WASHINGTON UNIVERSITY IN ST. LOUIS

Percutaneous Mitral Regurgitation Repair

Final Report

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Abstract

Mitral Regurgitation (MR) is a serious medical condition. MR is a progressive disease and can lead to a wide variety of other cardiac ailments. MR decreases cardiac output because the mitral valve does not completely close during ventricular contraction and blood flows back into the left atrium. There are multiple forms of MR, the most common being Type II MR. Type II occurs when the cordae tendineae elongate or break and the leaflet of the mitral valve prolapses into the left atrium and allows retrograde blood flow. In a healthy human heart, the cordae tendineae prevent the leaflet from extending back into the left atrium by anchoring it to a papillary muscle on the wall of the left ventricle. The cordae tendineae limit leaflet range of motion and help to guide leaflet motion. The goal of the MitraGuard device is to cinch two artificial cordae tendineae – one that is anchored to the papillary muscle and one that is anchored to the leaflet. While observing leaflet motion using a transesophageal echocardiogram (TEE), the free ends of the cordae tendineae are pulled through the device until MR is observed to be minimized; the cordae are then cinched. need to be adjustable and able to be cinched when MR is minimized. The surgical procedure required for this device uses a percutaneous catheter delivery system. It is less invasive, cheaper, and more physiologically sound than most current-day mitral valve replacements.

Contents

Background and Need

The mitral valve is a bi-leaflet valve and is the passageway for blood to flow from the left atrium and the left ventricle of the heart. The cordae tendineae are tendon-like cords that anchor the mitral valve leaflets to the papillary muscles on the wall of the left ventricle. The cords prevent the leaflets from prolapsing into the left atrium during ventricular contraction. Mitral regurgitation (MR) happens when the mitral valve does not close completely and there is retrograde blood flow into the left atrium. When there is retrograde flow in the heart, blood does not move efficiently through the heart, which reduces cardiac output and can cause shortness of breath (3).

Mitral regurgitation is the most common form of valvular heart disease. Two percent of the American adult population suffers from MR with similar prevalence in males and females. There are 20,000 to 25,000 mitral valve procedures performed each year in the United States with an 80% success rate (3). However, only 44.3% of patients who have MR actually undergo mitral valve repair. This is because current existing solutions to MR are complex and have many risk factors associated with them. Symptomatic patients have an annual death rate of 5% or more without intervention (2).

In the United States, degenerative mitral valve disease is the most common cause of MR (4). MR is a progressive disease and, if left untreated, will continue to become more severe.

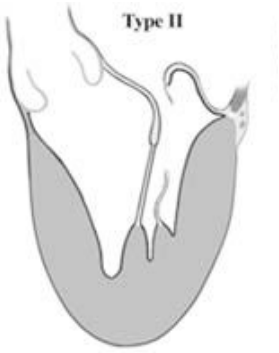

Figure 1. Type II Mitral Regurgitation

The most common cause of MR is detachment or elongation of the cordae that are attached to the posterior leaflet of the mitral valve, which results in increased motion of the leaflet (7). This is called Type II MR, which is what our device is designed to fix. Figure 1 shows Type II MR. MR often begins as a mild condition and progresses slowly. Severe MR can lead to heart failure, atrial fibrillation, endocarditis, and pulmonary hypertension. There is a positive feedback loop associated with MR, which is illustrated in Figure 2. Mild MR results in less blood flow out of the heart to the body and consequently less oxygen circulation. Receptors in the heart sense the lack of oxygen flow and dilate the annulus of the valve. This response leads to poor valvular function, which in turn results in greater retrograde flow in the heart, starting the positive feedback loop over again. Therefore, even patients with mild MR should undergo valvular repair because the condition will become progressively worse with time (1). However, current guidelines only require that surgery needs to be recommended to those with moderate-to-severe or severe MR (2).

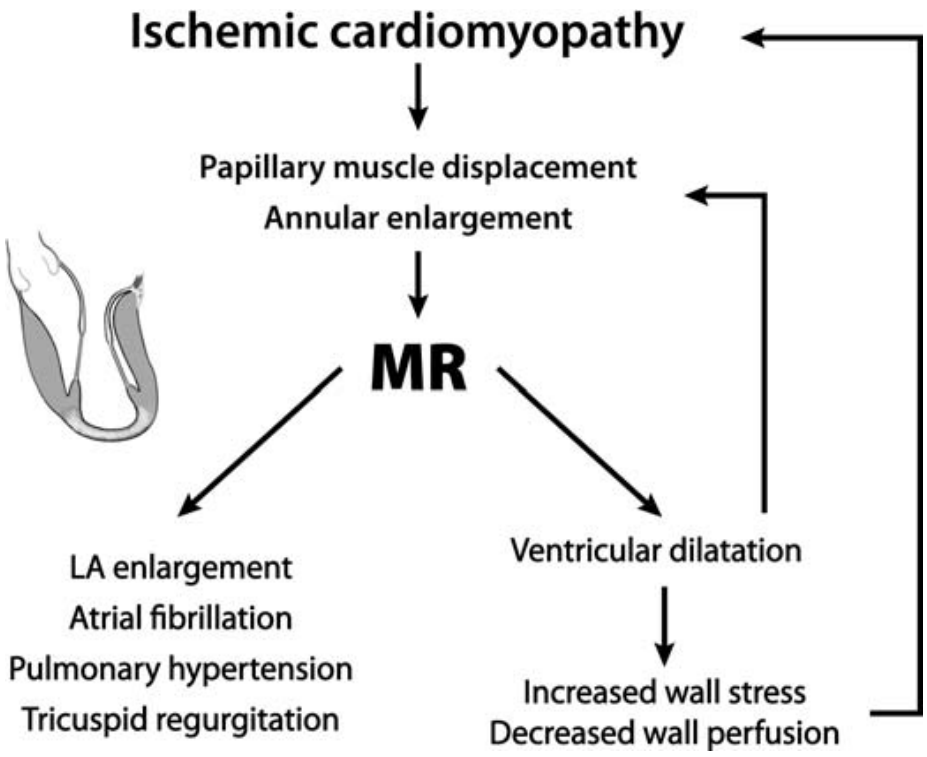

Figure 2. The Pathophysiology of Ischemic Mitral Regurgitation: Implication for Surgical and Percutaneous Intervention.

Our device is designed to fix minimal MR without the side effects and risks associated with current procedures. We are focused on providing a minimally invasive percutaneous procedure to repair Type II MR. Our project is the final step in a three-step process to repair Type II MR. The first step (completed in 2009) involves anchoring an artificial cordae to the mitral leaflet. The second step (completed in 2010) involves anchoring a separate cordae to the left ventricle wall. The focus of our project is to design a device that adjusts the lengths of the artificial cordae tendineae (ACT) and cinches the ACT together in order to reduce MR (3).

Introduction to the Project

The following three steps summarize the procedure to replace an elongated or detached cordae tendineae:

1. Attach an artificial cordae tendineae (ACT) to the mitral valve leaflet.
2. Attach a separate ACT to the papillary muscle on the wall of the left ventricle (LV).
3. Cinch the two ACTs together.

In 2009, a BME 401 group developed a method to attach an ACT to the posterior leaflet of the mitral valve using a catheter-based delivery system. In 2010, another BME 401 group designed a system to attach an ACT to the papillary muscle of the LV using the same catheter system. We are completing the cordae tendineae replacement procedure by cinching the two ACTs together. The goal is to have all three steps done through the same catheter delivery system. For the remainder of this report, we are assuming the ACTs have already been attached to the leaflet and papillary muscles and that their delivery systems have been removed from the catheter. The third step of this procedure begins with both ACTs extending from the LV, over the aortic arch, and out of the patient through the femoral artery.

Imaging Techniques

Minimally invasive procedures rely heavily on medical imaging to ensure accuracy and precision. Transesophageal echocardiograms (TEE) are used to image valves in the heart and are essential when performing a valve or cordae replacement.

Transesophageal Echocardiography (TEE)

Echocardiography uses ultrasound waves to image details of the heart, including heart valves, and the position of the catheter. A transducer and an ecomonitor are placed on opposite sides of the patient's chest. The transducer emits sound waves and the waves are distorted according to the types of cells they pass through. The ecomonitor detects these distorted waves and compares them to the emitted waves to create a picture. Echocardiography is not perfect; sound waves can be distorted fairly easily and objects such as the patient's ribs may partially distort the waves before they reach the heart.

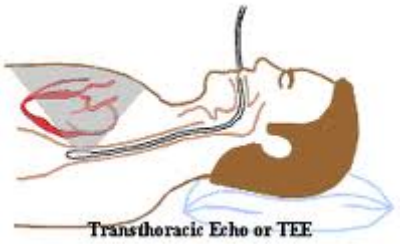

Figure 3. Echocardiogram of Heart with Mitral Regurgitation Diagram courtesy of www.metrohealth.org

However, transesophageal echocardiography (TEE) prevents distortion by placing the transducer in the esophagus of the patient, directly behind the heart. The ecomonitor is placed in front of the patient. TEE produces clearer pictures and can more accurately image a specific portion of the heart by adjusting the placement of the transducer and the ecomonitor. Figure 3 shows a patient undergoing TEE. During the third step of the cordae replacement procedure, the physician will look at the TEE image in real time while cinching the ACTs in order to determine what cordae length is minimizes MR.

Catheter Size

The ideal maximum size for a femoral artery catheter is 18-19 French (F), but 20-24 F catheters are used in some cases if the patient's artery is an appropriate size (A). Currently, 20-24 F catheters are used in minimally invasive procedures to insert percutaneous aortic valve devices, but they are bulky and cumbersome (B). Closing the resultant hole in the patient's thigh and stopping the bleeding can be done in several ways, including applying long-standing pressure, using "plug" techniques, and, as a last resort, stitching up the opening using surgical suture. The most common method is to pre-close the site with a percutaneous suture device called Proglide or by way of surgical arterial cut down (C).

Design Specifications

Our design specifications are divided into three categories:

- Metric design specifications
- Safety design specifications
- Clinical design specifications

Metric Design Specifications

Metric design specifications include restrictions that are necessary in order to allow the device to function properly during cardiac contraction in the LV and the selling price.

1. ACT Tear strength ≥ 9.8 N (1,000 g)
2. ACT Clipped strength ≥ 4.9 N (500 g)
3. Length of ACT: 30-45 mm
4. Device should allow a change of length of 1mm when a force of 12 N is applied to the leaflet
5. Diameter of catheter: < 24 French (8 mm)
6. Diameter of cinching device < Diameter of catheter
7. Selling price: $27,000

Safety Design Specifications

Safety design specifications prevent adverse and harmful side effects from occurring to the patient during or after the procedure.

1. Biocompatible

2. Shelf life of 2 years, plus a 40-year life span in the patient
3. Minimize possibility of blood clots
4. No sharp edges present once the artificial cordae have been cut
5. Does not inhibit blood flow
6. Does not inhibit heart motion
7. Does not inhibit electrical signals
    a. Within the body
    b. Detected by EKG

Clinical Design Specifications

Clinical design specifications establish requirements regarding how the procedure should be completed.

1. Procedure must be easily operable by a single physician
2. Procedure < 1 hour long
3. Device must be integrated with catheter delivery system
4. Lengths of the ACT must be adjustable before cinching
5. Device must be able to move within the LV in order to cinch the ACT when MR is minimized on TEE
6. Catheter and ACT must be visible under fluoroscopy and TEE

Design Alternatives

The four design alternatives for our cinching device were:

1. Knot Tying Device

2. Trap Device

3. Shorts Model

4. Box-Spring Model

We used a Pugh Chart in order to effectively determine which alternative was the best cinching device. The Pugh Chart is shown below in Table 1. The Box-Spring Model is our chosen device.

Pugh Chart Cinching Device

Table 1. Pugh Chart Analysis for Cinching Device. Scores are weighted based on importance with green indicating a perfect score (10), yellow a high score (9-7) and red a low score (6 or below).

Criteria	Weight	Knot Tying	Trap	Shorts	Box
Biocompatibility	10	10	9	9	9
Durability	10	7	3	6	10
Ease of Deployment	8	5	6	7	10
Ease of Adjustability	9	3	6	9	9
Mechanical Effectiveness	9	5	3	7	10
Cost	6	9	9	9	6
Total		336	303	404	477

Criteria for Cinching Device

The cinching device was scored according to the following design criteria: Biocompatibility, Durability, Ease of Deployment, Ease of Adjustability, Mechanical Effectiveness, and Cost. Our cinching device is designed to remain in the patient's body for the duration of his/her life and therefore must be **biocompatible** in order to avoid a negative immune response. The device needs to be **durable** so the mechanism does not degrade or become loose over time. **Ease of Deployment** is an important criterion we investigated in insuring the physician can maneuver the catheter attached to the device with ease. The device must be capable of being threaded or pushed with a guide wire into the femoral artery, around the aortic arch, and into the left ventricle. The ACTs also need to be **adjustable** to the correct lengths

where the cords will be cinched. Our goal is reduce MR and in order to do so the device need to be **mechanically effective**. Our criteria for mechanical effectiveness are: ability to replicate physiological tensions in the CT, ability to replicate change in length of the CT, and ability to undergo this change in length as slow as when the heart is at rest and as fast as when the heart is under maximum exertion. Finally we want to minimize **cost,** so we looked into the cost of production, materials and delivery systems we would need for each cinching mechanism.

We next weighted each of the above criterions on a scale of 1-10 based on its importance for our patients' needs. We assigned weights of 10 to the following criteria: Biocompatibility and Durability. We must make sure that our device does not cause any negative side effects to the patient, and the health of the patient post-procedure is our number one concern. Therefore, we must be certain that the device that we choose will not affect the patient's immune system and will work properly for a long duration. The Mechanical Effectiveness and Ease of Adjustability were rated a 9 because it is high on our list of priorities in term of reducing MR, however it does not have the ability to affect that patient negatively post operatively as the other criteria rated as 10. The Ease of Deployment criterion was weighted 8 because this criterion is based on the ease of the surgery for the doctor. Marketing our device to appeal to physicians performing the surgery is very important in terms of getting our product to market. However, we felt that the ease of surgery is of lesser importance than the safety of the patients. Lastly, we weighted Cost 6 because we found it to be of lesser importance than the physicians' ease of surgery but still and important criterion in terms of getting our product to market.

Scoring

We scored our four design concepts on a scale from 1 to 10 for each of the criteria given in the table above. In the Pugh Chart, green represents a perfect score (10), yellow a high score (9-7), and red a low score (6 and below).

Biocompatibility

The bodies of the Knot Tying Device, Trap Device, and Box-Spring Model are made of 316L stainless steel. The Shorts Model is made of Polypropylene (PP). The Knot Tying Device and the Trap Device use Gore-Tex as the material for the ACT. The Shorts Model and the Box-Spring Model use 316L stainless steel for the ACT.

There is a possibility that the devices using 316L stainless steel would require the patient to go on blood thinners. These device designs are comparable in size to typical stents used in blood vessels; thus, we anticipate the patient will need to take aspirin and go on blood thinners for approximately 1 to 12 months after the procedure, as that is what patients who have stents need post-operatively.

Though clot formation tendency does not fall directly under biocompatibility, it is an issue that needs to be addressed and fits best in the biocompatibility category. Gore-Tex does not require the patient to go on blood thinners so we rated the Knot Tying Device a 10 in biocompatibility, because the stainless steel device is removed from the patient and only the Gore-Tex ACT remain in the patient permanently. We gave the Trap Device, Shorts Model, and Box-Spring Model each a rating of 9 for biocompatibility due to the possibility that the patient will require blood thinners.

Durability

Each of our design alternatives cinches the free ends of the ACTs – the ends not anchored to the leaflet or papillary muscle. The different designs use either steel or Gore-Tex as the ACT material. The material used to anchor the ACTs dictates the material of the entire ACT because complications and risks are involved with having an ACT composed of more than one material.

The Knot Tying Device received a rating of 7 for durability because Gore-Tex does not hold onto the leaflet and papillary muscle as well as 316L stainless steel does. Stainless steel is a more rigid material than Gore-Tex so steel hooks are able to more firmly anchor the ACT. Therefore, over time, there is a greater chance that the ACT made of Gore-Tex will detach from the leaflet or papillary muscle. The Trap Device received a rating of 3 for durability because of the large potential for the Gore-Tex ACT to slip in the wire mesh trap. The diameter of the trap increases slightly when the mitral valve opens, allowing room for the Gore-Tex to move. Consequently, the length of the ACT can change, which reduces the success rate of minimizing MR. There is also the potential for the Gore-Tex ACT to detach from the leaflet or papillary muscle for the same reason as for the Knot Tying Device. The Shorts Model ACT is made of 316L stainless steel. Therefore, it is firmly anchored to the papillary muscle and leaflet. However, the device itself is made out of PP which is not as durable as 316L stainless steel and has the potential to wear over time due to the rubbing of the stainless steel ACT against the PP surface. Because to this concern, we gave the Shorts Model a rating of 6 for durability.

For the Box-Spring Model, both the ACT and the device itself are made of 316L stainless steel, which is very durable. We do not anticipate detachment of the ACT because of the rigid stainless steel flower hooks that grip the leaflet and papillary muscle (completed in 2010). All elements in the Box-Spring Model – springs, boxes, buttons, pins, sliding bars, and ACTs – are made of 316L stainless steel, making it the most durable design of our four alternatives. The

Box-Spring Model is the only design that is made completely out of steel; the body of the Shorts Model is made of bendable material with an elastic component, the Trap Device uses ACT made of a flexible material, and the Knot Tying Device uses Gore-Tex ACT that can be securely tied together. We rated the Box-Spring Model a 10 in durability.

Ease of Deployment

Ease of deployment scores were based on the ability of the physician to insert and cinch the device with minimal complications. We looked at the catheter size and mechanics of the cinching mechanism in order to determine ease of deployment scores. The smaller the catheter size, the easier it is for the physician to maneuver the device over the aortic arch.

The Knot Tying Device was given a score of 5 for ease of deployment. The Knot Tying Device is 8 mm wide and requires a 24 F catheter (the largest catheter able to fit within an average-sized femoral artery). The Knot Tying device fits snugly in the 24 F catheter, which could cause difficulties for the physician when pushing the Knot Tying device through the catheter. The Knot Tying Device also requires the physician to remove the cover of the device once inside the LV, which is an extra step and requires a higher skill level. The Trap Device, which can be inserted lengthwise into the femoral artery, requires an 18 F catheter. Once the Trap Device is in the LV, the physician must turn the device so that it is oriented lengthwise along the line stretching from the leaflet to the papillary muscle. The turning of the Trap Device requires the physician to torque the guide wire to create a hook or to use a guide wire with a mechanical clamp component. This extra complexity to the deployment of the Trap Device results in the Trap Device receiving a score of 6 for ease of deployment.

The Shorts Model requires an 18 F catheter, the same size as the Trap Device. Clamping devices must fit around the push buttons during deployment so that the buttons can be pushed to cinch the ACT. Yet because the Shorts Model is deployed at an angle, the device and the clamps have minimal movability during deployment. We rated ease of deployment a 7 because we believe the restricted movement will require the physician to have a higher skill level, but will not be as difficult as turning the Trap Device. The Box-Spring Model requires an 18 F catheter and has a spring releasing system to cinch the ACT, which is initiated by the physician outside of the patient's body. The Box-Spring Model requires the same sized catheter as the Shorts Model, yet is not inhibited during deployment by the bulky clamping devices due to its ability to cinch the ACT from outside of the body. Thus, we gave it a rating of 10 for easy of deployment.

Ease of Adjustability

The Knot Tying Device was given the lowest rating for ease of adjustability (score of 3) because the physician has minimal control over the slack in the knot created in the Knot Tying Device. It is important to cinch the ACT at a specific length – when MR is minimized – and it may be difficult to do so with this slack. The Trap Device was given a score of 6 for ease of adjustability because we anticipated complications associated with threading the ACT through the Trap Device lengthwise. Threading the ACT through the Trap Device and then delivering the device lengthwise will cause one of the ACT to be wrapped around the Trap Device, which could lead to issues of adjustability once inside the LV. The Shorts Model and the Box-Spring Model both use custom designed U-shaped clamps to guide them into and within the LV. Both models also allow the lengths of the ACTs to be easily adjusted by the physician, who pulls on the cordae from outside the body. This method is the easiest for the physician to control. Once in

the LV, the physician guides the Shorts or Box-Spring Model with the U-shaped clamp and pulls on the ACTs until there is minimal MR on the TEE. We gave both the Shorts Model and the Box-Spring Model rating of 9 for ease of adjustability.

Mechanical Effectiveness

Mechanical effectiveness assess the ability of the device to replicate the physiological condition of the heart with minimal MR. The Knot Tying Device was given a score of 5 because it has no component that accounts for the force and change in length. It is simply a string of Gore-Tex tied with a knot. The Trap Device was given a score of 3 because there is no component in the Trap Device that accounts for the force and change in length, but there is also the additional element of slippage, which drastically decreases the mechanical effectiveness of the Trap Device. The material of the Shorts Model, PP, accounts for the elasticity of the cordae. However, because of the angle between the sleeves of the Shorts Model, the ACT feed into the device at non-natural angles; the ACT do not form a straight line stretching from the leaflet to the papillary muscle. Thus, the force along the ACT is not equally applied at all the points from the leaflet to the papillary. Because of this complication, the Shorts Model was given a score of 7. The Box-Spring Model was given a high rating because the spring component adjusts for the change in length and elastic motion of the ACT. The spring responds instantaneously to an applied force; the spring extends as the LV blood pressure increases. The spring is able to relax and allow blood to flow into the heart as the LV pressure decreases. This replicates the physiological condition of the heart. The Box-Spring Model will allow for two spring options – one for patients with hypertension and one for patients with normal blood pressure.

Cost

Cost was based on the material of the cinching device and the material of other necessary devices needed to implement the cinching device. The Knot Tying Device, Trap Device and Shorts Model were all rated similarly for cost (score of 9) due to similar materials used. We anticipate the Box-Spring Model will be more expensive because of manufacturing constraints. Thus, the Box-Spring Model was given a rating of 6.

Chosen Design for Cinching Device

We chose the Box-Spring Model as the design for our cinching device because of its high Pugh Chart score of 477. Despite the expected higher cost, this model offers the safest approach and best replicates the physiological conditions of the heart.

Box-Spring Model

The Box-Spring Model is broken into:

- Design specifications
- Necessary items for procedure
- Detailed device description
- Procedure

Design Specifications

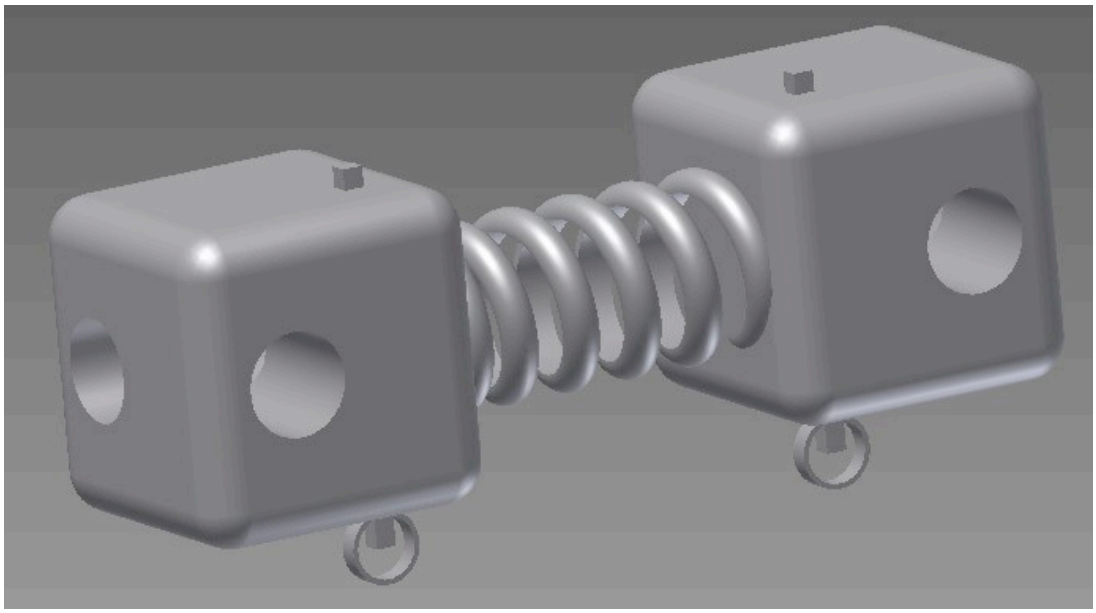

Figure 4. Box-Spring Model isometric external picture. Holes are the paths for the ACTs and pins are currently preventing the internal springs from releasing

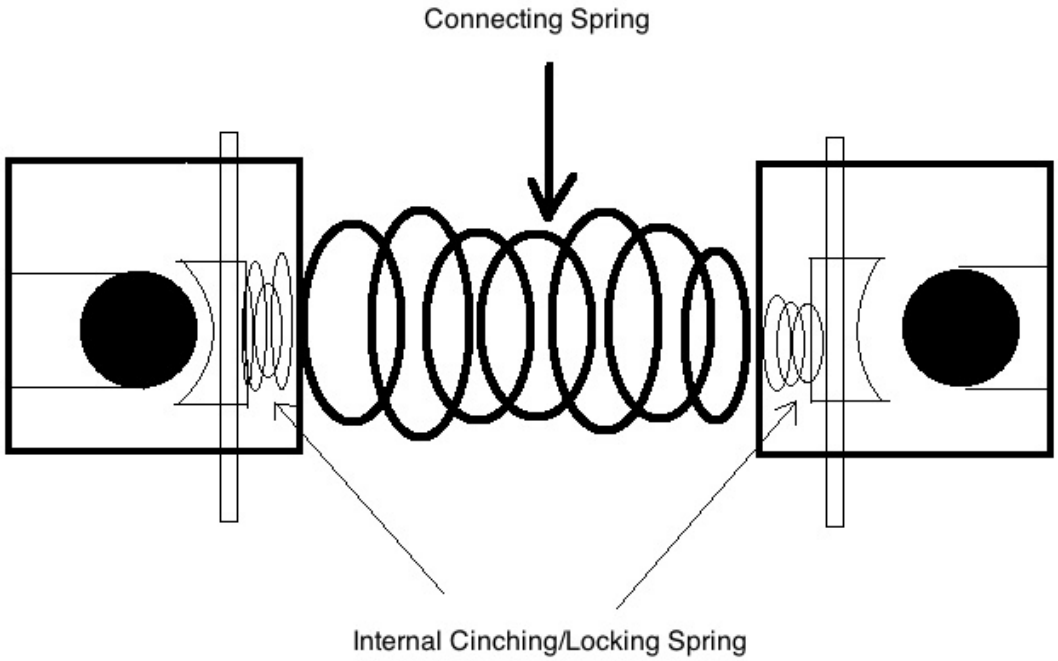

Figure 5. Depiction of the internal components of the Box-Spring Model

1. Materials of cord, boxes, and springs: 316L stainless steel
2. Boxes are 1.5x1.5x1.5 mm cubes
3. Boxes are connected by a spring of length 1 mm in the relaxed state
4. The connecting spring is designed to be extended ~1 mm during heart contraction
5. The connecting spring's standard extended length will be about 2 mm long
6. The four holes are centered on the face of the cube where they occur and have a diameter of 0.5 mm (1.5 French)
7. The holes meet and extend straight to the middle of the cube
8. Diameter of ACT: 0.5 mm
9. Diameter of connecting spring: 1 mm (3 French)
10. Extended surface area: 31.7 mm^2
11. Relaxed surface area: 28.6 mm^2

12. Extended volume: 8.32 mm^3
13. Relaxed volume: 7.53 mm^3
14. Weight: 60 mg
15. Diameter of internal locking springs: 0.75 mm
16. Compressed internal locking spring length: 0.375 mm
17. Extended internal locking spring length: 0.675 mm
18. Pins are 0.1mmx0.1 mmx1.8mm
19. Pin rings have an internal diameter of: 0.3 mm
20. Pin rings have an external diameter of: 0.36 mm

Necessary Items for Procedure

1. ACTs: one attached to the leaflet and one attached to the papillary muscle
2. 18 French delivery catheter
3. A U-shaped delivery guide wire that has a notch with a 1 mm diameter and a length of 2 mm. It will clamp onto the spring and deploy the device while the spring is in its extended state.

Detailed Device Description

The Box-Spring Model involves two small boxes joined by a connecting spring. The ACTs are threaded through the boxes. The boxes are in line with each other and each have a hole on side opposite the connecting spring, as shown in Figure 4. Inside of each box, there is a pin that holds the locking mechanism in its retracted (unlocked) position (refer to Figure 5) – this is when the internal springs are compressed. 4-0 Gore-Tex sutures are attached to rings on the

ends of the pins (refer to Figure 6). The Gore-Tex sutures extend over the aortic arch and out of the patient through the femoral artery. Once the ACTs have been adjusted to the correct length, the physician will pull the Gore-Tex sutures, removing the pins and releasing the locking mechanism to cinch the ACTs. This design is summarized in Figure 6 below.

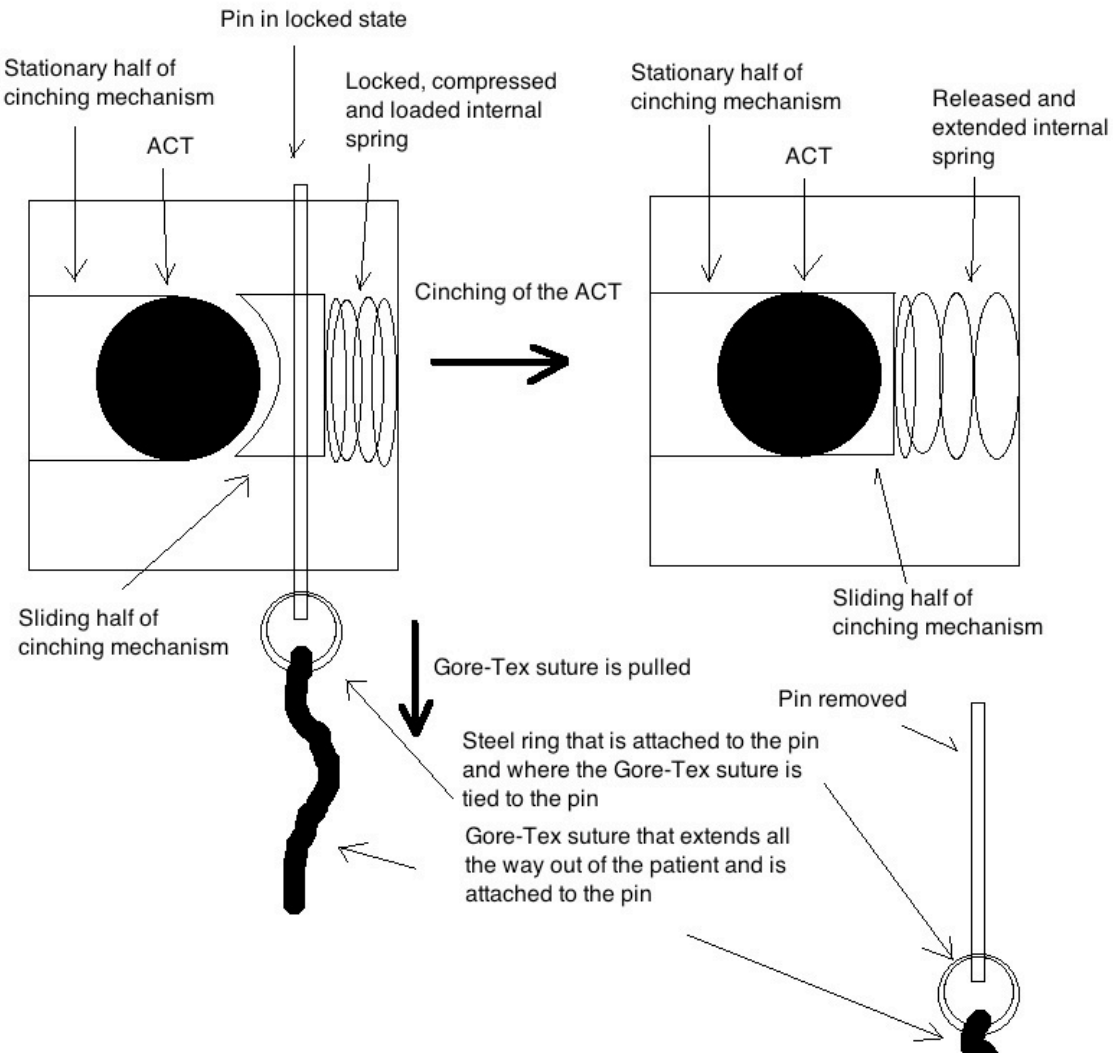

Figure 6. Detailed internal views of the cinching process and interaction of all the components

This device allows the ACT to extend in a straight line from the leaflet to the papillary muscle. In this way, all of the force applied along the ACT will go into extending the spring.

The boxes are made of a rigid material, 316L stainless steel, so the extension of the system is completely accounted for by the spring.

The ACTs are to be cinched while the spring is in its extended state and when the mitral valve is closed. The spring is deployed in its extended sate by using a specifically dimensioned U-shaped guide wire that fits around the spring and holds the boxes apart to keep the spring extended as the physician deploys the device. Each ACT is cinched independently. Cinching is controlled by the physician, who pulls the locking pins out (as described earlier) when mitral regurgitation is visibly minimized through TEE.

After deployment and cinching, the spring is in its relaxed state when the mitral valve is open. When the mitral valve opens, the spring length decreases to its relaxed state. During atrial contraction, the posterior leaflet opens into the LV because atrial pressure increases while LV pressure decreases. While the leaflet is open, the distance between the leaflet and the papillary muscle is minimized. This decrease in distance is accommodated by the spring, which decreases in length and returns to its relaxed state. During ventricular contraction, the force against the leaflet due to the pressure in the LV causes the spring to extend. Decrease in LV pressure during the subsequent atrial contraction then allows the spring to relax again. Figure 7 shows movement of the leaflet with the Box-Spring Model device.

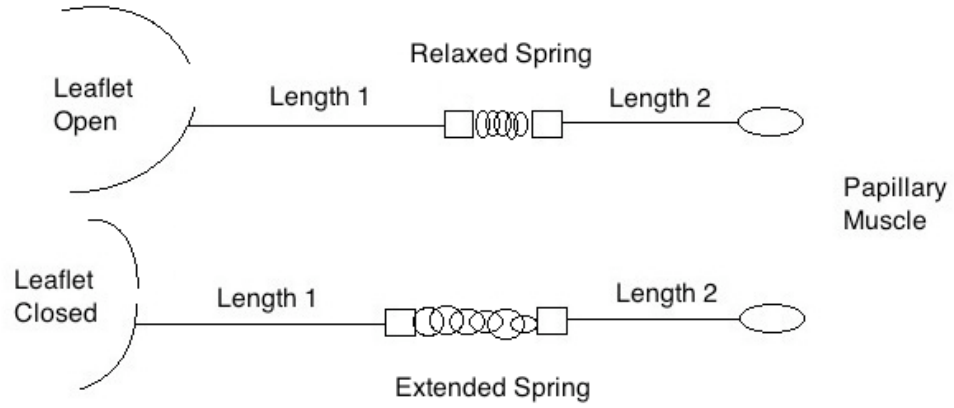

Figure 7. Diagram of how the Box-Spring Model reduces MR with spring extended when the mitral valve is closed and the spring relaxed when mitral valve is open.

Type II MR occurs when the leaflet has exaggerated motion and extends into the left atrium (LA) when it should be closed. When LV pressure forces the leaflet closed, the spring extends from its resting state. But the spring resists this extension, thereby applying a force on the leaflet directed towards the papillary muscle. This helps to prevent the leaflet from prolapsing. Figure 8 illustrates this effect.

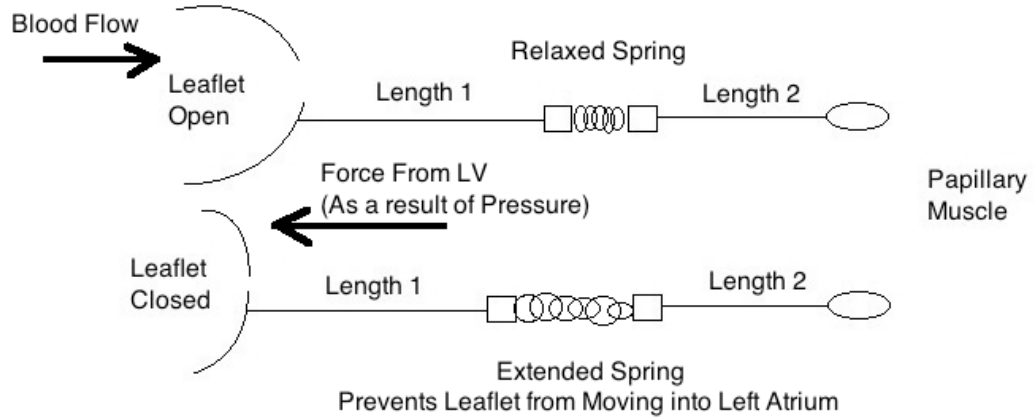

Figure 8. Diagram showing forces and blood flow of how the spring reduces MR with an extended spring when the mitral valve is closed and the spring relaxed when mitral valve is open.

Only a spring component is needed to adjust for the change in length because the heart undergoes elastic motion, not visco-elastic motion. The spring responds instantaneously to an

applied force, which allows it to relax in response to decreased LV pressure and extend in response to increased LV pressure. The spring compensates for the exaggerated motion of the leaflet by applying a slight force downwards towards the interior of the LV. The spring's relaxed state allows normal blood flow into the heart when the leaflet is open.

Overall, the spring allows the artificial system to change in length as the applied force from the left ventricle changes. The calculated spring constant is 12,000 N/m for a patient with normal blood pressure. This spring constant allows the artificial system to simulate biological cordae tendineae and heart motion. The spring constant is calculated in the section, *Box-Spring Model Force Calculation*.

The largest drawback to the Box-Spring Model is the intricacy of the design. The Box-Spring Model is difficult to manufacture due to the small dimensions of the device. The physician performing the procedure may have difficultly threading the ACTs through the device because the physician's hands will be bloody and slippery. A nurse or assistant may need to be present to help with the threading of the device. Once the device is threaded through, the physician will be able to perform the rest of the procedure in the single catheter delivery system.

Cinching in the Box-Spring Model

Specifications

1. Box-Spring Model
    a. The pins and springs are all made of 316L stainless steel
2. Diameter of steel cord: 0.5 mm
3. Diameter of grooved gripping section: 0.5 mm

The cinching device is a clamp that slides into place. Figure 6 above shows a detailed drawing of the different components of the cinching mechanism. The drawing is looking at the side perpendicular to the internal locking spring.

The curved surface in Figure 6 is grooved to be able to secure the steel cord. The curved surface works like pliers – the grooves create friction to ensure that the steel cord does not slip. The diameter of the clamp (formed when the mechanism is cinched) is exactly the same as the diameter of the cord (0.5 mm).

The cinching mechanism was described earlier in the detailed description of the device. For further illustrations, refer to Figures 9 and 10 below, which show internal views of the cinching mechanism. The internal spring is to the right of the pin, attached to the short sliding bar that will slide into place once the pin is removed. The spring is anchored to the internal wall of the box.

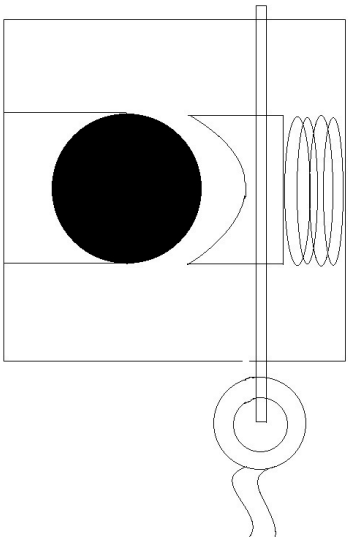

Figure 9. Un-cinched ACT with pin still in place

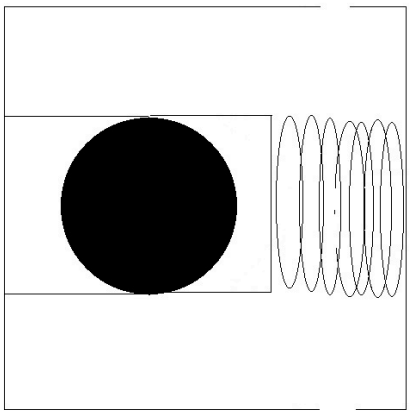

Figure 10. Cinched ACT with pin removed and spring released.

The internal spring that lock the ACT in place have the following dimensions.

Table 2. Constants associated with the internal springs of the boxes that cinch the ACTs.

Constant	Value
Change in Spring Length	0.3 mm
Compressed Spring Length	0.375 mm
Extended Spring Length	0.675 mm
Locking Force Applied to ACT	10 N

Ten Newton's is used as the locking force because that is the tear limit of the ACTs.

Equation 1. Relationship of force, change in length and spring constant of a spring

$F = -k(\Delta x)$ (F: force, k: spring constant, Δx: change in length of the spring)

Equation 1 is used to determine the spring constants in the Box-Spring Model.

Table 3 the calculation of the spring constant for the internal cinching springs

	Force	Δx (Change in spring length)	Normal k (Spring constant)
Internal Locking Springs	10 N	0.3 mm	33,333 N/m

Delivery of Box Model

Specifications

1. Material: Stainless steel
2. U-shaped delivery guide wire that has a notch with a 1 mm diameter and a length of 2 mm. It will mate to the whole length of the extended spring during delivery so it is deployed in the extended state.
3. Compressed spring made of stainless steel attached to the bottom plate.
4. Wide pin with a ring at the end and a Gore-Tex suture attached to the ring. The pin acts as a barrier between the spring and the top arm. The pin keeps the spring in its compressed state.
5. Spring diameter: 1 mm
6. Compressed spring length: 0.7 mm
7. Extended spring length: 1.7 mm
8. Spring constant: 10,000 N/m

The spring is released when the physician pulls the Gore-Tex cord to remove the pin. Once the spring is released, it pushes the arms apart and releases the device.

The main feature of the U-shaped delivery guide wire is the spring that is attached to the bottom plate. The spring is compressed and restrained by a wide pin that has a ring at the end. There is a Gore-Tex suture that is tied to the ring and extends out of the patient. Once the Gore-Tex suture is pulled, the pin is removed and the spring pushes upwards and forces the two arms

apart. Once the two arms are pushed apart, the Box-Spring Model is released into the LV. Figures 11 and 12 show asembled views of the U-shaped delivery guide wire.

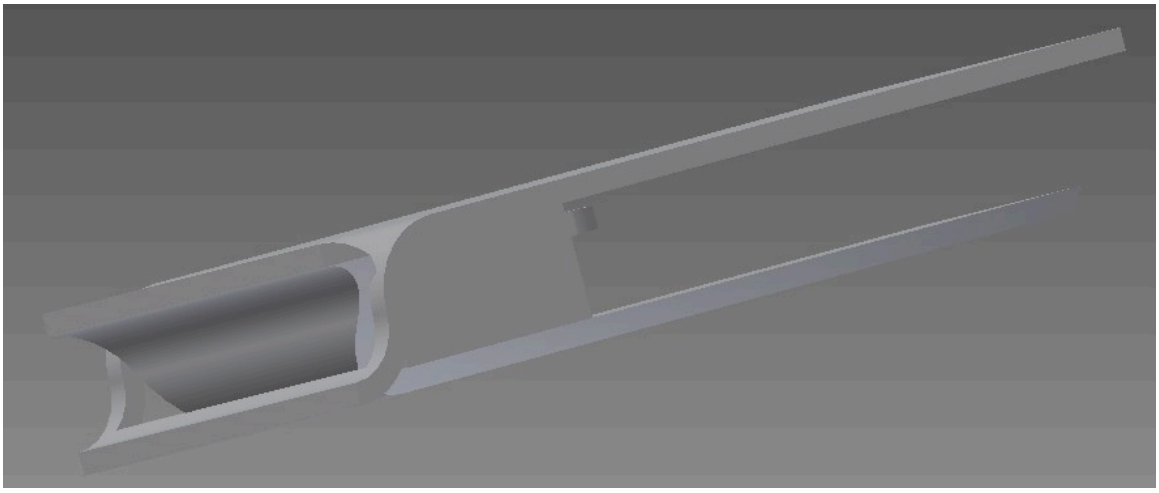

Figure 11. View 1 of the assembled U-Shaped delivery guide wire. The connecting spring of the Box-Spring Model fits between the two arms seen in the bottom left of the figure.

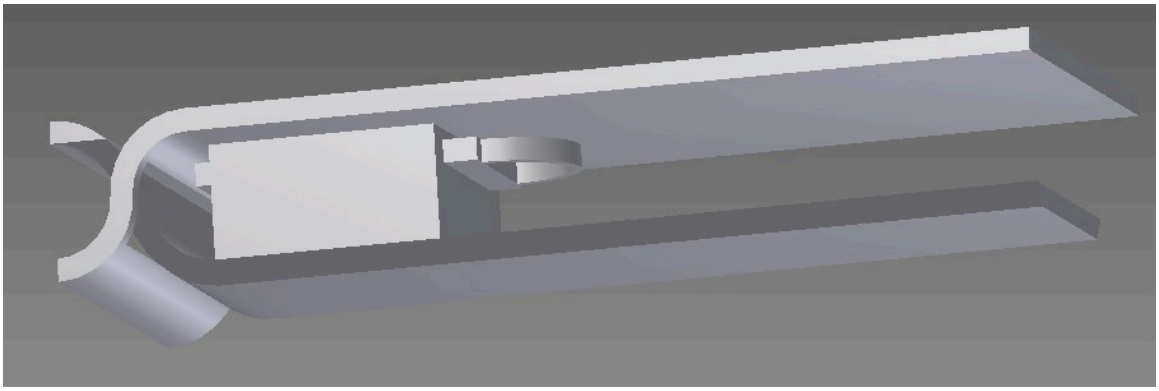

Figure 12. View 2 of the assembled U-Shaped delivery guide wire. The ring and wide pin that restrain the internal spring are seen between the top and bottom plates. The Gore-Tex suture will be connected to the ring.

The U-shaped guide wire will be made of 316L stainless steel. The guide wire will clamp across the entire extended spring, length 2 mm, so the spring does not deform during delivery. The U-shaped guide wire for the device is shown in Figures 11 and 12. The delivery guide wire and the Gore-Tex suture will be threaded out of the patient.

The guide wire allows the physician to push the device to desired position within the LV. After the ACTs are cinched, the Gore-Tex suture will be pulled. When the Gore-Tex suture is

pulled, the wide pin will pull out and release the spring. The spring will then push the two arms of the clamp apart and release the Box-Spring Model. The delivery U-shaped guide wire is then removed from the patient's body. Figures 13 and 14 show the bottom plate of the guide device, which connects to the top clamping arm.

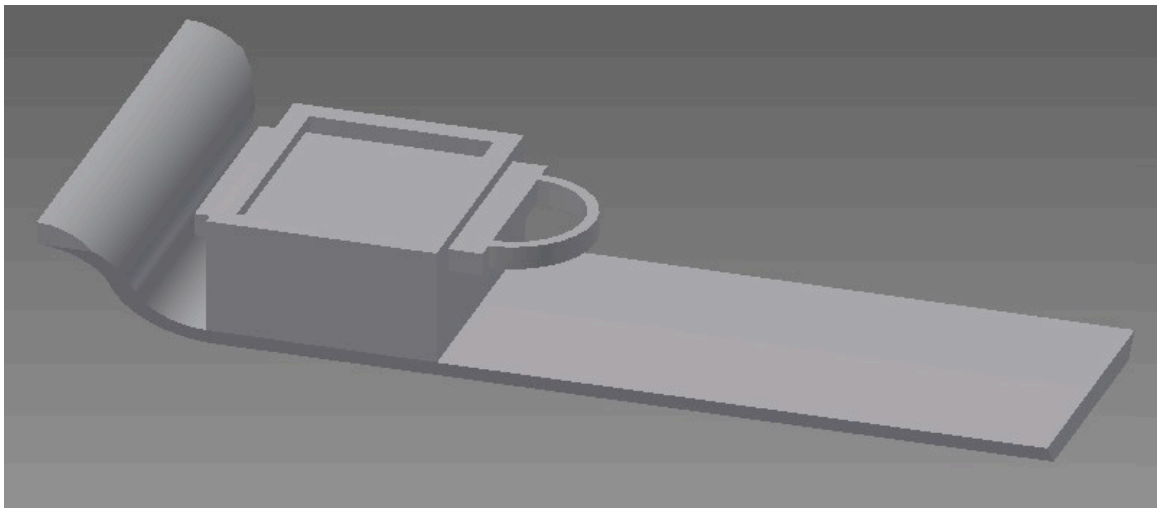

Figure 13. View 1 of the bottom plate-top arm of the U-shaped delivery guide wire. The box that contains the spring is clearly visible as well as the wide pin. The Gore-Tex suture will be attached to the ring.

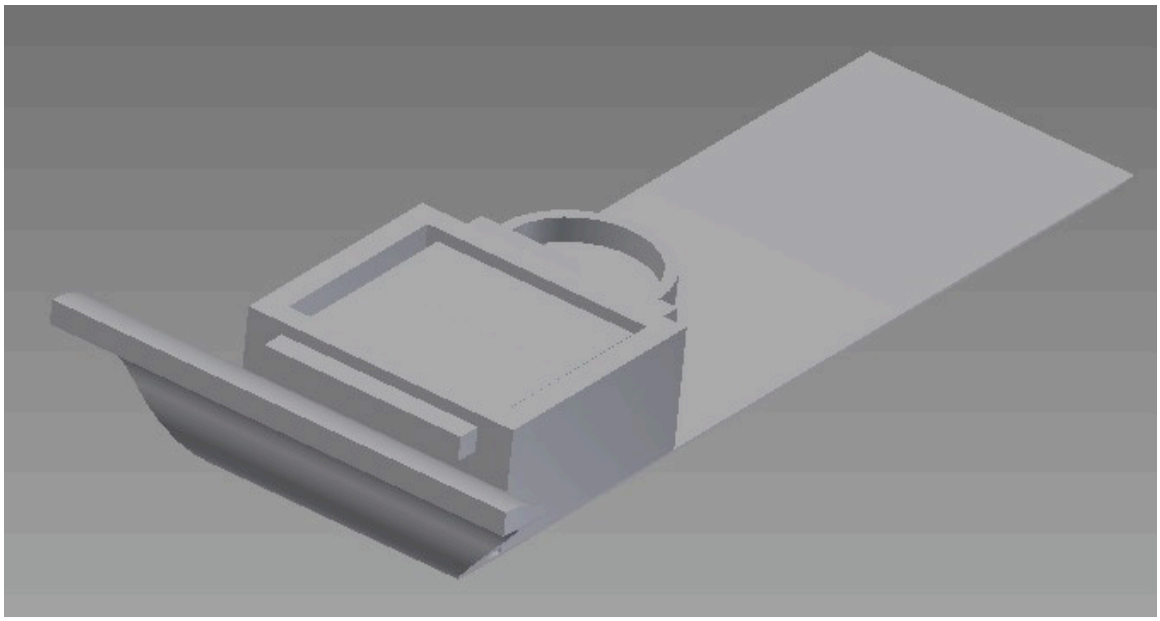

Figure 14. View 2 of the bottom plate-top arm of the U-shaped delivery guide wire

Figures 15 and 16 show the top plate of the guide device, which connects to the bottom clamping arm.

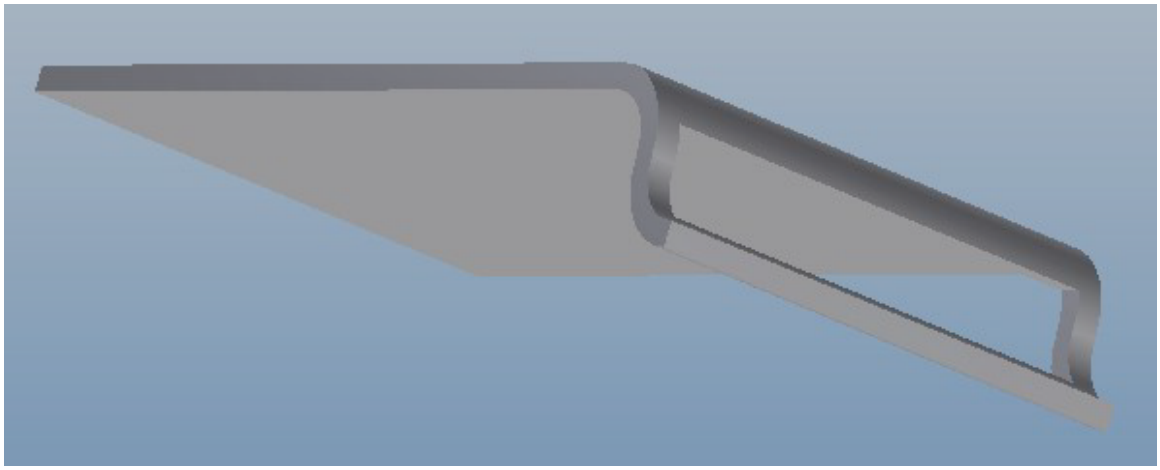

Figure 15. View 1 of the top plate-bottom arm of the U-shaped delivery guide wire. The hole in which to other half of the assemble fits into is clearly visible.

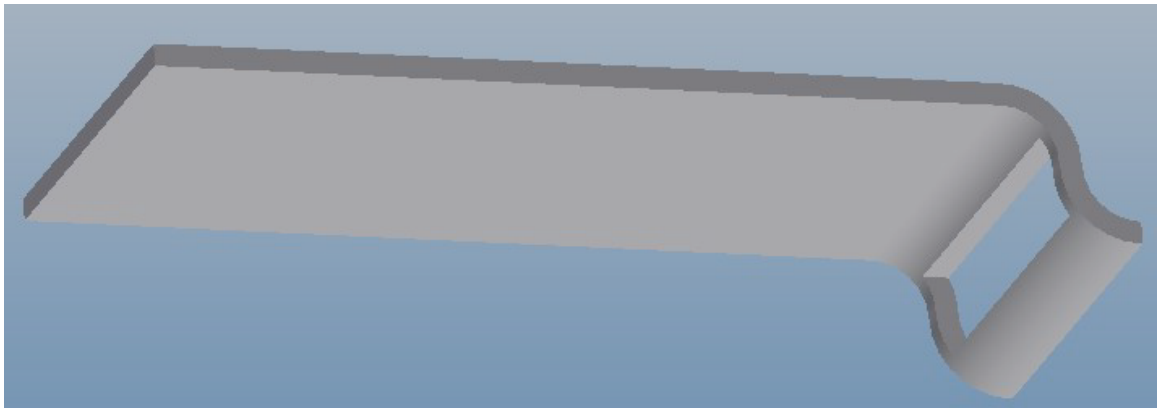

Figure 16. View 2 of the top plate-bottom arm of the U-shaped delivery guide wire. The hole in which to other half of the assemble fits into is clearly visible.

The bottom arm of the clamp has a hole that allows the top arm of the clamp (extending from the bottom plate) to slide through. When the spring of the guide device is compressed, the clamp fits securely around the spring of the Box-Spring Model device so that the Box-Spring Model device is released only when the spring pushes the two arms apart.

Procedure

After the ACTs have been attached to the leaflet and the papillary muscle (steps 1 and 2 of the repair procedure), they are pulled through the aortic arch and out of the patient through the femoral artery. The following steps are then done by the physician outside of the patient's body.

1. Thread the ACTs through the boxes – into the holes on the sides opposite the spring and out of the holes on the sides adjacent to the spring.
2. Place the U-shaped guide wire around the connecting spring.
3. Position the device at the opening to the femoral artery such that the spring is perpendicular to the axis of the femoral artery, as shown in Figure 17.

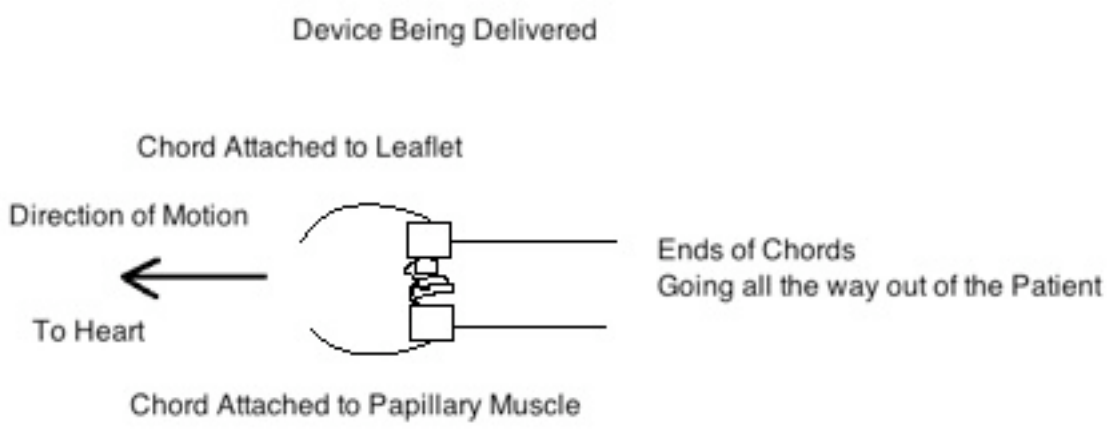

Figure 17. Diagram of how ACTs are threaded into the Box-Spring Model and the direction the Box-Spring Model is inserted into the femoral artery.

The device is then guided through the catheter from the femoral artery to the LV. The following steps are completed inside the patient's LV by the physician.

1. Once the device is in place (between the leaflet and papillary muscle), adjust the ACTs to the correct length. To determine the correct length, the physician watches for when MR is minimal on the TEE.

At this point, the ACTs are not yet cinched. The length of the system is preserved because the spring is being held in its extended state by the U-shaped guide wire so that no force is transferred to the spring. The ACTs have to be cinched when the leaflet is closed because that is when MR is visible. The cinching mechanism is flush against the holes on the sides of the boxes adjacent to the connecting spring. The cinching mechanism is described below.

2. Once MR is reduced, pull the Gore-Tex sutures attached to the pins to release the internal cinching mechanism.
3. Pull the Gore-Tex suture attached to the wide pin of the U-shaped delivery guide wire to release the Box-Spring Model device.
4. Remove the U-shaped delivery guide wire from the patient's body.

Box-Spring Model Force Calculations

The Box-Spring Model uses a spring to prevent the mitral leaflet from prolapsing into the LA. The total length of the artificial extended system is 5 mm. According Kara and Elkin's research summarized in Figure 18, the average change in length of the biological CT in the LV is 1 mm.

Average Distance between Spring-Loaded Clip and Apex Clip

Dog no.	No. of beats	Spring-loaded clip position	Rapid ventricular filling	Slow ventricular & atrial systole filling	Isovolumetric systole	Ventricular ejection
1	50	Free margin of anterior leaflet	40.0 mm (SD ± .97 mm)	42.4 mm (SD ± .20 mm)	43.4 mm (SD ± .85 mm)	42.2 mm (SD ± .16 mm)
2	24	Free margin of posterior leaflet	48.0 mm (SD ± .27 mm)	48.0 mm (SD ± .27 mm)	48.0 mm (SD ± .27 mm)	48.0 mm (SD ± .27 mm)
3	14	On chordae tendineae 2 mm above anterior papillary muscle	37.8 mm (SD ± .19 mm)	37.8 mm (SD ± .19 mm)	40.0 mm (SD ± .56 mm)	37.8 mm (SD ± .19 mm)
4	15	Free margin of anterior leaflet	41.0 mm (SD ± .78 mm)	41.5 mm (SD ± .09 mm)	42.8 mm (SD ± .55 mm)	41.5 mm (SD ± .13 mm)
5	14	On chordae tendineae 10 mm above anterior papillary muscle	46.7 mm (SD ± .78 mm)	47.5 mm (SD ± .05 mm)	48.8 mm (SD ± 1.15 mm)	47.5 mm (SD ± .14 mm)
		Free margin of posterior leaflet	56.2 mm (SD ± 1.35 mm)	60.0 mm (SD ± .16 mm)	61.2 mm (SD ± .70 mm)	60.0 mm (SD ± .05 mm)

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Figure 18. Shows change in length of CT in the left ventricle

Figure 19 shows the general physiology of the LV and how the Box-Spring Model will compensate for MR. The two lower illustrations in Figure 19 show the device in its relaxed and extended state. The spring naturally wants to be relaxed and short. The force due to the pressure in the LV extends the spring slightly. The change in length of the device is due only to the spring as the ACTs do not change in length.

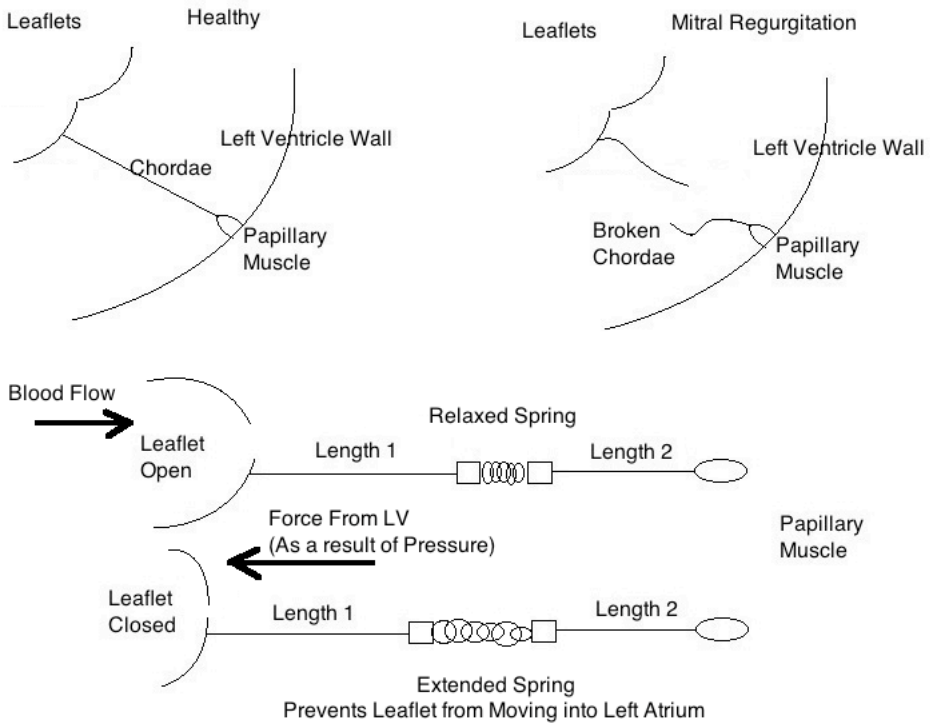

Figure 19. Box-Spring Model with spring components minimizes MR

Figure 20 shows the blood entering the LV, which forces the leaflet open and allows the spring to passively return to its relaxed state. The second image in Figure 20 shows that during ventricular contraction, a force is exerted upwards on the leaflet. The peak blood pressure in the LV can be used to calculate the force that extends the spring just enough to completely close the valve. The arrows show the direction of blood flow and the force that dominates the system.

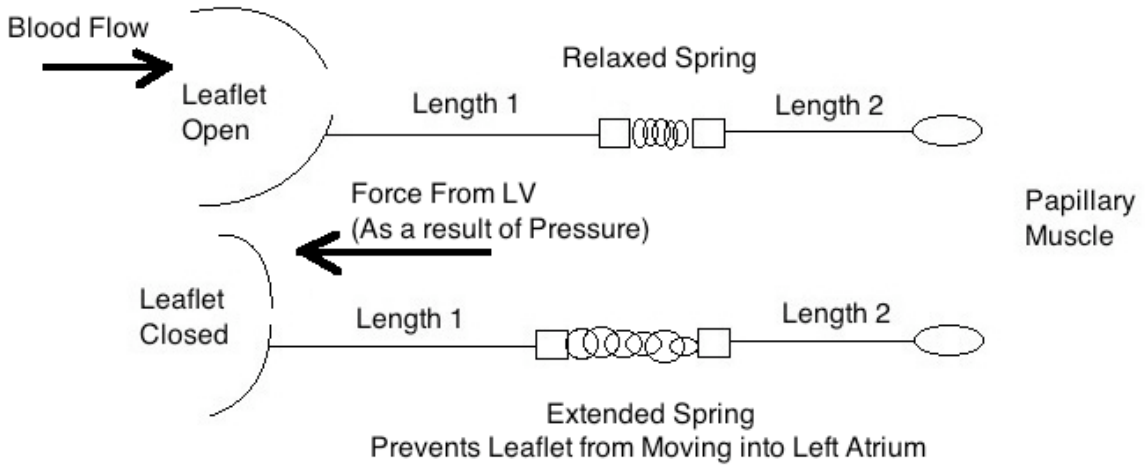

Figure 20. Force of Blood causing the mitral valve to open and shut

Table 4 shows the constants used to calculate the connecting spring's spring constant.

Table 4. Constants used to calculate the connecting spring's spring constant

Constant	Value
Change in Spring Length	1 mm
Relaxed Spring Length	1 mm
Total length of relaxed Device	4 mm
Area of anterior leaflet	3.8 cm^2
Area of posterior leaflet	7.6 cm^2
Normal systolic blood pressure (normal person)	120 mm Hg=15,998 Pa
Max systolic blood pressure (a person with hypertension)	140 mm Hg=18,665 Pa

Equation 2 is used in to determine the connecting spring's spring constant.

Equation 2. Relationship among pressure, force and area

$$P = \frac{F}{A}$$

The leaflets cannot exert any torque because they are very thin and pliable. The force is generated by the pressure acting on the cross sectional area.

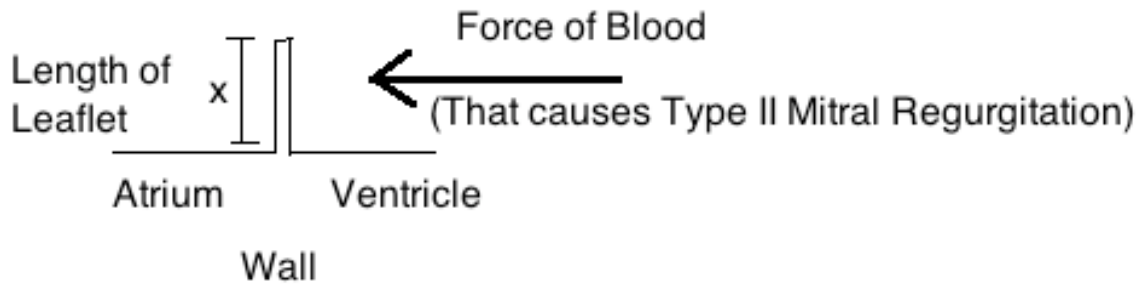

Figure 21. Leaflet model for force calculations

Table 5. Normal and Max Tension in the Anterior and posterior leaflet

	Area of leaflet	Normal systolic blood pressure	Max systolic blood pressure	Normal Tension	Max Tension
Anterior Leaflet	3.8 cm^2	15,998 Pa (1.5998 N/cm^2)	18,665 Pa (1.8665 N/cm^2)	6 N	7 N
Posterior Leaflet	7.6 cm^2	15,998 Pa (1.5998 N/cm^2)	18,665 Pa (1.8665 N/cm^2)	12 N	14 N

The ACT will be anchored at the edge of the leaflet to allow for maximum prevention of mitral regurgitation.

The posterior leaflet is the main leaflet involved in MR and therefore the leaflet considered through the remaining calculations. For a normal patient, the tension needed to cause an extension of 1 mm must be 12 N because that is the force perpendicular to the leaflet that causes leaflet motion. For our purposes, we will assume patients are normal.

Now, the spring constant is calculated. Equation 1 is used again to determine the connecting spring's spring constant.

Table 6. Spring constant for patients with normal blood pressure

	Normal Force	Δx (Change in spring length)	Normal k (Spring constant)
Posterior Leaflet	12 N	1 mm	12,000 N/m

The spring constant is such that, when the maximum upward force is exerted on the leaflet during ventricular contraction, the spring stretches so that the leaflet closes the valve and

does not prolapse into the LA. During ventricular relaxation, pressure in the LV decreases and the spring passively relaxes and shortens.

The spring constant for people with normal blood pressure is used in all cases to simplify the manufacturing process. It is assumed the normal spring constant will be adequate for all patients.

Blood does not instantaneously enter the LV, and the spring adjusts to that by opening an amount proportional to the force of blood entering the LV. As the LV pressure changes and the pressure differential favors a closed mitral valve, the spring begins to extend and helps the chordae close the valve to eliminate MR.

Material Analysis

The device will be in the patient's heart for the remaining life of the patient ranging from 20 to 50 years, depending on the age of the patient. Since the device will be in the heart for an extended period of time, the material chosen is of great importance. The device cannot have sharp edges or deep valleys to prevent cell build up on the device. There is a high likelihood there will be some tissue buildup on the device, despite the best efforts to make the device smooth. Therefore, there is the potential for the device to become larger overtime due to cell build up. The material chosen needs to be strong enough to withstand any possible degradation by the blood.

The device will be delivered using an 18 French catheter, which is standard. The catheter sheaths and guide wires are standard and disposable. They do not remain in the patient; therefore biocompatibility is not a main issue. The guide wire and catheter will follow the path from the femoral artery, through the aorta and into the left ventricle. The risks of puncturing an artery or the aorta are low as long as the physician is gentle, slow and trained well. If there were a puncture anywhere from the femoral artery to the left ventricle, the patient would be in great danger and could possibly die.

Infection is a risk in any operation. Catheters and guide wires come in sterile packaging and can be further sterilized if the physician thinks it is necessary. Transesophageal Echocardiography (TEE) will be used to guide the device into the left ventricle and view MR in real time. Since steel is metal, it will show up on TEE. The ACTs will be made of steel and the sutures attached to the pins will be made of Gore-Tex. Both of these materials will be available to be purchased in the lengths we need and not be a financial burden. Table 7 shows our materials list.

Table 7. Manufacturing parts list

	Part	Material	Manufacturer	Amount
Catheter System	Catheter	Polyurethane (FDA approved)	McMaster Carr (8787K712)	2
	U-shaped guide wire	316 Stainless steel wire	McMaster Carr (1305T11)	1
	Heparin	Protein/Saline Solution	Sigma Aldrich (H6508-5ML)	1
Box-Spring Model	Steel ACT	16 Stainless steel wire (0.5 mm Diameter)	McMaster Carr (1305T11)	2
	Boxes	316 Stainless steel	McMaster Carr (2317K11)	2
	Internal Spring	316 Stainless steel	McMaster Carr (2317K11)	2
	Connecting Spring	316 Stainless steel	McMaster Carr (2317K11)	1
	Box Locking Pins	316 Stainless steel	McMaster Carr (2317K11)	2
	Gore-Tex String	4-0 Suture	Gore Medical	3
	U-shaped Guide Wire (Top and Bottom)	316 Stainless steel	McMaster Carr (2317K11)	1
	U-shaped Guide Wire Internal Spring	316 Stainless steel	McMaster Carr (2317K11)	1
	U-shaped Guide Wire Pin	316 Stainless steel	McMaster Carr (2317K11)	1

Table 7 shows the parts needed, the materials they are made of, the manufacturers of the materials, and the numbers needed of each part. Because cinching is the third step in the repair procedure, guide wires and catheters have already been used to create a path from the femoral artery to the LV.

Table 8. Pricing parts list

	Part	Price	Lead Time	Amount
Catheter System	Catheter	$52.91	1 day	1
	Heparin	$63.90	1 day	1
Box-Spring Model	Steel ACT	$8.50	2 weeks	2
	Machining of Boxes	$61/hr	2 weeks	2
	Machining of Internal Spring	$61/hr	2 weeks	2
	Machining of Connecting Spring	$61/hr	2 weeks	1
	Machining of Box Locking Pins	$61/hr	2 weeks	2
	Gore-Tex String	$25	N/A	3
	Welding of Device	$61/hr	2 weeks	N/A
	Bottom Plate U-shaped Guide Wire	$61/hr	2 weeks	1
	Top Plate U-shaped Guide Wire	$61/hr	2 weeks	1
	Machining of U-shaped Guide Wire Internal Spring	$61/hr	2 weeks	1
	Machining of U-shaped Guide Wire Pin	$61/hr	2 weeks	1

John Kreitler, the head of the Machine Shop at Washington University Medical School, discussed the cost of producing the custom pieces of the device. He helped us form Table 8. Because the device is completely novel and unique, it will be fairly costly to produce until it becomes mainstream. Even the springs need to be manufactured specially because of their size and required spring constants. Steel is fairly inexpensive, but labor costs will contribute to most of the cost of our device because it must be specially made. The estimate of the time it will take to produce one complete device is 60 hours. With an estimated labor cost of $61/hour, labor costs total $3,660. This labor cost estimate is most likely a minimum number due to unforeseen complications and attention to detail.

Stent manufacturing companies are the most qualified to produce our device because some stents are made of 316L stainless steel and are of comparable sizes. Stent manufacturing companies have access to steel and manufacturing processes that create very small and delicate devices.

Gore-Tex

Specifications:

1. Breaking strength: 1,000 g.
2. Clip strength: 500-g threshold.
3. Typically Gore-Tex suture diameter is 5.0 French (1.667 millimeters).

Gore-Tex can withstand the physiological conditions of the left ventricle, making it the most commonly used material for the ACT. Yet Gore-Tex sutures are difficult to maneuver and anchor to the leaflet and ventricle wall because they are not sturdy and have little grip. We used Gore-Tex clip and tear strength as our minimal criteria for our material for the ACT.

316L Stainless Steel

316L stainless steel is a low carbon steel and is biocompatible and resistant to corrosion. These are the two of the most important criteria for our cinching device. 316L stainless steel is the traditional choice for bare metal and drug eluting stents. Stents are comparable in size to our device so we believe this is a strong candidate for the material for both the Box-Spring Model device and the ACTs.

- Biocompatible
- Strong (Tensile Strength 515 MPa, Rockwell Hardness 95)
- Durable: corrosive Resistant
- Easy to machine because of low carbon content

Properties:

Table 9. Properties of 316L Stainless Steel

Tensile Strength (MPa) min	Yield Strength 0.2% Proof (MPa) min	Elongation (% in 50mm) min	Rockwell B (HR B) max Hardness	Density (kg/m^3)	Elastic Modulus (GPa)	Brinell (HB) max Hardness
515	205	40	95	8000	193	217

Safety

DesignSafe Analysis

A DesignSafe analysis of the MitraGuard device and its procedure was completed. The full report can be found in the appendix. The potential victims that were taken into account include patients, surgeons, nurses, and technicians. The software indicates the following risks for the patient: administration of the wrong medication or dosage, puncturing of the skin to access the femoral artery, and bacterial infection due to improper dressing of the wound. In this procedure, an 18 French catheter is used so that the puncture size can be small enough to not require stitches. During the catheter procedure, an anticoagulant (eg. heparin) must be administered to the patient. In addition, because the MitraGuard device is made of 316L stainless steel, the patient may be at increased risk for blood clots, so he/she may need to be prescribed an anticoagulant post-surgery as well. In order to reduce the risks associated with administering the medication, the doctor and nurse need triple check that the drug and dosage are correct. They also need to keep the surgery area and equipment clean at all times and properly dress the patient's wound in order to avoid infection. Note that these sources of risk are associated with all catheter surgeries, not just this one in particular.

The device itself does not have any sharp edges or points, so machining, testing, and handling the device do not pose any serious risks. There is the possibility that skin could get pinched between the two boxes, yet because of the small size of the device, this would not cause any serious injury. Note that the device is very small and should be handled with care. Lastly, because the doctor and nurse are dealing with an open wound in the patient's thigh, they are at

risk for potential blood borne diseases. But as long as the usual preventative measures are taken, this risk should be negligible.

Table 10 DesignSafe analysis summary

User	Task	Hazard Category	Hazard	Severity	Probability	Risk Level	Risk Reduction Methods
Doctor	Operate on patient	Biological / health	Blood borne diseases	Moderate	Remote	Negligible	Be cautious during procedure and take preventative measures
		Mechanical	Pinch point	Minor	Unlikely	Negligible	Handle device with care
Nurse	Dress Wounds	Biological / health	Blood borne diseases	Moderate	Remote	Negligible	Be cautious during procedure and take preventative measures
Surgical Technician	Setup supplies/ equipment/ instruments for operation	Mechanical	Pinch point	Minor	Unlikely	Negligible	Handle device with care
Patient	Normal operation	Biological / health	Wrong medication/ dosage	Moderate	Unlikely	Low	Doctor or nurse administering the medication needs to triple check the drug and dosage
			Bacterial	Moderate	Unlikely	Low	Surgery area and equipment need to be kept clean and patient's wounds need to be properly dressed
		Mechanical	Stabbing/ puncture	Moderate	Unlikely	Low	Using an 18 French catheter allows puncture to be very small so that stitches are not required

Risks for the Patient

The table below provides an overview of the safety concerns for the patient associated with the MitraGuard device and the catheter procedure. The table does not cover every possible safety concern, but it does highlight the major safety concerns. It also provides explanations of how this device and procedure mitigate the risks.

Table 11 Major risks and mitigation of risks

Safety Concern	Risk Level	Design Mitigation	Final Risk Level
Steel material causes blood to clot	High	Patient receives heparin during procedure and is prescribed an anticoagulant as necessary	Low
Blood loss during surgery	Low	18 French catheter requires a very small puncture in thigh	Extremely Low
Valve function disrupted for too long during surgery	Moderate	Surgeon instructed to put as little tension on leaflet as possible when not critical to procedure	Low
Artificial chordae tendineae is of wrong length	Moderate	Surgeon instructed to view TEE for several different heart rates	Low
Device rubs left ventricle wall, causing irritation	Low	Device made very small to sit in the middle of the left ventricle	Extremely Low
Blood flow is altered by device in left ventricle	Low	Device made very small to limit its effect on fluid mechanics	Extremely Low

Conclusion

Problem Solved

The problem of MR is a complicated problem with many unforeseen complications. From a general sense, the Box-Spring Model solves the problem of MR. From a very practical sense, prototypes and clinical trials would be the only way to truly evaluate if MR is fixed by the Box-Spring Model.

Future Directions

There are 4 overall steps to this procedure.

1. ACT is attached to leaflet
2. ACT is attached to papillary muscle
3. ACTs are cinched
4. ACTs are cut

The first 2 steps have already been completed by past groups and the Box-Spring Model and U-shaped delivery guide wire complete step 3. Step 4, cutting of the ACTs is the last step that needs to be developed and designed.

Each piece of each of the 4 steps also needs to be prototyped. There are different opportunities for the pieces to be prototyped. Students could continue the project in BME 402, Dr. Crabtree could advise a group of students to independently pursue the prototyping, or Dr. Crabtree could prototype the pieces himself. Our mentor, Dr. Crabtree, is pursuing this process independently and with three consecutive BME 401 groups. He will be a large factor in moving this project to the prototyping phase.

One roadblock associated with prototyping any and each of the steps is the financial investment needed to complete the prototyping process. Even if the financial investment is

completed through fundraising, grants and donations, the restrictions of lab space, staffing and dedication are additional roadblocks. Testing materials and models would all need to be acquired, which could take years because heart (most likely pig hearts) and technical tools such as catheters and guide wires will all be required. Since undergraduate students are not trained in catheter procedures, a cardiologist or cardiac surgeon would need to be interested and invested to help in the testing and prototyping phase.

Once prototyping is completed, the next step would be to sell, license or patent the prototype. Stent companies would be the first choice of companies to sell the concept to because of their resources, capital and previous work with stainless steel and devices of comparable size. Catheter manufacturing companies are another potential investor of this process. Clinical trials would follow. Clinical trials are very expensive and time consuming. It is not feasible for undergraduates to conduct or manage a clinical trial. Therefore, the clinical trials would most likely be run by the company that purchased the concept.

After the clinical trials are completed, approval from the Food and Drug Administration would be needed. Considering all the road blocks, the most practical avenue is for a large stent or catheter manufacturing company to purchase the idea and fund all the necessary steps. The future directions of this project are extremely intricate and require expertise in a variety of areas.

Ethical Considerations

The goal of this project, procedure and device is to solve MR in patients. The goal inherently has ethical considerations because it is a device that will directly affect an essential organ in human bodies. The device will need to be tested in animals first to be confident it will not harm humans. Then, human clinical trials will need to follow to ensure the device is not only effective in correcting MR, but also safe for use in humans. The clinical trial process is very rigorous and to prevent unethical conduct, the most

important piece is to ensure all participants gave informed consent. Other regulations that will prevent unethical conduct are, HIPAA, the use of independent investigators that use the utmost discretion, competent project management and unbiased statistical analysis. Since participants will be people who are suffering from MR, it will be unethical to deny them treatment, and therefore, the clinical trial will need to be designed to compare current procedures against our procedure. It will also be impossible to keep the physician and patient blind to the treatment given. The inability to blind the study makes this a very complicated clinical trial to analyze. The clinical trial will also need to have a follow up time that is as long as the patients are alive to ensure there is no degradation of the device, cell build up, increase risk of heart attack or stroke or any other unforeseen negative consequences of the device being in the patient for an extended period of time.

The goal of this device and procedure are ethically genuine, but the potential for financial corruption is large due to the inability to blind the study. Everyone involved with the clinical trials and research will need to put the well-being and health of the people they are trying to help ahead of any potential financial or recognition benefits that could result from this device reaching the market.

Lessons Learned

Our whole group was new to the design and development process. A project of this size was new to all of us as well. We learned how to integrate research, existing solutions and creativity to produce something novel. The hardest part was developing and idea that would solve the problem and be practical.

The physiological condition of a beating heart produced much more complicated restrictions than working in a lab or machine shop. Every material used in the process needs to be biocompatible. As opposed to other engineering disciplines, we were much more restricted in size, material and options to cinch our device. Tying a knot is incredibly difficult to do outside the body and place exactly where

needed inside the LV. Welding steel inside the LV is impossible to do safely. Catheter size posed a difficult size and maneuverability constraint.

A critical lesson learned is doctors are busier than people realize. We had to work hard to schedule our weekly appointments with our mentor, Dr. Crabtree, and it took us almost 2 months to shadow a cardiologist in the catheter lab. One needs to make appointments with doctors a top priority because their time is extremely valuable. We also learned the importance of collaborating between clinical and engineering minds. Some terminology was used incorrectly and some practical constraints were hard to convey to the doctors, but we learned how to bridge this gap.

We learned a lot about time management. More time invested earlier always pays off more. This lesson is extremely true when it comes to designing something because there always slight adjustments that can make a model better.

An unexpected lesson learned is that our engineering background will give each of us a unique perspective in the fields we are going to pursue. One of us is going into biostatistics, another into OBGYN and the third into speech therapy. We will be able to think about issues in multiple ways and add a very analytic, detail oriented thought process to the fields we are pursuing.

Intellectual Property

About half of the tools used in our step of the process already exist and the other half are novel. The catheter and process of going from the femoral artery to the LV is a well-established procedure and the tools to get from the femoral artery to the LV are already patented.

Our Box-Spring Model and U-shaped delivery guide wire are both novel and unique. They both constitute intellectual property because they are not commercially available nor are concepts like them commercially available. The underlying pin-Gore-Tex suture-spring method is an underlying concept of each of our novel devices.

There are patents for procedures that involve clipping the mitral valve, replacing various heart valves, and open heart ACT attachment. However, the concept of a four step trans-femoral percutaneous ACT attachment procedure is novel.

Dr. Crabtree is one of the front runners with patents pending on aspects of this process. He has filed multiple patents on anchoring ACTs to the leaflet and myocardium, adjusting their lengths and then cinching them together. Our project is an extension of his research and is considered to be his intellectual property. As a concept, our device is unique, novel and would need patent protection.

What We Would Do Differently

We could potentially have explored more material options. We met with a material scientist in the Mechanical Engineering and Material Sciences department at the Washington University in St. Louis School of Engineering. We chose stainless steel for many reasons and wanted to use a spring system, but there is potentially a way an elastic material could be used.

Time management is always something that can be improved, but we all did our best despite our busy schedules.

Overall, our team worked very well together, was always able to meet when needed and each contributed something unique. Our design accomplishes the scope of our project and meets the requirements set by our mentor, Dr. Crabtree.

Evaluation

The scope of our project was to complete the third step of the noninvasive technique for treating MR while the heart is beating. We assumed the ACTs were already anchored to the leaflet and papillary muscle and we devised a process with corresponding devices to cinch the independent ACTs together. The ACTs are able to be individually adjusted and cinched while watching MR on TEE.

The Box-Spring Model and U-shaped delivery guide wire have been examined by Dr. Crabtree and Dr. Zajarias from the Washington University School of Medicine in St. Louis. They support our devices and procedure. The combinations of our devices with the methods created to anchor the two ACTs create an almost complete procedure.

Team Responsibilities

All members: design brainstorming, attending meetings and mapping out ideas

1. Kaitlin:
    a. Patent research
    b. Background information
    c. Physiology description
    d. Safety analysis and DesignSafe
2. Brooke
    a. Design specifications
    b. Analysis of devices and design requirements
    c. Pugh chart
    d. Manufacturing brochure
3. Tucker
    a. CAD and paint drawings
    b. Description of Box-Spring Model and U-shaped delivery guide wire
    c. Mathematical calculations
    d. Weekly reports

References

Doctors Consulted

(A) Dr. Robert Faul, MD

(B) Dr. Traves Crabtree, MD

(C) Dr. Alan Zajarias, MD

Sources

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Appendix

Abbreviations

ACT: artificial cordae tendineae

CT: cordae tendineae

MR: Mitral Regurgitation

PP: Polypropylene

TEE: Transesophageal Echocardiography

Headings

Black: Heading 1

Light Blue: Heading 2

Dark Blue: Heading 3

Detailed CAD Drawings

Other Materials Considered

L605 Cobalt Chromium

- Biocompatible
- Greater elasticity and strength than 316L Stainless Steel

MP35N Cobalt Nickel

- Biocompatible
- High Strength
- Toughness
- Ductility
- Corrosion resistance

We chose Gore-Tex for devices that need some flexibility and ACT that need to wrap and tie, as in the Knot Tying Device and Trap Device. We chose Gore-Tex for this use because it is an accepted material for ACT replacement.

We chose 316L stainless steel for the stiff ACT because it is biocompatible, durable, strong and easy to manufacture, which would reduce cost. All of these factors are criteria we looked for in the Pugh Chart of our device, and the other materials do not have all four of these qualities.

Safety

designsafe Report

Application:	MitraGuard	Analyst Name(s):	Kaitlin Ayer
Description:	Cinching device used to secure together the artificial chordae tendineae during percutaneous repair of the mitral valve	Company:	MitraGuard
Product Identifier:		Facility Location:	Washington University in St. Louis
Assessment Type:	Detailed		
Limits:			
Sources:			
Risk Scoring System:	ANSI B11.0 (TR3) Two Factor		

Guide sentence: When doing [task], the [user] could be injured by the [hazard] due to the [failure mode].

Item Id	User / Task	Hazard / Failure Mode	Initial Assessment Severity Probability	Risk Level	Risk Reduction Methods /Comments	Final Assessment Severity Probability	Risk Level	Status / Responsible /Reference
1-1-1	Doctor trouble shooting / problem solving	None / Other : Not a hazard						
1-2-1	Doctor operate on patients	biological / health : blood borne diseases	Moderate Remote	Negligible	Be cautious during procedure and take preventative measures.	Moderate Remote	Negligible	
1-2-2	Doctor operate on patients	mechanical : pinch point	Minor Unlikely	Negligible	Handle device with care.	Minor Unlikely	Negligible	
1-3-1	Doctor prescribe medications	None / Other : Not a hazard						
1-4-1	Doctor monitor patients	None / Other : Not a hazard						
1-5-1	Doctor monitor machines	None / Other : Not a hazard						
2-1-1	Nurse take vital statistics on patients	None / Other : Not a hazard						
2-2-1	Nurse dress wounds	biological / health : blood borne diseases	Moderate Remote	Negligible	Be cautious during procedure and take preventative measures.	Moderate Remote	Negligible	

Figure 22 DesignSafe report page 1

Item Id	User / Task	Hazard / Failure Mode	Initial Assessment Severity Probability	Risk Level	Risk Reduction Methods /Comments	Final Assessment Severity Probability	Risk Level	Status / Responsible /Reference
2-3-1	Nurse prepare / administer IV injections	None / Other : Not a hazard						
2-4-1	Nurse monitor patients	None / Other : Not a hazard						
3-1-1	Surgical Technician setup supplies / equipment / instruments for operation	mechanical : pinch point	Minor Unlikely	Negligible	Handle device with care.	Minor Unlikely	Negligible	
3-2-1	Surgical Technician assist doctor with surgery	None / Other : Not a hazard						
3-3-1	Surgical Technician trouble shooting / problem solving	None / Other : Not a hazard						
4-1-1	Patient All Activities	biological / health : wrong medication / dosage	Moderate Unlikely	Low	The doctor or nurse administering the medication needs to triple check that the correct dose of the correct drug is being given to the patient.	Moderate Unlikely	Low	
4-1-2	Patient All Activities	biological / health : bacterial	Moderate Unlikely	Low	The doctor, nurse, and surgical technician need to keep the surgery area and equipment clean at all times. The nurse needs to properly dress the patient's wounds.	Moderate Unlikely	Low	
4-1-3	Patient All Activities	mechanical : stabbing / puncture	Moderate Unlikely	Low	The puncture in the patient's upper thigh only needs to fit an 18 French catheter - it can be very small so that stitches are not required.	Moderate Unlikely	Low	

Figure 23 DesignSafe report page 2

Product Specification Information

GORE-TEX® Suture for Cordae Tendineae

Catalogue Number	Thread Size	Thread Length	Needle	Pledgets
3200A	CV-4	36" (91 cm)	TH-22	4 (3 x 6)
3201A	CV-5	36" (91 cm)	TH-22	4 (3 x 6)
3202A	CV-5	36" (91 cm)	TH-22	2 (3 x 6), 1 (2 x 4)

INSTRUCTIONS FOR USE FOR
GORE-TEX *SUTURE*
for Cordae Tendineae Repair or Replacement ePTFE Nonabsorbable Monofilament

Description

GORE-TEX® Suture for Cordae Tendineae Repair or Replacement is a nonabsorbable, monofilament suture manufactured from expanded polytetrafluoroethylene (ePTFE) that has been expanded to produce a porous microstructure which is approximately 50% air by volume. The suture is undyed and contains no additives. GORE-TEX® Sutures differ from USP requirements.
See the table below for diameter-strength relationship.

GORE-TEX® Mean Diam. GORE-TEX® Suture
Suture GORE-TEX® Knot-Pull Tensile
Size Suture (mm) Strength (kg)
CV-2 .518 3.50
CV-3 .422 2.64
CV-4 .307 1.67
CV-5 .246 1.00
CV-6 .168 0.65

USP Limits on Avg.
USP(mm) USP Diam. Knot-Pull Tensile
Size Min. Max. Strength (kg)
0 .35 .399 2.16
2–0 .30 .339 1.44
3–0 .20 .249 0.96
4–0 .15 .199 0.60
5–0 .10 .149 0.40
6–0 .070 .099 0.20

The GORE-TEX® Suture is not absorbed or subject to weakening by the action of tissue enzymes. It does not degrade in the presence of infection. The internodal spaces permit infiltration of fibroblasts and leukocytes. Tissue attaches to and collagen penetrates into the GORE-TEX® Suture.

Indications

GORE-TEX® Suture for Cordae Tendineae Repair or Replacement is indicated for the repair or replacement of cordae tendineae.

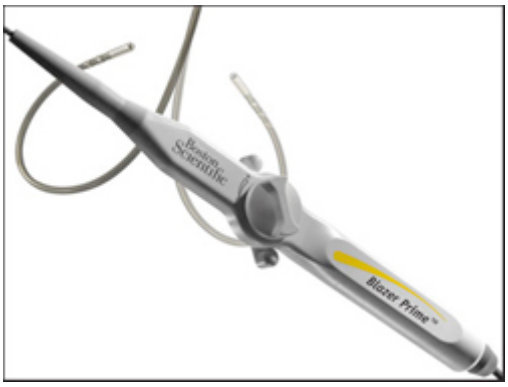
Contraindications

This device is contraindicated for use in ophthalmic surgery, microsurgery, and peripheral neural tissue.
Nitinol Wire (from fort wayne)

Kaitlin Ayer
Brooke Cheatham
J. Tucker Krone

MitraGuard

Boston Scientific – Sample Catheter



Blazer Prime Ablation Catheter
Intuitively Engineered for Exceptional Performance.

Better Torqueability

Extra support in proximal shaft is designed to:

- improve the "push" response from catheter handle to tip
- contribute to better overall torque of the catheter

Better Trackability

Smoother transition from distal tip to proximal shaft is designed to:

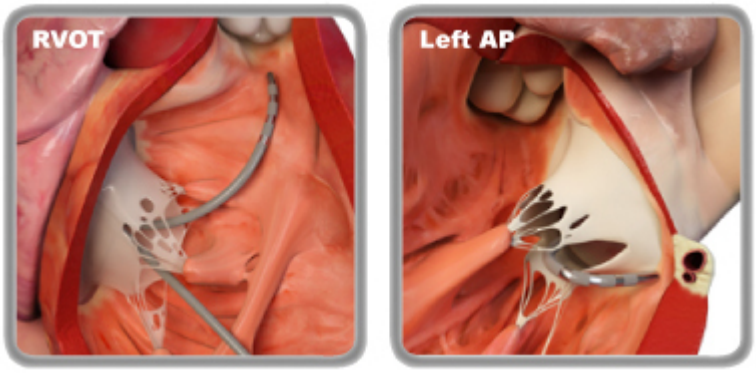
- navigate smoothly through complex anatomy
- aid banking maneuvers

Better Tip Stability & Durability

Fiber-reinforced distal section and more rugged center support provide flexible strength to optimize tip control and durability:

- improves lateral contact strength
- increases back steering strength
- enhances distal torque

Performance always matters.
Feel the difference.



[1] **Bench testing performed by Boston Scientific. N=5. Data on file.*

Medtronic Zinger Guidewire

Zinger® Guidewire is available in Light, Medium and Support versions offering different support levels for a variety of clinical situations.

Stainless Steel Workhorse Guidewire

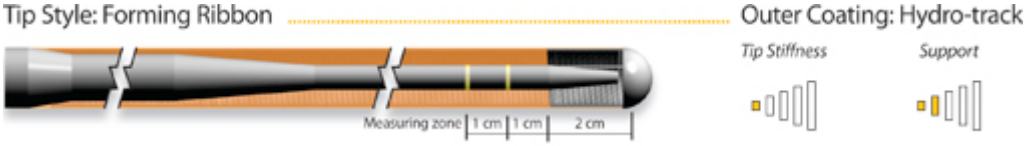
When You Need Steerability and Torque Control

- Stainless steel core wire provides torque transmission for steerability and optimal control
- Zinger® Guidewire is available in Light, Medium and Support versions offering different support levels for a variety of clinical situations

<u>Zinger Light</u>

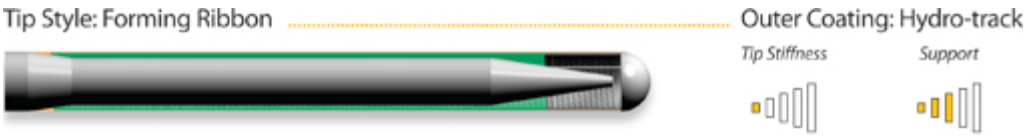
Zinger Light

<u>Zinger Marker</u>



Zinger Marker

Zinger Medium



Zinger Medium

Zinger Support

Zinger Support

Stainless Steel

Alloy	ASTM / ISO
304V (see PDF)	A313, A276
316LVM (see PDF)	F138, ISO 5832-1
316L	A276, A580
316	A313
22Cr-13Ni-5Mn	F1314
CUSTOM 465®	A564
CUSTOM 455®	A564
17-4PH®	F899, A564
17-7PH®	A313, A564
302 (see PDF)	F899, A276, A313
304	F899, A276, A313
304LV (see PDF)	A276, A580
420	A276, A580
440A	A276, A580
DFT® (Composites) (see PDF)	
18Cr-2Ni-12Mn	
21Cr-6Ni-9Mn	
321	
347	
446	
A286	
20Cb-3®	

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We would also like to thank Dr. Yin, our advisor on our project. He provided very helpful feedback on our design process. Through his comments on our papers and meeting in person we were able to redesign, rethink, and remodel our project to become a complete design.

Dr. Alan Zajarias allowed us to shadow him in the Cath lab and was our expert on catheter procedures. He was very helpful in providing his knowledge on operating procedures, catheter size, and existing catheter technology. He also showed us the imaging technologies he uses during procedures to allow the physician to guide the catheter through the patient.

John Kreitler gave us helpful and informative manufacturing and machining insight. We learned a lot about the pricing of specialty parts.

Dr. Faul consulted us on principles of percutaneous procedures and catheter size. We learned about ways to seal up entry wounds to the femoral artery when using large catheters.

Dr. Singamaneni met with us to discuss materials and their properties. We decided upon 316L stainless steel. We learned how to evaluate materials based on the properties needed.

We would like to thank last year's team (Brendan Cummings, Mike Dunphy, Travis May) for introducing us to this ingoing project. They did an excellent job in the second step of the project, which allowed for us to begin the third step of the project.

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