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Abstract - In the United States, about 4 million people have been estimated to suffer from severe mitral valve regurgitation [5]. Due to the high risks involved, about half of those patients are ineligible for surgery to repair the valve, because of their poor health [6]. Elongation of the *chordae tendineae* ***has been found to be one of the significant causes of regurgitation. To address this, the team has developed a device called "Chord Fastener", which will restore proper function to the valve via shortening of the chordae tendineae [1]. Via this shortening mechanism, the device will reduce mitral valve regurgitation and will be used in a minimally invasive cardiac procedure. Over the course of two academic semesters, the design and testing of the Chord Fastener was undertaken. The resulting prototype has demonstrated good promise that with refinement, it can function as intended and meet the project requirements.***

I. Introduction

Approximately four million people in the United States suffer from mitral regurgitation [1]. Mitral regurgitation occurs when the mitral valve does not close properly, allowing blood to flow backwards from the left ventricle into the left atrium. Improper mitral valve closing is a result of deterioration or elongation of the chordae tendineae (CT). The CT are fibrous biological chords that attach the mitral valve leaflets to the papillary muscle. In normal physiology, the papillary muscle contracts during asystole, pulling the CT to close the mitral valve. If the CT are not functioning properly, for instance due to elongation, the valve does not close properly, and blood is allowed back into the left atrium (4). Currently, pathological chordae tendineae can be repaired through open heart surgery. However, due to open heart surgery's rigorous nature on the body, only 50% of the patients needing open heart surgery to resolve a leaky heart valve, undergo the valve repair due to age or poor health [2].

Current options to treat mitral valve regurgitation include a replacement or a repair of the valve. Because of how it prolongs life expectancy, improves lifestyle, and minimizes risk of infection, repair of the valve is more ideal than replacement of a valve [3]. To repair the valve, moderately invasive methods that consist of small incisions to the chest are currently most popular [4]. However, there are a couple of current options for addressing mitral valve regurgitation using minimally invasive procedures. The MitraClip is a current product manufactured by Abbott, while NeoChord, Inc. has a product still under development. The Mitraclip is used via insertion into the right ventricle of the heart to bind the leaflets of the valve to minimize regurgitation [5]. In the NeoChord technique, artificial chords are implanted into the heart transeptally to attach to the valve leaflets and the papillary muscle [9]. With only one minimally invasive mitral valve repair device available to the biomedical market, the group decided to investigate other approaches to solving the problem. The resulting device was subsequently called the "Chord Fastener".

II. User Needs

In the first stage of the design process, the main goal was to perform background research to find a clinical problem that requires a solution. The group chose to find a problem within the cardiovascular area, so the team investigated potential problems with heart valves. The team finally agreed upon the clinical problems associated with mitral valve regurgitation. Initially, the team wanted to improve the design of prosthetic heart valves. Therefore, designs of current valve transplants were investigated, as well as patents for prosthetic valves that are being developed (refer to Appendix A for an image of current prosthetic valve options).

After more research, and interviews with physicians and professors, the team learned of the great need for a minimally invasive solution and of the significant role elongated chords played in regurgitation. Thus, it was decided to proceed with developing a plan to target the elongated tendineae. Alongside, the tortuous and lengthy nature of designing a replacement valve was an additional contributing factor to the decision to create a repair mechanism over a replacement

valve. The aim of the project was to develop a device to repair the elongated chords that can be inserted in a minimally invasive fashion (note: any reference to 'minimally invasive' in this report is referring to the procedure not the actual device, and this criterion is not to be confused with "a minimally invasive device"). This procedure would involve repairing the elongated CT, as they were found to be a leading cause of collapsing mitral valve leaflets [5]. Finally, this procedure would be intended for patients who cannot undergo open-heart surgeries to repair the mitral valve due to age or other risk factors.

From further interviews with cardiologists, a set of customer requirements were determined. The customer requirements were: (1) a minimally invasive procedure to implant the device, (2) a safe, secure, and repeatable placement of the clip, (3) ease of use, (4) low risk to the patient, (5) hemocompatibility/biocompatibility, and (6) restoration of proper tension to the leaflets of the valve. Achieving (1) a minimally invasive procedure, (2) a safe, secure, and repeatable placement, and (5) hemocompatibility/ biocompatibility were determined to be the 3 most important customer requirements for the device.

III. DESIGN INPUTS

In the design inputs stage, a comprehensive set of engineering requirements were developed. These were derived customer requirements using the Quality Functional Deployment (QFD) method. A preliminary risk assessment was also created at this stage, (refer to appendix B for the full QFD document). Engineering requirements are measurable and quantitative attributes that address customer requirements. These were assessed using the QFD approach to ensure that all user needs were satisfactorily addressed by at least one engineering requirement, and that quantitative target values were assigned. The relationships between engineering and customer requirements were determined and ranked as weak, moderate or strong based on readings from literature. (See Appendix B for the full QFD.)

Specific engineering requirements as inputs for our design were: (1) use of a catheter to implant, (2) tension of 0.22 ± 0.09 N for primary CT and 0.69 ± 0.37 N for secondary CT [13], (3) material composition to produce a moderate to low activation of the coagulation pathway, and (4) material durability against cycling over 200,000 cycles/day without failure. The required tension range of .22- .69 N range were derived from the average corresponding max and min tensions in a human heart [4]. Moderate to low activation was defined as less protein adsorption of fibrinogen to the device surface than that of Biolon, and less coagulation activation than that of glass (Biolon and Glass being known for their bad hemocompatibility properties). The 200,000/day-number requirement was found by applying a minimum safety factor of 2 to the average human number of beats per day (100,000 beats per day) [15]. By taking these correlations, the relative weights of the functional requirements were found to be 54.8, 30.3, 11.4, and 12.6 respectively (when testing the device, the values are used to evaluate whether the device passes or fails each test.). These target values of force and cycling allow the team to better quantify the engineering requirements.

To decide the relative importance of each engineering requirement, the relationships between engineering and customer requirements were determined. These were categorized as strong, moderate, or weak, where weak indicated they have little to no correlation. Requirements with strong correlations to the most important customer requirements were given priority in the design process.

The relationship between the procedure being "minimally invasive" and the "use of a catheter" was determined to be strong, because catheters have been found to have great minimally invasive procedure qualities. For in a study of 250 individuals who had undertaken a cardiac surgery involving a catheter very few individuals developed minor or serious health complications [17]. Specifically, after a 3-year period, less than 1% got stroke, and only 0.2% got femoral nerve injury (the nerve in which the catheter would go through for a chord tensioning procedure) [17].

The relationship between the "device being biocompatible/ hemocompatible" and whether the material causes clotting was determined to be strong. One material choice that was considered was Nitinol, a nickel-titanium alloy. In a Smith & Nephew study done on the hemocompatibility properties of different materials, it found that Nitinol has a significant effect on the protein adsorption and the effective activation of the coagulation pathway. By exposing different metals to a dilute blood plasma, it was found that depending on the metal used prekallikrein, a key initiator to the coagulation cascade, could vary from as low as 0.2 (moD/min/cm^2) for pyrolytic carbon, and to as high as 5 (moD/min/cm^2) for Zr-2.5Nb [18]. This indicates that the material choice and hemocompatibility/ biocompatibility would have a strong relationship. Additionally, data from a Smith and Nephew study was used to support the biocompatibility of Nitinol. The data is supplied and discussed further in section VI.

The relationship between the requirement of "safe, secure and repeatable placement" and "composition of the clip will produce a moderate to low activation of the coagulation pathway" was found to be moderate. The competitive device, MitraClip, is also made of Nitinol and was proven to be safe in a study performed over the course of 5 years [16, 19]. At the one-year timepoint, 0.0% of patients experienced thrombosis, 2.4% of patients experienced atrial septal defect, 2.4% of patients experienced mitral valve stenosis, 1.6% of patients experienced non-cerebral thromboembolism, and 7.1% of patients experienced major vascular complications [16].

The engineering requirements for our project were implemented into the QFD (Appendix B). They are as follows: (1) Catheter diameter 8 mm. (2) Chord tension 0.22 ± 0.09 N for primary CT and 0.69 ± 0.37 for secondary CT [13]. (3) The material shall not cause activation of coagulation cascade.

(4) The material shall be able to withstand 200,000 cycles/day (1 cycle defined as 1 stretching/ loading followed by an unloading of the sample). The importance (weight) of each requirement were calculated through the QFD after assigning relationships.

Because this device is intended for cardiac use, several severe risks were identified. Major concerns included the potential for blood clotting caused by the material, whether the device can withstand the required forces, and the possibility of the device being incorrectly sized. Various risk mitigation measures were also found, including using pre-approved materials and components and extensive testing (See Appendix D for the risk assessment).

IV. Design Process

Using our design inputs, the team moved forward in the third gate of the design process to determine the most effective method of fixing elongated chordae tendineae. To brainstorm, the team used method 365. In method 365 each member produced three ideas separately and then came together to add more details or feedback to each idea. From here the team was able to narrow down the best ideas from the brainstorming that would best meet the design inputs. The best three ideas were: (a) clipping the chords, (b) stapling the chords, and (c) a mesh wiring system to reinforce the valves. These three ideas were then compared using the previous QFD. In the QFD matrix, each idea was analyzed to see how well the device met both the customer and engineering requirements.

The team made multiple QFD charts, one for each of the three proposed methods. With each individual QFD chart the team investigated how the proposed method and solution compared with the design inputs from gate two (design input stage). The proposed approach went through a second QFD. This second QFD looked to compare the system and parts that go into the solution to help evaluate the pieces against the engineering requirements from gate two. The QFD process ultimately evaluated each of the three approaches against the engineering requirements to determine which one was best.

The finalized results of the QFD process (shown in the Appendix B) showed that the best method to move forward was binding the chords to shorten the length of elongated chords. At this point, the success of the MitraClip in the cardiac field was brought to the attention of the team through interviews with cardiologists. The MitraClip is a pronged clipping device used to clip the leaflets of the mitral valve together, all through a minimally invasive procedure (an approach that aligned with the team's objective). This inspired the team to redesign this clip for use specifically on the elongated chords themselves rather than the leaflets (as in the case of the MitraClip). It was reasoned that since regurgitation can be due to the elongated chords, shortening them back to their regular length, would allow the valve to close properly. Thus, the team decided that this project would (1) bring about a minimally invasive device to market to compete against the MitraClip and (2) improve upon the MitraClip by resolving the actual cause of the regurgitation (elongated chords), whereas the MitraClip aims to fix the valve itself.

After some research and the comparison to the engineering requirements, the team determined preliminary engineering specifications and sizing of the clip. The crown of the clip was determined to be 2mm in thickness [14], the leg to be 2.5mm long [14], the shaft of the catheter to be 6-8mm [14], and the mechanism for opening the clip needing to be thin and inelastic. From here, the team was able to move forward with figuring out more specifications as well as making initial prototypes.

V. Design Outputs

Through the design process and the use of a decision matrix, the team decided the best material to use is Nitinol, a nickel-titanium alloy that is approximately 56% nickel and 44% titanium by weight. This material has proven to be valid for many uses in biomedical engineering [18].

It was later determined that nickel-titanium was used in the MitraClip, after an updated design was released in 2016 [19]. When compared to other materials considered for this project, Nitinol had better mechanical properties and is more cost effective. Nitinol is known to have a high fatigue strength, low density, and is nonmagnetic. Also, it is very malleable and therefore, can be used to manufacture very small devices. When compared to stainless steel, nitinol has been shown to be much stronger against deformation and is much more cost effective than titanium 6-4 [11]. The design of the device is based on the MitraClip but allows for easy use in the smaller space while supporting the ability to add proper tension to the chordae tendineae. The device does this by clipping to two sections of the elongated chord and pinching it together to shorten its effective length and restoring the proper tension. In a general sense, the proposed device would be distinguished from the MitraClip because of how it would shorten the CT instead of the valve leaflets. As for technical differences, the Chord Fastener would be smaller but provide a greater surface area where the CT would be attached. Also, the MitraClip uses thinner and longer hooks to secure it in place on the valve leaflets while the Chord Fastener would use a smoother, grooved section to avoid piercing the CT and causing more damage. To operate the device, the user will pull on the center shaft which opens the upper, grooved section of the clip and allows the user more space to grab the CT. The user will then place the device in a way where the elongated CT is folded on itself, and the overall linear length is shortened. To close the upper arms and pull the CT together, the user will apply a small force via the delivery mechanism that pushes the center shaft back into the base where a locking mechanism will hold it in place (See appendix G and N). The grooves on the exterior arms line up with similar grooves on the interior arm to allow for increased surface area and grip of the CT. The overall size of the final product would be 3.125mm x 4mm x less than 11.5 mm (length, width, height). These dimensions keep the device compatible with the MitraClip Delivery System that uses a 16Fr catheter with an inner diameter of

approximately 5.5mm [4]. The 3D model presented is at an 8:1 scale model to allow for the device to be 3D printed with ease as there are many small dimensions that are crucial to the functionality of the device. (Appendix E, Appendix F for open clip).

The materials needed for manufacturing of the final product are listed below in the Bill of Materials (Appendix G). Included in the MitraClip Package is all necessary guide wires, catheters, and controls needed to properly implant the Chord Fastener device.

VI. Design Verification

To ensure that the design outputs of our device, the Chord Fastener, met the design inputs, a series of testing was undertaken as seen in Appendix C. The team began by testing if the width of the crown of the clip was small enough to enter the mitral valve, verification #1. The group tested this by measuring the width of the clip with a caliper. The device's width was smaller than the diameter of the valve (device width: 3.5 mm, valve diameter: 21mm), therefore passing the test. Next, the group tested if the device could meet the requirements of opening in the heart and closing. Since the device was physically observed to open and close using the spring mechanism it passed verifications #2 and #3. And since when it was in the open position the tip-to-tip measurement, via caliper, was less than 4 cm, it passed the verification #4. Because the clip's closure mechanism was seen to be retractable, via use of spring, it allowed the device to close in a succinct manner passing the verification #5. When in the closed position the clip had to be able to grab an at minimum of 3 chordae tendineae. Since the clip had 3 grooves our device passed this verification #6. Then to ensure that the clip still is locked in placed once it has grabbed the chordae tendinea, a series of weights were strung from the clip. Because our device withheld greater than the 0.7 newtons requirement it passed the verification #7. To ensure that once the Chord Fastener was inside the left ventricle there would be a proper initiation of the clipping mechanism, the material of the self-expanding Nitinol was used. Its shape change at different temperature would allow the Chord Fastener to be in the open temperature at room temperature and in the closed position at body temperature. This property was used to pass verification #8 and was tested via vendor descriptions. Then to ensure that there would be no nickel poisoning from the Nitinol material used, several stoichiometric calculations were undertaken to ensure that the percent weight of nickel content was well below the 0.2 µg/L, fulfilling verification #9. To make certain that the device was compatible with the catheter, the team made sure the device could be mounted on a rod. This was tested via SolidWorks and passed verification # 10. For verification #11, to ensure that the clip could detach from the rod, the team used a SolidWorks model to visualize detachment.

Finally, a Smith & Nephew article on protein adsorption to different materials was used to verify that the device met the low to moderate coagulation requirement. This article specifically addressed our material of choice, titanium nickel. In the article the authors analyzed different material surfaces for a protein adsorption test of fibrinogen and activation of prekallikrein.

Prekallikrein plays a crucial rule in the coagulation cascade. Activated prekallikrein will turn into kallikrein. Kallikrein is a protein that is made from the activation of the factor XIIa [22]. XIIa will turn prekallikrein into kallikrein and factor XI into XIa which will then lead to the intrinsic pathway [22]. Hence, prekallikrein is a good indicator for the activation of the intrinsic pathway.

Fibrinogen is pith for platelet activators and dictates the adhesion of platelets onto a material [22]. In addition, because fibrinogen has two receptor binding sites, it plays a crucial part in allowing for platelet–platelet bridging, this platelet-platelet bridging is what allows for thrombus formation [22]. Thus, looking at levels of fibrinogen adsorption serves as a great indicator of coagulation and thrombus formation.

The study found that the titanium oxide ceramic surface of Ti-13Nb-13Zr, Titanium Nickle, had only 25% of glass's prekallikrein activation, where glass was the positive control group. The study also found that oxide surface of the Titanium Nickle had a fibrinogen protein adsorption of 20 ng/cm2, which was only 33% of the positive control group, Biolon's 84 ng/cm2 [18]. In our device will have a titanium oxide layer that will be exposed to the blood plasma, which is why the study's publishing is relative. Since the team's device engineering requirement were to have a moderate to low activation and protein absorption. Thus, this study merited and verified the use of Nitinol, a Titanium Nickle alloy with a titanium-oxide surface, for the material of the clip passing verification # 12.

VII. Medical Device

In the final stage of the design process, the main goal was to implement any changes made after the design verification. As was found in the verification testing phase, the major design change needed was the inclusion of a mechanism for the device to detach from the catheter. It was determined that this would be rectified by adding a lock and key design on the crown of the device. Through use of a SolidWorks Motion Simulation, it visually showed how when the catheter is twisted during insertion, it detaches from the crown of the device.

For images related to validation testing and links to videos, please see Appendix H.

VIII. Validation Testing

To certify that the medical device outputs met or exceeded the user requirements, several validation tests were undertaken, broken down into two categories: Instron Machine Testing and SolidWorks flow simulation.

Instron Testing

The Instron machine was used to obtain the mechanical properties of ultimate tensile strength, Young's modulus, hysteresis, the coupled viscoelasticity, and effects of load rates. These properties were obtained by placing the clip onto bovine muscle tissue.

Testing how the Chord Fastener responds under controlled loading conditions supplies an understanding of how the device is expected to behave in a beating heart. Instron validation testing was done to highlight the clip's mechanical properties while gripping the bovine tissue. Load until failure was done to ensure the breaking strength of the clip was above the requirement and to obtain the Young's modulus. Hysteresis was done to seek energy lost via repeated loading and unloading.

To test for tensile strength, the sample was loaded onto an Instron Universal Testing Machine with a 1 kN load cell and BlueHill3 operating software. The testing machine was configured with fixtures for a tensile test. Standard protocol and calibration procedures were followed to accurately set up the Instron for testing. These procedures can be referenced in the device's user manual. The sample was tested under a 12-cycle hysteresis test and a load to failure test.

The hysteresis method placed the samples under several repeated loading and unloading cycles. The test parameters for the hysteresis test were defined within the Instron software such that the samples were subjected to a load rate of 0.5 cm/min for a total of 12 cycles. The end condition for the test was when it completed all 12 cycles.

After completion of the hysteresis test, the Young's modulus and tensile strength were obtained using the load until failure. The test parameters for the test were defined within the Instron software such that the samples were subjected to a load of 4 N - well above the 0.7 N - at a rate of 0.5 cm/min. There were two end conditions for the test: a 40% change in rate of load, which showed the material had fractured, or the maximum load of 3 N.

The results obtained was an average of 0.15 J lost per 15 cycles, this low value met the cut off requirement of below 0.25 J lost per 15 cycles (which was found to be the average ratio of energy loss to cycles over a 100,000-cycle period, with a safety factor of 2). Also, all trials were able to withstand the 3 N loading with little to no observed slip. These tests confirm that the device can withstand the dynamic conditions in the heart, and the device will conserve energy when in use and negate the energy lost in the valves to the device. It also validates that our device will withstand the forces applied onto it by the heart.

Next, a stress relaxation test was undertaken to illustrate that the devices' implantation did not negate the chordae tendinea's viscoelastic properties. The clipped tissue was put under a 2 N constant load for 12 minutes, while observing how the strain changed with time. Upon ending the test, there was a significant change in the strain going from 65% to 75% thus indicating that our setup allows for the tissue to retain its viscoelastic properties.

Finally, the effect of varying load rate was investigated. A 5-cycle hysteresis test was done on 3 separate rates of: 0.5 cm/min, 0.75 cm/min and 1 cm/min, to help capture how our instrument would react to the varying heart rates of a human heart. It was found that there was no significant difference in the energy loss from all 3 trials (as seen in the appendix S).

SolidWorks Flow Simulation

To ensure that the device would not induce a significant drag or turbulent flow in the mitral valve, thus causing shear stress induced thrombosis, a SolidWorks simulation was undertaken.

The Chord Fastener's SolidWorks model along with a pipe of 5 mm length and 3 mm diameter was placed into SolidWorks Flow simulation. A series of simulations of Cut Plot Velocity, Surface Plot, Pipe Trajectory and Surface Parameters, were undertaken to see the flow profile of blood around the device. There was no qualitative difference in the flow contours between the simulation with no clip and without clip (as seen in appendix O and P respectively). Alongside the shear stress rate without the Chord Fastener was 2.4 dyn/cm^2 and increased to 3.4 dyn/cm^2 after its addition. Thus, no significant difference in shear stress and ultimately supporting that the clip will not induce thrombosis via shear stress.

IX. Risk Mitigation Process

Through each step in the design process, the group went through the process of a Failure Mode and Effects Analysis (FMEA) model where risks were determined, and mitigations were developed to help ease or erase risks. Each gate required a new FMEA to be made as the group made changes to the design of the device. Risks were determined based on the design of the device and how it will be used in the human body. Although there were many risks determined, the most important risks were the mechanism of clipping the chord, the design of the crown/legs of the clip, the material that makes up the clip, and the size of the opened clip. The mechanism of clipping the chord could cause many issues such as bleeding or an embolism if the clipping is unsuccessful. This risk was mitigated by ensuring the surgeon is educated on the clip's design. In addition to educating the surgeon, designing the device's clips to withstand the forces inside the human heart, through tensile and fatigue testing, and remain attached to the chordae tendinea was another mitigation. The design of the legs and crown of the clip, if not designed based off the forces in the body, can make the surgery unsuccessful and the clip could fall off. This was mitigated by the team testing the device on bovine tissues to ensure it can withstand the tensile and fatigue forces from a heart. The material of the clip was

considered one of the biggest potential problems for the group. Most patients need to be on an anticoagulant medication after a surgery that inputs a device in the body due to the foreign body response that causes coagulation. To prevent this, the team will use Nitinol, a material that has already been tested in the body and is moderately successful regarding anticoagulation when following a natural oxidization of the material into titanium oxide, following implantation [12]. The material shows promise because Nitinol was already used for stents and the MitraClip, but further research will be needed to validate it for this application. More specifically, protein adsorption and platelet adhesion tests are needed to evaluate hemocompatibility [12]. Further options that may be needed to mitigate that risk are to surface modify the product by treating it with anticoagulants before insertion or to use the anticoagulant medication after surgery as a last resort. Recent studies have showed that surface modification with an antithrombin-heparin complex is a potential modification that could be used [10]. The sizing of the clip is the last important risk that could cause serious issues with the device. Mainly when the clip is open before clipping onto the chord, the sizing could cause rubbing against the heart walls which causes injury and potential bleeding. To mitigate this, the size of the clip being opened has been mathematically analyzed to ensure it is smaller than the chamber of the heart it is being inserted into. Also ensuring the surgeon is educated on how to use the clip will make sure they also are aware of opening the clip to its full size (see Appendix I for a risk summary table).

Although there were many risks that could not be completely mitigated, there are many benefits that outweigh the risks. The device can save many lives because many people with elongated chords are elderly and cannot undergo a full open-heart surgery. This device will help them to get the care they need to prevent mitral valve regurgitation. Mitral valve regurgitation can cause a shorter life expectancy because it can cause heart failure and other health problems. This device would help to lengthen a person's life expectancy. The small risks such as those listed above are considered minor after the mitigations are added to the design and use of the device. The small risks associated with the device therefore are outweighed by the benefits of the device to an individual's overall health.

X. Marketing And Manufacturing Considerations

In a study conducted in 2016, 598 patients, ages 12 to 81, were examined after fulfilling the echocardiograph criteria for mitral valve disease. Of the 598, 33.48% of the patients were determined to be suffering from elongated CT [3]. If this percentage is applied to the approximately 4 million patients with mitral valve regurgitation, it can be estimated that elongated CT is the cause for around 1.34 million people. Currently, the average cost of mitral valve replacement and repair surgery is around $45,000 and $31,000, respectively [5]. The proposed device would be compatible with the currently available MitraClip, which costs approximately $30,000 according to the manufacturer. If offered as a separate version of this device, the cost would remain similar. If the proposed device is offered as an add-on or separate attachment, the total cost is estimated to still be under $35,000 when considering the cost of other medical devices made of nitinol. This cost is still extremely competitive.

XI. Summary Feasability Discussion

This project addressed the clinical need for reducing mitral valve regurgitation. The proposed device design has the potential to achieve this through the tightening of elongated chords that cause valve prolapse. After exploring this problem, the team realized the benefits of making the procedure minimally invasive since half the affected patients cannot risk an open-heart surgery. This is possible with our design in that the clip can be inserted through a catheter. The clip addresses the prolapsed valve issue by addressing the problem at its source, the elongated chord.

The team was able to demonstrate a proof-of-principle device during this project. It is not classified as a prototype since it was made at an 8:1 scale out of 3-D printed materials. The device is still in the very early stages of development. More extensive testing should involve animal models with a properly scaled model made of Nitinol. This and further clinical testing of flow and coagulation will help solidify the design.

XII. Discussion, Lessons Learned, And Conclusions

Lessons Learned

This project helped us to gain knowledge and experience in the areas of market research, obtaining user requirements, defining engineering requirements, design development, testing, prototyping, and device validation. These experiences will bolster our ability to become practicing engineers. The technical capabilities we practiced include: 3-D modeling, analyzing biofluid flow, and conducting statistical analysis. Skills that are pertinent to being established engineers.

The process of mechanical testing show cased how essential of a practice it is, as it was used to certify that the device met user requirements. Our experience derived from the mechanical testing on the Instron machine is crucial to understanding examples of key tests used to validate medical technologies in the enterprise world. In this project the team was able to use load till failure test as well as hysteresis tests, to obtain profiles that validated our device. It is the understanding of these profiles and validation tests that contributes to medical devices being characterized.

This project allowed the team to build on the undergraduate career through using hands-on experience. Some of the project activities included: conducting interviews, doing background research on the problem of interest and patents relating to products on the market, working as a team, testing the device, and prototyping. All of which will prove valuable for intended professional careers. The research portions of this project helped increase the knowledge of medical devices as well as the human body. The project itself allowed us to better

understand and to be put through the engineering process of designing a medical device, like the FMEA, Validation and Verification processes. Learning the steps of design on paper only allows so much to be remembered by a student. By doing the process and walking through each step allows the design process to be completely solidified in our minds.

The team learned how to use better use SolidWorks software for a real design application, as well as how to set up, test, and critically analyze our mechanism's potential impact on mitral valve repairs. This project has made a big impact on us personally and professionally as it offered the opportunity for us to speak with cardiologists and to see firsthand the obstacles facing the medical community.

XIII. Future Work

After successful verification and validation of the design using the 3-D printed alpha prototype, the team would then make modifications to make the device compatible with the MitraClip delivery system or a similar system that allows for the device to be implanted using minimally invasive techniques. Also, the team would like to make small modifications to allow for a small, removable camera to be attached to give the surgeon better visibility and allow for better and easier placement of the device. Further testing would need to be conducted after the device is produced using Nitinol to show that material differences do not negatively affect performance.

Individual Roles and Responsibilities

Becca:
In earlier gates, I helped with research of the mitral valve regurgitation as well as solutions to that problem. I attended some of the interviews we conducted as well. Throughout each gate, I played a big part in the FMEAs, deciding the priorities, severities, occurrences, and how we could fine tune our device to mitigate risks. I focused on figuring out the risks and how the design we made could cause issues. From there I was able to produce ways we could prevent those risks. Looking at the risks also helped me play a role in researching to help determine engineering and functional specifications of the device as we moved towards making a SolidWorks prototype. Using some simple mathematical equations, I also did some analysis of the device to get a small look at the beginnings of forces the device would undergo.

Austin:
In the early stages of the design process, I helped with researching different causes of mitral regurgitation and the solutions that were already available. I also helped find different requirements for our device that would set the goals for the final design. In the later stages, my focus was on designing the device using SolidWorks and creating a 3D printed alpha prototype that could be used for the necessary testing.

Mary:
In the first stages of the design process, I helped to research patents for current devices and attended meetings with professionals in the field to help derive the engineering requirements for the project. I also contributed to the QFD and FMEA documents, helping to figure out which qualities should have priority and which risks were the most important to prevent. During verification testing, I performed some of the testing needed. During validation testing, I acquired some of the necessary materials needed.

Diana:
Throughout the whole design process, I helped with the first research process and choosing the project idea. I attended every interview the team had with stakeholders and faculty members. Following the user needs stage, I helped develop the customer and engineering requirements, helped fill out the QFD and FMEA reports, and supported the group members in any way that I could. Additionally, I made sure that the design history file stays updated with all the documents from all stages, as well as the Gantt chart with all the individual tasks that were completed.

Walid:
Interviewed Cardiologists to obtain user requirements. Read many articles and publications, to find the specifications of a CT repair mechanism. Orchestrated the FMEA for the first draft, finding some prodigious articles to support our decisions. Created the verification guidelines. And orchestrated some of the verifications. Created the Validation testing procedures and orchestrated the testing of the efficacy of our device on Instron machines and SolidWorks flow simulation.

XIV. Professional And Ethical Responsibilities

This device has the potential to help change how regurgitation is treated and allow more people to receive the care they need. However, this device also has the potential to be harmful or fatal to the patient if built or designed incorrectly. To prevent this from happening, extensive research was conducted, and when possible, the device incorporated already approved materials and components. Areas of concern included allergies, scraping of the device against the wall of an artery, and the possibility of the device slipping and getting dislodged inside the body.

XV. Acknowledgements

Dr. James Keszenheimer, Dr. Yang Yun, Dr. Hossein Tavana, Dr. Rebecca Willits, Dr. Rouzbeh Amini, Dr. Audrey Nguyen, Dr. Ihsan Haque, Dr. Ted Shaub, Amy Kanta RDCS, Dr. Brian Duncan, Steve Patterson, Mohamad Motaz Al Samman.

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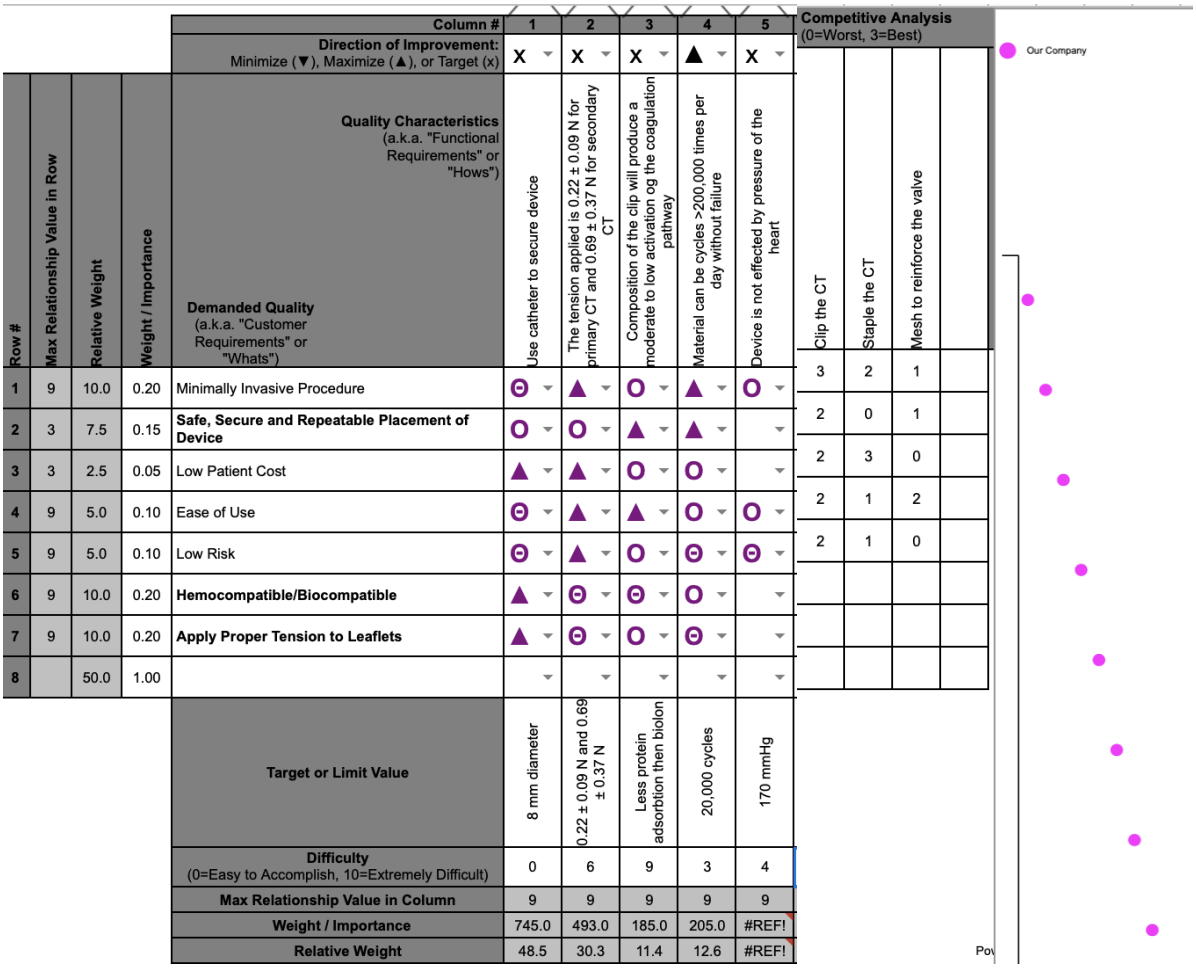
APPENDIX

Mechanical and Tissue Mitral Valves

A. Current options for prosthetic heart valves include mechanical or biological valves. The biological valves are either bovine or porcine valves. The mechanical valves are made of metal.

Legend		
⊖	Strong Relationship	9
O	Moderate Relationship	3
▲	Weak Relationship	1
++	Strong Positive Correlation	
+	Positive Correlation	
-	Negative Correlation	
▼	Strong Negative Correlation	
▼	Objective Is To Minimize	
▲	Objective Is To Maximize	
X	Objective Is To Hit Target	



Row #	Max Relationship Value in Row	Relative Weight	Weight / Importance	Demanded Quality (a.k.a. "Customer Requirements" or "Whats")	Use catheter to secure device	The tension applied is 0.22 ± 0.09 N for primary CT and 0.69 ± 0.37 N for secondary CT	Composition of the clip will produce a moderate to low activation og the coagulation pathway	Material can be cycles >200,000 times per day without failure	Device is not effected by pressure of the heart	Clip the CT	Staple the CT	Mesh to reinforce the valve	
				Column #	1	2	3	4	5	Competitive Analysis (0=Worst, 3=Best)			
				Direction of Improvement: Minimize (▼), Maximize (▲), or Target (x)	X	X	X	▲	X				
				Quality Characteristics (a.k.a. "Functional Requirements" or "Hows")									
1	9	10.0	0.20	Minimally Invasive Procedure	Θ	▲	O	▲	O	3	2	1	
2	3	7.5	0.15	**Safe, Secure and Repeatable Placement of Device**	O	O	▲	▲		2	0	1	
3	3	2.5	0.05	Low Patient Cost	▲	▲	O	O		2	3	0	
4	9	5.0	0.10	Ease of Use	Θ	▲	▲	O	O	2	1	2	
5	9	5.0	0.10	Low Risk	Θ	▲	O	Θ	Θ	2	1	0	
6	9	10.0	0.20	**Hemocompatible/Biocompatible**	▲	Θ	Θ	O					
7	9	10.0	0.20	**Apply Proper Tension to Leaflets**	▲	Θ	O	Θ					
8		50.0	1.00										
				Target or Limit Value	8 mm diameter	0.22 ± 0.09 N and 0.69 ± 0.37 N	Less protein adsorbtion then biolon	20,000 cycles	170 mmHg				
				Difficulty (0=Easy to Accomplish, 10=Extremely Difficult)	0	6	9	3	4				
				Max Relationship Value in Column	9	9	9	9	9				
				Weight / Importance	745.0	493.0	185.0	205.0	#REF!				
				Relative Weight	48.5	30.3	11.4	12.6	#REF!				

B. Quality Functional Deployment (QFD) document. The conditions and criteria to correlate the customer requirements with engineering requirements were based on information and values found in literature. The relationships assigned were determined by the design team and they are weak (triangle), moderate (empty circle), or strong (circle with a line in the middle). The weights of the engineering requirements were calculated by the QFD. Our top 3 Customer Requirements are bold faced.

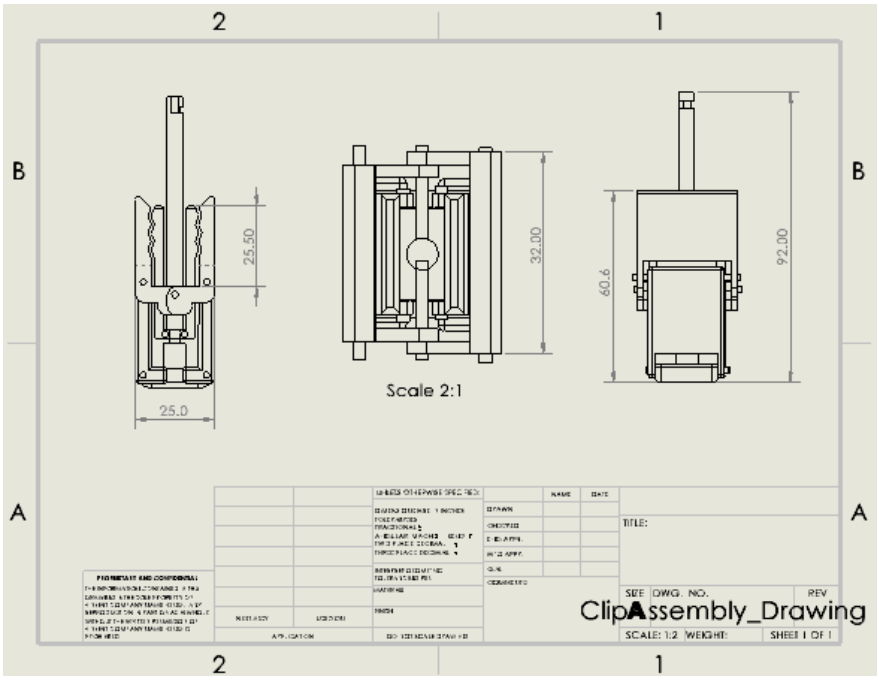
Verif #	Engineering Requirements	Range of Values it needs to meet	Testing	Evaluation
1	Width of Crown	Crown is **2.5 by 3.5 mm**. Valve D is **21mm**	Printed part measured via Caliper (Measurement)	Pass
2	Clip can Open	Spring mechanism can elongate	Physical movement on the clip was performed (Observation)	Pass
3	Clip can Collapse	Spring mechanism to help with closure	Physical movement on the clip was performed (Observation)	Pass
4	Open Position of Clip	Less than **4cm** (Chamber Diameter)	Actual device is .825cm when opened (Virtual)	Pass
5	Clip Remains Locked	Spring can withstand **.7N**	Tested on physical objects (Observation)	Pass
6	Clip tension	The clip can grip **1-3** tendineae	The clip has 3 grooves (Visual)	Pass
7	Clip Remains Locked	Spring can withstand **.7N**	Tested on physical objects (Observation)	Pass
8	Expandable clip	Clip can change chape in body tempeture	Nitinol's use in stents (Vendor)	Pass
9	Clip's Biodegradability	Acceptable level of Ni in blood **0.2 µg/L**	Weight fraction of nickel in Nitinol (Calculation)	Pass
10	Catheter Compatibility	Clip can be mounted on catheter	Solid works model includes catheter rod (Virtual)	Pass
11	Catheter Compatibility	Catheter can detach from Clip	Dismounting the clip via use of 3D printed part	Pass
12	Moderate to low Coagulation	Below Biolon's protein adsorbtion	Scientific results on titanium oxide's protein adsorbtion percentage (Article)	Pass

C. Verification Testing Results

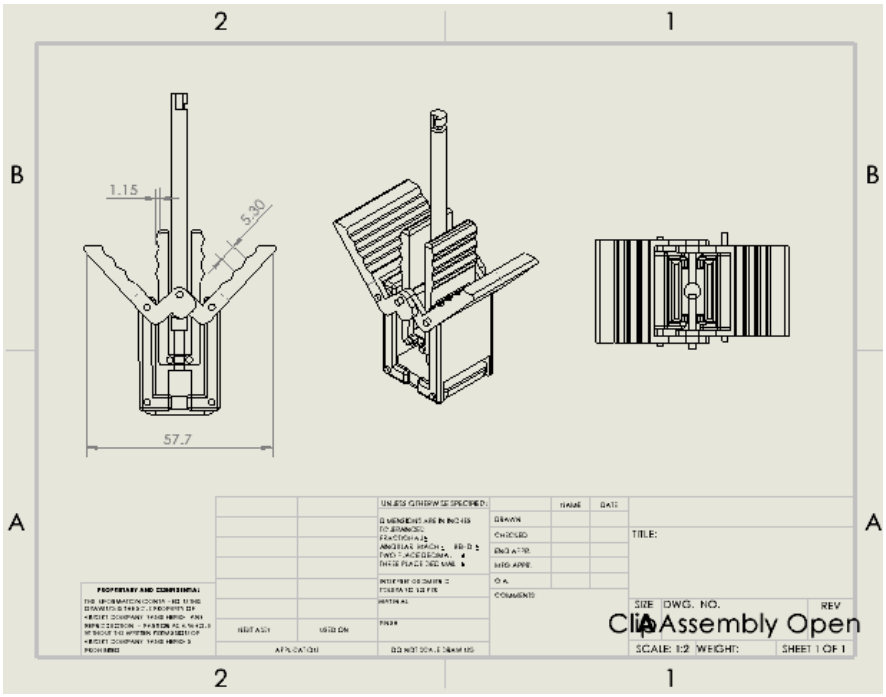
Name of Risk	Summary of Risk	Risk level and Risk Priority Number (RPN)	Mitigation
Material of Device	The material that makes up the device causes thrombosis or coagulation in a patient which can then cause stroke or heart attack.	Critical RPN: 180	Use a material that has already been tested and approved for human body use, surface modify the product with anticoagulants, or treat the patient with medication.
Clipping Mechanism	The clipping of the chord is unsuccessful, or a slipping occurs that knocks the clip out of place.	Serious RPN: 144	Ensure there is a surface that has ridges for friction to hold the chord in place.
Design of crown/legs	The design of the crown or legs does not withstand the forces of a dynamic heart and breaks.	Critical RPN: 105	Test the device on bovine tissue using tensile and fatigue testing to fine tune dimensions that will withstand heart forces.
Size of opened clip	The opened clip is too large and causes a puncture or rubbing against the heart wall.	Critical RPN: 96	Design the clip so that when opened it is less than the size of the chamber it is located in.

Spring	The spring does not allow the legs to open or close properly rendering the clip useless.	Serious RPN: 28	Use the correct spring based off its stiffness properties.

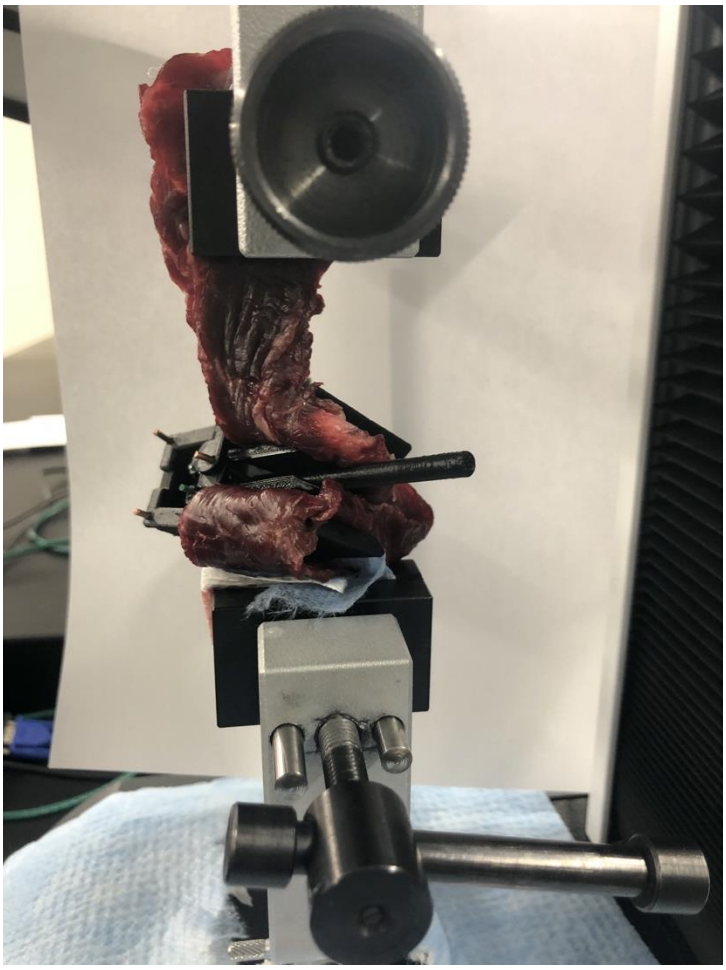
D. Table of risks with descriptions, risk level, and summary of mitigations. Risk priority number (RPN) is determined through multiplying preassigned numbers based on occurrence, severity, and detection.



E. SolidWorks drawing of the “closed” clip at an 8:1 scale of final product. This scale allows it to be 3D printed.



F. SolidWorks drawing of the “open” clip at an 8:1 scale of final product. This scale allows it to be 3D printed.



G. The apparatus used for Instron machine testing. The following is a link to video of the testing: http://bit.ly/InstronTesting

Part Number	Quantity	Name	Material	Procurement Type	Vendor/Source	Price Each	Typical Lead Time
20-001	1	Clip Base	Nitinol	MTS	FATHOM	requires quote	~5 Buisness Days
20-002	1	Clip Shafe	Nitinol	MTS	FATHOM	requires quote	~5 Buisness Days
20-003	1	Shaft Guide	Nitinol	MTS	FATHOM	requires quote	~5 Buisness Days
20-004	2	Clip Middle	Nitinol	MTS	FATHOM	requires quote	~5 Buisness Days
30-001	1	Clip Plate	Nitinol	MTS	FATHOM	requires quote	~5 Buisness Days
30-002	2	Clip Int. Arm	Nitinol	MTS	FATHOM	requires quote	~5 Buisness Days
40-001	1	Clip Arm - Sm	Nitinol	MTS	FATHOM	requires quote	~5 Buisness Days
40-002	1	Clip Arm - Lg	Nitinol	MTS	FATHOM	requires quote	~5 Buisness Days
50-001	1	MitraClip Package	N/A	OTS	Abbott	~$30,000	unkown
60-001	7	Pins	Stainless Steel	OTS	McMaster Carr	$3.76	~5 Buisness Days

H. Bill of Materials.

Gate 1 - User Needs				
Research Background	Everyone	100%	8/24/20	8/28/20
Research Patents	Mary and Walid	100%	8/28/20	8/30/20
Come up with Interview Questions	Everyone	100%	9/17/20	9/21/20
Interview with Dr. Yun	Walid, Rebecca and Diana	100%	9/21/20	9/26/20
Prepare Requirements	Everyone	100%	9/23/20	9/27/20
Prepare Presentation	Everyone	100%	9/21/20	9/28/20

I. Gantt Chart of the User Needs stage.

Gate 2 - Design Input				
Conduct Interviews	Diana, Mary, and Walid	100%	10/5/20	11/2/20
Determine Customer Requirements	Everyone	100%	10/7/20	10/27/20
Determine Potential Risks	Walid, Mary, Austin and Diana	100%	10/11/20	10/27/20
Prepare Gate 2 Presentation	Diana	100%	10/24/20	11/2/20
Write Honors Proposal	Everyone	100%	10/24/20	11/2/20

J. Gantt Chart for the Design Input stage

Gate 3 - Design Process				
Brainstorm Solutions	Everyone	100%	11/16/20	11/18/20
Pick Solution and Run QFD for Parts	Everyone	100%	11/19/20	11/20/20
Risk Assessment	Everyone	100%	11/24/20	11/24/20
Edit and Submit Honors Proposal	Everyone	100%	11/16/20	11/30/20
Gate 3 Presentation	Everyone	100%	11/27/20	11/30/20

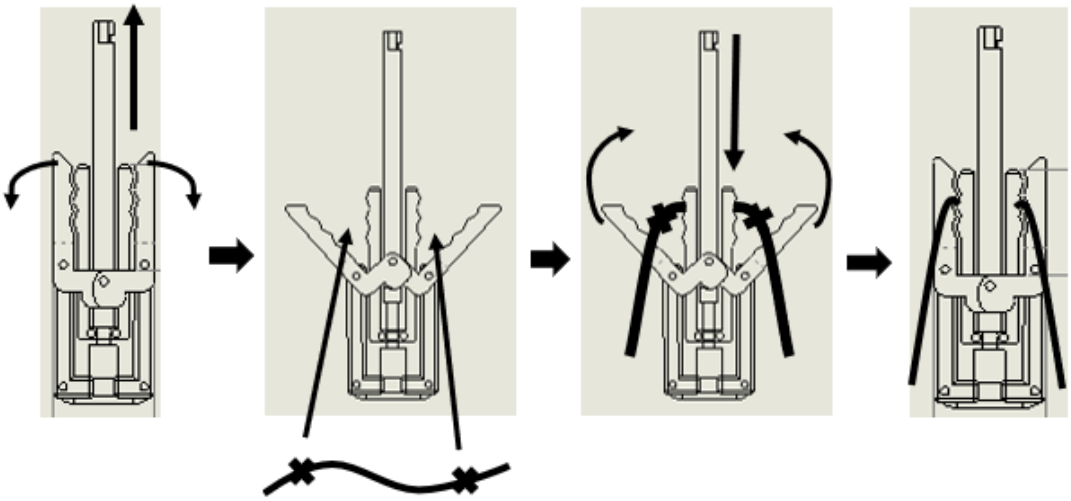
K. Gantt Chart for the Design Process stage.

Gate 4 - Design Output				
Device Specifications	Rebecca	100%	1/18/21	1/25/21
Device Drawings	Austin	100%	1/11/21	2/1/21
Decision Matrix	Diana	100%	1/11/21	1/25/21
Bill of Materials	Diana	100%	1/11/21	2/1/21
Analytical Calculations	Walid & Rebecca	100%	2/1/21	2/8/21
Risk Assessment	Rebecca	100%	1/25/21	2/1/21
Design Verification	Mary	100%	2/1/21	2/8/21
Design Validation	Walid & Mary	100%	2/8/21	2/15/21

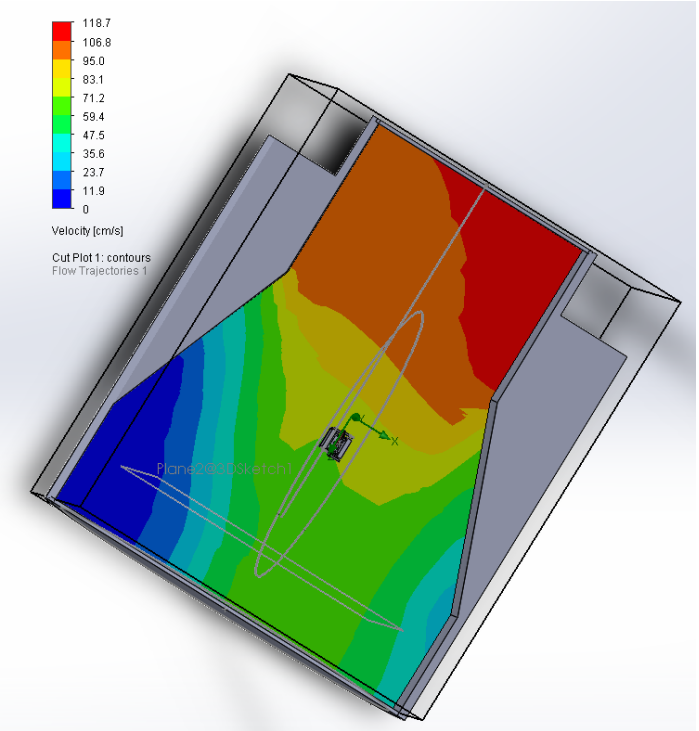
L. Gantt Chart for Design Output stage.

Gate 5 - Medical Device				
Validation Plan	Walid	100%	2/10/21	3/10/21
Validation Procedure	Mary	100%	3/12/21	3/22/21
Validation Testing	Everyone	90%	3/22/21	3/31/21
Risk Mitigation Summary	Rebecca, Diana	30%	3/31/21	4/15/21
Gate 5 PowerPoint	Everyone	40%	3/31/21	4/20/21

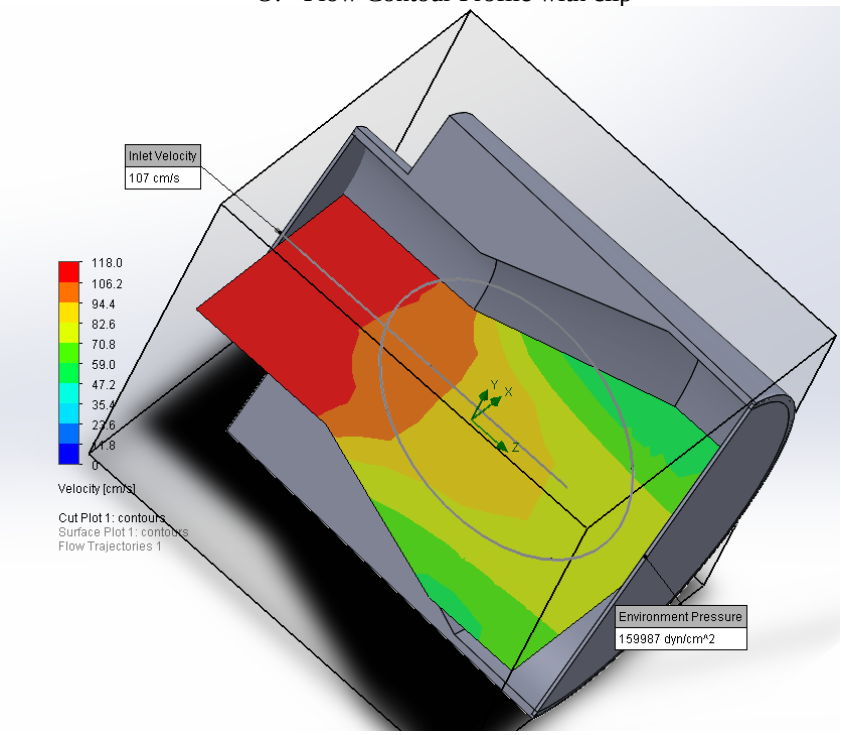
M. Gantt Chart for Medical Device stage.



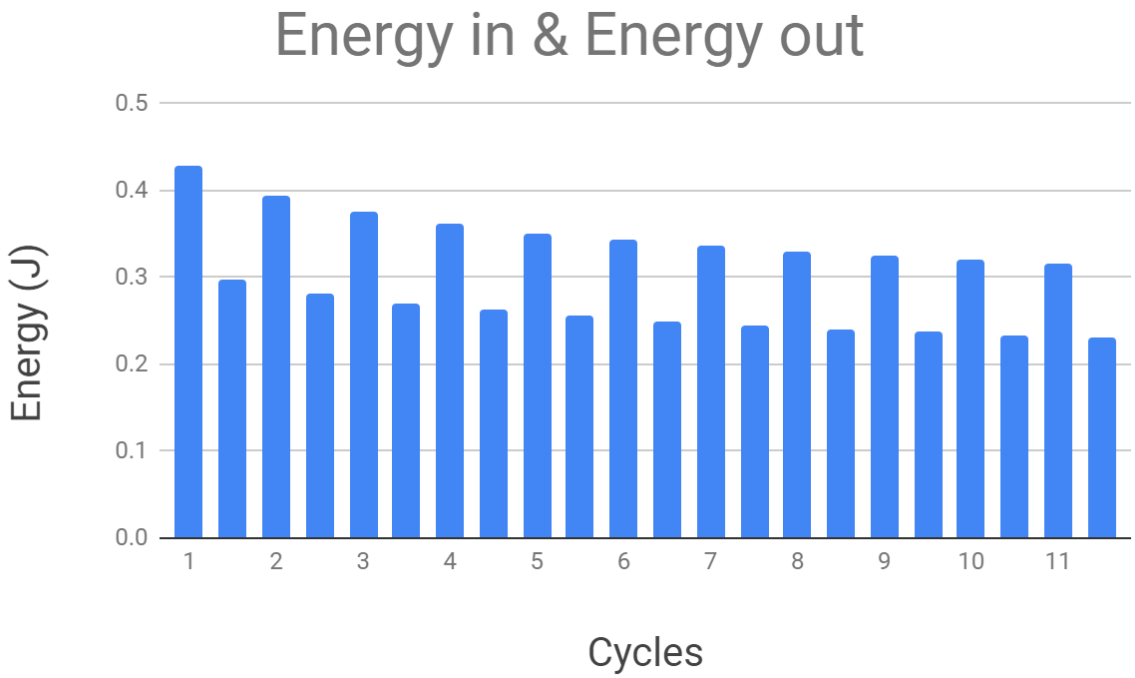
N. Diagram showing clipping mechanism step-by-step.



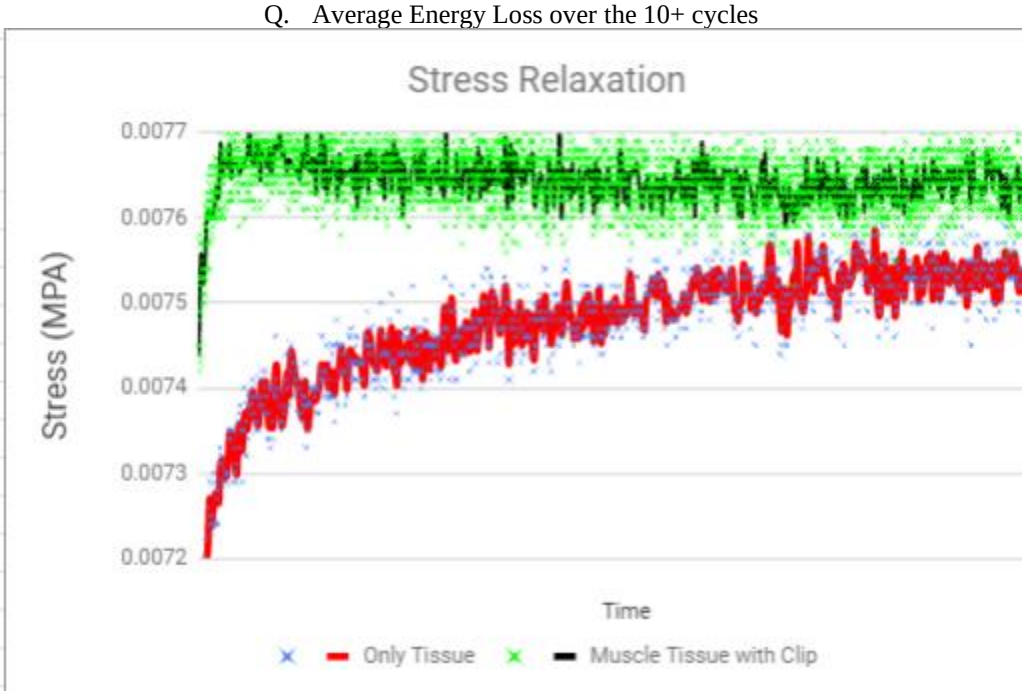
O. Flow Contour Profile with clip



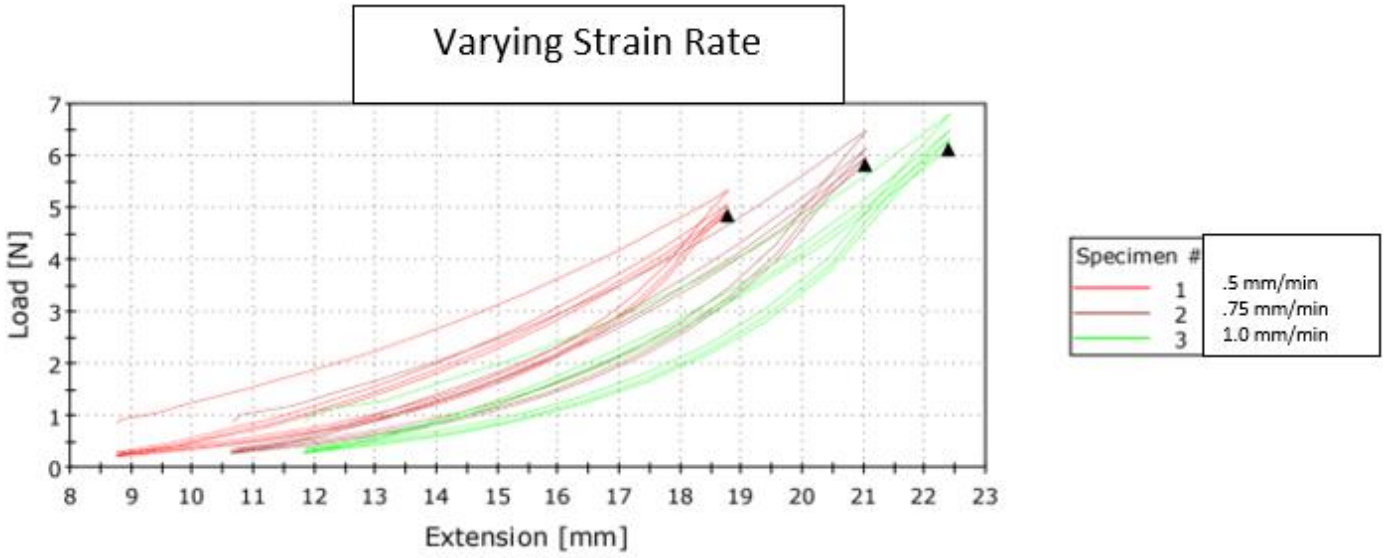
P. Flow Contour Profile with NO clip



Q. Average Energy Loss over the 10+ cycles



R. Stress Relaxation Results



S. Stress Strain graph of varied loading rates

T.