTFE chordae tendineae began to grow, a chordae replacement study compared its properties against traditional leaflet resection to fix mitral regurgitation. The study took 211 patients, all of whom underwent isolated mitral valve repair for degenerative posterior mitral leaflet prolapse and all of whom received an annuloplasty ring. Results were collected after 5 years. 156 patients went under leaflet resection and 55 received PTFE neochordae. Results showed a 98.2 % in PTFE and 93.9% in resection group from a mitral repair study, freedom from all cause reoperation 100% in PTFE, 93,9% in resection, freedom from mitral regurgitation 89% PTFE and 96.1 in resection, freedom from endocarditis 100% PTFE and 98.3% in resection group. Overall, PTFE neochordal repair can allow for a larger mitral annuloplasty ring and is associated with a better hemodynamic performance then leaflet resection (Ragnarsson, 2015).

There have been advances in tissue engineering to make surfaces more biocompatible through coatings and surface modifications. These coatings have been incorporated into different cardiac implants and devices to make devices more suitable for implantation in the heart. Some of these methods have included adding a layer of polyethylene glycol (PEG). PEG is an important polymer because it can combat the inflammatory effects and has photolithography capabilities that can pattern different electrodes to accept stimulation (Ravenscroft-Chang, 2010).

Nitinol

Nitinol has been widely used in cardiac applications due to its shape memory characteristics. Nitinol can be given desired properties by treating it a certain way. One treatment is heat treating and it determines the final properties of the Nitinol wire and can be modified to a desired outcome. This is due to the crystal structure of the different alloys. While in the martensitic phase, the Nitinol is able to be bent into a shape that can be remembered. This aligns the crystals in a different structure that can then be heated to a certain temperature to "lock" them in a shape that can be remembered later on. The different phases between austenitic and martensitic are shown in Figure 2. The crystal structures can then align and then be remembered and then once the object is deformed, it can be returned to that when heat is applied.

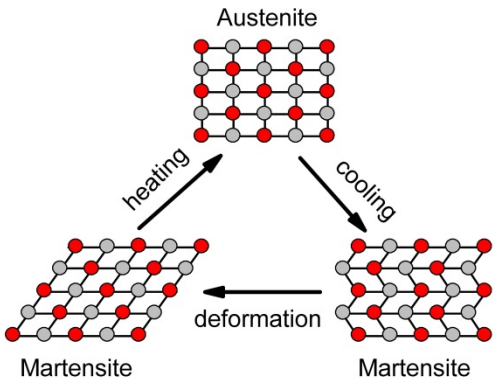


Figure 2. Nitinol Austenite to Martensite phase change

III. Project Strategy

Initial Client Statement

The following client statement was presented by advisor Professor Glenn Gaudette for this Major Qualifying Project.

> "Design a functional replacement for the papillary muscle that incorporates the use of fibrin microthreads. Design considerations include implantability, handling and function."

Background on the topic of interest was also provided to give more insight into the problem:

> "The papillary muscles are small muscles located in the ventricles of the heart. These muscles are connected to the cusps of the atrioventricular valves via the chordae tendineae,

and prevent inversion and prolapse of the valves. Damage to these muscles leads to valve prolapses and blood regurgitation increasing the chances of severe complications in the heart. Cardiac surgeons generally prefer to keep native atrioventricular valves rather than replace them with mechanical or bioprosthetic valves. One method to do this includes re-orienting the valve leaflets. A tissue engineered papillary muscle may be able to re-align the valve leaflets while also providing the contractile benefits of a normal papillary muscle."

Our initial client statement had the implied solution to use fibrin microthreads as a replacement of the papillary muscle. After investigating and going through the design process, our group came to the conclusions that although this implied solution was presented to us by the client, that did not mean it was the best option in solving it. We found we did not need fibrin microthreads to replace the papillary muscle, we just needed to bring the edges of the mitral valve leaflets together again to eliminate mitral regurgitation. Once we were able to think outside the confinement of the initial client statement, we were able to come up with a revised client statement as well as a list of functions and objectives that better suited the problem needed to be solved.

Revised Client Statement

"Design a device that will repair closure of the leaflets in the left ventricle of the heart after myocardial infarction, through the repositioning of the papillary muscles. Design considerations include being implantable, minimally invasive, and biocompatible"

Functions and Objectives

A list of functions and objectives was developed based on the initial and revised client statement.

- **Non-immunogenic:** The device cannot cause an immune response within the body that could lead to additional health problems.

- **Non-toxic; biocompatible**: the device and materials need to be able to welcome cell growth so they do not cause problems and kill the cells that will be growing on them. If the device causes more problems for the body, given that it will be located in the heart, then more harm could occur than benefit.
- **Degradation rate should match the rate of new tissue formation (initial):** The device and tissues have to be matched with a degradation rate so one does not fail sooner than the other. It cannot give off negative byproducts from degrading to ensure that its safe for internal body use, especially when it has contact with the blood stream.
- **Provide physical support for cardiac cells when seeded (initial)**: Making sure the cells are able to grow properly and they have enough support will help ensure that they can grow properly and become proper cardiac cells. This also ensures that they should be grown on a surface that will not negatively impact their properties.
- **Provide chemical and biological cues which mimic the papillary muscle (initial)**: If the material used can either take electrical signals to contract properly (if needed) or even be able to know when the heart needs to pump more or less to follow bodily function.
- **Display viscoelastic material properties (initial):** Ideally having a viscoelastic material should last longer and display similar properties to the original physiology of that its replacing.
- **Light weight (revised):** Having a low weight, high strength material would be ideal in the heart for minimal interference.

- **Easily manufactured into desired shape (revised): S**hape memory will ensure that our material is not overly brittle.
- **Biomimetic strength to the papillary muscle**: Having the material used match the shape of the papillary muscle will ensure the elimination of extraneous cost and less material waist.
- **Contract with the left ventricle**
- **Account for cell viability, proliferation, and differentiation during and after engraftment:** making sure that the cells don't continuously grow into a mass that becomes a problem down the road would be another important factor.
- **Cannot tear the leaflets (revised)**: making sure that the device does not break the leaflet or does not damage the heart will be important. The device has to be securely anchored so that does not cause damage to the patient.
- **Alters the orientation of the leaflet to close properly and stop mitral regurgitation (revised):** the device cannot cause more problems than it is trying to fix. If the valves and leaflets get altered too much then this would cause more harm than benefit.

Based on these functions and objectives, a pairwise comparison chart was used to help organize the major function on the list (Table 1).

Table 1: Pairwise Comparison Chart

Pairwise Comparison Chart					
	Biocompatible	Cell Growth	Mechanical Properties	Contractile	Total
Biocompatible	x	1	1	1	3
Cell Growth	0	x	0	1	1
Mechanical Properties	0	1	x	1	2
Contractile	0	0	0	x	0

Through the chart, biocompatibility and strong mechanical properties showed to be the most important aspects in the design. It also showed that contractile properties were not as important, meaning this may not need to be incorporated into the final design. These tests allowed a revised client statement to be produced.

Project Approach

For our project approach, we intend to design a papillary muscle repositioning device using the shape memory alloy nitinol. We plan on developing a proof of concept to show that our device will work when applied to cardiovascular applications. We will use computer aided design simulations, data analysis, and in vitro experiments to determine if our device will allow for a new orientation of the papillary muscle thus allowing for proper closure of the leaflets and elimination mitral regurgitation.

IV. Design Process

Needs Analysis

After developing our project approach one the client statement was revised, we specified the needs required for our device. The length of the papillary muscle was researched to determine the size our device should be. The average displacement of the papillary muscle was calculated to help determine the possible vectors needed to return the papillary muscle to its initial position. And finally different reactions on the papillary muscle when the heart is in systole and diastole were researched to understand how our device should account for those changes.

Table 2: Needs Table

Ranking	Need
6	The material used needs to properly fit the length of the papillary muscle.
1	It must readjust the papillary muscle to it's original location and account for displacement after myocardial infarction in order to eliminate mitral regurgitation which is occurring from improper closure of the leaflets
3	Account for the maximum forces and pressure changes that act on the papillary muscles to assure our material will be able to withstand such force inside left ventricle
5	Account for angular displacement of the papillary muscle after myocardial infarction in relation to the myocardial wall
2	The material we use must be biocompatible so it will be accepted by the body and function properly
8	Calculate how to train the nitinol to desired shape in order to force the papillary muscle back to its original location
4	Solve the problem of mitral regurgitation without causing additional issues
7	PTFE needs to be the proper length to account for a 10% strain within the cardiac cycle

Length of Papillary Muscle:

The material used needs to properly fit the length of the papillary muscle. A study measured the length of the papillary muscles of different age groups in Bangladeshi cadaver. Group A where <20, Group B were between the ages of 21 to 40 and Group C was 41 to 60 years of age. The mean +/- SD length of the anterior papillary muscle in the left ventricle of the heart was 1.53 +/-0.34, 2.05 +/-0.39 and 2.01 +/-0.25 cm in Group A, B, and C respectively. The mean +/- SD length of the posterior papillary muscle in the left ventricle was 1.33 +/- 0.34, 1.95 +/- 0.89, and 1.81 +/- 0.76 cm (Li, 2014).

Displacement of Papillary Muscle after Myocardial Infarction:

Based off a study, "Ring plus String", that was conducted to better understand the precise 3-dimensional geometry changes of the mitral valvular-ventricular complex in chronic ischemic mitral regurgitation to better devise a surgical repair technique, the average displacement of the posterior papillary muscle after myocardial infarction was 7 +/- 3 mm to the left perpendicular to the tip, 8 +/- 5 mm at 45 degree angle of the tip, 1 +/- 1 mm down and for the anterior papillary muscle was 3 +/- 2 mm to the left perpendicular to the tip, 1 +/- 1 mm down (Tibayan, 2015).

Geometric Orientation during Systolic and Diastolic Cardiac Cycles:

The onset of systolic pressure in the left ventricle causes the length of the papillary muscle to increase sharply, reaching its maximum length at the opening of the aortic valve. In the geometric orientation of the left ventricle, the mitral annulus is placed somewhat forward, whereas the aortic orifice is adjacent and directed upward. The anterior leaflet is oriented parallel with the line of flow out of the aorta, meaning that in the systolic cardiac cycle, it is pushed further out of the way. The vector of systolic forces is mainly tangential to the anterior leaflet, which, despite its large surface area, is protected from stress (Farner, 1973). As long as the mitral valve is open, only moderate tangential forces act on the papillary muscle. Pre-tension of the papillary muscles is low during diastole. After the valve closes, the pressure in the left ventricle sharply rises to stretch the muscle and in turn causes the mitral leaflets to act as a secondary anchoring point for the papillary muscle (Duran, 2013).

Strain on Papillary Muscles during Cardiac Cycle:

Based off of our research, the average strain on the papillary muscles from systole to diastole is approximately 10% (Komeda, 1997 and Semafuko, 1975).

Maximum Forces on Papillary Muscle:

On average, a mean force of 4.1 +/- 9 N is transferred to each papillary muscle from the mitral valve and the chordae tendineae. Values found in a study, Forces on the Papillary Muscle, measured peak papillary muscle force at 5.3 N in the anterior papillary muscle and 5.1 N in the posterior papillary muscle at a left ventricular pressure of 94 mmHg, this is an average range of a heart during the systolic phase of the cardiac cycle of a healthy adult (Askov, 2011).

Angular Displacement of Papillary Muscle after Myocardial Infarction:

A study called "Angle Displacement during Cardiac Cycle", obtained short-axis measurements of left ventricular cavity at the level of the papillary to obtain individual frames were the muscle was in systole and diastole. Degrees of angular displacement of the papillary muscle were obtained by subtracting the measured angle in diastole from the measured angle in systole. This final value was assumed to represent the degree of angular displacement of the left ventricle about its longitudinal axis. The study showed that patients with heart diseases, such as myocardial infarction, had a mean papillary muscle angular displacement of 3.2 degrees. Values ranged from 0-7 degrees. These results confirmed that patients with mitral regurgitation do not have exaggerated left ventricular rotation and no significant difference from that of a normal papillary muscle (Mirro, 2015).

Pressures of Diastole and Systole:

Diastole is defined as "the pressure exerted on the walls of the various arteries around the body in between heartbeats when the heart is relaxed", and occurs at a normal range of 60-80 mmHg in healthy adults. Systole is defined as "the measure of the amount of pressure the blood exerts on arteries and vessels while the heart is beating". The average range in a normal healthy adult is 90-120 mmHg (American, 2015).

Pressure of Diastolic and Systolic after Myocardial Infarction:

A study conducted hemodynamic monitoring in patients with acute myocardial infarction to better understand the pathophysiology of myocardial infarction and allowed an objective assessment of left ventricular filling pressure, cardiac output, and aortic pressure. The study included thirty-eight patients, aged 39 to 77 with acute myocardial infarction (conducted within 48 hours of onset of symptoms). Results showed that the left ventricular end-systolic volume was 125 +/- 41 ml/m^2 compared to 82 +/- 10 ml/m^2 in normal, healthy adults. The left ventricular ejection fraction 36 +/- 8% compared to 56 +/- 3% in normal, healthy adults. Overall, patients with acute myocardial infarction had significant increase in the left ventricular end-systolic volume and decrease in ejection fraction compared to those in normal hearts. The end-diastolic volume was, however, increased only in those with an elevated left ventricular filling pressure or decreased cardiac index (Rigo, 1974).

Design Requirements and Functions

For our device, insertion will occur from the outside of the heart wall and will be placed inside the papillary muscle. This will be done through port access surgery, allowing our device to be minimally invasive. Current devices are inserted through open heart surgery, which is very invasive compared to port access surgery. This will help decrease the recovery time for the patient, allowing them to return to their daily activities.

The typical displacement of the papillary muscles after myocardial infarction is 2.5-5mm. The material chosen for our device will allow the papillary muscle to return to a position that will allow for proper closure of the mitral valve leaflets.

Our device needs to be durable because we want it to last the remainder of the patients' life time. A problem with current devices are that they are a temporary fix and another surgery is needed 10 years later. Our device will be a permanent one-time surgery for the patient.

We also want our device to be easy for the surgeon to use. Because current devices on the market have been used for so long, it could be difficult to introduce a new product if the surgery is more complicated than the current method.

Functions

The purpose of our device is to be minimally invasive. This will be accomplished through port access surgery. We also want this to be a permanent, one time surgery for the patient. Our device will be placed inside the papillary muscle of the left ventricle of the heart to reposition the muscle in a new orientation that will allow for proper closure of the mitral valve leaflets in order to eliminate mitral regurgitation after myocardial infarction.

Specifications

Specifications were determined for our device to ensure that it would function properly when placed inside the papillary muscle of the left ventricle.

The first specification was that the device could not be longer than the papillary muscle itself, which is typically 13-19mm. We did not want to cause more damage to the heart, so the device needed to be smaller than the typical size of the papillary muscles. However, the device must also be long enough to enter the papillary muscle through the heart wall. The heart wall after myocardial infarction is typically 10-20mm. The final specification was that in order to reposition the papillary muscle, it needs to be within the range of 2.5-5mm, which is the typical displacement seen after myocardial infarction.

The device also need to be biocompatible by not damaging the biological environment it would be placed in. Fragility was also another specification when focusing on the mitral valve leaflets. The leaflets are very fragile so we had to ensure that our device could not cause tearing of the leaflets, leading to further complications. And our last specification was cost. We had to make sure we stayed within our budget and that our device did not cost more than current devices on the market.

Important Industry Standards

Industry Standards allow for regulation, legal liability, ethical research and development, clinical practice, and patient safety. Since our device falls under cardiovascular standards, it would be classified as a division three: medical/surgical device. Many of the regulations enforced by the FDA regarding medical devices are found in Title 21 Code of Federal Regulations Part 800 to Part 1299. This involves device classification, 510 k clearance to market, pre-market approval (PMA), good manufacturing compliance (GMP) compliance, establishment registration, device listing, and medical device reporting (MDR).

Conceptual Designs

After determining the requirements and functions for our device alternative designs were developed to solve the problem addressed by the initial client statement as well as the revised client statement.

Design 1: Webbed Polymer Coating

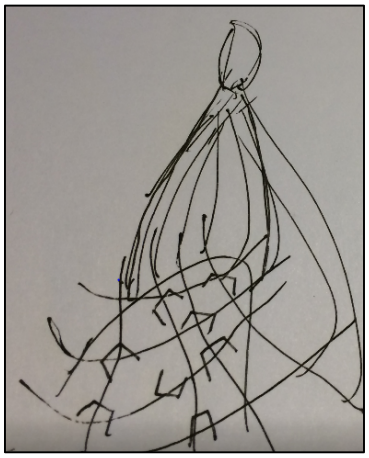


Figure 3: Webbed Polymer coating

Spider silk is becoming an attractive biomedical material used in tissue engineering applications. The interlocked webs add a greater attachment to the location it is placed (Figure 3). This was used as a design alternative because it could better withstand the conditions in the left ventricle. This design showed properties of interest such as, high-energy absorption rates, rupture elongation, and high strength (Table 3). The material would take aspects of an actual spider web and be coated with a polymer to make more elastic. This design would also allow for the papillary muscle to be not be removed because the webbing would be placed over the current dead muscle. This device would be used in the case that the papillary muscle has died, allowing for stable attachment sites. This attachment would make the surface of the papillary muscle rougher, which can lead to a more secure attachment.

Table 3: Pros & Cons Design 1

Pros	**Cons**
Use of Ideal Mechanical Properties from web	Use of Staples in heart
Use of Polymer Coating	Polymer hard to locate
	Invasive
	Web could dislodge
	Coagulation

Design 2: Surface Modification for Chordae Attachment

Figure 4: Surface modification of the dead papillary muscle. The dots represent the surface modification with a polymer string allowing for reattachment.

If the chordae tendineae of the valve were to become detached from the papillary muscle, a design was created to reattach the chords. The surface of the papillary muscle will once again be roughened to allow for easier attachment (Figure 4). The papillary muscle is dead in this method as well, and staples will be placed on the surface. The surface modification would be done to increase the surface roughness, increasing the amount of attachment. However, there has not been much research into this method, which makes this idea not as viable.

Similarly, a table was created of this designs pros and cons (Table 4).

Table 4: Pros & Cons Design 2

Pros	Cons
Not as invasive	Unknown Polymer to be used
Increased surface area for attachment	Not strong mechanically
	Biocompatibility

Design 3: "Silly Putty" Attachment

This design addresses the need to reattach the chordae tendineae or a dislocated papillary muscle. The premise of this idea is that at the end of the chordae, a portion of putty-like material will be placed so that the chordae could be securely attached in a new location (Figure 5). This design is a plus because of its strength and attachment properties, however this is a novel idea that has not been widely researched (Table 5).

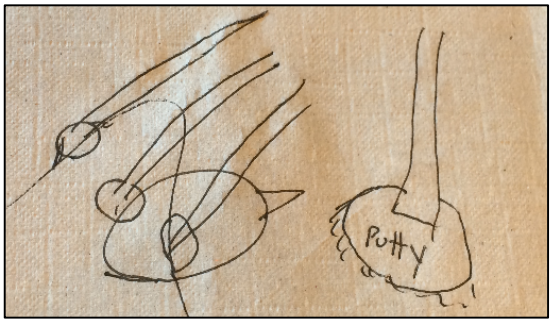


Figure 5: The "Silly Putty" Idea for attachment

Table 5: Pros & Cons Design 3

Pros	Cons
Versatility for each Patients Heart	Attachment with material might be difficult
Not as Invasive	Biocompatibility
	Proper Symmetry might be hard to come by

Design 4: Attachment of Cardiac Cells to Surface

The fourth design explored the possibility of regenerating the papillary muscle. This design would seed the surface of the papillary muscle with stem cells to return the contracting function, in the case that it had died (Figure 6). The attachment of the cells would be achieved through a bonding method that would allow the cells to remain on the papillary muscle. However, after much research, it showed that this may not be a realistic solution. In a few studies, it showed that regeneration was only possible in <1 percent of papillary muscles and the rate decreased with increasing patient age. Due to this research, this idea is not feasible (Bergmann, 2009). Other studies used skeletal muscles in the heart, but led to failure due to the differences between the cell types (Marasco, 2008). Below is the table of the designs pros and cons (Table 6).

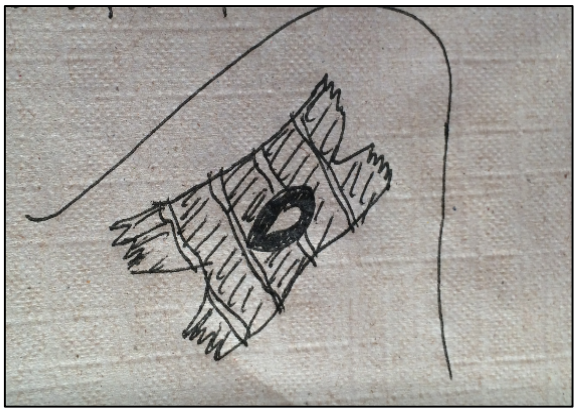


Figure 6: Seeding Cells on Surface of Papillary Muscle for Returned Function

Table 6: Pros & Cons Design 4

Pros	Cons
Idea sounds nice of putting new cardiac cells	Probably not as strong as thought
Some function returns	Such a minor amount of function
	Question of how to stick the cells to surface

Design 5: “Suction Cup” Method

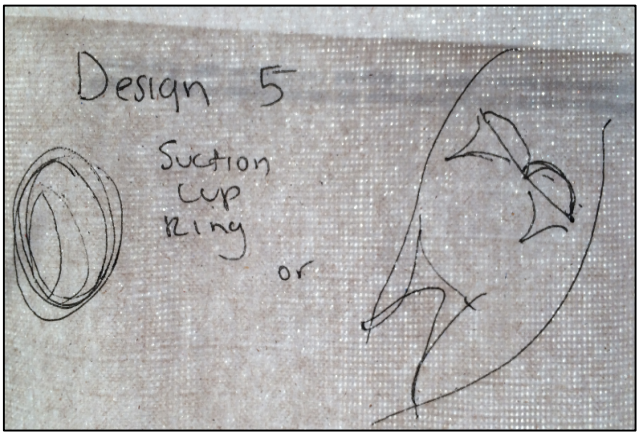


Figure 7: The Suction Cup Method/ Ring method.

In the fifth design a suction cup technique was explored to utilize the pressure changes between the systolic and diastolic phases of the heart for a mock leaflet (Figure 7). The suction cups could be on both sides of the mitral valve or in the left ventricle. The leaflets are very fragile, so this idea is not the most feasible. It would most likely result in ripping or destruction of the leaflet. More research would have to be done on this technique. The figure to the right shows the two design modifications for the pressure ring around the valves on either side and the suction device on the papillary muscle. Below is a list of pros and cons (Table 7).

Table 7: Pros & Cons Design 5

Pros	**Cons**
Capitalize on Natural Pressures	Might lead to misshapen heart
No more leakage	Valves too thin most-likely
	Might cause more complications

Design 6: Full Replacement with Polymer

A few designs were created that involved the removal of the dead papillary muscle. In this design the muscle would be completely removed and replaced by a biocompatible polymer (Figure 8). There were a wide range of different polymers, some were piezoelectric while others were conducting polymers. Upon further discussion, full removal of the papillary muscle was not ideal due to the amount of bleeding that would occur. Determining which polymer would be best depends on the mechanical properties of each polymer. The polymer would need to not lead to inflammation or coagulation on the surface, so coating this polymer with a protective covering or performing surface modification would be needed to ensure that it would not fail. The table below is the pros and cons list for this design (Table 8).

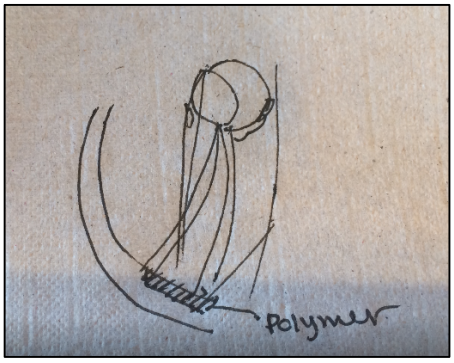


Figure 8: The full replacement of the papillary muscle with a polymer *a*ttachment

Table 8: Pros & Cons Design 6

Pros	**Cons**
No more dead papillary muscle	Changes shape of heart
Better mechanical properties	Severe Bleeding
Degradation factors?	Not what the surgeon wants
	Invasive

Design 7: Insertion of Polymer Loop

In this design the papillary muscle has died and is removed from the heart. A polymer will be attached to the ventricular wall and the mitral valve leaflets (Figure 9). Causing the angle of the leaflets to be changed to address for proper closure. The drawback to this design is that the leaflet may not support the polymer used for attachment (Table 9). Also if the polymer is attached by a loop, this could lead to increased blood volume.

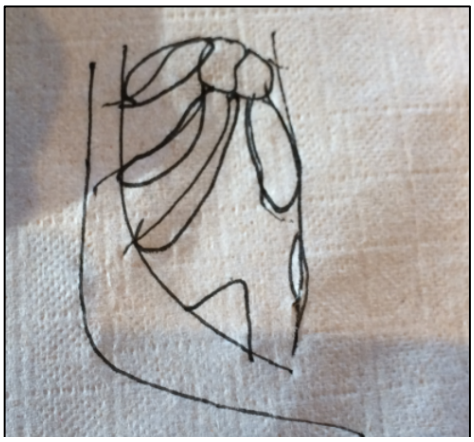


Figure 9: Looped Polymer attachment

Table 9: Pros & Cons Design 7

Pros	Cons
Not as invasive	Valves too thin
Creative Solution	Idea, not actuality
Tested. So it works for valve regurgitation	Leads to more problems

Design 8: Papillary Anchor

In this design the dead papillary muscle is used as an anchor for the chordae tendineae to be reattached (Figure 10). It is assumed that the chordae tendineae is still attached to the mitral valve, which will allow for the chords to be reattached to the papillary muscle, or a biocompatible chord could be inserted that attaches. The papillary muscle would be used as the attachment site for the chords so that the leaflets close at an angle that decreases mitral regurgitation. Instron testing would needed to be done to decide which polymer would be best used. Also surface

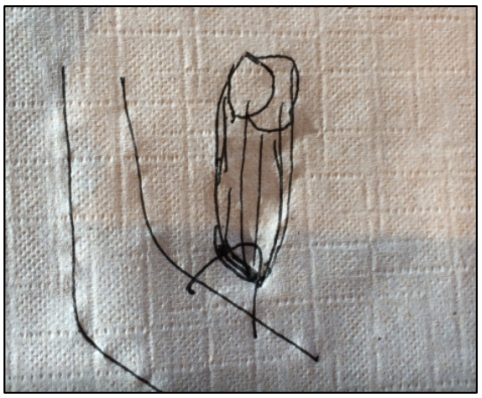


Figure 10: Papillary Muscle Anchor Design

modification techniques and coatings would need to be incorporated to make the material more biocompatible (Table 10).

Table 10: Pros & Cons Design 8

Pros	Cons
Can mix use of current chordae with polymer	Might not work
Fixed to one location	Not good under deformed heart

Design 9: Velcro Design

This design involved using a Velcro-like material for attachment of the chordae to the papillary muscle (Figure 11). The Velcro design would be executed through hooks and loops that create a secure system. With this Velcro design, the attachment would be interchangeable depending on what angle the chords needed to be pulled in to establish proper closure of the mitral valve leaflets. This design would require a coating to make sure it is biocompatible and that there is no coagulation. The limitations to this are that it is not highly explored in research; so many trials would have to be performed to decide which material to use and how the device would be constructed (Table 11).

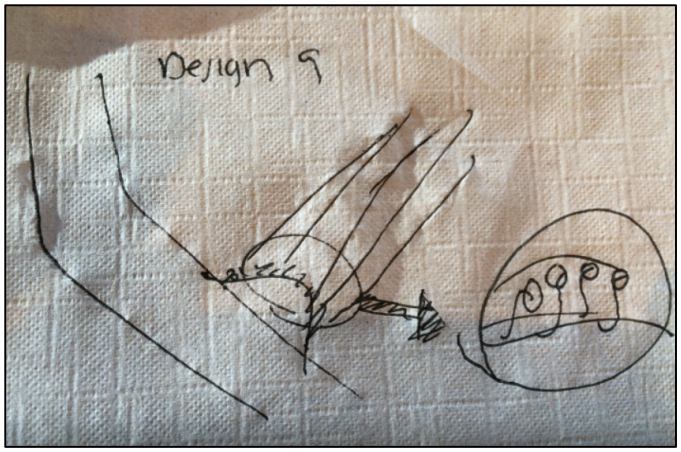


Figure 11: The Velcro Design

Table 11: Pros & Cons Design 9

Pros	Cons
Movable	A lot of foreign material
Strong	Coagulation

Design 10: Conducting Polymer Addition

The tenth design included using a conducting polymer to allow the papillary muscle to contract. The polymer would receive signals from the nodes of the heart, allowing it to contract (Figure 12). A conductive polymer that was investigated was PTFE due to its high conduction and biocompatibility. Through the addition of PTFE, the papillary muscle would be able to contract, if it had died. However, through research it was discovered that a previous Major Qualifying Project Team researched using a conductive polymer for papillary muscle regeneration. Ultimately it was deemed too expensive and the results did not exhibit the same qualities as hypothesized. Although PTFE has high contractile properties, it was difficult for this polymer to regenerate the papillary muscle (Table 12).

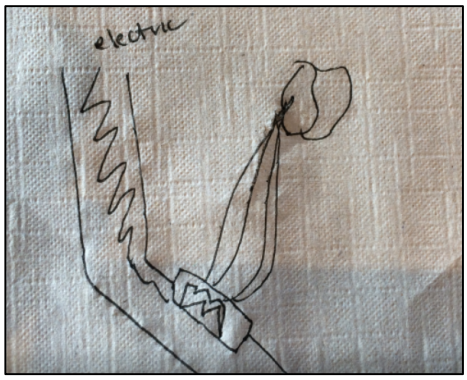


Figure 12: The PTFE polymer model

Table 12: Pros & Cons Design 10

Pros	Cons
Contracts	Too expensive
Biocompatible	Timed contractions
	Displacement not good.

Design 11: Regenerate a New Papillary Muscle

A new papillary muscle would be able to be regrown through the use of induced pluripotent stem cells (Figure 13). This would be done in the case of papillary muscle death. The stem cells would be cultured to contract in order to give this function into the tissue engineered papillary muscle. This new papillary muscle would

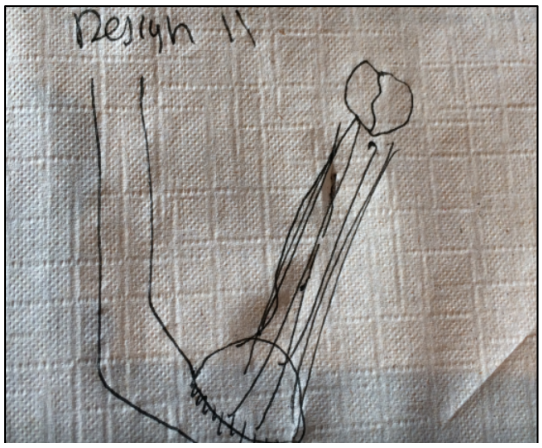


Figure 13: Regeneration of a Papillary Muscle

then be inserted into the heart in place of the dead muscle. Through research, it was found that the cell properties, especially in cardiac cells could be altered depending on what surface the cells are grown on. Culturing a large quantity of cells to contract simultaneously and finding a material to seed these cells on, that have similar properties to those of the papillary muscle proves to be a challenge (Table 13).

Table 13: Pros & Cons Design 11

Pros	**Cons**
Full function, new muscle	Fantasy vs reality
Contractile Properties.	Muscle Failure
	Poor Mechanical Properties

Design 12: Collagen Cross-linked Hydrogel with Cardiac Cells

Through research on hydrogels, it was found that seeding of cells on crosslinked collagen hydrogels can make this biocompatible. When placed in the body the cells can help regenerate the function of a dead papillary muscle, and also fix the displacement (Figure 14). Cardiac cells can be used because they will exhibit the least foreign body response (Table 14).

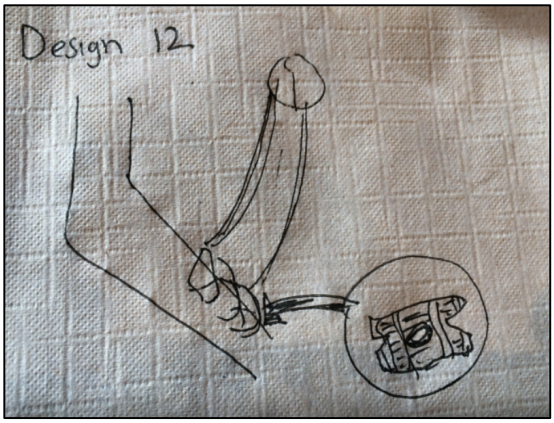


Figure 14: Hydrogel - Collagen Cross-link design

Table 14: Pros & Cons Design 12

Pros	**Cons**
Biocompatible	Hydrogels Properties
Good Mechanical Properties	
Movable.	

Design 13: Annuloplasty Ring Idea

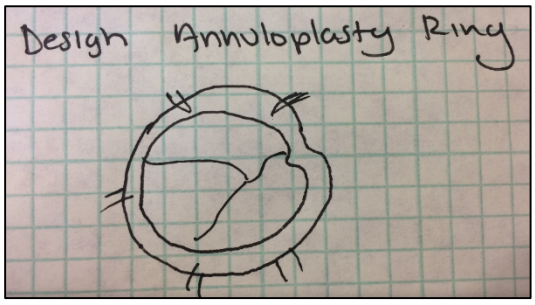


Figure 15: The Annuloplasty Ring Design

This design is based off of current patents and devices out on the market today. To help reduce turbulence in blood flow created by the annuloplasty ring, a saddle horn shape would be incorporated on the design (Figure 15). A saddle horn would be an indent on the circle to make it more like the normal shape of the mitral valve. The ring would be created out of a durable polymer that will help correct the position of the heart valve back to its original shape. The design would allow the mitral valve to maintain the natural shape, function and movement. Although the gold standard for correcting mitral regurgitation are annuloplasty rings, incorporating the saddle horn would cause further complications (Table 15).

Table 15: Pros & Cons Design 13

Pros	Cons
Proven that it fixed mitral regurgitation	Makes blood flow faster
Can be minimally invasive.	Not innovative enough
	Solves one problem, leads to more

Design 14: Retractable Suture Method

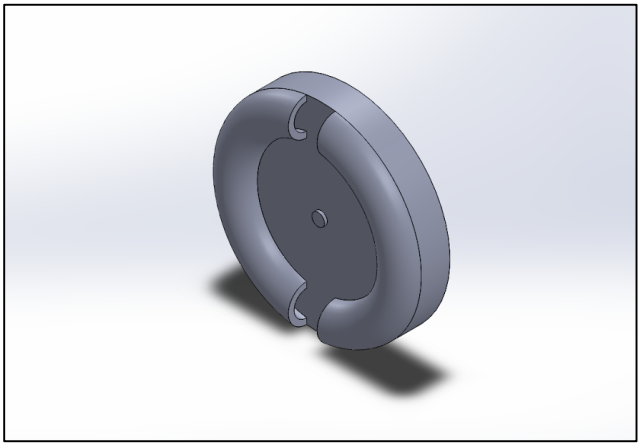


Figure 16: SolidWorks Drawing for Retractable ID Design

This design was based on the concept of a retractable ID badge (Figure 16). It would allow for a string to be pulled to a particular length and excess string to be retracted into the base. This function makes the device applicable for different heart geometries. The CAD design is in Figure 15 It would be a two tier system to allow for the device to be pulled in two different directions. Surgeons would use MRI data or other

forms of digital imaging to know where to suture the string to the myocardial wall. A nitinol spring would be placed inside the base and attach to PTFE string, allowing the string to be pulled out to a certain amount. PTFE is the ideal polymer for this device because it is a synthetic fluorocarbon polymer that is currently being used for different cardiovascular applications. PTFE has low surface free energy and hydrophobicity, which prevents particles from sticking to its surface. The use of PTFE is the polymer of choice because it has been very successful with other heart applications that have been utilized. In Figure 16, the base of the device is placed on the outside of the myocardium wall. This idea was introduced after realizing the limited surface area offered by the papillary muscle making it near impossible to create a device large enough to incorporate everything we wanted. A Pros and Cons list is in the tables on the next page (Table 16).

Table 16: Pros & Cons Design 14

Pros	Cons
Versatility for each Patient's Heart	Device might be too small on tip of papillary muscle
Not as Invasive	Potential Blood Clotting in heart
Innovative Design	Might be hard to maneuver around the chordae

Design 15: Nitinol Cantilever Design

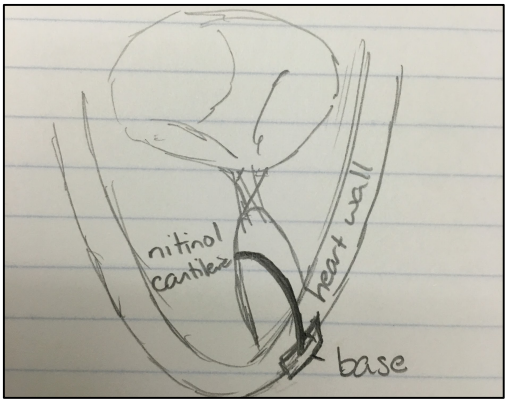


Figure 17: Nitinol Cantilever Design

The incorporation of a Shape Memory Alloy, Nitinol, has been a common component in other cardiovascular devices. Nitinol is a very durable and strong material that can be treated to change shape at different temperatures (Figure 17). The use of nitinol as a cantilever is beneficial because it is contained within the papillary muscle, eliminating the need for sutures or other aspects that could cause further damage to the infarcted heart. The Nitinol can be bent or

trained at the angle necessary to return the papillary muscle to its original position. The insertion of this device will also be minimally invasive (Table 17).

Table 17: Pros & Cons Design 15

Pros	Cons
• Durable	• If train the nitinol to the wrong geometry, it is difficult to take back out
• Minimally invasive	• Possibility of poking out of the papillary muscle/cutting the muscle
• Easily shaped to fit whatever geometry we need	• It could not move the muscle at all
• High strength	• Possible toxic wear particles
• Coat with a material to minimize chance of cutting through the muscle	• If train the nitinol to the wrong geometry, it is difficult to take back out

Design 16: PTFE String through Heart

This design inserts a string of PTFE through the papillary muscle with the use of a minimally invasive procedure such as thoracoscopic surgery (Figure 18). This design will allow for the PTFE string to exit from the apex of the papillary muscle and it will be pulled in the direction that will regain proper closure of the leaflets. The PTFE adds flexibility to the device, making it easier to move the muscle in the desired direction. The PTFE will then be sutured to the heart wall in the location of the needed vectors. When sutured to the wall, the string will have 10% slack to account for length changes during the cardiac cycle. Majority of the movement of the papillary muscles occurs from repositioning at the apex, so our device is ideal for this function (Table 18).

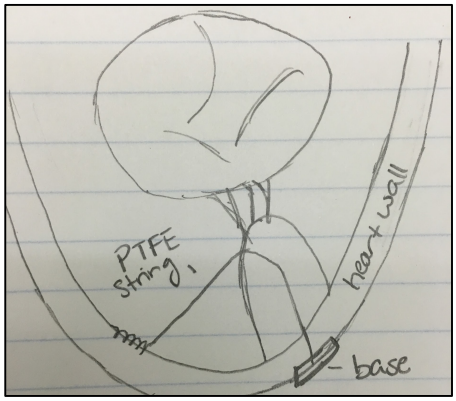


Figure 18: PTFE String Design

Table 18: Pros & Cons Design 16

Pros	Cons
• PTFE is used in many cardiovascular applications so it won't be rejected	• Cost
• Easily adjust to the different heart geometries	• Only account for geometry shape changing at the top of the muscle
• Room to account for error right away	• Blood clots
• Wont interact with chordae tendons	• Suturing to a weakened heart wall- will that have detrimental effects?
• Slack on wire to account for change in volume during systole and diastole	• In a device were you would need to know the exact vectors, doctors may be more inclined to go off of their own knowledge and estimate suturing visually rather than MRI
	• Account for pressure of fluids, anatomical structures around the papillary muscle,
	• Worry about how it will pull out of the papillary muscle so it's not entangled in the chords

Alternative Designs

Many designs were created that met the needs of the client in order to reposition the papillary muscle to its original position after displacement through myocardial infarction. This is done to eliminate mitral regurgitation, occurring from improper closure of the mitral valve leaflets. However, many of the designs had large amounts of complications associated with their functions. Through further research, meetings with our advisor, and defining our client statement we developed a final design that will be tested as our papillary muscle repositioning device.

Many of the preliminary designs were not used because they did not fully address the need. They may have interfered with the chordae tendineae, or attached to the mitral valve leaflet making it weaker and more prone to prolapse. Below are the pros and cons for each of our alternative designs.

Design 1: Webbed Polymer Coating

Table 19: Pros and Cons Design 1

Pros	Cons
Use of Ideal Mechanical Properties from web	Use of Staples in heart
Use of Polymer Coating	Polymer hard to locate
	Invasive
	Web could become intertangled or dislodged
	Coagulation

Design 2: Surface Modification for Chordae Attachment

Table 20: Pros and Cons Design 2

Pros	Cons
Not as invasive	Unknown Polymer to be used
Increased surface area for attachment	Not strong mechanically
	Biocompatibility

Design 3: "Silly Putty" Attachment

Table 21: Pros and Cons Design 3

Pros	Cons
Versatility for each Patients Heart	Attachment with material might be difficult
Not as Invasive	Biocompatibility
	Proper Symmetry might be hard to come by

Design 4: Attachment of Cardiac Cells to Surface

Table 22: Pros and Cons Design 4

Pros	Cons
Idea sounds nice of putting new cardiac cells	Probably not as strong as thought
Some function returns	Such a minor amount of function
	Question of how to stick the cells to surface

Design 5: "Suction Cup" Method

Table 23: Pros and Cons Design 5

Pros	Cons
Capitalize on Natural Pressures	Might lead to misshapen heart
No more leakage	Valves too thin most-likely
	Might cause more complications

Design 6: Full Replacement with Polymer

Table 24: Pros and Cons Design 6

Pros	Cons
No more dead papillary muscle	Changes shape of heart
Better mechanical properties	Severe Bleeding
Degradation factors?	Not what the surgeon wants
	Invasive

Design 7: Insertion of Polymer Loop

Table 25: Pros and Cons Design 7

Pros	Cons
Not as invasive	Valves too thin
Creative Solution	Idea, not actuality
Tested. So it works for valve regurgitation	Leads to more problems

Design 8: Papillary Anchor

Table 26: Pros and Cons Design 8

Pros	Cons
Can mix use of current chordae with polymer	Might not work
Fixed to one location	Not good under deformed heart

Design 9: Velcro Design

Table 27: Pros and Cons Design 9

Pros	Cons
Movable	A lot of foreign material
Strong	Coagulation

Design 10: Conducting Polymer Addition

Table 28: Pros and Cons Design 10

Pros	Cons
Contracts	Too expensive
Biocompatible	Timed contractions
	Displacement not good.

Design 11: Grow a New Papillary Muscle

Table 29: Pros and Cons Design 11

Pros	Cons
Full function, new muscle	Fantasy vs reality
Contractile Properties.	Muscle Failure
	Poor Mechanical Properties

Design 12: Collagen Cross-linked Hydrogel with Cardiac Cells

Table 30: Pros and Cons Design 12

Pros	Cons
Biocompatible	Hydrogels Properties
Good Mechanical Properties	
Movable	

After eliminating the above ideas. Two more were established; PTFE String through the Papillary Muscle and Nitinol Cantilever. Both designs are minimally invasive options for papillary muscle readjustment. The devices will be inserted through Thoracoscopic surgery and enter the heart through the heart wall. In Thoracoscopic surgery, the procedure is done through small holes

on the right side of the patient's chest. This surgery is a benefit because the patient does not have to get their breastbone split, resulting in a quicker recovery time.

PTFE String through the Papillary Muscle

The PTFE string through the Papillary Muscles inserts the PTFE string through the heart wall and into the papillary muscle. The wire will be pulled out from the edge of the papillary muscle closest to the apex, to not interfere with the chordae tendineae. From there, the string will be pulled in the proper vector direction to account for the displacement of the papillary muscle and return to its original position. The string will then be sutured to the heart wall.

Advantages to this device are that Polytetrafluoroethylene (PTFE) is the main material used and it has been used widely in cardiovascular applications. PTFE is currently used as sutures for repair of the mitral valve in myxomatous disease and it has also been used in surgery for anterior and posterior leaflet prolapse. PTFE is also used as the material for implantable prosthetic heart valve rings (Jaganathan, 2014). Another advantage of this device is that because it is a string, it can easily adjust to the different heart geometries of each patient. When patients hearts infarct, the papillary muscles will not all be displaced in the same manner, making it hard to adjust from the papillary muscles. Another advantage is because it is being implanted by port insertion, once it is in place it does not become permanent until it is sutured to the heart. So if the doctor had to move the papillary muscle a few centimeters in a different direction, the device allows for this to occur. Another advantage is that through further research this device could be modified to incorporate the use of fibrin microthreads seeded with contracting cells to aid in making this a more biocompatible device.

There are a few drawbacks to this device that include the possibility of blood clots on the exposed string. Because a foreign particle is being added to the heart, there is a higher risk of blood

clotting or disrupting the flow of blood through the heart. Also because the heart wall has been slightly compromised due to the reshaping from the myocardial infarction, there could be further complications in suturing the PTFE string to the heart wall. This device is very dependent on following the vectors received from MRI in order to know the position of readjustment. However, doctors may be more inclined to use their own knowledge when performing the surgery instead of following the guidelines. Another drawback to this device is that it only moves the papillary muscle at the tip, it does not adjust the shape at the base or middle of the muscle. Moving the entire papillary muscle will result in more movement versus just adjusting the tip of the muscle.

Nitinol Cantilever

The second design is a nitinol cantilever that will also be inserted through the papillary muscle by port insertion. The nitinol wire will be designed so that its shape moves the papillary muscle back to its original position. The wire will remain inside the muscle and force movement internally.

There are many advantages to this design, one being the high strength of nitinol. This strength will cause enough force to allow the papillary muscle to move back to its original position. This design is also minimally invasive because of the use of port insertion. This device will also remain inside the papillary muscle, avoiding interference with other sections of the heart. Because nitinol is very easy to train, it can be formed into any shape needed for proper movement of the papillary muscle, which will allow for easier processing. The transformation temperature of nitinol is normally 30°C, which is a bit lower than body temperature. In order to avoid the nitinol wire forming shape before proper insertion, it can be constrained by a retractable sheath or other material (Stoeckel, 2003). Nitinol is also a very durable material so it will be able to last in the heart for a long period of time.

There are a few constraints associated with this device as well. A major problem will be in the training and processing of the nitinol wire. It will have to be trained with the exact geometry needed to move the papillary muscle back to its original position. If it is not, it will difficult to remove the wire from the patient and retrain it to another position. If this were to occur, an entirely new wire would have to be created, which causes the price of the device to increase. Another possible issue with this device is the wire cutting the papillary muscle, or creating a hole by sticking through the muscle. The wire will have to be developed so that it contains no sharp ends that could cause this damage. Another concern is that this device may not be strong enough to move the papillary muscle without other assistance. The Young's Modulus of nitinol is between 28 - 40 GPa when in the martensitic phase and around 83 GPa when in the austenite phase (Johnson, 2015). And because nitinol is a metal alloy made from nickel and titanium, toxic wear particles are a concern. Also patients could be allergic to the nickel wear particles.

Final Design

Table 31: PTFE String through Papillary Muscle Pros and Cons

Pros	**Cons**
PTFE is used in many applications	Only accounts for shape changing at top of muscle
Easily adjust to the different heart geometries	Possible blood clotting on exposed string
Room to account for error	Suturing to a weakened heart wall
10% slack to account for change in volume during systole and diastole	Could cause turbulence of blood flow
Could add contractile cells to PTFE string	Possible entanglement with chordae tendineae

Table 32: Nitinol Cantilever Pros and Cons

Pros	**Cons**
Durable Material	Very specific shape geometry needed to move papillary muscle
Minimally invasive	Could protrude out of papillary muscle
Easily shaped to specific geometry	Could not move the papillary muscle
High elastic modulus	Possible toxic wear particles

After creating the pros and cons list for both the PTFE String Through the Papillary Muscle design and the Nitinol Cantilever design, we chose our final design idea to be the Nitinol Cantilever design. We as a group decided to use Nitinol as our cantilever material for multiple reasons. Nitinol is a shape memory alloy with great mechanical properties. Important factors to consider when choosing our material was its biocompatibility, since it would be placed in the heart, as well as its mechanical properties and whether it would be able to withstand the forces and pressures of the left ventricle. The Ultimate Tensile Strength of Nitinol when it is fully annealed is 895 MPa. This value is much higher than the forces and pressure the heart will exert on the material making it an ideal candidate to be used for our device. Nitinol has "a passive titanium oxide layer which protects the base material from corrosion and nickel release", by removing Ni atoms from the surface of the material (Nitinol, 2015). Out of all the shape memory alloys on the market today, NiTi has the best superelasticity, biocompatibility, corrosion resistance, and overall engineering properties. Other alloys such as copper-aluminum-nickel, copper-zinc-aluminum, and iron-manganese-silicon are less stable and more brittle than Ni-Ti, have limited shape memory strain, and lack ductility. Under normal conditions, nitinol has an infinite shelf life *and is not affected by humidity changes*

(Nitinol, 2015). Additionally, characteristics that make NiTi a standout material for our application is its hardness, impact toughness, high fatigue strength, machinability, and naturally low density.

Feasibility Study

Preliminary tests were performed to test the mechanical strength of the different chordae tendineae in a pig's heart. These values would be compared to that of the literature. For the first experiment, we isolated the papillary muscles of the left ventricle and prepared them for testing. This can be seen in Appendix A. We wanted to test the difference in tensile strength between a papillary muscle with all of the chords attached, versus a papillary muscle with only one chord. Tensile testing was created using Bluehill software, however, due to time constraints we were only able to test the papillary muscle with all of the chorea attached. The results of the testing were compromised due to slippage, so values from the literature were used to create our designs.

More anatomical features were observed in pig hearts to test if our design ideas could be applied *in vivo*. Heart dissection videos were watched to understand the proper procedure for cutting into the left ventricle while leaving the mitral annulus intact. The design idea of inserting the device through the heart wall into the papillary muscle was tested to see if it was feasible or not. We viewed the thickness of the ventricle as well as the mobility of the papillary muscle through insertion of a zip tie. The zip tie was used to move the muscle in all directions. The zip tie was then inserted through the wall into the papillary muscle and moved. By testing the movement of the papillary muscle with the zip tie, it validated our final design of moving the papillary muscle with a Nitinol cantilever.

The use of Finite Element Analysis (FEA) was researched to see whether it would be useful for our project. FEA is a computer modeling software that helps predict what a product will do under real world situations. The finite element model is a system of points, or nodes. These nodes

are what create the shape of the design. The finite elements are connected to these nodes and this is what forms the finite element mesh. This mesh contains the material and structural properties of the model and this determines how it will react in certain conditions (Siemens, 2015). Some of the situations that could be modeled with FEA that are applicable to our project are forces, fatigue, fluid flow and heat transfer. There are many different softwares that are available for the analysis of these computer meshes such as "Abaqus" and "Ansys".

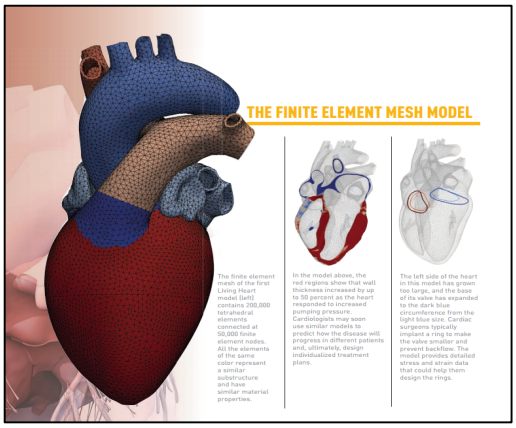


Figure 19: Finite Element Mesh Model

At Worcester Polytechnic Institute, Professor Sergey Makarov developed a highly detailed digital model of the human body, "The Living Human". This FEA model has the capabilities to be used by doctors to help them conduct medical experiments or procedures before performing them on live patients. We wanted to utilize this project to model the heart of a patient who suffered from myocardial infarction. An advanced model of Finite Element Analysis was done by *Dassault Systemes* called the "Living Heart Project". The mesh system that they used is shown in *Figure 19* and the model was specified for an enlarged left side of the heart. We hoped to use this type of system to determine if our device would function in the heart. However, upon meeting with Professor Makarov, he suggested not using this system due to time constraints and lack of the proper computer science knowledge to develop this type of FEA model. Professor Makarov did mention the use of either "Comsol" or "Ansys" for our project.

Design Calculations

The following chart displays the calculations researched and solved for to determine the dimensions are device should contain, forces it should withstand, and amount of angular displacement it should account for.

Table 33: Design Calculations

Average Length of Anterior Papillary Muscle	20 years old or younger: 1.53 +/- 0.34 cm 21 to 40 years old: 2.05 +/- 0.39 cm 41 to 60 years old: 2.01 +/- 0.25 cm
Average Length of Posterior Papillary Muscle	20 years old or younger: 1.33 +/- 0.34 cm 21 to 40 years old: 1.95 +/- 0.89 cm 41 to 60 years old: 1.81 +/- 0.76 cm
Displacement Length of Anterior Papillary Muscle after Myocardial Infarction	3 +/- 2 mm to the left perpendicular to the tip, 1 +/- 1 mm down
Displacement Length of Posterior Papillary Muscle after Myocardial Infarction	7 +/- 3 mm to the left perpendicular to the tip, 8 +/- 5 mm at 45 degree angle of the tip, 1 +/- 1 mm down
Average Strain on Papillary Muscle from Systole to Diastole	10 %
Maximum forces on the papillary muscle at 95 mmHg	Mean force: 4.1 +/- 9 N Anterior Papillary Muscle: 5.3 N Posterior Papillary Muscle: 5.1 N
Angular Displacement	Mean angular displacement: 3.2 degrees Range: 0-7 degrees
Left ventricular end-systolic volume for patients who have experience myocardial infarction	125 +/- 41 ml/m^2
Left-ventricular ejection fraction for patients who have experienced myocardial infarction	36 +/- 8 %

Modeling

Models of our device were created with the use of SolidWorks. Figure 20 below shows the cantilever papillary muscle repositioning device. This modeling was used to determine the forces that would be on our device from the chordae tendinae, papillary muscle itself, as well as the heart wall.

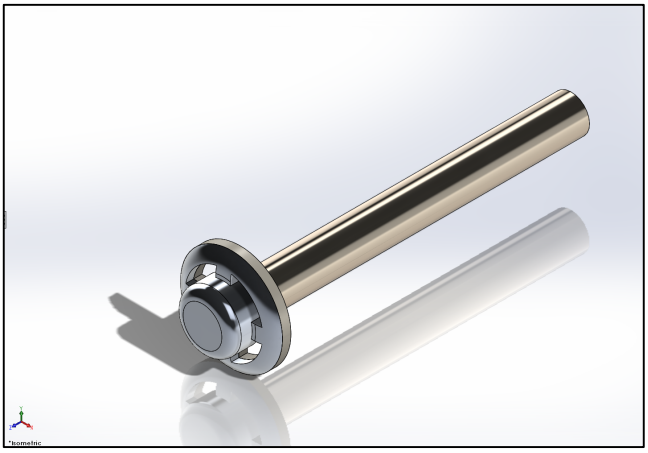


Figure 20: Cantilever Papillary Muscle Repositioning Device in SolidWorks

Preliminary Data

All testing was performed in vitro on pig hearts to allow for a visual of the papillary muscle movement. However, testing with this method had limitations. Cutting the heart in half to isolate the left ventricle did not allow for an accurate visual of how the muscle react in vivo. An attempt to solve this problem was done by purchasing a camera that could be inserted into the aorta/pulmonary valve of a pig heart and insertion of the nitinol could be done in a full heart with the use of the camera. However, during testing we discovered our camera did not have a brightness adjustment nor an attachable flashlight, so a proper image of the papillary muscle was hard to capture. Another difficulty was knowing the exact location of where to place the nitinol without having a proper visual.

We began our experiments with determining which size of nitinol wire would show the greatest movement of the papillary muscles. Our project accounts for the displacement after myocardial infarction; typically the papillary muscle moves 2.5-5 mm towards the heart wall from its original position when in an infarcted state. We took measurements of the original distance between the anterolateral papillary muscle and the posteromedial papillary muscle in the left ventricle before and after the insertion of nitinol. The nitinol was inserted into the posteromedial papillary muscle and the displacement when the muscle was moved towards the heart wall and the anterolateral papillary muscle was measured. This was done to test if the muscle could be moved enough to overcome the amount of displacement experienced after myocardial infarction. The original distance from the two papillary muscles (center-to-center) of our experimental heart was 3.5 cm.

We had ordered nitinol with a range of thickness. This resulted in nitinol of 0.025cm, 0.051cm, and 0.076cm of thickness. When inserting the nitinol of 0.025 cm, there was no movement in either direction, towards the anterolateral papillary muscle or the heart wall. The 0.051cm thick nitinol had a displacement of 0.3cm when moved towards the heart wall and 1cm when moved towards the anterolateral papillary muscle. The 0.076cm had a displacement of 0.5 cm when moved towards the heart wall and 1.2 cm when moved towards the anterolateral papillary muscle. This validated that all thicknesses except the 0.025cm nitinol, could move within a range that would account for the displacement of the papillary muscle after myocardial infarction. The 0.076 cm nitinol was chosen for our final design because it had the largest degree of movement and could correct for the largest amount of displacement.

To test whether the nitinol wire should be straight or curved, we inserted the different shaped nitinol wires into the papillary muscle to determine which had the best movement. The

nitinol was trained to have a curved shape by using pliers. This curved wire was then placed in boiling water of 276.6°F. When the wire was removed, it was quenched by being placed in cold water allowing the wire to keep its shape. After completing this experiment, we concluded that the trained curved nitinol was not as effective as the straight nitinol. Insertion of the curved nitinol into the papillary muscle was difficult due to the head of the wire would protrude out the side of the papillary muscle instead of reaching the tip of the muscle. When the nitinol was successfully inserted, little to no movement was seen. The 0.051cm curved nitinol did not move the papillary muscle. While the 0.076cm curved nitinol only allowed for back movement of the papillary muscle, due to how the curved portion of the wire was inserted into the muscle.

V. Design Verification

Myocardial infarction generally causes a displacement of the papillary muscle of about 2.5 - 5 mm from its original position. Ideally, our device would be able to move the papillary muscle to allow for proper closure of the leaflets. Through simulations and calculations, the length of the device needed to move the papillary muscle as well as the choice of material would be confirmed.

AutoDesk ForceEffect and Calculations

In order to ensure that our device was feasible, hand calculations, along with computer simulations were used. For the hand calculations, free body diagrams and cantilever equations for a distributed force and a specific force were used. The hand calculations were also supplemented by Autodesk ForceEffect to create a comprehensive free body diagram of the system as seen in Figure 21. These steps are important to help verify the results of our device and compare them to the computer models.

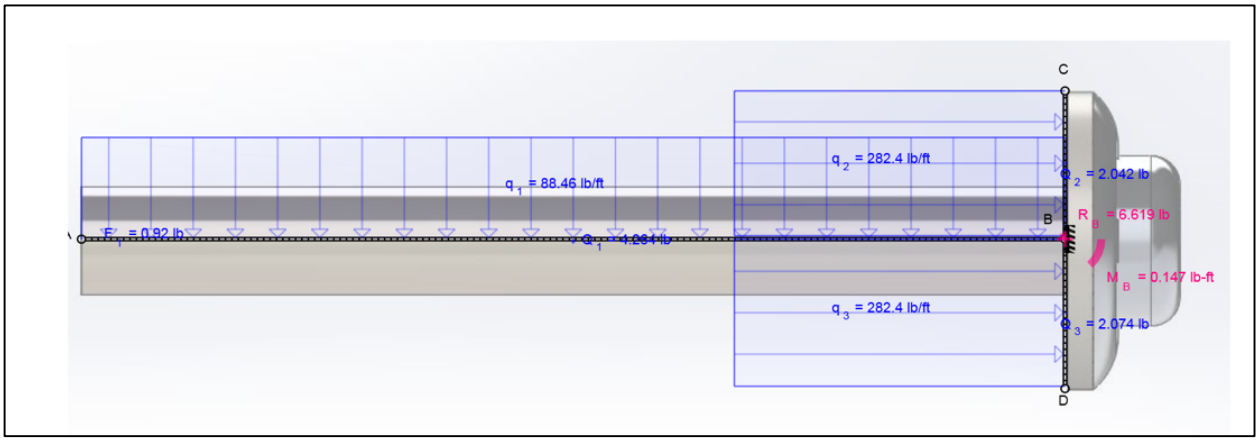


Figure 21: The Free Body diagram of the device when inserted into the heart with its forces. The F1 is from the chordae tendinae on the papillary muscle, F2 and F3 is the forces being exerted from the heart wall, and the distributed force is that being exerted on the papillary muscle.

This free body diagram was paired with the hand calculations to help lead to the proper equations. The device is a cantilever rod that is fixed on one end. In the heart, there are different forces that are based on the cardiac cycle. For the analysis, it was assumed that the device was in the diastole phase because it will present us with the data when the heart is at rest. The heart does exhibit variation in pressures during the different cycles. The equations below represent the initial equations that were used in our analysis.

$$v_{max} = \frac{PL^3}{3EI} \qquad (1)$$

$$v_{max} = \frac{wL^4}{8EI} \qquad (2)$$

The equations are for each of the different forces that are being exhibited onto the device. Equation 1 is related to F1 and its isolated load on the end of the device. Equation 2 is related to the distributed force across the device in the heart. For a more exact breakdown of the calculations, please refer to Appendix A. The solutions were then totaled to determine the deformation of the nitinol in the device. Table 1 below shows a summary of what the forces values that were used for the different forces in the calculations.

Table 34: The list of values used for the calculations

Force	Value [units]
Chordae Tendinae Force (F1)	4.1 N
Papillary Muscle Force (Q1)	5.1 N or 3834 N/m
Forces from Heart Wall (F2, F3)	5 N

Autodesk ForceEffect outputs different outcomes from the free body diagram that was created. These values are shown in Table 35 below. The values from this simulation verified the hand calculations and brought us to ask what the added moment would be. This simulation could also take into account the forces from the heart wall, adding variation in the results. Displacement is the most important calculation because it determines the amount of movement our device will be able to have on the papillary muscle.

Table 35: Autodesk ForceEffect Outputs

Output from Program	Value [units]
Shear Force	9.2 N
Moment	25.7 N/m

SolidWorks Nitinol Material Model Simulation

Along with the calculations, SolidWorks15 was used to create the material simulation of our nitinol model. As seen in Figure 22, the same numbers were used from the hand calculations and this showed a three dimensional model of the change that the device would undergo. The nitinol does have a lot of potential to deform if needed which is partly due to its Shape Memory Alloy effects. It was expected that the nitinol would deform a lot, but the model showed a higher degree of movement than expected. The ideal range of movement would be 2.5 - 5 mm to match that of the papillary muscle displacement after myocardial infarction.

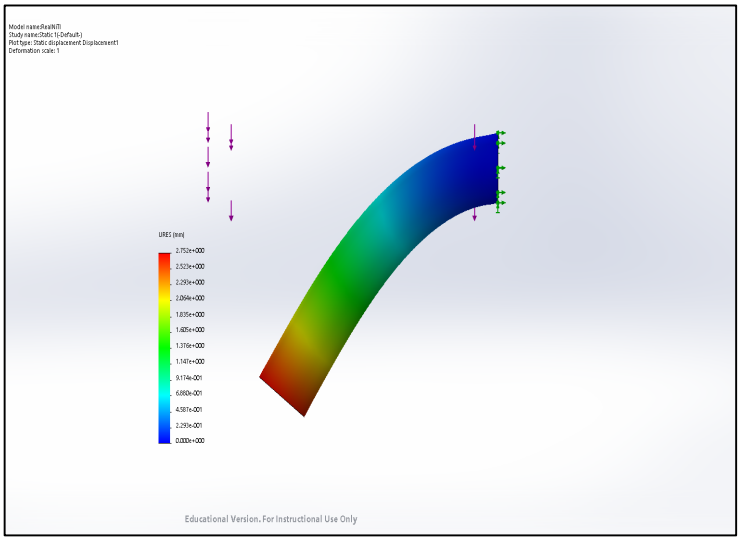


Figure 22: 14mm length nitinol showing a displacement of 2.7mm

The SolidWorks nitinol material model is based off the use of Lagrangian formulas. It uses nitinols different finite strains and its loading and unloading potential, all while maintaining its shape and properties. The model also takes into effect the logarithmic strains, along with the Kirchhoff stress which then goes into a matrix that demonstrates the transformed material. SolidWorks wanted to have the ability to show how the nitinol would behave without the permanent deformations that would occur from other materials. This model helps show the superelastic properties of the nitinol and provide a visual of them. Other factors like the yield criterion and the flow rule were taken into effect to help show the phase changes.

The green arrows show where the cantilever beam would be fixed which is under the assumption that would be contained by the forces of the heart wall, this will be about 1cm of the nitinol cantilever device. The purple arrows show the different forces that would be put onto the device from the chordae tendineae and the papillary muscle. The different simulations were conducted to obtain the length of the nitinol that would be inserted into the papillary muscle. The minimum and maximum length was obtained by the results of the graph. The displacement diagram in Figure 22 shows the that the 14 mm nitinol wire would have a displacement of about 2.7 mm which is in the desired range of 2.5-5mm.

A diagram was also run to get a maximum displacement closer to the 5 mm. The diagram in Figure 23 shows that the amount of movement was about 4.9 mm as a result of a 15.5mm nitinol wire.

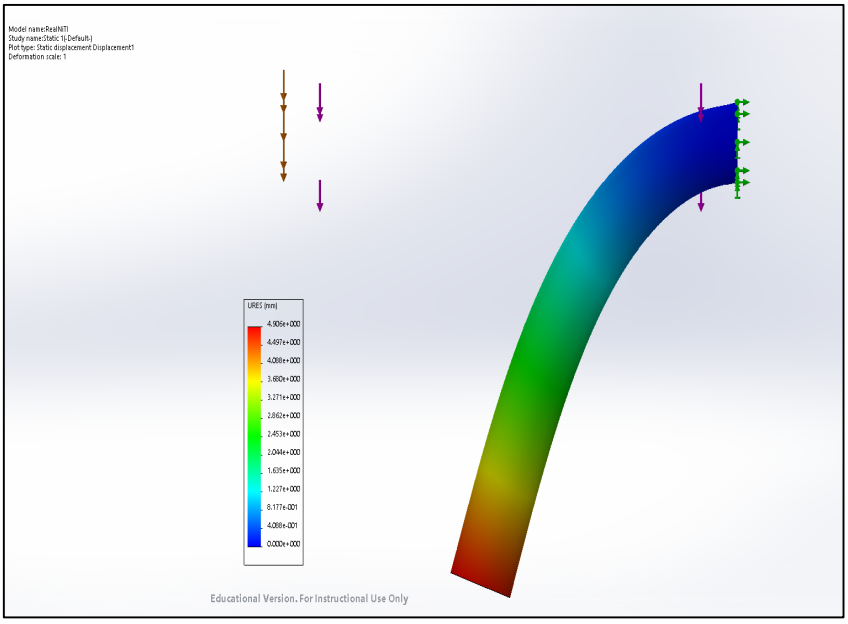


Figure 23: 15.5mm length nitinol showing a displacement of 4.9mm

Before the simulation was run, the rod was placed horizontally and the end was where the floating purple arrows are located. The total amount of deformation is greater than the total amount needed for the device. An example of this would be on the 14 mm device shown in Figure 24.

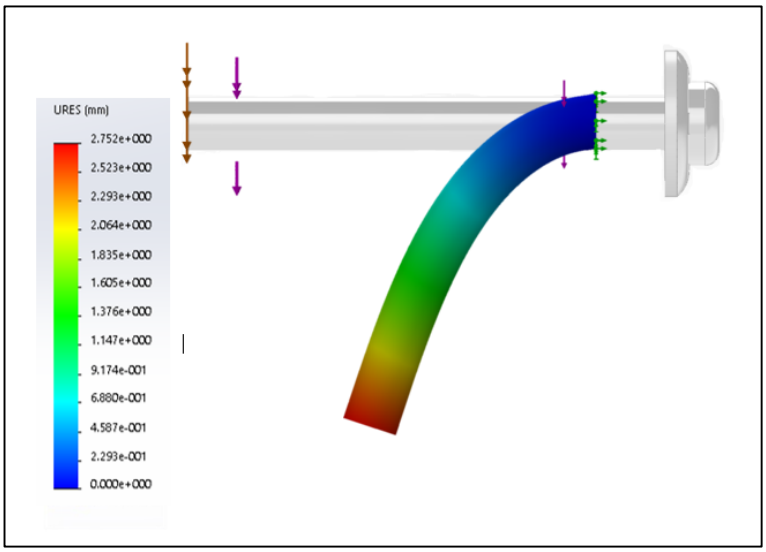


Figure 24: The results for the 14 mm cantilever device compared to the device. Note: this is not to scale.

The one setback about the SolidWorks model was that some of the numbers are not accurate. Another setback was that the simulation could not be conducted on the whole assembly, which is one the forces are focused solely on the nitinol wire. This would eliminate the forces from the heart wall which would help counteract some of the deformation and require less movement. The simulations are also a check to ensure that the devices work in the body the way that we intend them to. Again, the SolidWorks simulation only accounted for the part inserted into the papillary muscle.

The benefits of having a range of values that the simulations produced helped verify that the device is customizable. Based on the amount of papillary muscle displacement of each patient, the length of the device could be modified. The adaptability of the device makes it more marketable. The ability to have the device customizable will allow more patients to benefit from our device.

VI. Final Design Validation

Our final device was a cantilever papillary muscle repositioning device. The SolidWorks drawing shows the isometric view of the device in Figure 25.

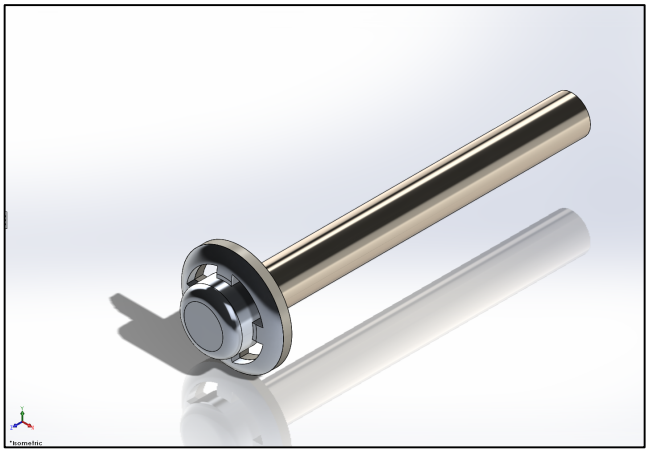
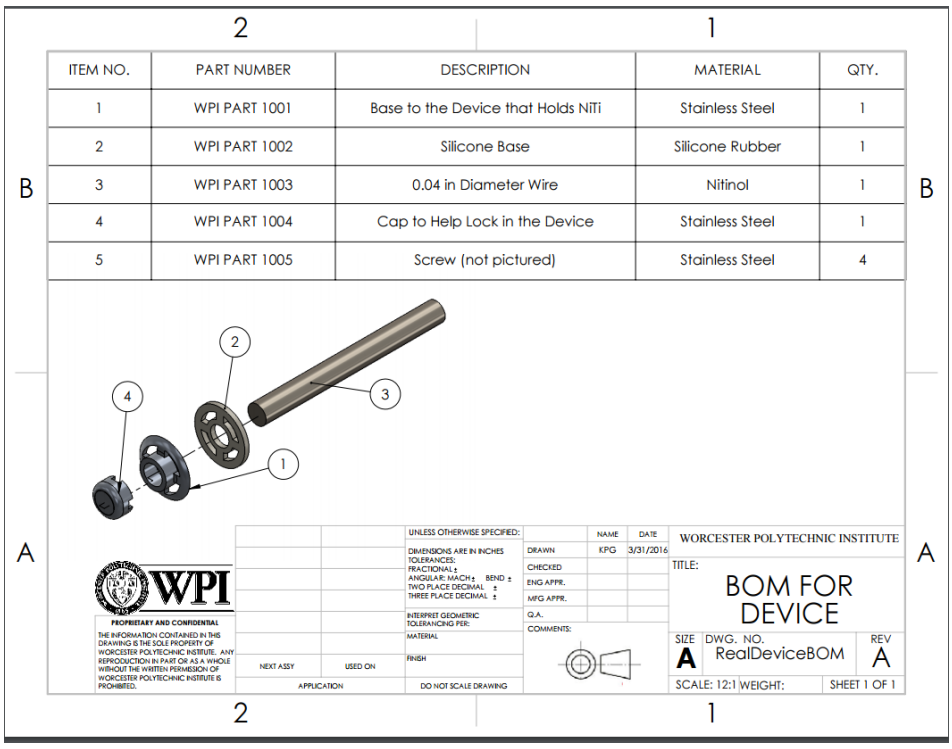


Figure 25: SolidWorks Isometric View of Papillary Muscle Repositioning Device

This design would be inserted through the outside of the heart wall, allowing for a larger surface area. This also avoids the entanglement issues that would occur on the internal devices that were in the left ventricle. This device would stay internal of the papillary muscle so there would not be interaction with the device and the fluids inside the heart. The device would be sutured to the heart wall on the supportive base to allow for more stability.

The bill of materials, along with the exploded view is shown in the SolidWorks drawing. This bill of materials outlines the parts of our final device shown in Figure 26.



ITEM NO.	PART NUMBER	DESCRIPTION	MATERIAL	QTY.
1	WPI PART 1001	Base to the Device that Holds NiTi	Stainless Steel	1
2	WPI PART 1002	Silicone Base	Silicone Rubber	1
3	WPI PART 1003	0.04 in Diameter Wire	Nitinol	1
4	WPI PART 1004	Cap to Help Lock in the Device	Stainless Steel	1
5	WPI PART 1005	Screw (not pictured)	Stainless Steel	4

Figure 26: Bill of Materials for Device

There are five main components of the device which include: the nitinol rod, the silicone base, the stainless steel base, the cap, and the screws. The nitinol rod was trained straight for easier insertion and improved movement. The length of this rod depends on the displacement of the papillary muscle due to myocardial main parts. The silicone rubber component has the ability to conform to the geometry of the heart wall allowing for a more secured placement upon insertion. And the stainless steel base has been used in other cardiovascular applications, such as annuloplasty rings. The last component is the stainless steel cap that helps secure the nitinol in place. This portion ensures the stability of the device and prevents the nitinol from losing its position during the cardiac cycle.

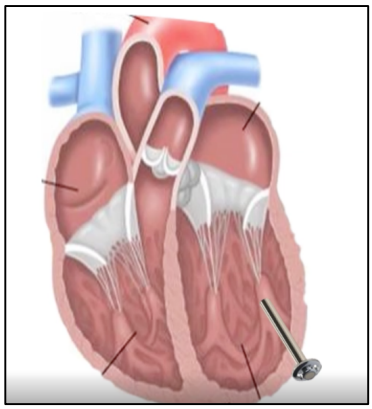


Figure 27: Placement of Nitinol Cantilever Device in Papillary Muscle

Our device would be inserted into the heart via port access surgery which would meet the objective to be minimally invasive. The length of the nitinol rod for each device would be determined based off of the CT scans and the amount of displacement of the papillary muscle. The device will be inserted at the proper angle that will account for the amount of displacement that occurs after myocardial infarction. Figure shows the proper insertion of the nitinol cantilever in the papillary muscle. Once the device is in place, the base of the device will be sutured to the heart wall for security.

VII. Discussion

When presented with the initial client statement, our group came to the realization that although the initial solution was to use fibrin microthreads, that was not the aim of the client statement. By going through the design process and evaluating what the client was asking, we determined that the client was not focused on the use of fibrin microthreads but wanted a solution to eliminate mitral regurgitation after myocardial infarction. Once we were able come up with a revised client statement that we felt better answered the problem being asked of us, we were able to refine our list of functions, objectives, and constraints.

The decision to choose Nitinol was based on in depth investigation of biomaterials used in cardiovascular applications as well as which material best suited the needs of our device. We needed the material to move the papillary muscle 2.5-5mm as well as adhere to the length of both the papillary muscle and heart wall so it would not protrude out into the ventricle and cause more problems. In vitro experiments where nitinol was inserted into the posterior-medial papillary muscle of the left ventricle of a porcine heart and manually maneuvered towards the anterolateral papillary muscle and the heart wall were executed. This was done to get the maximum displacement the material would allow to determine if nitinol would successfully work in moving

the papillary muscle within the typical displacement range after myocardial infarction. Stainless steel and silicone rubber were suitable materials for the base because of stainless steels uses in cardiovascular applications as well as silicones ability to conform to the geometry of the heart wall allowing for a more secured placement upon insertion.

The SolidWorks material model simulation was used to determine how the material would displace when placed in vivo. The forces from the papillary muscle, chordae tendinae, and stresses acting on the heart wall from contractions were derived from literature and applied on the cantilever beam. These forces were applied to the solidworks model of the nitinol rod in order to determine the required length needed to achieve the typical displacement experienced by the papillary muscle post myocardial infarction. Taking the unique properties of nitinol into effect helped give a more accurate example of what the Shape Memory Alloy would do in vivo to show the amount of movement that would occur. The model only showed the portion of the nitinol that was in the papillary muscle so 10 mm had to be added to the final length of each of the lengths to account for the uniform forces from the heart wall. The minimal displacement of 2.7 mm was achieved with a length of 14 mm. The maximum displacement of 4.9 mm was achieved with a length of 15.5 mm. This opens up many possibilities to make our device customizable based off of the CT scans taken of the patient, showing how much displacement their papillary muscle experienced. Having this minimally invasive option also be customizable will make it easier for the surgeon to efficiently insert our device. Combining these results, with the hand calculations, demonstrated our device could reposition the papillary muscle to a location that accounts for the displacement seen after myocardial infarction.

ABET Criteria

Economics

The current cost of a mechanical or biological heart valve is between $5,000 and $7,000 (Pick, 2010). Economists have measured the economic value of improved health and longevity and determined that there is an enormous return on investment for patients, especially the elderly, who receive aortic valve replacements. However, the initial investment is extremely cost consuming. In the United States, the average cost of heart valve replacement surgery is $137,184 and this includes materials for the valve (man-made if it is mechanical and made from animal tissues for biological valves), as well as anesthesia.

Our device will be inserted through port access surgery, a minimally invasive surgery that allows for decreased recovery time. For 24 hours, the patient cannot drive a car, drink alcohol, or make important personal decisions. After a week the patient should be able to resume their usual activities (UW Medicine, 2015). Because time needed to recover is decreased, the patients' hospital stay will be decreased as well.

Current mechanical heart valves will put a patient on anticoagulants for the remainder of their life. And biological heart valves will require a replacement surgery about 10 years later. Our device will only require a one-time surgery with no need of post medications.

Environmental Impact

The material chosen for this device are biocompatible meaning there will be no damage to the body when placed in vivo. Nitinol is about 50% Ti, so molten Nitinol is very reactive and has to be processed in a vacuum. Vacuum induction melting and vacuum consumable melting are very commonly used. To machine nitinol, conventional methods such as milling, turning and drilling can be used. However, these methods can be difficult and cause tool wear. That is why carbide tools with chlorinated lubricant are recommended (Wu, 2002).

The base of our device is formed from stainless steel, which is a recyclable material. Because they are designed to have a long life they can be used for multiple different purposes. Also, the main alloying elements of stainless steel are chromium, nickel and molybdenum. These three elements are valuable and can be easily separated from stainless steel. Stainless steel itself is typically made from recycled material; 25% end of life products, 35% scrap returned from production, 40% raw materials that are just being added (Salman, 2015).

Societal Influence

The targeted patient age for our device is between 60-90 years old. Many of these patients are not as healthy as they were in the earlier stages of life. Because of this, the current treatment of mitral regurgitation is a very invasive surgery for patients of their age. They have to undergo open heart surgery with a long recovery time. Patients should wait up to six weeks after surgery before driving a car and up to 12 weeks before returning to work. Also immediately after surgery there are several symptoms that a patient will experience. For example, loss of appetite, difficulty sleeping at night, mood swings and feeling depressed, and experience muscle pain or tightness (Murkin, 1999).

Our device will inserted through port insertion surgery. This is a much less invasive procedure than open heart surgery for a full mitral valve leaflet replacement. The recovery time is less as well. For 24 hours, the patient cannot drive a car, drink alcohol, or make important personal decisions. After a week the patient should be able to resume their usual activities (UW Medicine, 2015). Allowing the patient to return to their life as fast as possible and not feel as if they have missed months of what was happening in the world.

Current mechanical heart valves will put a patient on anticoagulants for the remainder of their life. Our device will only need a one-time insertion into the heart by port insertion with no need of post medications.

Political Ramifications

The surgical procedure for correcting mitral regurgitation after myocardial infarction is a world-wide procedure typically corrected with the use of a mechanical or biological heart valve. Our papillary muscle repositioning device has the potential to advance the cardiovascular field. It is an affordable alternative that can be brought into markets around the world. By tackling the problem at the papillary muscle, our device avoids the possibility of ripping the leaflets and causing additional problems to the mitral annulus.

However, because our device will be inserted through the heart wall it is classified as a class 3 device by the FDA. This means that there is the highest amount of risk with these devices and are subject to the highest level of regulatory control. They also must be approved by the FDA before being marketed. A current class 3 device on the market are replacement heart valves (Whitmore, 2013)

Our device falls under the medical device tax which will impose a 2.3 percent sales tax on the medical device supplies.

Ethical Concern

When designing and biomedical device, an engineer must consider the biomedical ethics established by the Belmont report in 1979. The Belmont report considers the three basic principles of ethics to consider when a device or research pertains to human subjects: beneficence, respect for autonomy, and justice. Our original client statement included the use of fibrin microthreads that we were going to seed stem cells onto to help with the regeneration of the papillary muscles.

Stem cells have been causing large debates on the ethics of utilizing them. The controversy began when scientists discovered they could remove stem cells from human embryos. However, the general public did not believe in destroying human embryos (Learn.Genetics, 2016). Through research and speaking with our advisors, we realized that stem cells were not needed for the completion of our project, so that eliminated the ethical concern of using stem cells.

We would be using nitinol to reposition the papillary muscle in the hopes to improve the lives of patients and eliminating the possibility of mitral regurgitation. Making this correction will extend the lifespan of the patient and allow them to continue to live a normal and healthy lifestyle. We do consider and respect the patient's decision to not want the device implanted into their body or the possibility of the patent not wanting to undergo the port access procedure.

An ethical concern that has been raised in previous biomedical implants is the issue of human identity and dignity. The question of whether an individual can still be considered human once they incorporate an artificial structure and system into their body has been debated for years. This controversial topic is one we have considered and will live up to the opinion of the intended user.

Health and Safety Issue

Nitinol is a biocompatible material, however, there is the potential for hazardous contamination. Although nitinol has an oxide layer that prevents corrosion and removes toxic Ni atoms from the surface of the material, there is still the potential for these particles to degrade into the body causing damage, and in some cases death. There is also the possibility of people being allergic to nickel which makes nitinol potentially problematic if exposed to an immune system that can not tolerate the material; especially if one were unaware of this allergy.

Another safety issue is that our device will be inserted through port access surgery. Although this procedure is less invasive than open heart surgery it still has risks associated with it. Port access surgery involves the medical professional inserted tubes into the blood vessels of the thigh and neck and threading those tubes through the vessels until the heart is reached. These tubes are delivering drugs that stop the heart in order to protect the patient while going through the surgery. They are connected to a heart-lung machine which circulates blood through the body although the heart is stopped. Then the surgeon makes two small incisions between the ribs, these are the "ports". The surgeon will insert the nitinol papillary muscle repositioning device using one of the holes while a miniature camera is inserted in the other (Mohr, 1998).

Manufacturability

All materials chosen for our device are easy to manufacture. They are accessible and inexpensive products that may be purchased within the United States. Nitinol has begun to increase in the industrial and commercial markets. The manufacturing process of nitinol configures and programs the shape memory alloy to a specific shape through thermal manipulation between the martensitic and austenitic phases based on the intended final use and environment of the nitinol. Manufacturing begins with melting and is followed by shaping of material which is typically performed by laser machining, wire EDM, swiss machining, and milling. The chemistry behind melting nitinol must be performed carefully and precisely. The transformation temperatures are very fragile and may cause a imbalance concentration between Ni and Ti. "For alloys having greater than 55.0 weight percent Ni, a one weight percent deviation in Ni (or Ti) 2 concentration will result in approximately a 100°C shift in transformation temperatures (Wu, 2002)." When incorporated in medical devices, nitinol must be electropolished to remove dross, machining

artifacts, and heat affected zones resulting from thermo-cutting processes in order to eliminate crevices between grains, as well as improve lifespan and performance.

Silicone Rubber

Through the processes of manufacturing the silicone rubber portion of the device, the method of choice would be liquid injection modeling. This is a cost effective option that makes it easier to make more complicated objects. Since the base has the double circle design with the cutouts, it would be easier to use the liquid injection molding. Using liquid injection modeling allows for our device to be produced on a large scale due to the simplicity of this method (Dow Corning, 2015).

Stainless Steel

The process to manufacture the stainless steel components would be based on the normal stainless steel manufacturing process. This is done by using normal alloying methods. Stainless steel would be melted and put into the casting of the mold of interest. This would then follow into the forming and heat treatment phases that determine the proper mechanical properties. Once the shape is made, different quality assurance positions would be tested to ensure that the stainless steel would be able to be placed in the heart (Turing, 2015).

Sustainability

The materials used to assemble our device are easily accessible as well as readily available. The amount of each material for our final product is relatively small and will not cause a major consumption of these resources during manufacturing.

VIII. Conclusion and Recommendations

Through our Major Qualifying Project the engineering design process was heavily implemented to create a cost-effective product that meets the client's needs. We began with

understanding that although a client may have an implied solution associated with the initial client statement, that does not mean it is the only solution to the problem. The client wanted to address the need to treat mitral regurgitation after myocardial infarction with the use of fibrin microthreads. However, after conducting research on fibrin microthreads and the causes of mitral regurgitation, we discovered a better approach. What the client truly needed was for the mitral valve leaflets to return to a location that would allow for proper closure. We did not need to regenerate the papillary muscles, we needed to reposition them to create that proper closure of the leaflets. Current devices that solved this problem were either very invasive or not a permanent solution. Our device was designed to improve upon that by making it minimally invasive through port access surgery as well as having it be a one-time surgery for the patient.

The final device developed was a cantilever papillary muscle repositioning device. The device would be inserted into the papillary muscle through the outside of the heart wall allowing to reposition the papillary muscle to a position that would allow for proper closure of the mitral valve leaflets. The typical displacement seen after myocardial infarction is 2.5-5mm, and the amount of displacement per patient would be determine via CT scans. The length of our device determines how much displacement will be seen in the movement of the papillary muscle. The range of length is 14-15.5mm giving a displacement of 2.7-4.9mm. This was calculated through the use of SolidWorks Nitinol Simulations. Determining this range in lengths allows our device to be customizable per patient depending on the severity of their papillary muscle displacement.

There were a few limitations associated with our project however. The biggest limitation that occurred from this project was the time constraint. We did not have enough time or resources to perform an extensive Finite Element Analysis that would work as our proof of concept of our device.

During our experiment, we experienced limitations with the morphology of the hearts. The porcine hearts obtained came from a local butcher. When received, many of the hearts had cuts that went through the ventricle and in some cases had the papillary muscle cut out or dislocated the chordae tendinea. With the internal destruction of important components, it was not possible to do accurate dissection.

Many of the initial specimens developed a moment when compressed against the heart wall and resulted in a failed experiment. In order to fix this problem was, nitinol was shortened in length to decrease that moment that caused bending, allowing nitinol to enter more efficiently. This allowed for accurate results of data.

Our proof of concept was backed up by the SolidWorks Material Simulation. This is a reliable stimulation for our device because it is based on the characteristics of the shape memory alloy (SMA) of NiTi. Using an FEA model would have been the best and most ideal method, however the CT scans we obtained were not able to be created into a finite element model of the left ventricle alone.

Our project was designed to be a proof of concept, so further testing and research need to be conducted. In vitro experiments with the use of porcine hearts were conducted throughout our project, however in vivo testing with the use of animal models will be the next step in the development of our device. If these tests supported our findings from the year, the device would then be moved to clinical trials. This device would also be considered a class 3 device through the FDA, making it more difficult to gain approval. And finally further research would have to be conducted on the cost of our device and if insurance would be able to cover the expenses, so that our device could be available for a large population.

References

Ahmed, M. (2013). "MyHeart.net". [Online]. Available: http://myheart.net/articles/mitral-valve-prolapse-flail-leaflet/.

American Heart Association. (2015). "Understanding Blood Pressure Readings," *Understanding Blood Pressure Readings*. [Online]. Available at: http://www.heart.org/heartorg/conditions/highbloodpressure/abouthighbloodpressure/understanding-blood-pressure-readings_ucm_301764_article.jsp. [Accessed: 2015].

Anatomy Expert, "Chordae Tendinae," [Online]. Available: http://www.anatomyexpert.com/app/structure/8037/1151/.

Askov, J.B., Honge, J.L., Nygaard, H. (2011). "Papillary Muscle Force Transducer for Measurement In Vivo," *Springer*. [Online]. Available at: http://link.springer.com/article/10.1007/s13239-011-0043-9. [Accessed: 2015].

Autodesk ForceEffect (2012). *Entertainment Close-Up,*

Bergmann, O. (2009). "Evudence for Cardiomyocyte Renewak in Humans". *Science Magazine,* vol. 324, 98-102.

Bhat, S.V. Biomaterials, Boston: Narosa Publishing House, 2002.

Clough, N.E. "Innovations in ePTFE Fiber Technology," *ePTFE Innovations,* 2015.

Clinical Anatomy Associates, Inc, "Chordae Tendineae," 2015. [Online]. Available: http://clinanat.com/index.php/291-chordae-tendineae.

Dean Kerste. (2014). *SolidWorks 2015* Infinite Skills. Retrieved from http://proquestcombo.safaribooksonline.com/9781771373074

Dennis, A.R. "Prognostic signifigance of ventricular tachycardia and fibrillation induced at programmed stimulation and delayed potentials detexted on the signal-averaged elextrocardiograms of survivors of acute myocardial infarction". 1986. *Pathophysiology and Natural History,* vol. 74, no. 4, pp. 731-745. \

Dow Corning.Rubber fabrication processes. Retrieved from https://www.dowcorning.com/content/rubber/rubberprocess/

Duan, Y., Liu, Z., O'Neill, J., Wan, L. Q., Freytes, D. O., & Vunjak-Novakovic, G. Hybrid Gel Composed of Native Heart Matrix and Collagen Induces Cardiac Differentiation of Human Embryonic Stem Cells without Supplemental Growth Factors. *Journal of Cardiovascular Translational Research*, 4(5), 2011, 605–615.

Duran, C. (2013). “Recent Progress in Mitral Valve Disease,” *Google Books*. [Online]. Available at: https://books.google.com/books?id=2bzlbaaaqbaj&pg=pa405&lpg=pa405&dq=what forces act on papillary muscle&source=bl&ots=lajrbjsgav&sig=5hh4vnqhzpof06cfwtajwcdnmyc&hl=en&sa=x&ved=0ahukewjcsdgflcvjahxxpomkhyina5yq6aeijtab#v=onepage&q=what forces act on. [Accessed: 2015].

Farner, D. (1973). "Breeding Biology of Birds" *Google Books*. Web. 15 Dec. 2015.
Fradley, G.M., Picard, H.M. Rupture of the Posteromedial Papillary Muscle Leading to Partial Flail of the Anterior Mitral Leaflet. Images in Cardiovascular Medicine. 123, 2011, 1044-1045.

Georgia Perimeter College, "Muscle and Muscle Tissue," 2015. [Online]. Georgia.

Grasso, W.A., Brener, J.S. Complications of Acute Myocardial Infarction. 2014, 1-14.

Gulati, A.K. "Regeneration pattern of cardiac and skeletal muscle," *Pub Med,* pp. 188-194, 1995.

Hetzer, R., Rankin, S.J., Yankah, A.C. Mitral Valve Repair: The Biological Solution. 2011, 106-107.

Holubec, T. , Sündermann, S.H., Jacobs, S., Falk, V. Chordae replacement versus leaflet resection in minimally invasive mitral valve repair. 2013. Ann Cardiothorac Surg, **2**(6): 809-813

How Products Are Made.Stainless steel. Encyclopedia.

Hung, J., Guerrero, J.L., Handschumacher, J., Supple, G., Sullivan, S., Levine, R.A. Reverse ventricular remodeling reduces ischemic mitral regurgitation. *Echo-guided device application in the beating heart*. 106, 2002, 2594-2600.

Inner Body, "Cardiac Muscle Tissue Interactive", 2015. [Online].

Jaganathan, S. "Biomaterials in Cardiovascular Research: Applications and Clinical Implications," *Biomed Research International,* p. 11, 2014.

Johnson Matthey Medical Components. (2015). Nitinol Technical Properties. [Online]. Available at: http://jmmedical.com/resources/221/Nitinol-Technical-Properties.html. [Accessed: 2015].

Jolly, S., Hutchison, S. Papillary Muscle Rupture Post-Myocardial Infarction. Cardiology Rounds. 8, 2003, 1-6.

Kobayashi, Y., Nagata, S., Ohmori, F., et al. Mitral valve dysfunction resulting from thickening and stiffening of artificial mitral valve chordae Circulation, 94 (Suppl II) (1996), pp. II-129–132.

Komeda,M., Glasslon, J.R., Bolger, A.F., Daughters II, G.T., Ingels Jr, N.B., Miller, C.D. (1997). “Papillary muscle–left ventricular wall ‘complex,’” *Cardiovascular Surgery*. [Online].

Available at: http://www.sciencedirect.com/science/article/pii/s002252239770326x. [Accessed: 2015].

Learn. Genetics.The stem cell debate: Is it over? Retrieved from http://learn.genetics.utah.edu/content/stemcells/scissues/

Li, J., and L. Ackermann. (2014). Cobalt-catalyzed C-H Acylations with Weakly-coordinating Amides and Tetrazoles: Expedient Route to Angiotensin-II-receptor Blockers. *National Center for Biotechnology Information*. U.S. National Library of Medicine. Web. 15 Dec. 2015.

Marasco, S., Rosenfeldt, F., Lim, H., Mennen, M., Cairo, S., Bain, C. Correction of Posteromedial Papillary Muscle Displacement in Repair of Ischemic Mitral Regurgitation. 2008 *The Journal of Heart Valve Disease*. 17: 620-627.

Medscaoe, "Chordae Tendinae," 2015. [Online]. Available http://www.medscape.com/viewarticle/713894_3

Melton, D. "How to Grow a Heart: Transforming Stem Cells Into Live Organs" 2011. *Big Think.*

Millard, "Mechanical Properties of Chordae Tendineae of the Mitral Heart Valve" 2011. *Journal of Mechanics in Medicine and Biology,* vol. 221.

Millington-Sanders, C. et al. "Structure of Chordae Tendineae in the Left Ventricle of the Human Heart." Journal of Anatomy 192.Pt 4 (1998): 573–581.

Poly Fluro Ltd., "Unraveling Polymers," 2009. [Online]. Available: http://polyfluoroltd.blogspot.com/2009/08/expanded-ptfe.html.

Mirro, M. (2015). "Angular Displacement of the Papillary Muscles During the Cardiac Cycle," *http://circ.ahajournals.org/content/60/2/327.full.pdf*. [Online]. Available at: http://circ.ahajournals.org/content/60/2/327.full.pdf. [Accessed: 2015].

Mitral valve - symptoms, causes and treatment on themitralvalve.org. Retrieved from http://www.themitralvalve.org/

Mohr, F. W., Falk, V., Diegeler, A., Walther, T., van Son, J. A. M., Autschbach, R., & Borst, H. G. (1998). Minimally invasive port-access mitral valve surgery. *The Journal of Thoracic and Cardiovascular Surgery, 115*(3), 567-576. doi:10.1016/S0022-5223(98)70320-4

Murkin, J. M., Boyd, W. D., Ganapathy, S., Adams, S. J., & Peterson, R. C. (1999). Beating heart surgery: Why expect less central nervous system morbidity? *The Annals of Thoracic Surgery, 68*(4), 1498-1501. doi:10.1016/S0003-4975(99)00953-4

Murphy, M. (2008). *Fibrin mircothreads promote stem cell growth for localized delivery in regenerative therapy*

Nitinol Devices & Components, Inc. (2015). "Nitinol Facts." *NDC*. [Online]. Available at: http://www.nitinol.com/. [Accessed: 2015].

Ragnarsson, R. "Polytetrafluoroethylene Neochordae Versus Resection Repair of Isolated Posterior Mitral Valve Relapse," *AATS,* 2015.

One on one: Adam collette, president and chief executive officer, VitaThreads, worcester. (2015, October 18). *Telegram & Gazette* Retrieved from http://search.proquest.com/docview/1722952775

Pick, A. (2010). How much do heart valve replacements cost? Retrieved from http://www.heart-valve-surgery.com/heart-surgery-blog/2010/09/20/mechanical-tissue-valve-replacements-cost/

Ravenscroft-Chang, M. "Altered Calcium Dynamics in Cardiac Cells Grown on Silane-modified surfaces," *Biomaterials,* vol. 31, no. 4, pp. 602-607.

Readers respond: Your hospital bill nightmares, via CNN iReport. (2013, February 28). *Time,*

Rigo, P., M. Murray, H.W. Strauss, and D. Taylor. (1974) "Left Ventricular Function in Acute Myocardial". *Circulation*, Volume 50. Web. 15 Dec. 2015.

Roberts, C.W., Cohen, S.L. Description of the Normal and a Survery of Conditions Causing them to be Abnormal. Left Ventricular Papillary Muscles. 46, 1972, 138-152.

Salman, M., Dubois, M., Maria, A. D., Van Acker, K., & Van Balen, K. (2015). Construction materials from stainless steel slags: Technical aspects, environmental benefits, and economic opportunities. *Journal of Industrial Ecology,* , n/a. doi:10.1111/jiec.12314

Selder, J., Riezebos, R. 2015. Double jeopardy: two major complications of a myocardial infarction in one patient. *BMJ Case Reports 2015*: published online 6 July 2015.

Semafuko, W. and Bowie, W. (1975). "Papillary muscle dynamics: in situ function and responses of the papillary muscle". *Papillary muscle dynamics: in situ function and responses of the papillary muscle*. [Online]. Available at: http://ajplegacy.physiology.org/content/228/6/1800. [Accessed: 2015].

Shah, P. 2010. *Journal of Cardiology*. 56, 2010, 125-133

Siemens.(2015).FEA/Finite Element Analysis. [Online]. Available at: http://www.plm.automation.siemens.com/en_us/plm/fea.shtml. [Accessed: 2015].

Solis, J. et al. "Polymer Injection Therapy to Reverse Remodel the Papillary Muscles: Efficacy in Reducing Mitral Regurgitation in a Chronic Ischemic Model." Circulation. Cardiovascular interventions 3.5 (2010): 499–505. PMC. Web. 13 Oct. 2015.

Stoeckel, Pelton, Duerig. (2003). “Self-Expanding Nitinol Stents - Material and Design Considerations”. *European Radiology*, 1-13.

The Mount Sinai Hospital. "Mitral Valve Function". Mitral Valve Repair Reference Center. Icahn School of Medicine at Mount Sinai, 13 Dec. 2005. Web. 12 Oct. 2015.

The Mount Sinai Hospital. "Chordae Tendinae.": Mitral Valve Repair Reference Center. Icahn School of Medicine at Mount Sinai, 10 May 2006. Web. 12 Oct. 2015.

Tibayan, F., Langer, F., Rodriguez, F., Zasio, M.K., Bailey, L., Liang D., Daughters G.T, Ingels, N.B., Miller, C. (2015). Geometric Distortions of the Mitral Valvular-Ventricular Complex in Chronic Ischemic Mitral Regurgitation. *Geometric Distortions of the Mitral Valvular-Ventricular Complex in Chronic Ischemic Mitral Regurgitation*.

Tomita, Y. "Extensive use of polytetrafluoroethylene artificial grafts of posterior mitral leaflet," *The Annals of Thoracic Surgery,* vol. 78, no. 3, pp. 815-819, 2004.

Trinity College Dublin, "World Study to Test Cardiac Tendons," Dublin, 2015.

UCSF. Complications of Myocardial Infarction. 2004, 1-2.

UW Medicine.Chest port. Retrieved from http://www.uwmedicine.org/health-library/Pages/chest-port.aspx

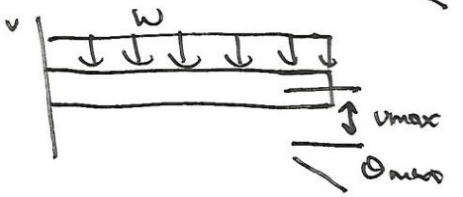
Whitmore Elaine. (2013). *Development of FDA-regulated medical products - prescription drugs, biologics, and medical devices*. United States: American Society for Quality (ASQ).

Wu, M. H. (2002). Fabrication of nitinol materials and components. *Materials Science Forum, 394-395*, 285-292. doi:10.4028/www.scientific.net/MSF.394-395.285

Appendix A: Hand Calculations for Cantilever Beam

Equations:

$$v_{max} = \frac{PL^3}{3EI}$$



$$v_{max} = \frac{wL^4}{8EI}$$

Nitinol Properties

Young's Modulus

Austenite: 83 GPa

Martensite: 28 - 41 GPa

Moment of Inertia: (Rod @ End)

$$I = \frac{1}{3} m L^3$$

density = 6.45 g/cm³

volume = $\pi r^2 h$ = 0.0236 cm³

mass = 0.1522 grams

Rod @ End MOI

$$I = \frac{1}{3}(0.1522\,g)(1.3\,cm)^3 =$$

0.111 g/cm³

or $1.11 \cdot 10^{-8}$ kg/m³

Deflection from Cords

$$v_{max} = \frac{PL^3}{3EI}$$

P = 4.1 N

L = 1.3 cm = 0.013 m

E $3 \cdot 10^{10}$ N/m²

$$\frac{(4.1\,N)(0.013\,m)^3}{3(3\cdot10^{10}\,N)(1.11\cdot10^{-8}\,\frac{kg}{m^2})} = 9.02^{10-9}\,m$$

Deflection from Papillary Muscles

$$v_{max} = \frac{wL^4}{8EI}$$

w = 5.1 N / 0.00133 = 3834 N/m

L = 0.013 m

E = $3 \cdot 10^{10}$ N/m

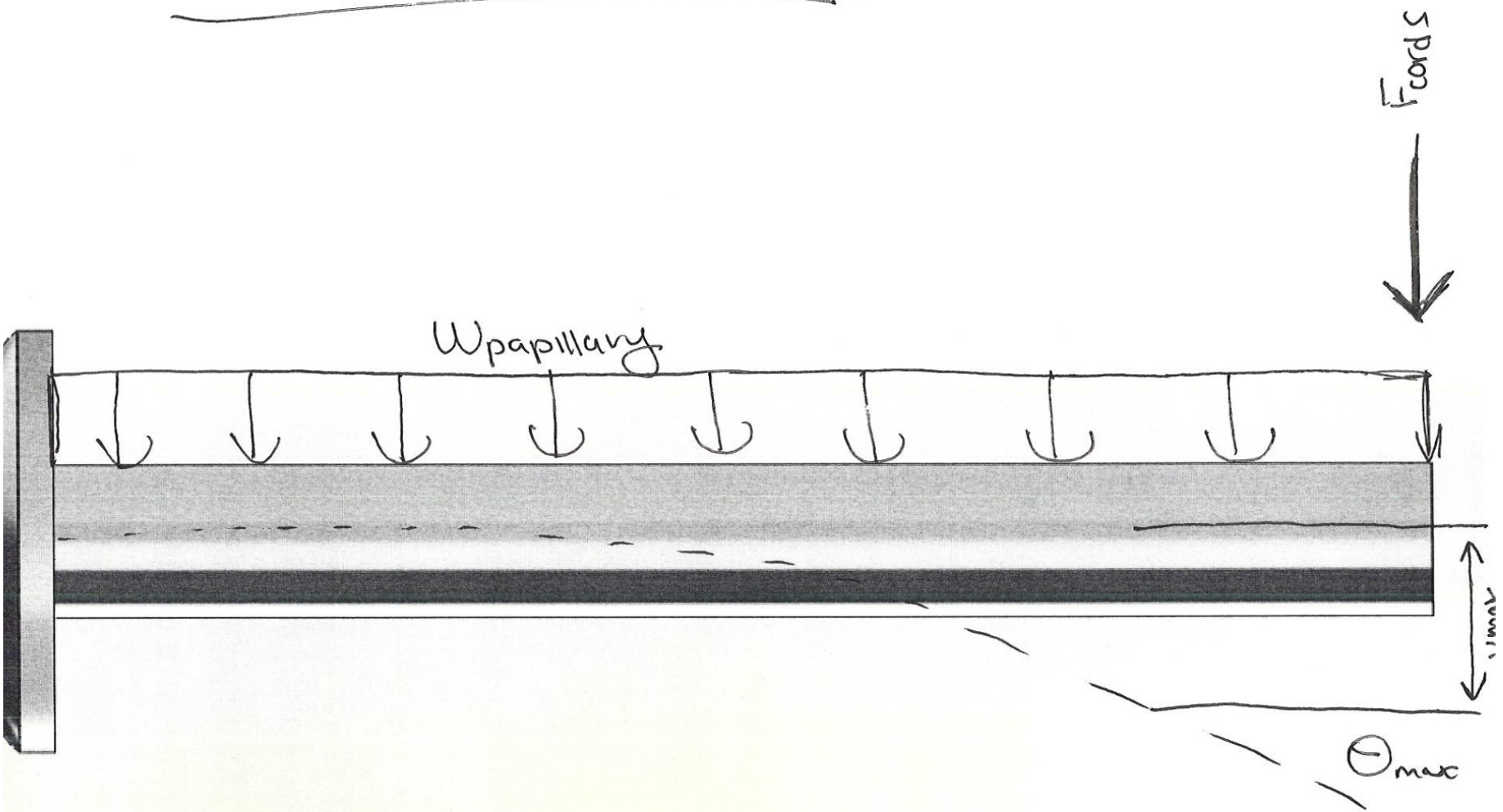
$$\frac{(3834\,N/m)(0.013\,m)^3}{8(3\cdot10^{10}\,\frac{N}{m})(1.11\cdot10^{-8}\,\frac{kg}{m})} = 3.16\cdot10^{-6}\,m$$

Summation of Displacement from Cords and Papillary

$$\Sigma \text{Displacement} = V_{papillary} + V_{cords}$$

$$V_{total} = 3.17 \cdot 10^{-6}\ m$$

FREE BODY DIAGRAM - DEVICE



Appendix B: Lab Notebook Scans

16

Group Meeting # 16 — 10/4/2015

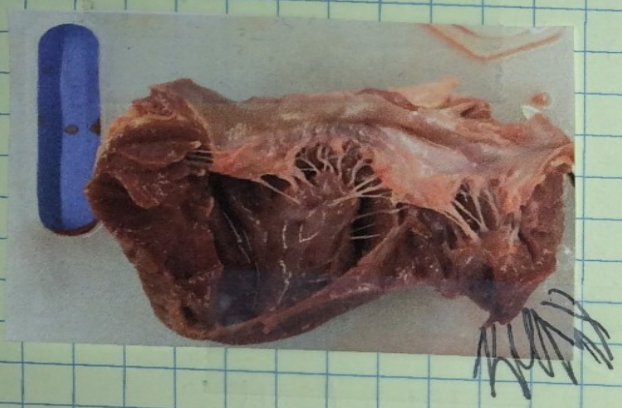
Location GFT 206

Attendees: Danielle, Nadjia, Keith

Test Parameters. [board off studies]

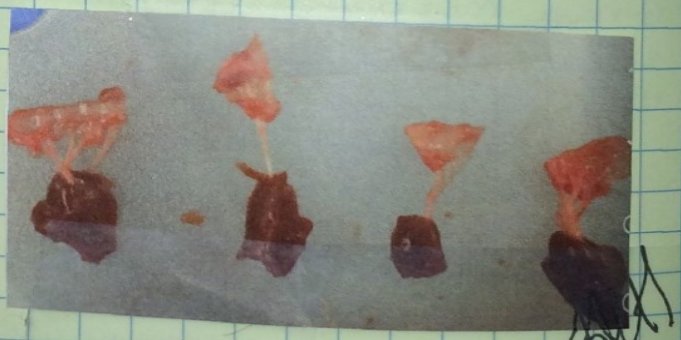
- Prepare the heart to isolate papillary
  -> leave one with a single chordae, leave the other with multiple cords.
  -> to be then Instron Tested later on.

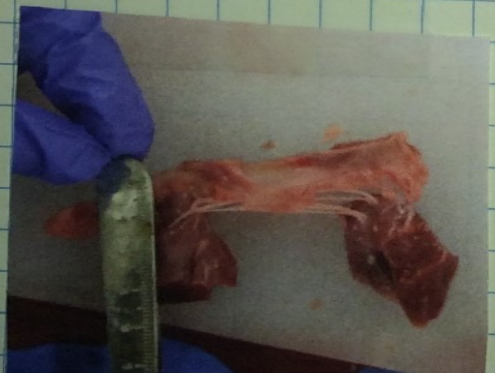
·Notes for future, plan for more time to prepare the heart for isolation.



The team cut the pig heart in half to look at the left ventricle and isolate some of the chordae to test on Instron machine.

The team then isolated the papillary muscles to be tested later on. One has all the chordae, the others have a single one.





Some measurement of the papillary muscle.

Group Meeting # 16 10/4/2015

This is a picture of the multiple chordae tendinae on the papillary muscle to be tested in the Instron machine. This test slipped on us and we ended up running out of time for a lot more. We then looked into research and journals for this number.

The Results from the first three trials are on the next few pages. They are in three columns.

Test # 1	Test # 2	Test # 3

Test results on next pages

10/4/2015

Results from Initial Instron Testing 20-4-15

Page 1

Specimen label	Chord1	
Geometry	Circular	
Length	25.82	mm
Maximum Load		N

Time (s)	Extension (mm)	Load (N)
0	0.019	0
0.1	0.996	1.9
0.11	1.107	2
0.112	1.13	2.1
0.212	0.539	0.5
0.26	-0.02	-0.3
0.262	-0.044	-0.3
0.362	0.529	0
0.452	1.554	2
0.454	1.576	2.1
0.554	1.002	0.6
0.642	-0.018	-0.6
0.644	-0.041	-0.6
0.744	0.545	-0.3
0.844	1.694	1.4
0.87	1.985	2
0.872	2.007	2
0.972	1.405	0.2
1.072	0.243	-0.7
1.094	-0.006	-0.8
1.096	-0.029	-0.8

Specimen label	Chord Length
Geometry	Circular
Length	25.82mm
Maximum Load	7.05499N

Time (s)	Extension (mm)	Load (N)	Time (s)	Extension (mm)	Load (N)
0	-1.422	0.1	0	0.023	0
0.1	-0.407	2	0.1	1.105	0
0.102	-0.384	2.1	0.2	2.33	0.1
0.104	-0.362	2.1	0.3	3.52	0.2
0.106	-0.34	2.2	0.4	4.689	0.4
0.108	-0.318	2.3	0.5	5.845	1.3
0.11	-0.297	2.3	0.548	6.396	2
0.114	-0.262	2.4	0.55	6.42	2.1
0.116	-0.249	2.5	0.65	5.698	1.3
0.118	-0.238	2.5	0.75	4.377	0.3
0.12	-0.23	2.5	0.85	3.126	0.1
0.122	-0.225	2.6	0.95	1.925	0
0.124	-0.221	2.6	1.05	0.75	0
0.126	-0.22	2.6	1.116	-0.017	0
0.128	-0.218	2.6	1.118	-0.04	0
0.13	-0.217	2.6	1.218	0.676	0
0.132	-0.215	2.6	1.318	1.994	0
0.134	-0.213	2.6	1.418	3.242	0.1
0.136	-0.209	2.6	1.518	4.443	0.3
0.138	-0.205	2.6	1.618	5.617	0.9
0.14	-0.199	2.7	1.69	6.452	2

Specimen label	Chord Length
Geometry	Circular
Length	28.52mm
Maximum Load	6.19013N

Results from Initial Instron Testing 10-4-17

Page 2

1.378	2.639	2
1.38	2.661	2.1
1.48	2.044	0.3
1.58	0.874	-0.6
1.658	-0.002	-0.8
1.66	-0.024	-0.8
1.76	0.587	-0.7
1.86	1.754	-0.1
1.96	2.87	1.4
2.002	3.327	2
2.004	3.348	2
2.104	2.742	0.3
2.204	1.567	-0.6
2.304	0.444	-0.8
2.346	-0.015	-0.9
2.348	-0.037	-0.8
2.448	0.588	-0.8
2.548	1.763	-0.5
2.648	2.885	0.5
2.748	3.966	2
2.75	3.988	2
2.752	4.009	2
2.852	3.374	0.3
2.952	2.191	-0.6
3.052	1.066	-0.8
3.152	-0.018	-0.9
3.154	-0.04	-0.9
3.254	0.573	-0.8
3.354	1.754	-0.7
3.454	2.879	-0.1

0.144	-0.187	2.7	1.792	5.758	1.4
0.146	-0.181	2.8	1.892	4.441	0.3
0.148	-0.175	2.8	1.992	3.192	0.1
0.15	-0.171	2.9	2.092	1.991	0
0.152	-0.168	2.9	2.192	0.818	0
0.154	-0.166	2.9	2.264	-0.018	0
3.414	0.088	2.3	2.266	-0.041	0
3.436	-0.007	2.2	2.366	0.676	0
3.438	-0.02	2.2	2.466	1.994	0
3.44	-0.034	2.2	2.566	3.242	0.1
3.442	-0.046	2.2	2.666	4.443	0.3
3.444	-0.058	2.2	2.766	5.616	0.9
3.446	-0.069	2.2	2.84	6.475	2
3.448	-0.079	2.3	2.842	6.498	2.1
3.45	-0.087	2.3	2.942	5.781	1.4
3.452	-0.094	2.3	3.042	4.463	0.3
3.454	-0.1	2.3	3.142	3.215	0.1
3.456	-0.105	2.3	3.242	2.014	0
3.458	-0.109	2.3	3.342	0.841	0
3.46	-0.112	2.3	3.416	-0.019	0
3.462	-0.115	2.3	3.418	-0.042	0
3.464	-0.118	2.3	3.518	0.676	0
3.466	-0.121	2.2	3.618	1.993	0
3.468	-0.124	2.2	3.718	3.242	0.1
3.47	-0.128	2.2	3.818	4.443	0.3
3.472	-0.131	2.2	3.918	5.617	0.9
3.474	-0.135	2.1	3.992	6.475	2
3.476	-0.139	2.1	3.994	6.498	2
3.478	-0.143	2.1	4.094	5.781	1.4
3.48	-0.147	2	4.194	4.463	0.3

Results from Initial Instron Testing - 10/4/2018

3.554	3.963	1.1
3.654	5.025	1.6
3.754	6.073	0.5
3.854	7.115	0.2
3.954	8.153	-0.2
4.054	9.189	-0.5
4.154	10.223	-0.7
4.254	11.257	-0.8
4.354	12.29	-0.8
4.454	13.323	-0.8
4.554	14.356	-0.8
4.654	15.388	-0.8
4.754	16.421	-0.8
4.854	17.454	-0.8
4.954	18.487	-0.8
5.054	19.52	-0.8
5.154	20.552	-0.8
5.254	21.586	-0.8
5.354	22.618	-0.8
5.454	23.651	-0.8
5.554	24.684	-0.8
5.654	25.717	-0.8
5.754	26.75	-0.8
5.854	27.782	-0.8
5.954	28.815	-0.8
6.054	29.847	-0.8
6.154	30.881	-0.8
6.254	31.914	-0.8
6.354	32.946	-0.8
6.454	33.979	-0.8

3.482	-0.15	2	4.294	3.216 0.1
3.582	-0.104	2.3	4.394	2.015 0
3.682	0.165	2.5	4.494	0.841 0
3.798	0.075	1.9	4.568	-0.018 0
3.936	-0.03	1.7	4.57	-0.042 0
4.074	0.004	1.7	4.67	0.676 0
4.174	-0.176	1.9	4.77	1.994 0
4.274	0.2	2.9	4.87	3.242 0.1
4.374	0.049	1.6	4.97	4.443 0.3
4.474	-0.057	2.4	5.07	5.616 0.9
4.574	0.415	2.6	5.144	6.475 2
4.674	-0.159	1.6	5.146	6.498 2
4.774	0.329	3	5.246	5.781 1.4
4.876	0.025	1.4	5.346	4.463 0.3
4.976	0.06	2.2	5.446	3.215 0.1
5.076	0.203	1.8	5.546	2.014 0
5.176	-0.119	1.6	5.646	0.84 0
5.276	0.2	2	5.72	-0.019 0
5.376	-0.099	1.6	5.722	-0.042 0
5.476	0.258	2.7	5.822	0.676 0
5.576	0.11	1.5	5.922	1.994 0
5.676	0.008	1.4	6.022	3.242 0.1
5.776	-0.149	1.5	6.122	4.443 0.3
5.876	0.382	2.8	6.222	5.616 0.9
5.976	0.008	1.3	6.298	6.498 2
6.076	0.12	2.6	6.3	6.521 2.1
6.078	0.098	2.6	6.4	5.804 1.4
6.178	-0.03	1.2	6.5	4.486 0.3
6.278	0.115	1.7	6.6	3.238 0.1
6.378	0.261	2.3	6.7	2.037 0

Results from Initial Instron Testing 10/4/2015

page 4

6.554	35.012	-0.8
6.654	36.045	-0.8
6.754	37.077	-0.8
6.854	38.11	-0.8
6.904	38.627	-0.8

6.478	0.401	3
6.578	0.535	3.6
6.678	0.668	4
6.778	0.799	4.3
6.878	0.929	4.6
6.978	1.059	4.7
7.078	1.187	4.9
7.178	1.317	5.1
7.278	1.446	5.2
7.378	1.575	5.3
7.478	1.705	5.4
7.578	1.833	5.5
7.678	1.962	5.6
7.778	2.092	5.7
7.878	2.221	5.8
7.978	2.35	5.9
8.078	2.48	6
8.178	2.608	6.1
8.278	2.738	6.1
8.378	2.866	6.2
8.478	2.995	6.2
8.578	3.125	6.3
8.678	3.254	6.3
8.778	3.383	6.4
8.878	3.512	6.6
8.978	3.641	6.8
9.078	3.77	6.9
9.178	3.899	7
9.278	4.029	7.1
9.378	4.158	7.1

6.8	0.863	0
6.876	-0.019	0
6.878	-0.042	0
6.978	0.676	0
7.078	1.994	0
7.178	3.242	0.1
7.278	4.443	0.3
7.378	5.616	0.9
7.454	6.498	2
7.456	6.521	2.1
7.556	5.804	1.4
7.656	4.486	0.3
7.756	3.238	0.1
7.856	2.037	0
7.956	0.864	0
8.032	-0.019	0
8.034	-0.042	0
8.134	0.676	0
8.234	1.993	0
8.334	3.242	0.1
8.434	4.443	0.3
8.534	5.616	0.9
8.61	6.498	2
8.612	6.521	2.1
8.712	5.827	1.4
8.812	4.51	0.3
8.912	3.262	0.1
9.012	2.06	0
9.112	0.887	0
9.19	-0.019	0

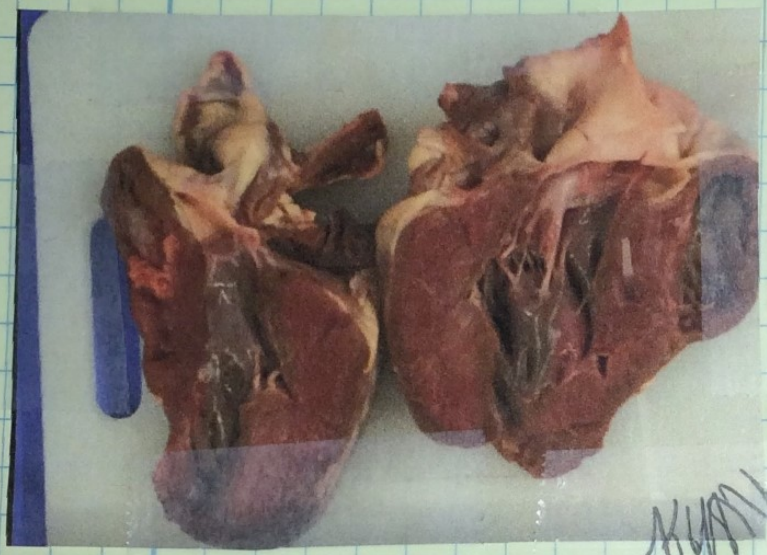
Group Meeting #19 12/2/2015
Location: Goddard Hall 206 @ 8 am
Attendees: Keith, Danielle, Nadjia.

- Purpose = to see how the papillary muscle would move based off current device idea.

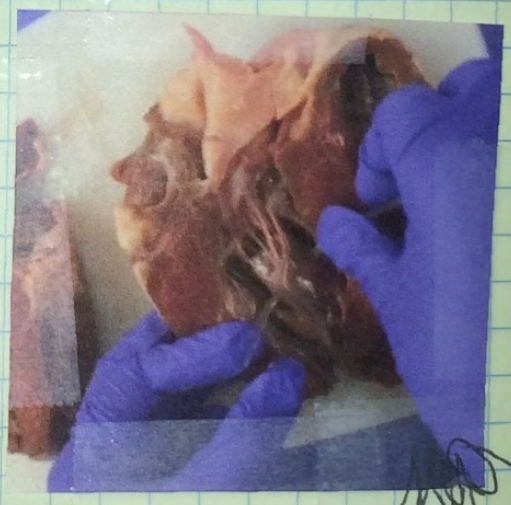
↳ prepare the heart to be tested.

Preparation:
watched videos to isolate the left ventricle to get the papillary muscle in full view

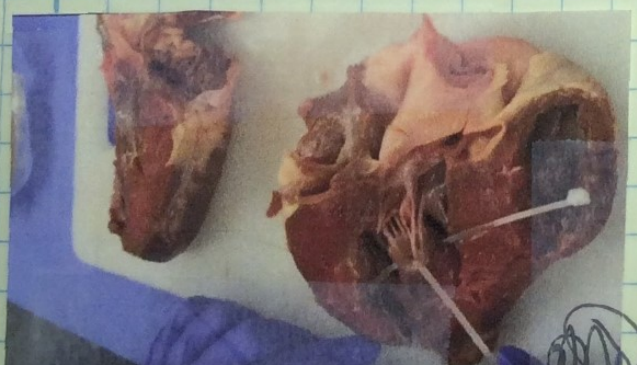
*Note; the heart seemed a little old.



Followed an online video to cut the heart in half so we could have a solid view of a papillary muscle for future tests.
← to left.



Through the use of tiptics we pulled the papillary muscle forward and back to see movement.



The second test was to pull the papillary muscle to the left and right to see how the

Group Meeting # 19 12/7/2015

Through pure testing, the team decided to see how the zip ties would work going through the pap muscle. We wanted to base this off an idea that Prof. Gaudette suggested at an Advisor meeting

The testing at this time was just to check to see if the ideas were implementable or not.

Ls other alternative designs stemmed from this meeting.

12/9/2015