

**DESIGN, PROTOTYPING AND TESTING OF A TOOL FOR  
INTRACARDIAC DELIVERY AND ANCHORING OF A  
PROSTHETIC MITRAL VALVE**

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## **Abstract**

The mitral valve in the heart sometimes struggles with diseases and complications, and needs to be replaced. This problem becomes more frequent with the ageing of the population in developed countries. The most common practice consists of suturing a prosthetic valve into place. However, newer methods are being devised and tested to make the surgery faster and less invasive. In particular, various types of new sutureless heart valve systems exist on the market. However, there is still a need for a tool designed for the intracardiac delivery and anchoring of a prosthetic mitral valve, as addressed here.

A number of criteria and specifications were set by researchers at the Robarts Research Institute (London, ON) who came up with the design task. To address their request, ten conceptual designs of a sutureless, virtual-reality guided, self-anchoring, intracardiac system were developed to hold a prosthetic mitral valve, deliver it safely, and quickly affix it in position. The winning concept adequately met the design criteria.

Two prototypes were manufactured. The attachment of a prosthetic valve to a simulated mitral valve annulus was tested with the first prototype to verify feasibility and measure leakage. The second prototype was pressure tested in a dynamic surgical phantom reproducing the circulatory conditions during surgery. While the preliminary feasibility of the concept was established, recommendations were made to develop a less bulky design.

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# 1 Introduction

## 1.1 Context of the research

Heart disease is the leading cause of death worldwide (1). The heart may suffer from a number of diseases and complications (details are presented in Appendix A: Cardiovascular diseases), including abnormal heart beats (arrhythmia), buildup of plaque (atherosclerosis), birth defects, thickened cardiac muscle (cardiomyopathy), high blood pressure (hypertension), blood clots (thrombosis), and heart valve diseases. Of particular interest in the present work is the mitral valve, which regulates blood flow between the left atrium and the left ventricle of the heart. It may suffer from a number of complications, including bacterial infections (endocarditis), and numerous diseases that may lead to the valve's incomplete closure causing blood leakage (regurgitation) or cause the valve to narrow (stenosis) (details are presented in Appendix B: Mitral valve complications).

As medical technology progresses, safer surgeries have become possible to treat the various diseases and complications of the heart and its valves. More than half a million heart surgeries are performed each year in the United States (2). The most common heart surgery is called coronary artery bypass surgery, whereby one or more of the heart's blood vessels (blocked due to coronary artery disease) are replaced with healthy ones taken from other parts of the body (3).

A traditional open-heart surgery, first pioneered in the 1950s, requires access to the heart by opening the patient's chest wall by cutting through the breast bone, and use of a heart-and-lung machine to take over the heart's pumping action (4; 2). This allows for the

patient's heart to be stopped, so that it is blood-free and motionless for the surgeon to easily perform the operation (3). However, as the baby boomers population ages, and may develop several simultaneous diseases (comorbidity), cardiac surgery becomes more risky, therefore it would be advantageous if the operating times (cardiopulmonary bypass and aortic/mitral cross clamp) were reduced and the cardiac surgery was less invasive (5).

Surgeons are always striving to improve patient comfort during and after heart surgery. With recent advancements in technology, heart surgeries have evolved into new, potentially faster and less-invasive procedures called off-pump bypass, and minimally invasive surgeries. Instead of using a heart-and-lung machine and stopping the heart, in an off-pump surgery, the heart is left beating and new technologies allow the surgeon to “hold and stabilize portions of the heart” to perform the required surgery while the rest of the heart still circulates and pumps the blood (3). In minimally invasive heart surgery, instead of splitting the breastbone, only “three to four inch incisions” are made and advanced operating tools are used to access the heart, thus offering a less painful, better and a safer surgery (6).

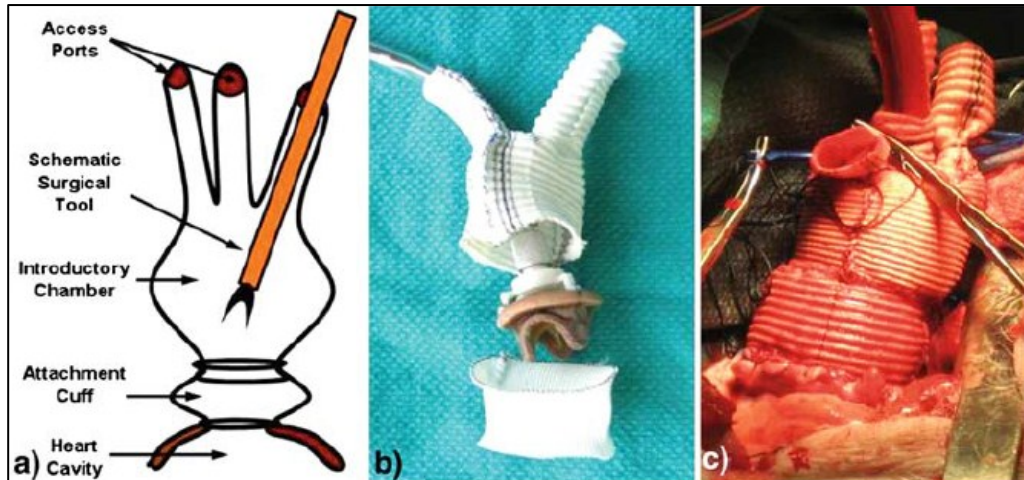
Over the last five decades or so, to correct diseases and complications of the aortic and mitral valves, advancements have been made in the design of prosthetic valves, and the valve replacement or valve repair surgeries. Numerous prosthetic valve designs have been developed, not only those that are manually sutured into place by the surgeon, but also sutureless prosthetic valves that utilize other means of attachment, and sutureless catheter based valves that utilize the benefits of catheter based insertion methods.

Open heart valve replacement surgery is considered a low risk, but still a serious surgery that entails replacing the valve with a prosthetic one. However, this type of procedure is now challenged by minimally invasive surgeries which can be used for repair or replacement of the heart's aortic or mitral valve (6). New technological devices, such as the Universal Cardiac Introducer (UCI), described below are being developed to increase the applicability of minimally invasive surgery (7).

## **1.2 Universal cardiac introducer**

The UCI was developed by Dr. Gerard Guiraudon, a world renowned cardiac surgeon (Robarts Research Institute, London, ON), with the goal to offer a safe and effective access to any heart chamber during a closed, off-pump (i.e. beating heart), minimally invasive heart surgery (8). As shown in Figure 1, the UCI consists of two parts: an attachment cuff and an introductory-airlock chamber. Both parts are tightly connected to each other and are equipped with an easy-release mechanism. The attachment cuff is sutured unto the left atrial appendage, and the introductory-airlock chamber has two to four ports to allow the use of surgical tools (7).

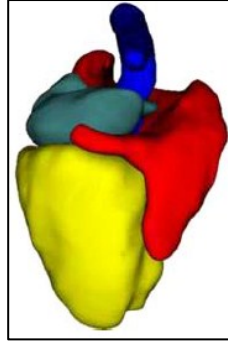
The materials used for the cuff and the introductory-airlock chamber are impervious, soft, and collapsible; the impenetrable coating protects against possible bleeding and air embolism (air bubbles in the blood stream). A soft and collapsible material must be used to easily occlude the cuff with clamps (7).



*Figure 1: a) Schematic representation of the UCI; b) physical UCI; c) UCI used during surgery. Source: (9).*

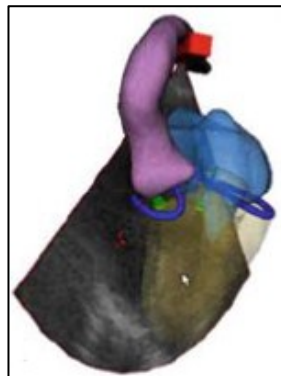
The lack of direct vision when performing a minimally invasive, closed cardiac procedure requires some type of imaging modality. Ultra sound (US) imaging was first used and caused many limitations for the navigation of instruments which interfered with the ultra sound. Therefore, an instrument-tracking system was introduced and coupled with a virtual reality environment.

To create this virtual reality environment, computed tomography (CT) or magnetic resonance imaging (MRI) can be used to make high-resolution geometric models of the heart anatomy before surgery (pre-operative imaging), which allows one to see clearly the anatomical parts of interest, see Figure 2 (9).



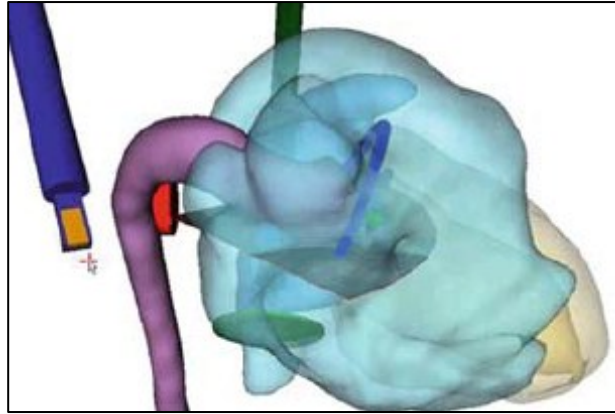
*Figure 2: Anatomical model built from pre-operative MRI. Source: (9).*

Then, during surgery, the imaging arrangement that can be used consists of a 2-D US transesophageal echocardiography (TEE) and a Philips X4 3-D US transducer probe, combined with pre-operative CT or MRI information (Figure 2), and virtual, real-time tracked representations of surgical instruments using magnetic tracking system (MTS) (9; 7). See Figure 3 and 4 for typical results that will be displayed on a screen for the surgeon to follow. Such virtual reality environment, for example, based on AtamaiViewer software, can be used to position a prosthetic mitral valve in the same manner as it would be positioned in a regular clinical procedure.



*Figure 3: Pre-operative anatomical model with intra-operative 2D ultra-sound imaging.*

*Source: (9).*



*Figure 4: A pre-operative anatomical heart model, 2D ultra-sound imaging and virtual surgical instruments, all combined in a virtual reality environment. Source: (9).*

This virtual reality guidance has been shown to allow positioning accuracy of  $0.99 \pm 0.29$  mm and makes it possible to see important details which would not be visible if 2-D/3-D US imaging was used alone (7). Using these enhanced imaging techniques, Guiraudon et al. reported no complications associated with accessing the cardiac chamber and no complications in positioning the prosthetic valve (7). The goal of this vision technology is to make a “virtual reality (VR) platform” that shows more information than normal direct vision can provide (7).

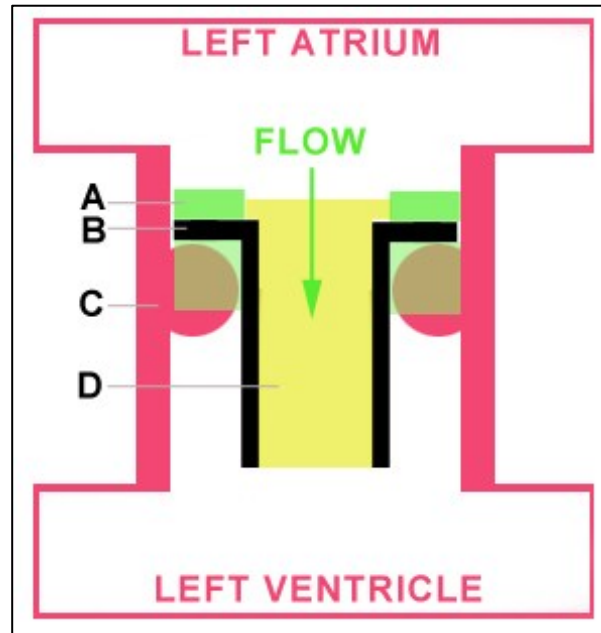
It should be noted that static anatomical models are not applicable to the beating heart; therefore, the heart’s motion needs to be rebuilt throughout its cycles (9). To make a dynamic heart model, the trajectories of all points in the model must be analyzed; the motion vectors of these points are calculated by looking at 4-D (space and time) images at various cardiac cycles (9). A dynamic model is thereby created by “propagating the static model (taken at mid-diastole) throughout the cardiac cycle using the computed motion vectors” (9).

As reported in a study performed by Guiraudon et al., the UCI has been used in 47 animals and has proved to be versatile, safe, and effective: a long-term study of 17 animals for atrial fibrillation did not show any complications due to UCI or air embolism (7). However, the tools used with the introductory-airlock chamber were considered to be bulky because they were equipped with sensors for 3-D tracking, therefore they interfered with each other, causing positioning of the prosthesis to be quite difficult (7). This prompted the need for new tools.

The need for new tools was also stressed with regard to the current anchoring and imaging techniques used. The anchoring mechanism used is a laparoscopic clip applicator, which attaches the prosthesis into position by means of clips (9). However, the clips have poor penetration into the tissue, thus sometimes fail to properly secure the prosthesis; they also have the risk of coming loose and are not easily removable if placed incorrectly (9). If the clip applicator is not used with the virtual reality environment and is used with 2D US alone, its tip and the clips cannot be seen, so its manipulation becomes difficult (9).

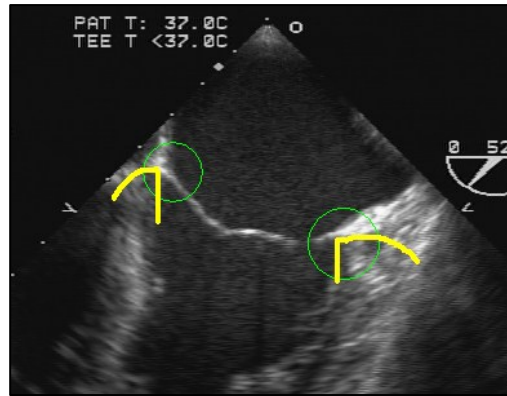
The task of designing a new tool, to be used in conjunction with the UCI during a closed, minimally invasive, off-pump, mitral valve replacement surgery was presented to myself and Dr. Michel Labrosse (University of Ottawa, Ottawa, ON) by Dr. Gerard Guiraudon, John Moore, Dr. Terry Peters, and Dr. Doug Jones (Robarts Research Institute, London, ON). The complete problem definition for the design of a non-metallic, non-bulky, fast and effective sutureless anchoring tool is as follows.

### 1.3 Problem definition



*Figure 5: Schematic working environment showing (A) the permissible working area in green, (B) mitral valve cross-section, (C) annulus cross-section, (D) and blood flow in yellow.*

Figure 5 illustrates the working environment for the tool to be designed. The left atrium and left ventricle are the two chambers, between which blood flows through the mitral valve (Figure 5-B). When the natural mitral valve no longer functions properly, a prosthetic valve needs to be implanted and held in position between these chambers.



*Figure 6: Ultrasound imaging of possible anchoring locations for a prosthetic mitral valve: (yellow) cardiac tissue, and (green) mitral valve annulus. Image is courtesy of John Moore, Robarts Research Institute (London, ON).*

The device, or intracardiac tool, to be designed must hold the prosthetic valve, allow its delivery and positioning into the cardiac tissue, anchor it in place, and finally release it. The duration of surgery is critical, therefore the anchoring mechanism must be quick (say, under 30 seconds) and efficient; after the valve is anchored to the tissue, the intracardiac tool must be promptly removed.

The device must meet a number of requirements, as requested by the researchers from the Robarts Research Institute, and they are presented as follows.

The tool can only be given a certain permissible working volume around the mitral valve (Figure 5-A), where the anchoring mechanism can be deployed into the cardiac tissue (Figure 6).

The device must not cause any significant blood flow (Figure 5-D) restriction between the two heart chambers, or only minimal restriction for a short duration of time (e.g. a maximum reduction time of up to 30 seconds).

For safety reasons, the reversibility or the potential for the intracardiac device and the prosthetic mitral valve to be removed, in case of any difficulties, is ultimately of great importance. However, for the initial design stages, it may be assumed that reversibility is not a concern.

The intracardiac device should not have metallic parts, as any ferro-magnetic material can interfere with the magnetic field generated by the magnetic tracking system (MTS), used for tracking surgical tools during this specific surgery (9). An assumption can be made that small metallic components cause little interference with the MTS, therefore it may be acceptable to use metallic components as anchoring mechanisms. Metallic parts were also viewed as the most efficient mechanisms for providing grip by the researchers at the Robarts Research Institute.

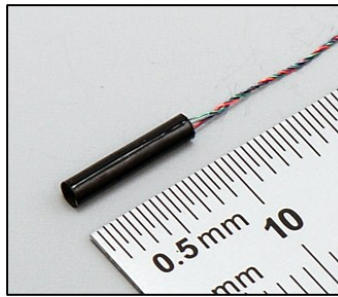
The insertion of the intracardiac tool holding the prosthetic mitral requires a path that is not straight from the surgeon to the location of implantation; instead it requires a 70-degree bend. Therefore a 70-degree bend is a requirement to be considered when designing the intracardiac tool. However, for the initial design, a straight path of approximately 15 cm in length is assumed.

It was recommended that a MOSAIC 310 bioprosthetic mitral valve be used as a reference for the design of the intracardiac tool. However, a mechanical prosthetic mitral valve (model: ONXM-25, by On-X Life Technologies, Inc.) was chosen instead, mainly for

simplicity reasons and accessibility of geometric data. Any prosthetic heart valve is designed to allow proper blood flow during its operation; therefore any modifications brought about by the device holding it, should not interfere with the blood flow. For instance, this means that the device must be located on the outside of the prosthetic valve, because the inside is reserved for the leaflets and maintaining the correct flow through the valve.

For safety reasons, the intracardiac tool must be designed such that wires/sutures/threads running to the tool, if pulled accidentally or over-pulled, must not break, damage the tool, or interfere with the surgery.

The intracardiac tool must be equipped with a sensor that must be positioned as close to the prosthetic valve as possible, to enable better magnetic imaging navigation during surgery. The sensor to be used, as shown in Figure 7, is an NDI Aurora Mini 6 degrees-of-freedom (DOF) sensor, it is 1.8 mm in diameter, and 9 mm in length (10).



*Figure 7: NDI Aurora Mini 6 DOF Sensor. Source: (10).*

The sensor is encased in a hard plastic shell, and is suitable for any disposable medical tools. For the initial design of the intracardiac tool, the use of epoxy may be considered for attaching the sensor.

## **1.4 Thesis outline**

The thesis is arranged in the following manner. The literature review is presented in Chapter 2 and includes a brief overview of the anatomy of the heart and of its various properties pertinent to the design of an intracardiac tool, as well as the prior art on sutureless prosthetic heart valves. Chapter 3 presents the conceptual designs developed for the intracardiac tool, along with their advantages and limitations, leading to a decision analysis. The design analysis of the winning concept, its prototype manufacturing and testing are presented in Chapter 4. Conclusions and recommendations for future work are reported in Chapter 5.

## **2 Literature Review**

The first purpose of this section is to review the literature pertinent to heart anatomy and physiology, mitral valve anatomy, the forces involved in myocardium puncture, and the pressures inside the heart. The second purpose of this section is to evaluate the existing medical technologies related to the sutureless implantation of artificial heart valves, including different anchoring devices and different types of artificial valves. The third purpose of this section is to demonstrate the need for a sutureless, quick-deploying, non-metallic, virtual-reality guided, artificial mitral valve anchoring device.

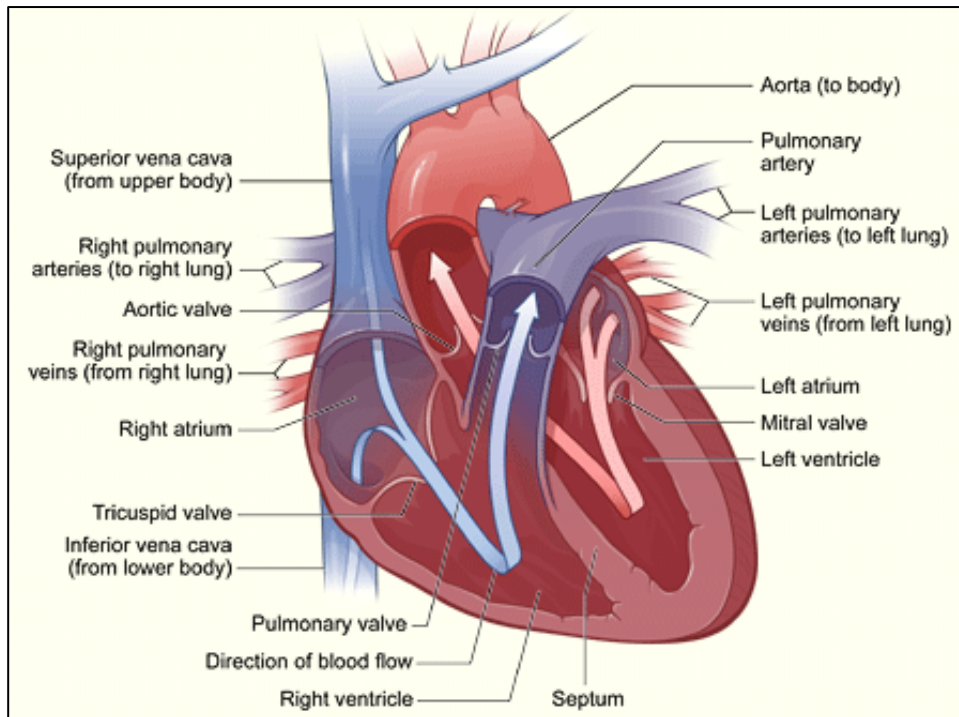
### **2.1 Heart anatomy and physiology**

“With what words will you describe this heart,  
so as not to fill a book...?”

– Leonardo da Vinci

#### **2.1.1 Introduction: heart, blood, arteries, veins, capillaries**

The cardiovascular system consists of the heart, blood vessels, and the blood. The heart is a double pump whose main function is to force blood into arteries and throughout the body. The size and weight of the heart varies according to gender and age, but typically a heart is 12 cm in length, 9 cm in breadth, 6 cm in thickness, and weighs about 230 to 340 grams (11).



*Figure 8: Basic heart anatomy. Source: (12).*

The heart is a conical, muscular organ located just above the diaphragm and between the lungs (11). As shown in Figure 8, it is divided into right and left halves with each half further divided into upper and lower chambers; the upper chambers are called atriums, the lower are called ventricles (11). Thus, the heart consists of four main components: right atrium, right ventricle, left atrium and left ventricle (11).

The heart has four valves: the tricuspid (between right atrium and right ventricle), pulmonary (between right ventricle and pulmonary arteries), aortic (between left ventricle and aorta) and mitral valve (between left atrium and left ventricle). The heart valves' function is to control blood flow at regular intervals: due to the heart's pumping action, the valves are forced to open allowing blood to pass, then the back pressure from the blood

forces them to close, and the process repeats. For this thesis, the mitral valve anatomy is of great importance and will be discussed in more detail later.

### **2.1.2 Blood circulation**

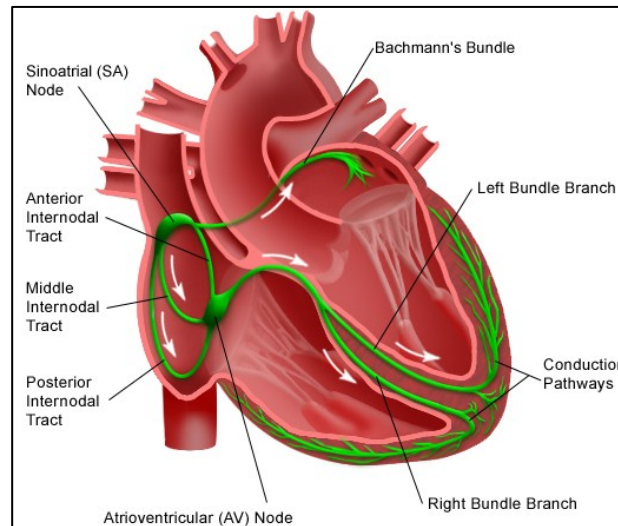
Referring to Figure 8, blood coming into the heart does so through the superior vena cava (from upper body) and the inferior vena cava (from lower body), which are veins that deliver deoxygenated blood to the heart's right atrium from the rest of the body, and through pulmonary veins which deliver oxygenated blood from the lungs to the heart's left atrium. The blood coming out of the heart travels into the aorta and the pulmonary arteries. The aorta is the largest artery in the body; with a diameter of 2-3 cm, it transports blood from the heart to the rest of the body by progressively branching out to different organs (13). The pulmonary arteries transport blood from the heart to the lungs (14).

The heart is itself a major organ, and as such requires oxygen and removal of carbon dioxide. Therefore, it has its own blood supply: branching out from the aorta just at the exit of the heart, the right and left coronary arteries deliver much needed oxygenated blood to the myocardium (14). Large coronary veins, like the coronary sinus, are responsible for waste removal by transporting blood back to the right atrium (14).

### **2.1.3 Cardiac cycle and heart's electrical system**

The heart's pumping action is controlled by an electrical system. The sinoatrial node (Figure 9), the heart's natural pacemaker, is located in the right atrium and creates electrical impulses (at a rate of 60 to 100 impulses per minute) that stimulate the heart muscle (15). These impulses travel through conducting pathways to the different regions of the heart (15). For example, impulses travel to the atrioventricular node where they are slowed down and

then continue on to the ventricles (15). The impulses then travel back to the sinoatrial node, which then generates more electrical impulses to start another cycle (14).



*Figure 9: Electrical system of the heart. Source: (15).*

During the initial stage of a contraction of the heart, called atrial systole, the sinoatrial node generates electrical impulses that stimulate contraction of the atrial walls, forcing the right atrium to push blood into the right ventricle through the tricuspid valve, and forcing the left atrium to push blood into the left ventricle through the mitral valve (14). During this stage, the aortic valve and the pulmonary valve both remain closed due to the existing back pressure in the aorta and pulmonary arteries.

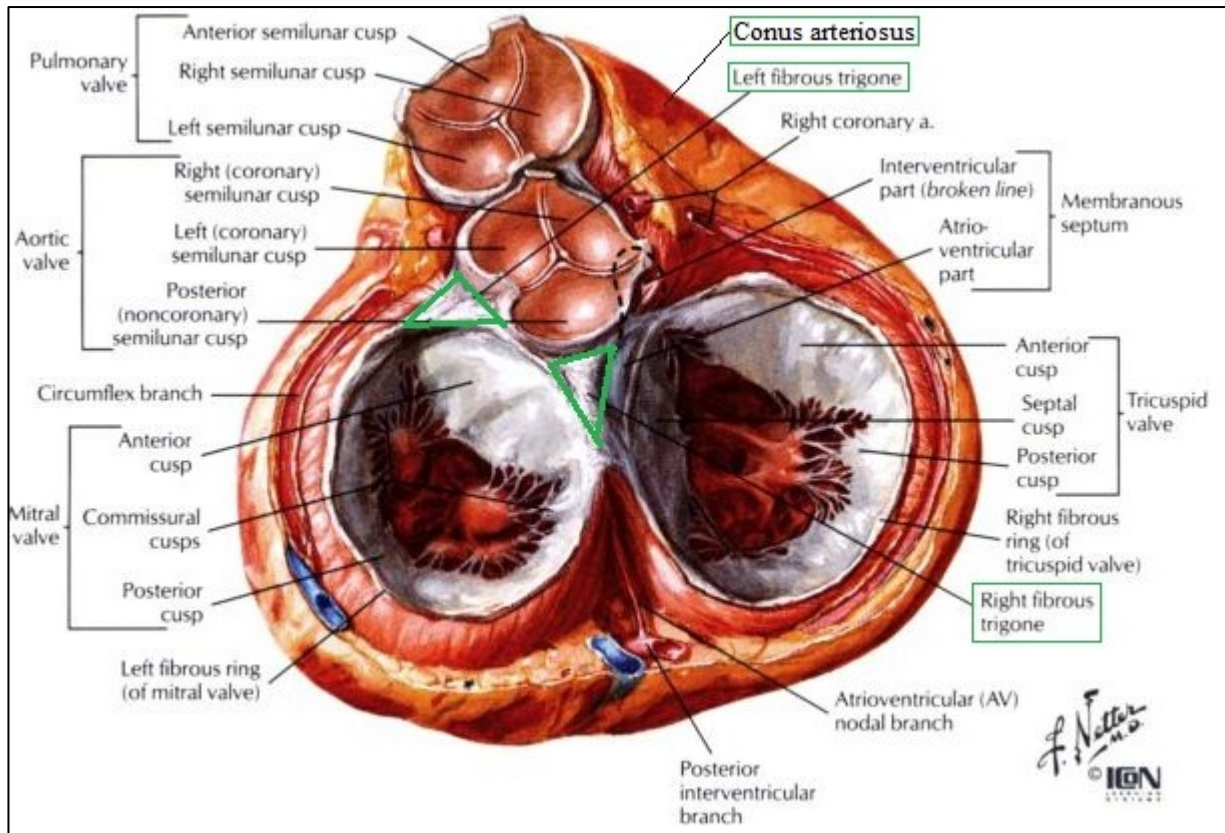
During the second stage of a contraction of the heart, called ventricular systole, the larger and thicker walls of the ventricles contract due to electrical impulses from the atrioventricular node (12). This contraction forces the blood into the pulmonary artery through the pulmonary valve from which the blood travels into the lungs, and also forces oxygenated blood from the left ventricle into the aorta through the aortic valve and to the

rest of the body (12). During the ventricular contraction, the mitral and the tricuspid valves are forced shut due to the blood pressure generated. After the ventricle contraction is complete, the ventricle walls relax (diastole), the mitral and tricuspid valves open and begin to fill the ventricles with blood coming from the atriums (14). Before the beginning of next systole, the ventricles are filled to about 80% capacity (14).

#### **2.1.4 Fibrous cardiac skeleton**

Of great importance for the support it provides to the heart muscle and valves, the heart's dense fibrous skeleton is composed of rings that wrap the heart valves, the right and left fibrous trigones, and the tendon of the conus arteriosus as shown in Figure 10 (16). The rings or annuli around the valves are fairly rigid, and thus prevent deformation of the valves during normal cardiac cycles (14). The rings serve as an attachment point for the muscle fibers of the atriums, ventricles, bicuspid and tricuspid valves (11). They are stronger on the left side than on the right side to handle larger pressures on the left side of the heart (11) as will be detailed later.

As shown in Figure 10, the right fibrous trigone is a triangular thickening of the fibrous cardiac skeleton “underlying the right posterior leaflet of the aortic valve” (17); whereas the left fibrous trigone is also a triangular region “between the left side of the left atrioventricular ring and the aortic ring” (18).



*Figure 10: Cardiac skeleton showing right and left fibrous trigone regions, the conus arteriosus, the right fibrous ring of tricuspid valve and the left fibrous ring of mitral valve.*

*Source: (19).*

The tendon of the conus arteriosus originates from the right atrioventricular fibrous ring and functions as a connection between the posterior conus arteriosus and the aorta (11). The conus arteriosus is essentially a cone-like pouch running from the right ventricle to the pulmonary artery (11).

Very importantly, the fibrous cardiac skeleton needs to be preserved as much as possible during heart valve surgery. Therefore, the information in this paragraph needs to be kept in mind when evaluating the viability of an anchoring mechanism for the mitral valve.

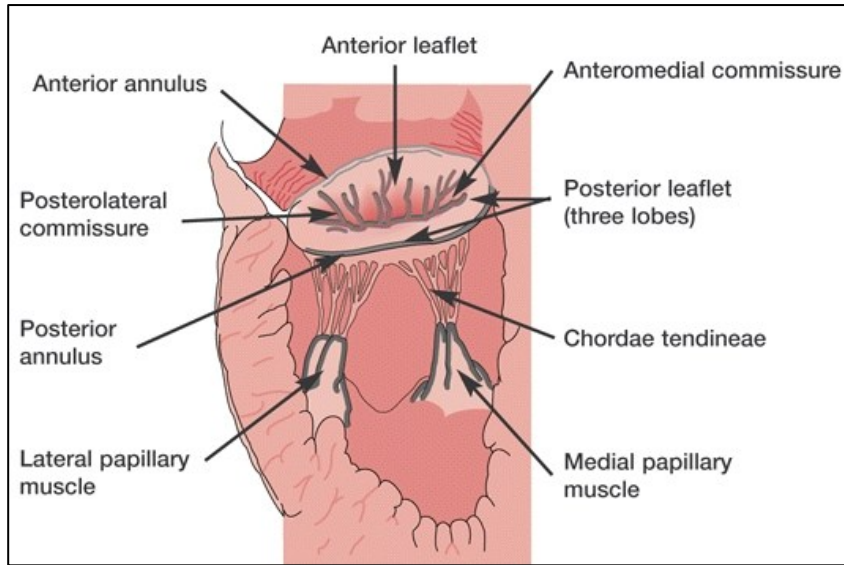
## **2.2 Mitral valve anatomy**

### **2.2.1 Overview**

It is apparent that the intracardiac tool to be designed will puncture and grip certain tissues near the mitral valve; we must therefore closely examine the mitral valve anatomy and the composition of its surrounding tissues. As noted earlier, the mitral valve is located between the left atrium and left ventricle, as shown in Figure 11, it can be described as a system consisting of a fibrous annulus ring, two anterior (aortic) and posterior (mural) leaflets or cusps, chordae tendineae, and papillary muscles (20). The mitral valve undergoes dynamic changes in shape during a cardiac cycle (21).

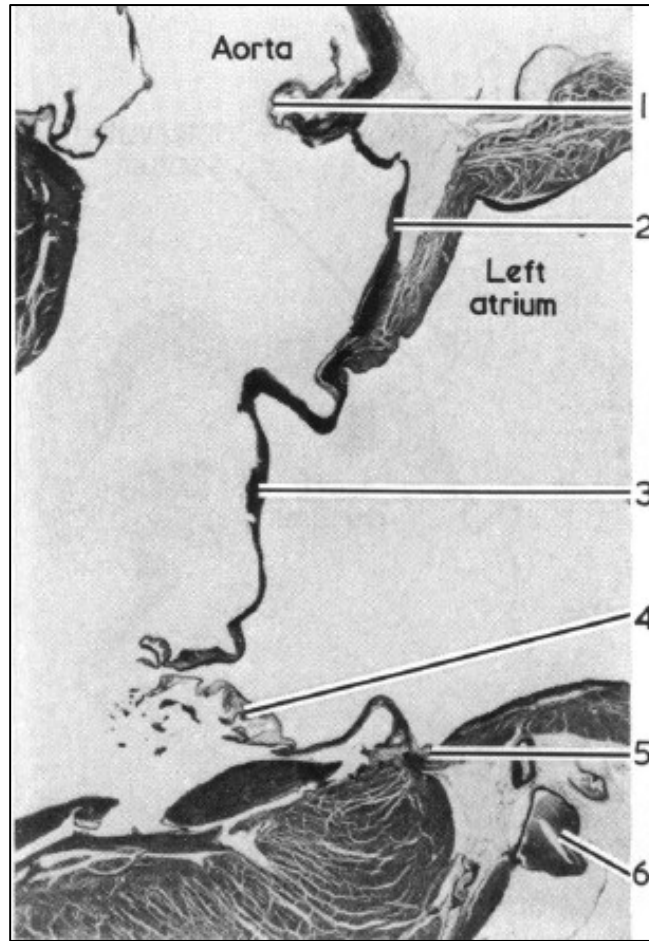
### **2.2.2 Mitral valve annulus**

The mitral valve annulus, as shown in Figure 11 can be further distinguished between the anterior and posterior annulus. It is a fibrous ring that supports the shape of the mitral valve and serves as attachment for the leaflets; its function is to anchor the leaflets to the myocardium (21) and to also contract (albeit passively, following its muscle support) during systole to ensure complete valve closure (22). The annulus is more in a D shape than circular, with the anterior leaflet being along the straight part (23). The microstructure of the annulus consists of collagenous and elastic fibers that connect to the heart's myocardium (21).



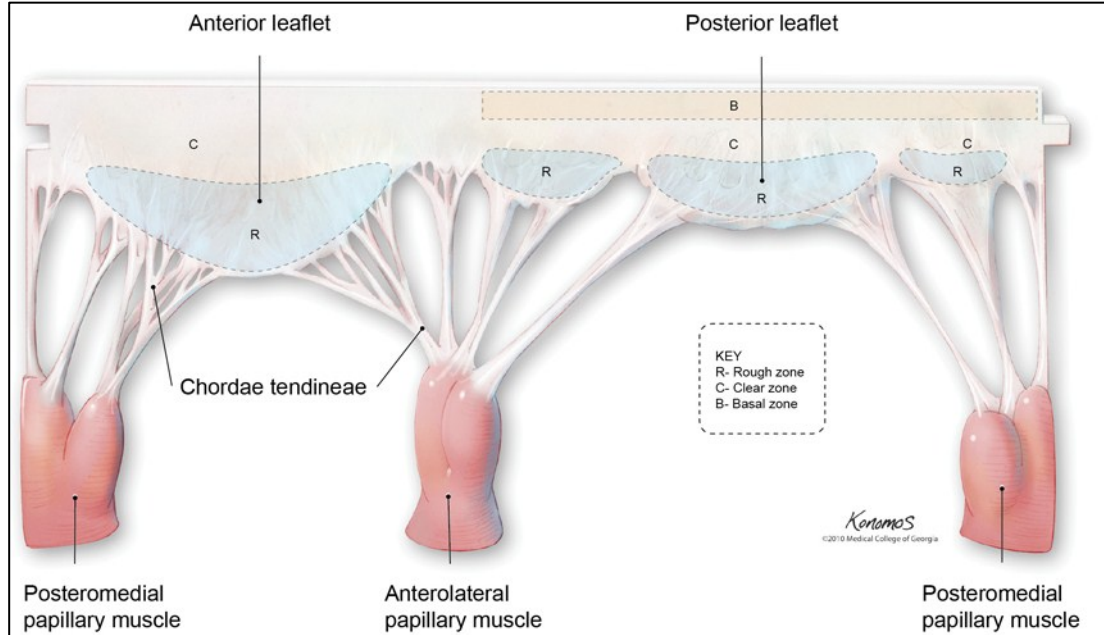
*Figure 11: Mitral valve anatomy. Source: (24).*

With reference to Figure 12, it can be seen that the annulus ring is not continuous, but is limited to a region where atrial and ventricular myocardia are next to each other (20), mainly on the posterior side, where the annulus ring is a distinctive band of collagen (20). On the anterior side of the mitral valve, the mitral valve annulus is not considered to be very well defined (20).



*Figure 12: Magnification of mitral valve leaflets showing absence of mitral annulus at anterior leaflet side. Also seen are (1) the left cusp of aortic valve, (2) the intervalvar septum, (3) the anterior cusp of mitral valve, (4) rough zone of mitral valve leaflet, (5) mitral valve annulus is also clearly visible, (6) and the branch of left coronary artery. Source: (20).*

### 2.2.3 Mitral valve leaflets



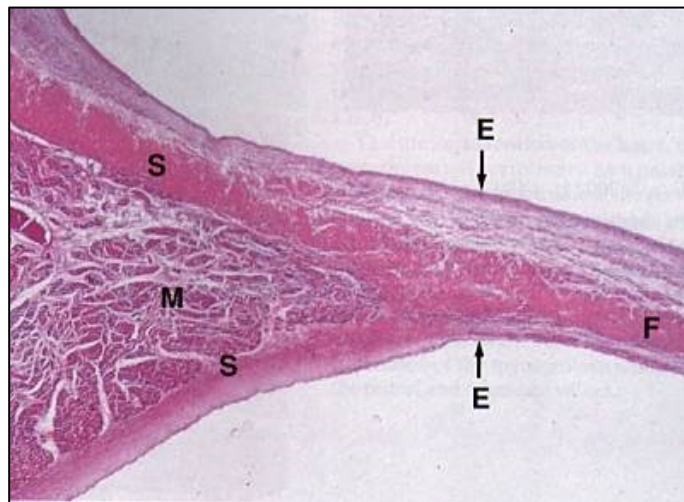
*Figure 13: Anterior and posterior mitral valve leaflet zones. Source: (22).*

As can be seen in Figure 13, the mitral valve has two main leaflets, the anterior and the posterior leaflets. The anterior leaflet is more triangular in shape and takes up about a third of the mitral valve circumference (23) whereas the posterior is more rectangular in shape (20). The leaflets are soft, thin and translucent (23).

The two mitral valve leaflets are divided into two zones that have distinct functions, the distal appositional or rough zone and the free or clear zone (20). The appositional zone is composed of loose meshwork of collagen fibers; when the valve closes this appositional zone comes into contact with the matching appositional zone on the opposing leaflet (20). This is due to the fact that the area of the leaflets is larger than the area of the mitral valve orifice (20). The free zone is composed of much denser collagen called the lamina fibrosa; the free zone does not come into contact with the opposing leaflet (20). A 'ridge of

demarcation' or the 'line of closure' may be a distinct ridge present between the appositional and free zones (20).

Referring to Figures 14 and 15, the mitral valve leaflets' microstructure consists of an outer endocardium layer, and a dense connective tissue core (lamina fibrosa) which connects to the mitral valve annulus (22). The anterior and posterior outer layers of endocardium are continuous with chordae tendinae, are thicker on the anterior side (20), and consist of squamous endothelium and a thin subendothelial tissue (22).



*Figure 14: Mitral valve leaflet microstructure: [E] endothelium, [F] lamina fibrosa, [S] fibro-elastic supporting layer, [M] myocardium. Source: (25).*

During ventricular systole, the leaflets close to prevent backflow into the left atrium (22); this is made possible by the chordae tendinae, which act as tough strings that connect the mitral valve leaflets' free edges to the papillary muscles in the left ventricle (26).

The anterior leaflet's basal attachment is achieved through the continuity of its lamina fibrosa (part of free zone of the leaflet) with the intravalvar septum, effectively

making the anterior mitral leaflet continuous with the aortic valve (23), because there is an absence of mitral valve annulus ring in this location (20), as noted earlier.

The posterior leaflet's lamina fibrosa has a basal attachment to the mitral valve annulus fibrous ring extending along its entire length (20). This part of the annulus ring may be thicker than 1.5 mm, and merges with the subendocardium of the left ventricle (20).

Aside from the two major mitral leaflets, the two regions between the anterior and posterior leaflets can be considered as small commissural cusps, and there is a large variation in the number of commissural cusps present in human hearts, therefore it may occasionally appear that there are more than two leaflets in the mitral valve (26).

#### **2.2.4 Tissues potentially affected by the anchoring of the mitral valve**

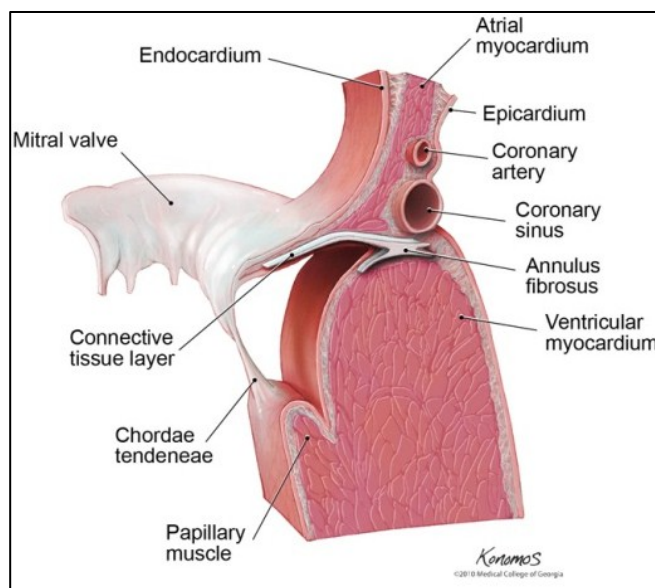
It is evident that along the circumference of the mitral valve, more specifically on the posterior and anterior sides along the mitral valve annulus, the structure and tissue through which the intracardiac tool's anchors must puncture and grip varies considerably. The design of the anchors should take these variations into consideration.

The ventricular myocardium does not completely encircle the mitral valve orifice, but is limited to the posterolateral region (20). This affects the design of the attachment anchors as some will puncture myocardium and others will puncture other tissues.

Due to the lack of the mitral valve annulus on the anterior leaflet side and the relatively thin myocardium between the aorta and the right atrium, the deployment of the anchors may cause puncturing into the aortic valve and negatively affect the aortic valve and the flow in the aorta. Therefore, keeping in mind that the left cusp of the aortic valve lies

above the attachment point of the anterior cusp of the mitral valve to the left atrium wall (20), the design of the anchors must carefully take into consideration these specific attachment conditions and spacing requirements on the anterior leaflet side.

Part of the fibrous cardiac skeleton, on the anterior side the left and right fibrous trigones (Figure 10) can provide a stable attachment location for the anchors, while avoiding too close proximity with the aorta or the aortic valve.



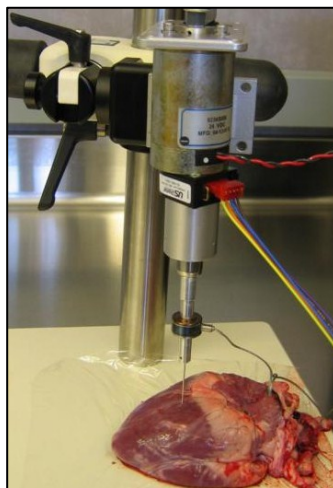
*Figure 15: Mitral valve leaflets anatomy. Source: (22).*

On the posterior leaflet side of the mitral valve, the mitral valve annulus is more prominent, and so is the myocardium (Figure 15). Therefore, the anchors either should puncture through or puncture near the endocardium layer, the mitral valve annulus, the connective tissue layer and ultimately into the myocardium. Very importantly, the coronary sinus, the coronary artery and any nearby conduction pathways for the heart's electrical system must not be affected or disturbed by the attachment anchors.

### 2.3 Forces involved in myocardium puncture

One anchoring method considered in this work consists of puncturing the cardiac tissue around the mitral valve annulus. This requires some understanding of what changes occur in the cardiac tissue during anchor insertion in response to applied forces. However, very little literature exists about “forces and deformations” of tissues during surgeries, since surgical dissection relies mainly on “gentle tissue handling” acquired through many years of experience (27).

As demonstrated by Mahvesh and Dupont, the general process of needle insertion into a pig heart (as shown in Figure 16, in vitro, using a rigid trocar needle) can be described as four force-displacement steps: initial loading deformation (0-1, Figure 17); rupture of the tissue (1-2, Figure 17); cutting of the tissue (2-3, Figure 17); and unloading deformation (3-4, Figure 17) (28). The forces generated during these four steps are due to friction (Coulomb friction, tissue adhesion, and damping), cutting (including plastic deformation), and internal stiffness (due to elastic properties of tissue before puncture) (29).



*Figure 16: Needle insertion experiment into the myocardium. Source: (28).*

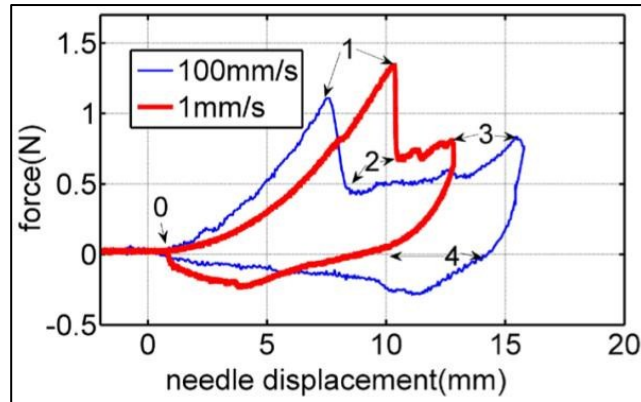


Figure 17: Force-displacement curves for trocar needle insertion/removal into a pig heart at 1 mm/s and 100 mm/s velocities, includes friction forces. Source: (28).

Of interest in the present work is the maximum puncture force required during this four step process, as this force needs to be sustained by the anchoring mechanism as well as, in the end, by the surgeon activating the mechanism.

Mahvesh and Dupont argue that during puncture though several tissue layers, maximum forces along with great deformations are generated at rupture events when “strain energy is suddenly released to the cracks” (28). Step 1 through step 2 in Figure 17 demonstrate a rupture event of the porcine heart tissue with a maximum generated puncture force of approximately 1.3 N at a velocity of 1 mm/s, including friction forces.

Puncture forces in porcine liver and spleen were measured as 0.35 N and 0.45 N respectively; in sheep liver and spleen, they were 0.29 N and 0.53 N respectively (27). Alja’afreh reports puncture forces of 0.9 N in lamb heart and 1.7 N in a rabbit heart (at 5 mm/s velocity, with a tri-pointed 1.1 mm surgical needle) (30). Frick et al. measured the puncture force for sheepskin to be 0.9 N (5 mm/s velocity, with a straight 2-0 cutting suture

needle), under an existing 2.9 N tensile load of the sheepskin. They also demonstrated that increasing the existing tensile load will increase the required puncture force (31).

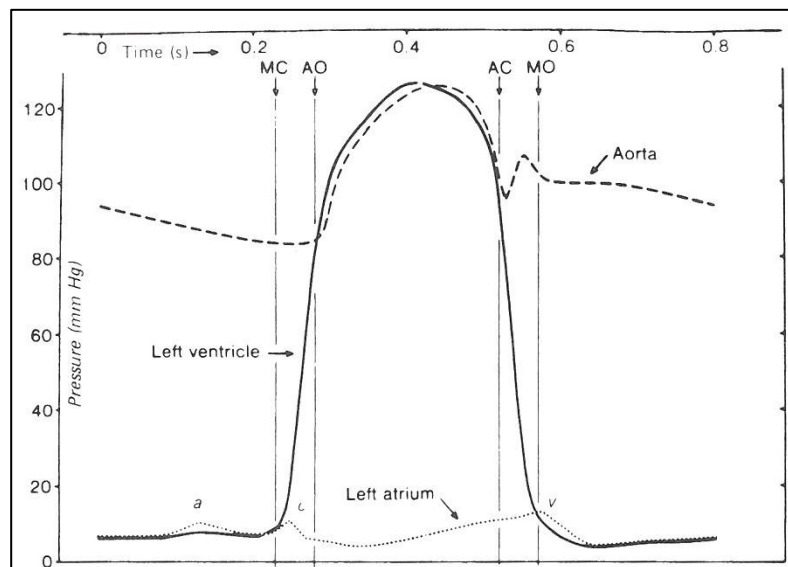
The type of needle or device used to puncture the tissue yields different force-displacement values. As stressed by Okamura et al., larger diameter needles require higher forces due to increased cutting and friction forces (29). Therefore, the maximum forces (at point of rupture) that must be overcome by the anchoring mechanism to be designed may vary considerably. However, the general force-displacement profile during needle insertion is not expected to change (32). Thus, from the experimental data of Mahvesh and Dupont (Figure 17), and the puncture forces reported by Alja'afreh, and including a design factor of 1.5, the maximum force to be overcome by the anchoring mechanism was set at 3 N (including needle friction forces).

Increasing the velocity of the needle as it punctures the tissue has been shown to reduce the maximum puncture force and tissue damage (30), “partly due to the viscoelastic and fracture properties of the material” and due to “increased energy release rates into the extended cracks” (28), therefore the deployment speed of the anchoring method should ideally be as fast as possible, which would also minimize surgical time.

## 2.4 Pressures involved

The design of an anchoring device for a prosthetic mitral valve also requires a good understanding of what operating pressures the prosthesis will be subjected to once in position.

According to Figure 18, showing typical blood pressures during a cardiac cycle, the maximum pressure generated in the left ventricle (LV) is about 120 mmHg, and the left atrial (LA) minimum pressure is about 8-10 mmHg. This means that the anchoring mechanism must withstand a maximum LV-LA pressure differential of about 110 mmHg when the mitral valve is closed.



*Figure 18: Pressures (mmHg) in the aorta, left ventricle, and left atrium as functions of time during a cardiac cycle; (MC/MO - mitral valve closing/opening, AO/AC – aortic valve opening/closing). Source: (33).*

Depending on the size of the prosthetic valve used, the mitral valve orifice area is known, and therefore the force applied onto the prosthetic valve and the anchoring mechanism can be calculated from the estimated operating pressures. For example, given an area of  $4.5 \text{ cm}^2$ , which is a usual area for a mitral valve cross-section (24) and a pressure of 110 mmHg (14.7 kPa), the force that the intracardiac tool's anchoring system must withstand will be approximately 6.6 N. Therefore, including a design factor of 1.5, the anchoring mechanism must withstand forces close to 10 N.

The intracardiac tool that will hold the mitral valve prosthesis and anchoring mechanism takes up space and, therefore, has the potential to reduce the effective mitral valve area for blood flow, thereby changing the pressure gradient across the left ventricle and the left atrium when the mitral valve is open. This pressure gradient is called the transvalvular pressure gradient and is defined as the "pressure difference between the upstream and downstream regions of a valve" (34). The instantaneous transvalvular pressure gradient can be calculated from the blood velocity across the valve using the simplified Bernoulli's equation such that:  $\Delta P = P_1 - P_2 = 4V^2$  (35). The maximum velocity across the mitral valve is typically 0.9 m/s in an adult (36). A typical normal mitral valve has a negligible transvalvular pressure gradient ( $\Delta P$ ), usually about 3 Pa; any reduction in the mitral valve area (MVA), due to the presence of the intracardiac tool and the prosthetic mitral valve, will cause an increase in  $\Delta P$  if the same flow rate is to be maintained. The flow rate is dependent on the cardiac output: a low cardiac output generates a low flow rate and a low  $\Delta P$  (36). The relationship between MVA,  $\Delta P$ , and flow rate is usually expressed by the simplified Gorlin formula:

$$MVA (cm^2) = \frac{\text{Flow rate across the valve}}{\sqrt{\text{Mean Pressure Gradient}}} \quad (37)$$

Increases in the pressure gradient are graded based on their severity: Grade 1 (up to 25 mmHg, considered acceptable); Grade 2 (25 to 50 mmHg, considered unacceptable); and Grade 3 (more than 50 mmHg, severe). Higher  $\Delta P$  increases the chances of complications such as ventricular hypertrophy, i.e. increased wall stresses lead to larger wall sizes of the left ventricle (38; 35). Therefore the design of the intracardiac tool must be as unobtrusive as possible, to limit any potential increases in  $\Delta P$ .

In concrete terms, if one is to allow a 25 mmHg  $\Delta P$  across the mitral valve during surgery, this means, based on a flow rate of 4 l/min, that the mitral valve area can be reduced to 0.8 cm<sup>2</sup> by the intracardiac tool.

## 2.5 Prosthetic valves

With the overview of the environment faced by the prosthetic mitral valves now completed, it is necessary to present the different existing prosthetic valves that could be used with the tool to be designed.

For a typical heart valve replacement surgery, prosthetic valves are normally sutured into place by the surgeon, thus they are referred to as sutured valves. Different sutured valves are available on the market, including bioprosthetic and mechanical designs to replace either or both the aortic and mitral valves. They are manufactured by various companies, including: On-X Life Technologies, St. Jude Medical, Edwards LifeSciences, and Medtronic.

As examples, Medtronic's bioprosthetic aortic/mitral sutured valve is shown in Figure 19, and a St. Jude Medical® Regent™ aortic mechanical sutured valve is shown in Figure 20.



*Figure 19: Medtronic's bioprosthetic (porcine) tissue valve. Source: (39).*



*Figure 20: St. Jude Medical® Regent™ aortic mechanical valve. Source: (40).*

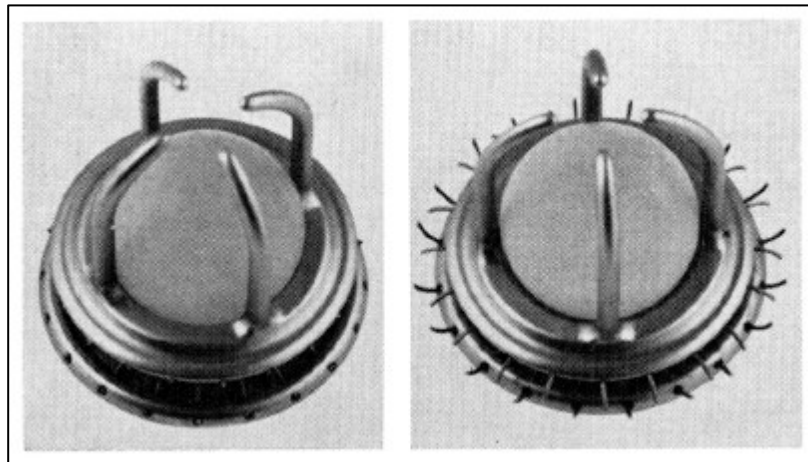
Also available on the market are sutureless valve designs that have their own methods of attachment, and newer tools such as catheter-based sutureless valves; the technologies behind these are greatly relevant to the present design of the intracardiac tool and are discussed below.

## 2.6 Sutureless valves

The objectives of sutureless valves are: to reduce surgery times; provide less invasive treatment; possibly improve hemodynamics and durability (by using a larger valve than what used to be possible), all the while “without compromising clinical outcome” (41; 42).

### 2.6.1 Magovern-Cromie ball valves

In the 1960s, any valve replacement surgery was much more risky than it is today, so to reduce the duration of surgery and thus the risk, first attempts at creating a quick deploying sutureless valve were made by Magovern and Cromie (5). They developed fast-deploying and very commercially successful designs of the aortic and mitral valves (43). The mitral prosthesis is shown in Figure 21.



*Figure 21: Magovern-Cromie mitral prosthesis in closed and deployed states. Source: (43).*

As shown in Figure 21, the Magovern-Cromie mitral prosthesis consists of an open-cage for the ball valve, and two donut-shaped rings with 24 pins per ring (30-degree angled) (43). The rings are attached to a central cylinder (not shown), which when rotated deploys the pins from the lower ring approximately 3 mm out toward the upper ring (and vice versa),

as well as moves the rings closer together, thus achieving excellent and quick grip with 48 actuating pins (43).

First implantation was performed in 1962 and demonstrated faster insertion (initial cross clamp time was around 30 minutes in 1962, declining to about 18 minutes over the next two years) (5). It also benefited from a large valve diameter, and exhibited no loss of fixation (43). Early complications included thromboembolism, endocarditis, insufficient anticoagulation, paravalvular leakage, and design problems such as ball variance (43).

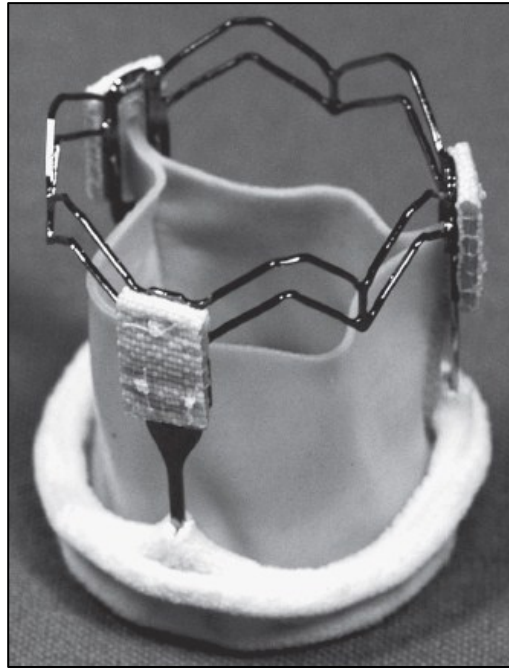
Thromboembolism is an inherent problem in valve replacement surgery (5). However, in the Magovern-Cromie case, its formation depends on the hemodynamics of the closed cage ball valve (Magovern later changed the design to an open cage design), the materials used (eliminating sutures and cloth ring from the valve should lessen thrombus formation), and the proper use of anticoagulants (43).

The Magovern-Cromie aortic sutureless valve showed great durability, as reported by Amnon Zlotnick, when in 2008 a valve was explanted from a 65 year old patient after 42 years of implantation (44); overall, approximately 7,300 Magovern-Cromie prostheses were implanted between 1962 to 1980 (5).

A number of companies and individuals, as presented below, are still involved in developing sutureless valves, each with its own specific advantages or disadvantages.

### 2.6.2 Medtronic 3F Enable

The 3F Enable Model 6000 sutureless aortic valve (equine pericardial trileaflet) shown in Figure 22, with a self-expandable Nitinol-based stent, was first developed by 3F Therapeutics (5). Nitinol is a shape-memory alloy.



*Figure 22: 3F Therapeutics 3F Enable Model 6000 sutureless aortic valve. Source: (5).*

When the company was bought by ATS Medical in 2006, the valve was modified to have a double flange design to further prevent paravalvular leakage (5; 45). When Medtronic bought ATS Medical in 2010 (46), the valve was further improved to closely mimic the “function of a native human aortic valve” (47).

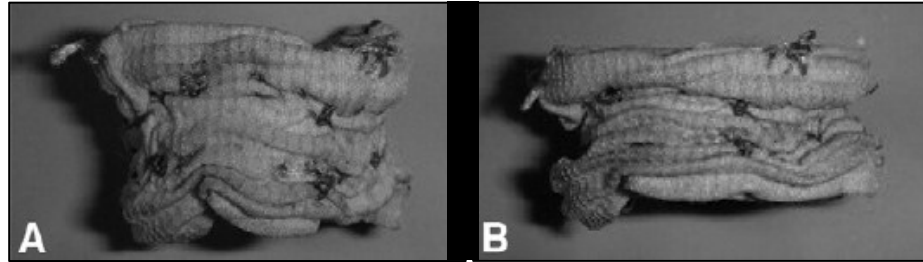


*Figure 23: Medtronic 3F aortic bioprosthesis. Source: (47).*

Medtronic claims that the valve (Figure 23) “preserves aortic sinuses (i.e. preserves sinus shape and function), restores native stress distribution (increases durability), and offers excellent hemodynamics (maintains aortic root geometry, helps restore non-turbulent transvalvular flow)” (47).

In a European clinical study conducted in five countries on 140 patients, the results showed minimal early complications (1.4% valve related mortality, 2.1% major paravalvular leak), and at 1-year follow up, the results showed “no valve migration, valve thrombosis or structural deterioration”, as well as minimal late complications (48).

### 2.6.3 Berreklouw sutureless valve attachment ring



*Figure 24: A) a textile covered Berreklouw device in cold shape; B) the same device in its warm, expanded shape. Source: (49).*

Berreklouw et al., have developed a unique attachment device based on the utilization of current commercially available sutured valves with a suture ring (49). The device consists of a valve attachment ring (VAR) shaped to match the aortic annulus, made of Nitinol and covered with a textile to aid in paravalvular leakage, with flexible upper and lower flanges to replace the suture ring of a conventional sutured valve (49; 5). Figure 24-A shows the device in its cold shape (maintained by low temperature and restraints) that is necessary to fit through the aortic annulus, and Figure 24-B shows its warm, expanded shape after body temperature is applied and restraints are removed (49) (shape-memory effect).

In a study performed by Berreklouw et al., the device has shown quick actuation, demonstrated normal heart function and valve operation, with a strong grip of the aortic annulus (“withstanding 5 kg of pulling force” in ex vivo pig heart experiments) (49).

#### 2.6.4 Perceval® S by Sorin Biomedica

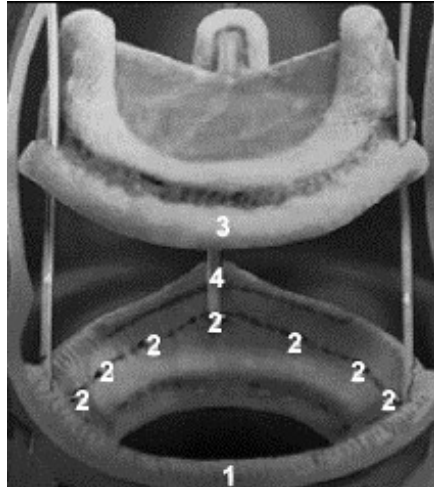


*Figure 25: Perceval® S sutureless aortic bioprosthesis. Source: (50).*

The Perceval® sutureless aortic bioprosthesis system, as shown in Figure 25, is a bovine pericardium stabilized in a buffered glutaraldehyde solution trileaflet valve (50). It is available in 21 mm and 23 mm sizes and built in conjunction with a Nitinol stent designed to take the shape of the aortic root and sinuses (5; 50). It is self-expanding, self-anchoring (with specially designed sinusoidal struts), sutureless, with good hemodynamic properties, and predictable long term outcomes (50).

Shrestha et al. confirmed the safety of this valve in a European clinical study including 30 high-risk patients (51). The results showed one hospital death, one death in a one year follow up, no observed dislodgement of the valve, two mild paravalvular leakages and two mild insufficiencies (51). The mean aortic cross-clamp time was  $34 \pm 15$  min, and the extracorporeal circulation time was  $59 \pm 21$  minutes (51).

### 2.6.5 Trilogy valve by Arbor Surgical Technologies, Inc.



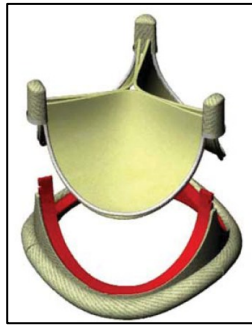
*Figure 26: Trilogy aortic valve by Arbor Surgical Technologies, Inc., showing (1) SecuRing, (2) aortic annulus, (3) valve crown and (4) guiding and locking mechanism. Source: (52).*

The Trilogy aortic valve by Arbor Surgical (Figure 26) consists mainly of two parts: the valve crown (Figure 26-3), which is a trilobal bovine pericardial valve with a Nitinol frame and independent leaflet suspension; and the SecuRing (Figure 26-1), which is essentially a Nitinol ring that is attached onto the aortic valve annulus by means of special attachment clips (52). It acts as a firm foundation for the valve crown (52). The valve was designed to reduce tissue stress, improve leaflet kinematics, and “with advanced antimineralization treatment, can exhibit superior calcification resistance” (53).

According to a study conducted on 32 patients by Breitenbach et al., the mean bypass time was  $111 \pm 42$  minutes, the cross-clamp time was  $70 \pm 23$  minutes, and the valve implantation time was  $21 \pm 7$  minutes (52). Although there was some regurgitation present (the SecuRing needed to be redesigned to correct this problem), Breitenbach et al. claim that the patients’ outlooks were positive, with good transvalvular pressure gradients (at discharge

and at two year follow-up) due to Trilogy valve's excellent effective orifice area (52). This suggests long-term survival and valve durability (52). The study showed that overall, the aortic valve replacement surgery using the Trilogy valve is feasible, safe, and quick (allowing for a learning-curve) (52). Another study by Flameng et al. concluded that the Trilogy valve is a “promising breakthrough in the effort to develop a more durable and hemodynamically efficient bioprosthetic valve” (53).

#### **2.6.6 ValveXchange, Inc. Vitality™ Heart Valve System**



*Figure 27: ValveXchange Vitality™ Heart Valve System. Source: (54).*

The ValveXchange system, as shown in Figure 27, is a two-part aortic valve system with a permanent support frame or “a docking station that provides a structurally sound foundation” and an exchangeable bovine pericardium leaflet set (55; 54). According to Salinas et al., it is in “early stages, with no human implants yet” (55). According to the manufacturer, its main advantage is that “when needed, the tissue leaflet set can be exchanged for a new set without open heart surgery, providing patients a lifetime tissue valve solution” (54).

## 2.7 Sutureless transcatheter valve implantation

About a third of patients are considered “high-risk” and are rejected for aortic valve surgery (55). To offer an alternative to sutureless aortic valves for these patients, great advancements have been made to deliver replacement valves by means of a catheter tube using transfemoral (small incision in femoral artery) or transapical<sup>1</sup> methods (5). Such methods are referred to as transcatheter aortic valve implantation (TAVI) (5).

More specifically, TAVI comprises of “an aortic valvuloplasty (the original valve remains in-situ and gets dilated into the aortic wall (5)), followed by the implantation of biological prosthetic valve stitched to a metallic stent crimped into a catheter” (55).

Since its first utilization in 2002, TAVI has shown great success in high risk patients, demonstrating decreases in mortality rates, reduced hospitalizations, and no deterioration of the prosthetic valve (56; 55); however, since the original valve is not removed, one significant complication may arise: the prosthesis may be implanted in a non-circular and inhomogeneous layer (typically in bulky leaflet calcification) causing it to change shape and thus leading to paravalvular leakage or coronary obstruction (5; 57).

As reported by Salinas et al., other TAVI complications include valve malapposition<sup>2</sup>, embolization, aortic regurgitation (severe in about 5% of cases), need for open heart surgery or a pacemaker, stroke, myocardial infarction, coronary obstruction, and

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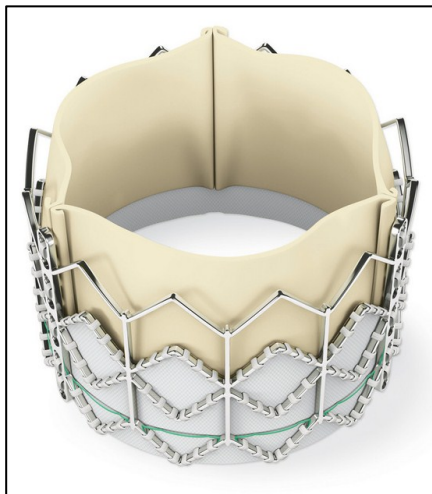
<sup>1</sup> “access to the left ventricular apex gained through the left anterolateral minithoracotomy in the fifth intercostal space” (122).

<sup>2</sup> “when a stent is not positioned properly (flush) against the interior arterial wall; late incomplete malapposition occurs when the stent later pulls away, or degrades, leaving a space.” (123).

kidney injury (55). In addition, access site complications including severe hemorrhaging, tears, and hematomas (55).

A number of different companies are involved in transcatheter aortic valve replacement surgeries. Their products are briefly described below.

### 2.7.1 Edwards SAPIEN



*Figure 28: Edwards SAPIEN transcatheter aortic heart valve. Source: (84).*

The Edwards SAPIEN valve, shown in Figure 28, is a bovine pericardial balloon-expandable valve sutured onto a cobalt chromium metallic stent (55), with a polyethylene terephthalate skirt, available in 23 mm and 26 mm sizes, to be used to with a special RetroFlex 3 delivery system (58).

As compared to a standard aortic valve replacement surgery for high risk patients, one year after the TAVI procedure, this valve showed an approximately 20% decrease in rate of death from any cause, a decreased rate of hospitalization, however increased incidence of major strokes and vascular complications (56).

## 2.7.2 Medtronic Engager™

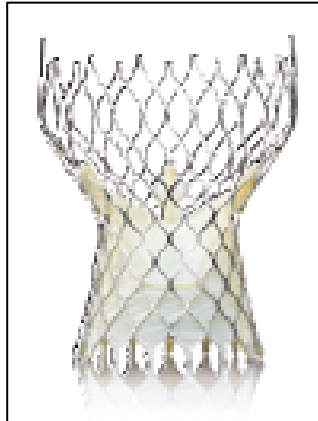


*Figure 29: Medtronic Engager valve system. Source: (59).*

Figure 29 shows the Medtronic Engager™ valve system, which is a trileaflet, flexible, bovine pericardium, aortic valve prosthesis mounted on a compressible and self-expanding Nitinol frame, with “a shape that is intended to minimize pressure losses at the inlet, and maximize pressure recovery at the outlet” (59).

As reported in a study done by Volkmar et al. on 30 patients, accurate valve placement is achievable, and in most cases, no more than grade 1 paravalvular leakage was observed (59). “Thirty day and in-hospital mortality were 20% and 23% respectively, and 6-month survival was 56.7%” (59).

### 2.7.3 Medtronic CoreValve ReValving System



*Figure 30: Medtronic CoreValve ReValving TAVI system. Source: (60).*

Figure 30 presents the CoreValve system, which “uses a self-expandable porcine pericardial valve sutured to a large Nitinol frame” (55). It comes with a much larger Nitinol frame than usual designs, to “cover both the left ventricular outflow tract and the aortic root.” (55). It is not retrievable and only partially repositionable before release (60).

### 2.7.4 Sadra Medical Lotus™ Valve

The Lotus™ valve is fully repositionable and self-centering and has the ability to be re-sheathed and retrieved, which provides physicians with more control over the implantation procedure (61; 55).

“The Lotus™ Valve System consists of the Lotus™ Valve, a bovine tissue tri-leaflet bioprosthetic aortic valve supported by a self-expanding Nitinol stent structure, and the Lotus™ Delivery Catheter, a delivery system for guidance and placement of the Lotus™ Valve” (61).

### 2.7.5 JenaValve™ by JenaValve™ Technology



*Figure 31: JenaValve™ prosthesis. Source: (62).*

The JenaValve™ aortic prosthesis, shown in Figure 31, is a “self-expanding Nitinol stent” design that “minimizes valve stresses and avoids contact between leaflets and the stent, for enhanced durability” (62). A unique feature of this valve is that it has a mechanism to capture the diseased leaflets, and avoid potential coronary obstruction (62).

### 2.7.6 Direct Flow Medical™ valve and inflation media



*Figure 32: Direct Flow Medical™ aortic valve. Source: (63).*

The Direct Flow Medical™ aortic valve shown in Figure 32 consists of “bovine pericardial leaflets that are attached to an inflatable polyester fabric cuff with independently

inflatable ventricular and aortic rings that encircle and capture the native valve annulus to provide positive axial anchoring of the device” (63).

Injected into the cuff, a saline and contrast solution enables fluoroscopic visualization; afterwards it is exchanged with a special inflation media (a water-soluble epoxy and a radiopacifier) and “hardens to form a permanent support structure” (63). According to Salinas et al., six patients have been implanted with this valve (55; 64).

Other catheter-based valves that have been developed are the AorTx™ valve by Hansen Medical, the HLT™ by Heart Leaflet Technologies, the Paniagua™ by Endoluminal Technology Research, and the St. Jude™ by St. Jude™ Medical (55).

In conclusion, as can be seen from this review of the existing medical technologies related to the implantation of artificial heart valves (sutureless and catheter-based), there is still a need for a sutureless, quick-deploying, non-metallic (so as to not interfere with magnetic imaging equipment), virtual-reality guided, artificial mitral valve anchoring device.

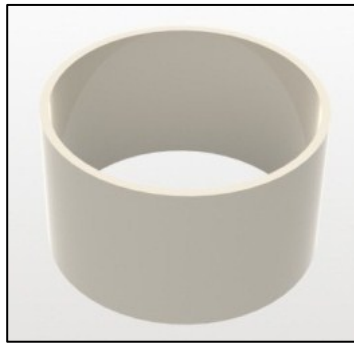
Indeed, all the designs found were for aortic valve replacements (with the exception of dated Magovern-Cromie designs), for which the requirements of the anchoring mechanism are very different from those in mitral valve replacement. In addition, most current designs rely on fairly large metallic stents that would prohibit magnetic tracking of the surgical tools and limit imaging modalities.

In the following section, conceptual designs are proposed to address the requirements expressed at the onset of this research project.

### 3 Conceptual Designs

#### 3.1 Design assumptions

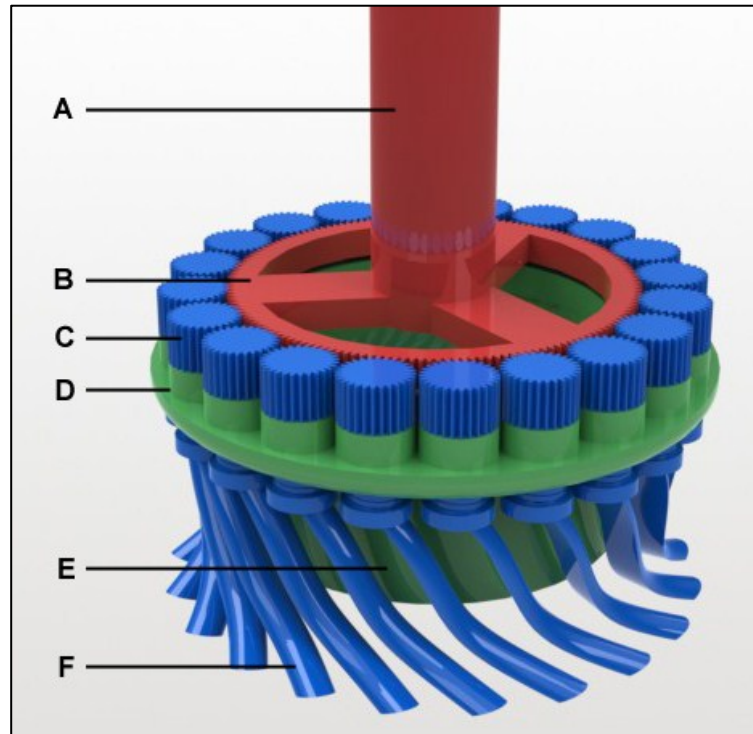
1. The mitral valve annulus shape is assumed to be a flat circular one with a perimeter equal to the perimeter of an actual D-shaped annulus.
2. Unless stated otherwise, parts are assumed to be made out of plastic.
3. For drawing purposes, the selected reference prosthetic mitral valve, On-X model ONXM-25 (Figure 33), was simplified to a simple hollow cylinder with an outer diameter of 25 mm, inner diameter of 23.4 mm, with a height of 14.2 mm, according to manufacturer data (65).



*Figure 33: Simplified version of an On-X 25 mm mitral valve (model: ONXM-25).*

4. Sutures or suture lines are not shown in CAD model parts or assemblies unless otherwise stated.

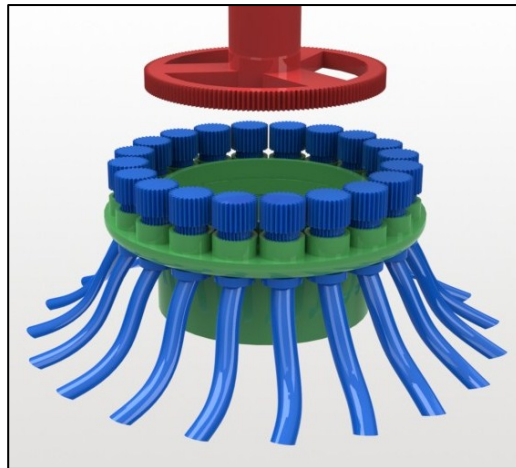
### 3.2 Concept 1: “Compression Legs”



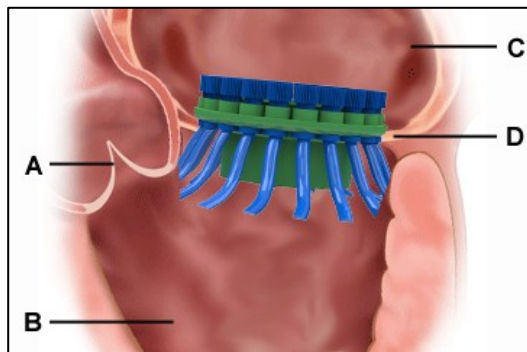
*Figure 34: Un-deployed view of Concept 1: "Compression Legs" consisting of (A) a holder, (B) main gear, (C) compression legs system, (D) an attachment to the prosthesis valve, (E) prosthetic mitral valve, and (F) rotating leg extensions.*

Concept 1 titled “Compression Legs” shown in Figure 34 is based on “leg” extensions (F) that rotate into position underneath the mitral valve annulus. The rotation is initiated by the surgeon rotating the holder (A). The deployed position is shown in Figure 35, and a deployed model inserted into the mitral valve annulus is shown in Figure 36.

Not illustrated is how the main gear (B) is supported for rotation only, but this does not affect the basic operating principle underlying this concept.

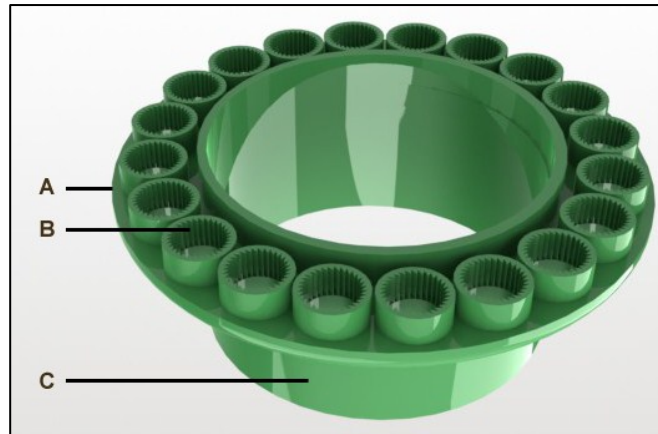


*Figure 35: Deployed Concept 1 (extension legs rotated into position under the annulus).*

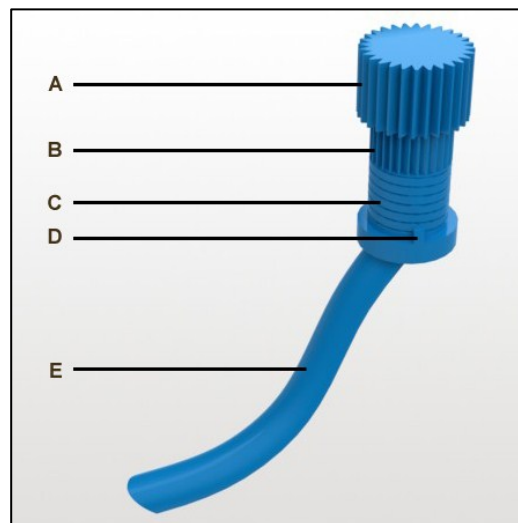


*Figure 36: Deployed Concept 1 shown in position with respect to (A) the aortic valve, (B) left ventricle, (C) left atrium, and (D) the mitral valve annulus. Original heart image source: (66).*

The On-X 25 mm prosthetic mitral valve (Figure 37) must be modified to have an addition (Figure 37) that rests on top of the mitral annulus and can support the compression legs system.



*Figure 37: Valve assembly consisting of (A) attachment to the valve, (B) legs locking ratchet system, (C) On-X 25mm mitral valve.*



*Figure 38: Single compression leg showing (A) the driven ratchet, (B) locking ratchet, (C) thread, (D) the stopper, (E) and the ventricle-shape-conforming leg extension.*

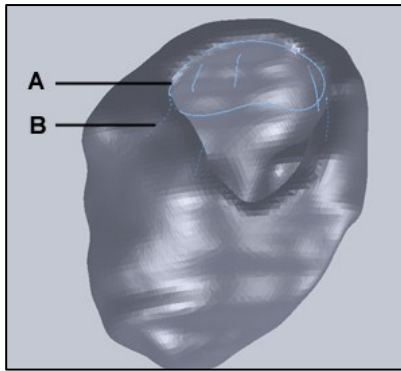
There is a threaded design along the axis of each leg (Figure 38). As the leg rotates along the thread, it will displace upwards. Therefore, when the surgeon rotates the main gear (Figure 34) it drives the legs in rotation as well as in translation to compress the mitral valve annulus.

A locking ratchet (Figure 38) is used to stop the legs from returning to their original position. A stopper, a small plastic extrusion (Figure 38), prevents the leg from over-turning during initial deployment; the location of this stopper on different legs can dictate different stopping distances along the annulus.



*Figure 39: Bottom view of a single compression leg showing the ventricle-shape-conforming leg extension.*

The shape of the legs was designed to conform to the shape of the left ventricle (Figure 39), based on average ventricle geometry data provided by John Moore (Robarts Research Institute, London, ON). This was done by generating curves running from the top (near the annulus) to the bottom of the ventricle (Figure 40), and taking an average curve to construct the shape of the leg extensions.



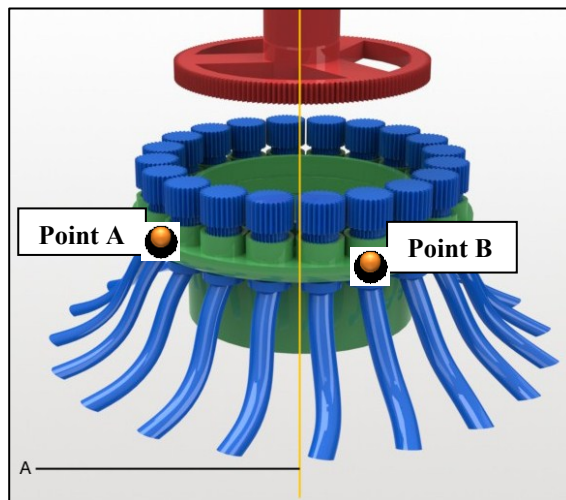
*Figure 40: Geometry of the left ventricle (imported from AtamaiViewer data courtesy of John Moore), showing (A) annulus defined as saddle-shape curve, and (B) curves added along the inside of the ventricle to define its shape.*

Concept 1 has a number of advantages and disadvantages. Its main advantage is that it is easy and quick to operate: just hold and rotate the extensions into place. Another advantage is that varying the properties of each thread (Figure 38) (for example the pitch or diameter) enables the legs to rise and compress at different rates, therefore independent compression control can be obtained.

Navigating the mitral valve prosthesis into the annulus becomes more difficult when the thread properties are varied, so some landmark must be chosen along the mitral valve annulus. Precise rotating or navigating of the assembly is necessary so as to align this landmark with say Point A and not Point B in Figure 41. Such navigation is possible using the NDI Aurora Mini 6 Degree-of-Freedom (DOF) sensor, but adds an extra step requiring monitoring an extra DOF. This may increase surgery times and may become a disadvantage.

A simpler navigation case is when there is no independent compression along the annulus, i.e. when the leg extensions all rise/compress at the same rate. Then, no landmark

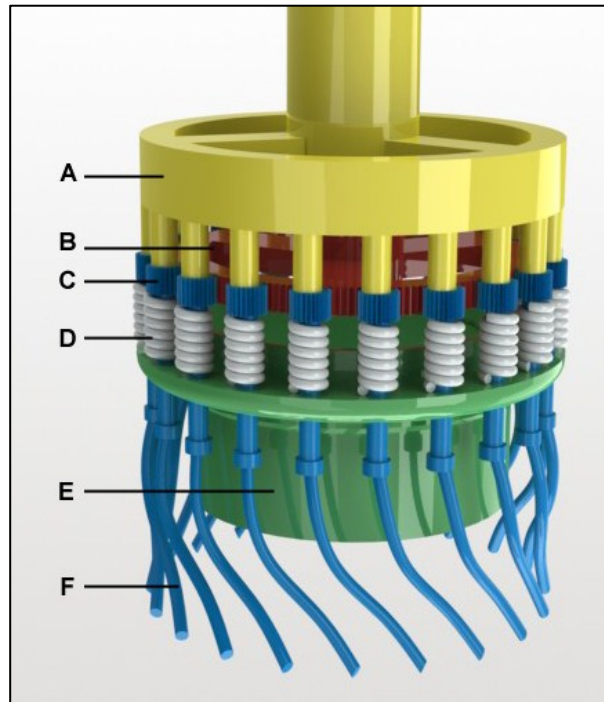
or alignment is necessary. In this case, all the leg extensions rotate together at the same rate. However, the likelihood for all the legs to have good contact with the heart muscle decreases, as the annulus and shape of ventricle is not same at all locations; this may cause some leg extensions to have a good grip, while others may jam, or have poor grip, and may lead to gear damage. The leg extensions may also get in the way of proper blood flow, especially near the aortic valve side. These issues may render independent leg extension rotation and compression indispensable to better control the grip around the mitral valve annulus.



*Figure 41: Concept 1 positioning, indicating (A) the main longitudinal axis. A complex navigation case consists in aligning Point A at a designated spot along the annulus; a simple navigation case does not involve any alignment.*

A number of other disadvantages to Concept 1 are present: the reversibility may only be possible if small plastic components are broken, e.g. when leg extensions are over-rotated. If care is not taken, a large torque on the main gear (Figure 34) may develop and cause damage to the gear teeth.

### 3.3 Concept 2: “Springs”

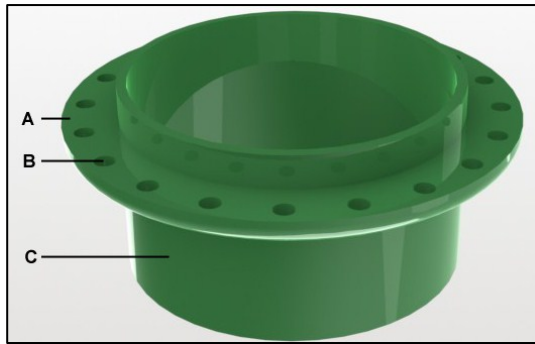


*Figure 42: Un-deployed view of Concept 2: "Springs", consisting of: (A) a main holder, (B) main driving gear, (C) compression leg system, (D) springs, (E) On-X 25 mm valve, (F) and leg extensions.*

Concept 2 is similar to Concept 1, but instead of using threads, it uses springs to generate a force that compresses the mitral valve annulus.

The On-X 25 mm mitral valve is modified to have an attachment that sits on top of the mitral valve annulus and contains spaces for compression leg systems (Figure 43).

The compression leg system (Figure 44) consists of a gear mechanism and leg extensions; the design of the leg extensions mimics the inside shape of the ventricle as done in for Concept 1 (Figure 40).



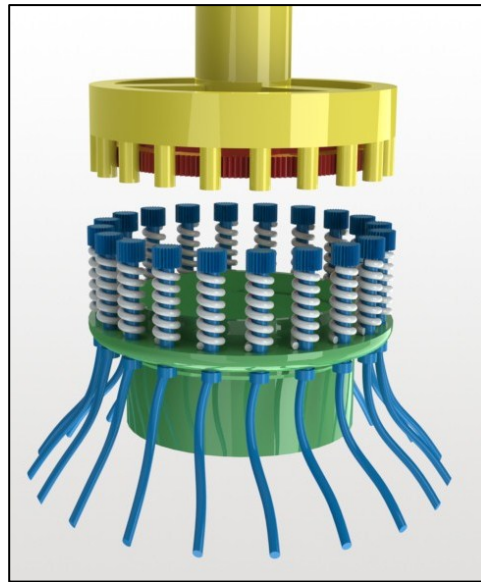
*Figure 43: Valve assembly showing the (A) attachment to the valve, (B) space for the compression leg system, (C) On-X 25 mm valve.*



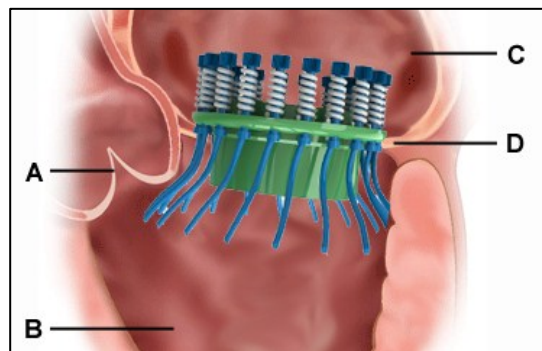
*Figure 44: Compression leg system used for Concept 2, consisting of (A) gear mechanism, (B) leg extension.*

Once positioned, the main gear (Figure 42) is rotated by the surgeon, thus rotating the compression leg systems and expanding the leg extensions, which grip the underneath of the mitral valve annulus.

Once the rotation is complete, suture lines (not shown) which attach the holder to the rest of the mechanism are cut. This releases the springs (Figure 42) which create a compressive force on the mitral valve annulus. The holder and main gear are removed and the procedure is complete (Figure 45, Figure 46).



*Figure 45: Deployed Concept 2, with leg extensions rotated into position under the annulus.*



*Figure 46: Deployed Concept 2 shown in position with respect to (A) the aortic valve, (B) left ventricle, (C) left atrium, and (D) the mitral valve annulus. Original heart image source:*

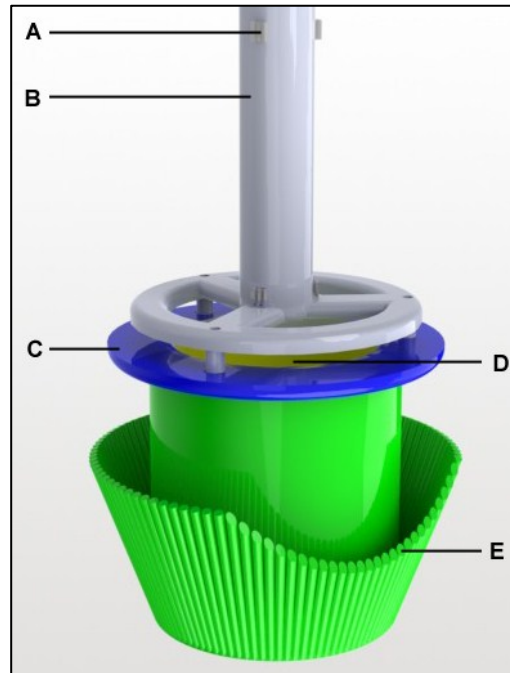
(66).

Concept 2 presents a number of advantages and disadvantages. Its primary advantage is that the springs allow for independent compression of mitral valve annulus, without complicating the initial positioning of the entire system. Another advantage is that reversibility may be possible, as the compression leg systems can be pushed back down again and simply rotated to a folded position.

A number of disadvantages are also present: the springs used must be very small, causing strength and manufacturing concerns; the springs may have to be made from metal if plastic can not be used, which may cause interference with magnetic imaging equipment.

A large torque arising from the main gear may also damage the small gears on the compression leg system (Figure 44). As with Concept 1, all compression legs rotate at the same time. This may lead to some leg extensions having a good grip, while others are over-rotated or under-rotated. This prompted the search for an independent rotation and compression system for each leg.

### 3.4 Concept 3: “Brush Bristles”

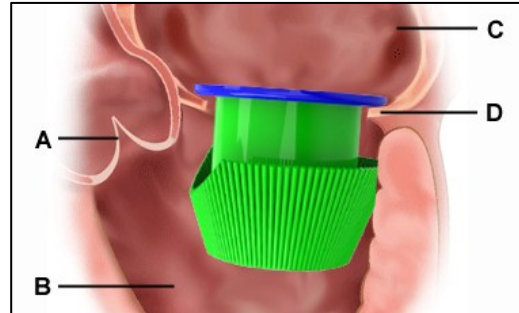


*Figure 47: Concept 3: "Brush Bristles" showing (A) suture guides, (B) the holder, (C) top attachment, (D) modified On-X 25 mm mitral valve, (E) bottom attachment with a half-circular cutout for aortic valve side.*

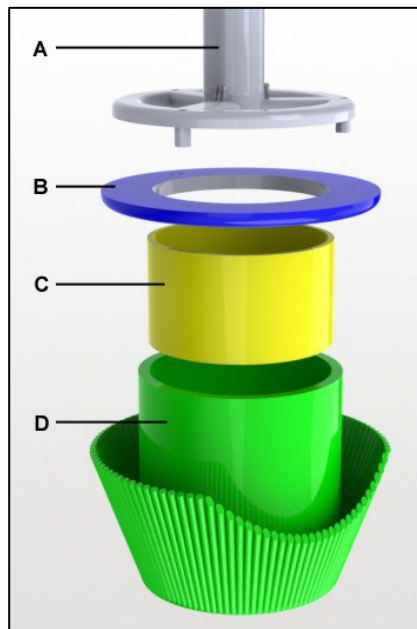
Concept 3 shown in Figure 47 is a simple concept with no moving or rotating parts. It consists of the following: a top attachment that rests on the mitral valve annulus, and prevents the valve from dropping into the left ventricle, a bottom attachment that is wrapped around the On-X 25 mm mitral valve and consists of multiple “brush bristles” protruding at a specified angle, upwards and away from the valve assembly.

The principle of operation is as follows: the brush bristles are able to deflect inwards when the entire assembly is inserted from the left atrium past the mitral valve annulus, and then after it passes the annulus, the brush bristles expand underneath, hence preventing the

entire assembly from moving back into the left atrium. The final deployed position is shown in Figure 48.



*Figure 48: Deployed Concept 3 shown in position with respect to (A) the aortic valve, (B) left ventricle, (C) left atrium, and (D) the mitral valve annulus. Original heart image source: (66).*



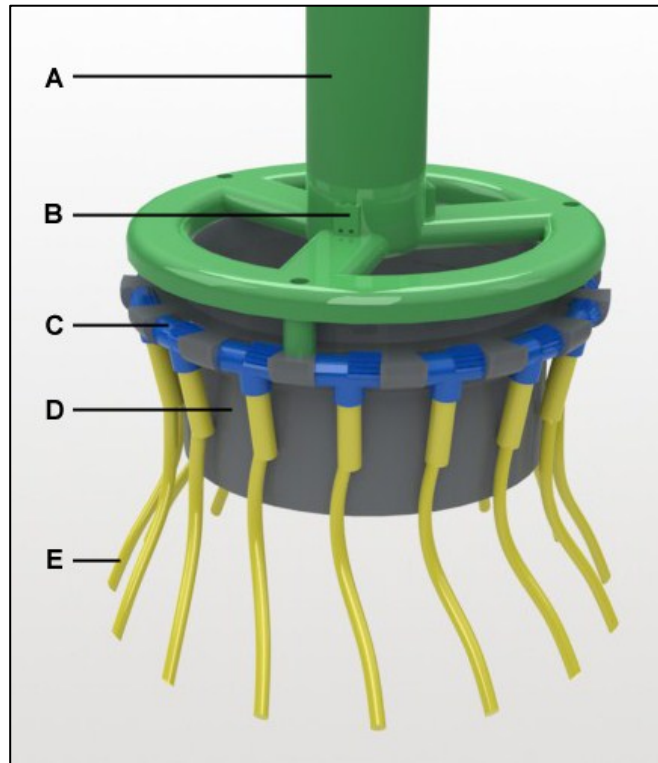
*Figure 49: Exploded view of concept 3: "Brush Bristles" consisting of: (A) a holder, (B) top attachment, (C) On-X 25 mm mitral valve, (D) and a bottom attachment with "brush bristles".*

The holder (Figure 49) is fixed to the top attachment with sutures (not shown); it also provides pathways for sutures that secure the holder to the top attachment (Figure 47).

This concept's main advantage is its simplicity (no moving or rotating parts), and ease of use (simply push into the annulus); however, there are a number of drawbacks, including that the brush bristles or the entire lower attachment may interfere with the blood flow, which may lead to complications such as thrombus formation. The brush bristles must not interfere with the aortic valve region, as this may greatly affect blood flow. Therefore the bristles length must be carefully designed, as illustrated by a half-circular cut-out on the aortic side (Figure 47). Utilizing all six degrees-of-freedom of the NDI Aurora Mini 6 DOF sensor, it would be possible to precisely position the entire assembly so as to not interfere with the aortic valve region.

This concept is currently not reversible; if it is considered for further work it will have to be redesigned to be made reversible.

### 3.5 Concept 4: “Winding Legs”



*Figure 50: Un-deployed view of Concept 4: "Winding Legs" consisting of: (A) a holder, (B) suture guides, (C) winding leg system, (D) On-X 25 mm valve with an attachment on top that holds the winding leg systems, (E) and leg extensions.*

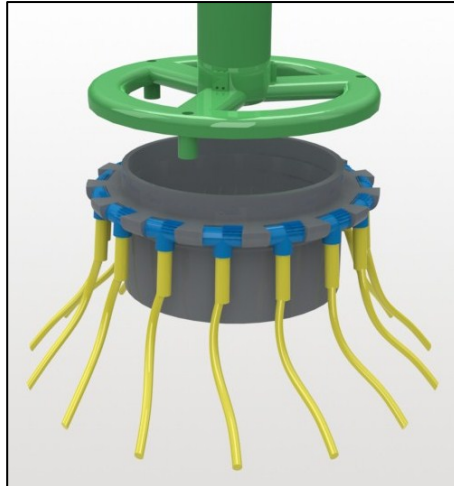
Concept 4 “Winding Legs” shown in Figure 50 consists of the following: a top holder, a top attachment that rests on top of the mitral valve annulus, and mounted to a modified On-X 25 mm valve, a winding leg system, as well as small extrusions that help guide suture lines along the holder to the winding leg system. Introduction of suture lines to activate the mechanism came from the realization that other powerful and small enough actuators were not available. Suture lines are made of non-metallic materials and are very strong. After activating the anchoring mechanism, they can be removed completely. Care

must be taken so that the suture lines are not pinched or do not make any sharp turns. Therefore, plastic guide tubes will be used to enclose suture lines with rubber seals used inside these tubes to prevent any blood leakage. The seals must not be too tight so as to allow for easy movement of the suture lines.

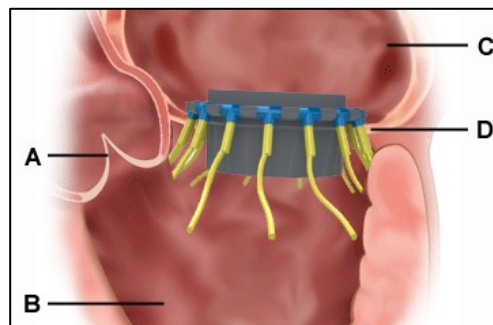


*Figure 51: Valve assembly consists of (A) a top attachment, containing (B) a ratchet-like extrusion and an axis to support the winding leg systems, mounted to (C) an On-X 25 mm valve.*

Similarly to Concept 1, Concept 4 is based on using leg extensions that rotate into position underneath the mitral valve annulus. The rotation is initiated by the surgeon by pulling on sutures that rotate the winding leg system. A deployed Concept 4 is shown in Figure 52 and Figure 53.

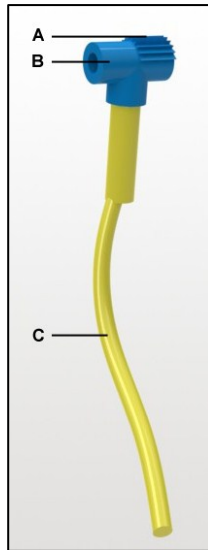


*Figure 52: Deployed Concept 4, with the leg extensions extended, holder partially removed.*



*Figure 53: Deployed Concept 4 shown in position with respect to (A) the aortic valve, (B) left ventricle, (C) left atrium, and (D) the mitral valve annulus. Original heart image source:*

*(66).*



*Figure 54: Winding leg system, consisting of (A) rotator ratchet side, (B) rotator smooth side, and (C) the leg extensions.*

As shown in Figure 54, the winding leg system consists of a rotator, and leg extensions. The rotator consists of two sides, a smooth side and a ratchet side. The ratchet side works to prevent the leg extension from moving back down into their un-deployed position, the smooth side is the location for a coiled suture line. Once the suture line is pulled on by the surgeon, it uncoils and forces the rotator to move the leg extension radially outward. A ratchet extrusion on the top attachment (Figure 51-B) prevents the leg extrusions from rotating backwards into their un-deployed position.

Similarly to Concepts 1 and 2, the design of the leg extensions imitates the inside shape of the left ventricle as determined from a CAD model of the left ventricle (Figure 40).

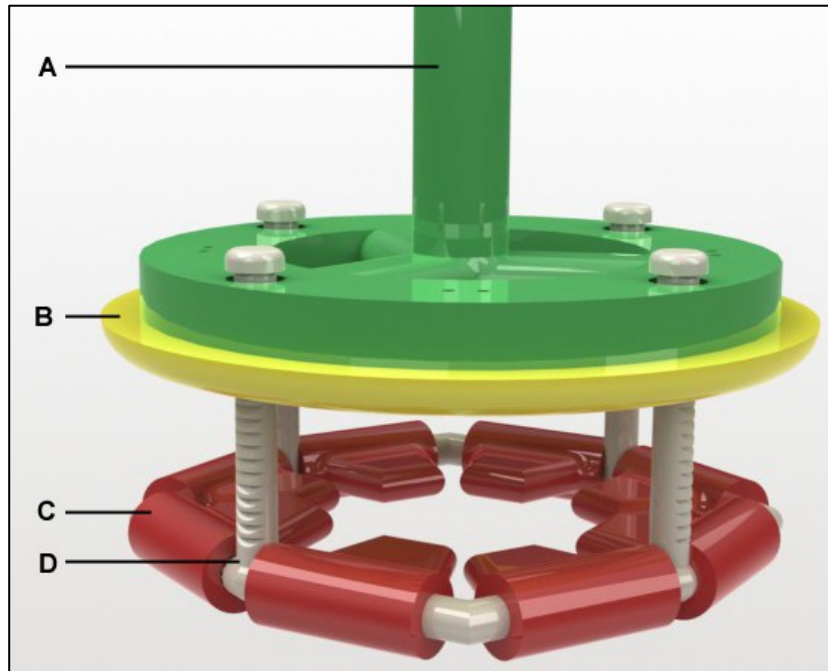
The leg extensions are able to grip underneath of the mitral valve annulus and they are also locked in place, so the suture lines can be cut and the valve assembly left in place.

The sutures securing the holder to the valve can also be cut to completely remove it and finish the procedure.

This concept's main advantage is the independent grip-control of each leg extension, because the surgeon pulls on individual sutures that run to each winding leg system; this is a significant advantage as the regions around the mitral valve annulus do not uniformly provide grip ability. Another advantage is that there are no large moving parts, and no gear teeth under large torques; therefore, the possibility of parts breaking is reduced.

Yet, a number of disadvantages are present: the extensions legs may interfere with the flow near the aortic valve, thus causing potential for thrombus formation. To alleviate this problem, some leg extensions may be shortened and then all six degrees-of-freedom of the NDI Aurora Mini 6 DOF sensor located at the bottom center of the holder may be utilized to position the entire assembly accurately. The size of certain parts is very small which may cause manufacturing problems. Reversibility may also prove difficult.

### 3.6 Concept 5: “Two step”

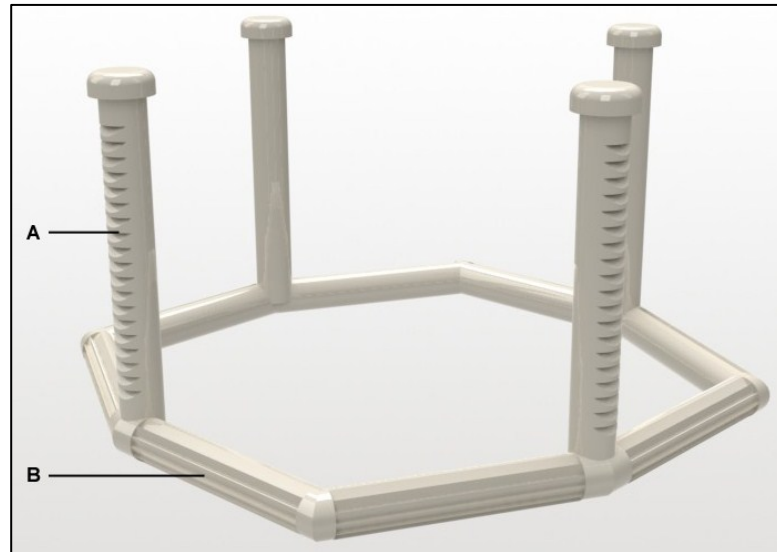


*Figure 55: Un-deployed view of Concept 5: “Two step” attachment base, consisting of (A) a holder, (B) top compression ring, (C) rotating flaps, and (D) bottom compression ring.*

Instead of a single step process as in Concepts 1-4, whereby the valve holder device is brought towards the mitral valve annulus, deployed, and removed in one step, a two-step process is proposed in Concept 5. Concept 5 (Figure 55) consists of a holder, a top compression ring, and a bottom compression ring which holds rotating flaps.

The first step of the process aims to establish an attachment base at the mitral valve annulus. The attachment base is shown in Figure 55. It is first introduced into the annulus. As the surgeon pulls on suture lines, the flaps are rotated to expand underneath the annulus. The flaps are fitted with a ratchet mechanism (Figure 56) which prevents them from moving

back into their un-deployed position. In principle, the flaps are similar to the leg extensions in Concept 4; however they can be larger because the valve assembly is not yet present.



*Figure 56: Bottom compression ring, with ratchet extrusions (A) for vertical elements, and (B) ratchet extrusions for flaps.*

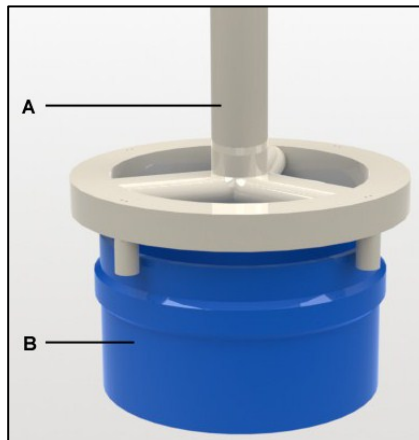
After the flaps are deployed, a compressive force can be created between the flaps and the top compression ring (Figure 55), as the surgeon pulls on suture lines that raise the lower compression ring (Figure 56), with a vertical ratchet mechanism preventing the lower compression ring from moving back down.

The mitral valve annulus may now be compressed by the flaps and the top compression ring. Once this attachment base is in place, all the sutures of the holder and lower compression ring are cut and the surgeon removes the holder; the deployed Concept 5 is shown in Figure 57.

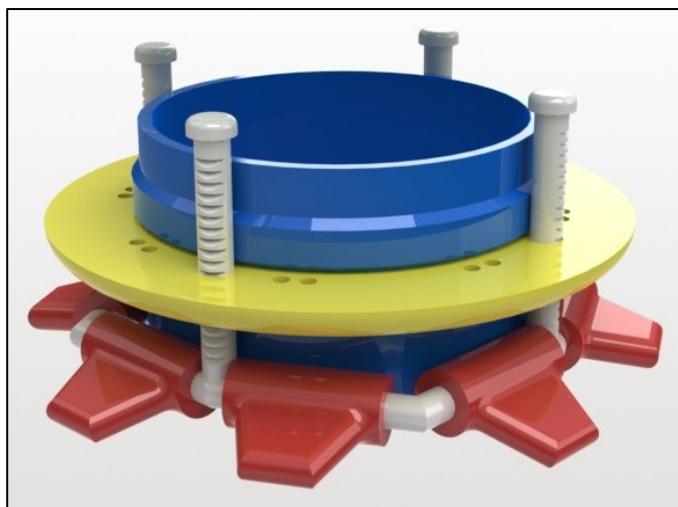


*Figure 57: Deployed Concept 5 attachment base, with flaps extended and the holder partially removed.*

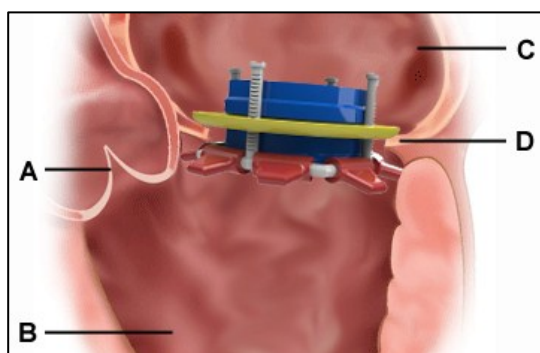
The second step of the process brings the On-X 25 mm mitral valve (Figure 58) to the attachment base and locks it there. The sutures of valve holder are cut and removed to finish the procedure. The final deployed position of Concept 5 is shown in Figure 59 and Figure 60.



*Figure 58: Concept 5 valve assembly, consisting of (A) a valve-only holder and (B) On-X 25 mm valve.*



*Figure 59: Deployed Concept 5, showing the flaps extended, lower compression ring raised, with the attachment base holder and valve holder removed.*



*Figure 60: Deployed Concept 5 shown in position with respect to (A) the aortic valve, (B) left ventricle, (C) left atrium, and (D) the mitral valve annulus. Original heart image source: (66).*

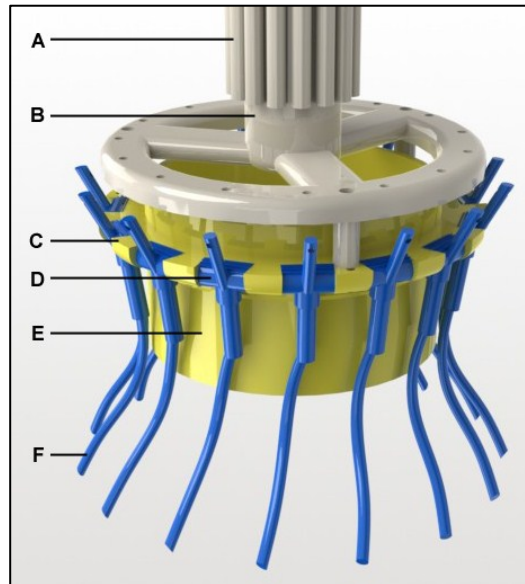
There are a number of advantages and disadvantages to Concept 5. Its main advantage is that using a two-step process may lead to a better grip of tissue, as the flaps (Figure 55) can be manufactured to be much larger and effectively stronger than the leg extensions of Concept 1 (Figure 34), Concept 2 (Figure 42), or Concept 4 (Figure 50). A

two-step process allows for these larger flaps because the valve prosthesis is not yet introduced in the first step and does not cause interference. Individual control of each flap is possible, meaning that compression along the perimeter of the mitral valve annulus can be different when some flaps are over or under-rotated; however this requires precise initial positioning of the attachment base by utilizing all six degrees-of-freedom of the NDI Aurora Mini 6 DOF sensor.

Navigating the artificial mitral valve to the already in place attachment base is achieved through guiding suture lines, which run from the attachment base to the prosthetic heart valve assembly, so that the assembly moves along the lines towards the attachment base. This eliminates the need to use any other navigating devices or extra sensors.

This concept's main disadvantage is that surgery times may be increased. The purpose of the present work is to have a design that will accomplish the placement of the artificial heart valve in as few steps as possible. Multistep design hinders that ability and may complicate the surgery procedure. Reversibility may also become difficult as the number of steps is increased.

### 3.7 Concept 6: “Rotating Legs”



*Figure 61: Un-deployed view of Concept 6: "Rotating Legs", showing the (A) suture guides, (B) main holder, (C) a top attachment to the artificial valve, (D) the rotating leg system, (E) On-X 25 mm mitral valve, and (F) leg extensions.*

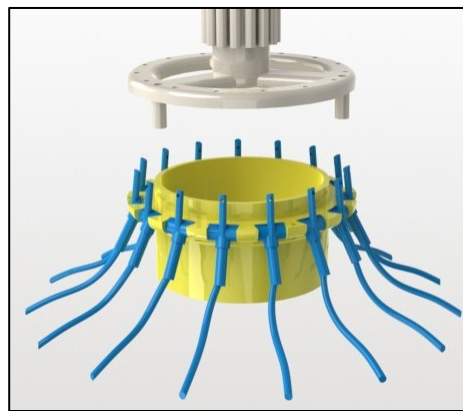
Concept 6 in Figure 61 is a variation of Concept 4. It consists of a holder, a top attachment to the prosthetic On-X 25 mm mitral valve, a rotating leg system, and leg extensions.

The ratchet side of the rotator, part of the “winding leg system” in Concept 4 (Figure 50) has been removed, and instead the rotating leg system now pivots about an axis fitted with a ratchet mechanism to make sure the leg rotates only one way as the corresponding suture line is pulled by the surgeon.

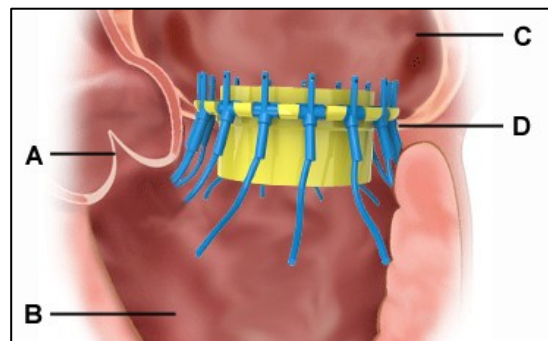
Guides for the suture lines have been added to the main holder (Figure 61). The number of rotating leg extension system is variable, with 15 shown in Figure 61; similarly to

other legged concepts, the design of the leg extensions mimics the inside shape of the left ventricle.

Fixation of the assembly to the annulus is similar to that in Concept 4: the suture lines are pulled by the surgeon to deploy the leg extensions and thus fix the assembly in the mitral valve annulus. Thereafter, sutures are cut to release the main holder. The deployed position is shown in Figure 62 and Figure 63.



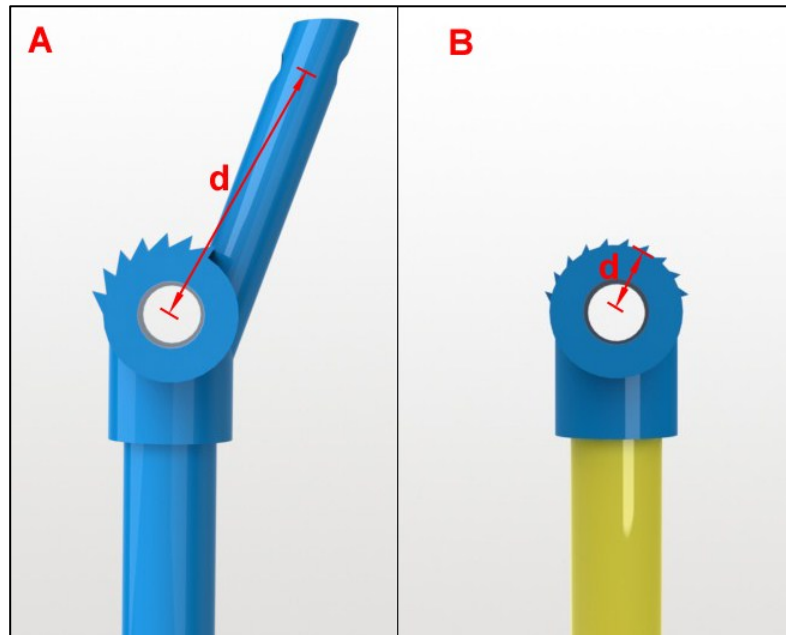
*Figure 62: Deployed Concept 6, showing rotating leg systems extended.*



*Figure 63: Deployed Concept 6 shown in position with respect to (A) the aortic valve, (B) left ventricle, (C) left atrium, and (D) the mitral valve annulus. Original heart image source:*

*(66).*

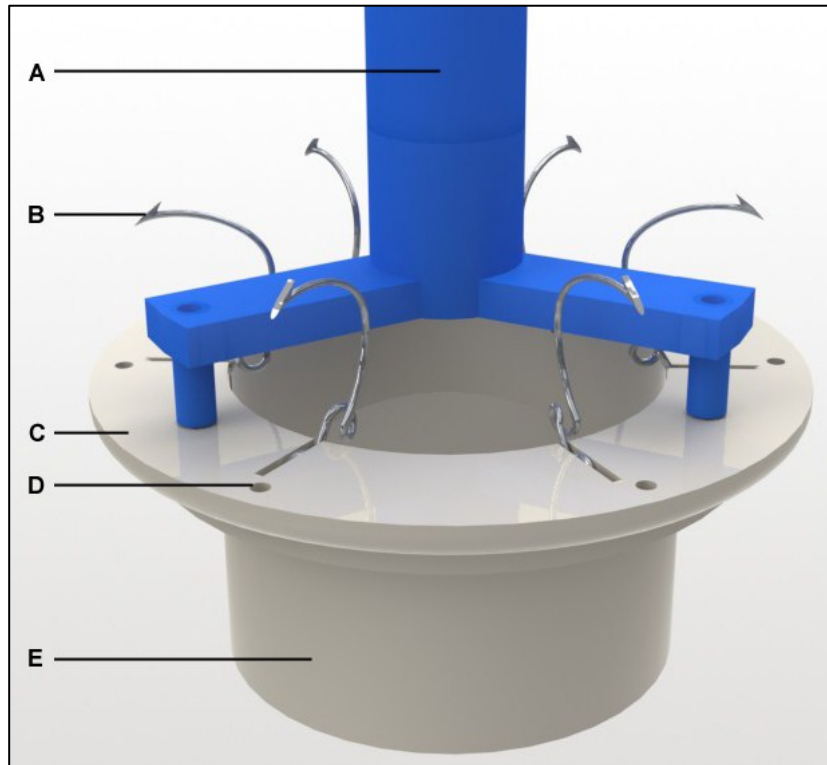
This concept's advantages are similar to that of Concept 4. The main improvement is that coiled sutures in Concept 4 have been modified. The coiled sutures in Concept 4 work with a small moment arm (distance between attachment of a suture and pivot point, Figure 64-B) that requires larger forces to rotate the leg extensions and puts large strains on the rotating components. In Concept 6, the moment arm is much larger, making it easier to extend the leg extensions (Figure 64-A).



*Figure 64: Working moment distances of (A) Concept 6: “Rotating Legs” and (B) a much smaller moment arm in Concept 4: “Winding Legs”.*

This concept's main disadvantage is that some parts, especially the rotating ratchet, are quite small and may potentially be difficult to manufacture. Reversibility is possible, but must be further worked on if this concept is to be pursued.

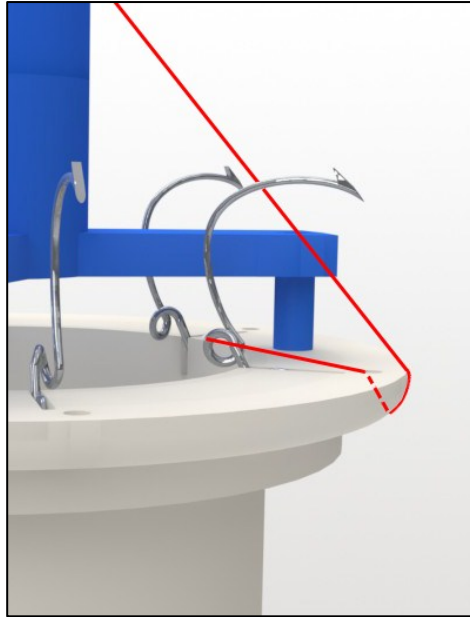
### 3.8 Concept 7: “Simple hooks”



*Figure 65: Un-deployed Concept 7: " Simple hooks", consisting of (A) a holder, (B) barbed metallic hooks, (C) a top attachment, (D) slots for the sutures that rotate the hooks, (E) modified On-X 25 mm mitral valve.*

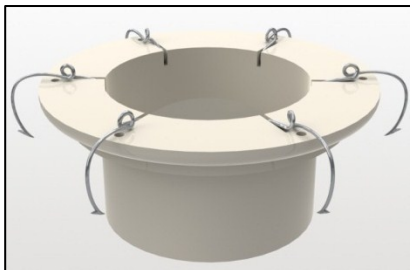
As noted before, the ideal concept should not have any metal parts so as to not interfere with the magnetic imaging equipment and the positioning sensor. However, this requirement can be relaxed if metallic parts are relatively small and made of high grade stainless steel, which minimizes magnetic interference, as proposed in Concept 7.

Concept 7: “Simple hooks” shown in Figure 65 consists of small barbed hooks arranged in a circular pattern along the top attachment mounted onto On-X 25 mm mitral valve. A holder and suture lines control the entire assembly.

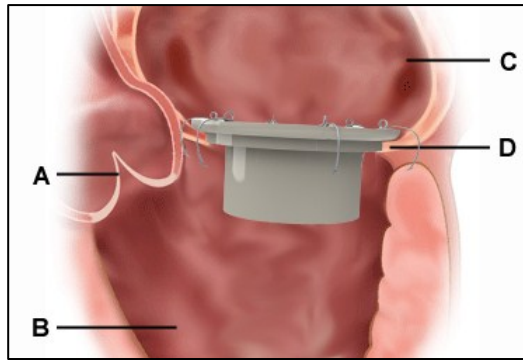


*Figure 66: Concept 7 path of one suture, shown in red, from surgeon to rotating hooks.*

Figure 66 shows the pathway of one suture line. It is held by the surgeon at the upper end of the holder, runs down the holder, and then through the slots in the top attachment, and towards the hooks. As the surgeon pulls on the suture line, the hook pivots and punctures the mitral valve annulus, with the barbs preventing any backwards motion. The final deployed position is shown in Figure 67 and Figure 68. Any sharp changes of direction in the path of the suture lines should be minimized.



*Figure 67: Deployed Concept 7, showing hooks rotated into position.*



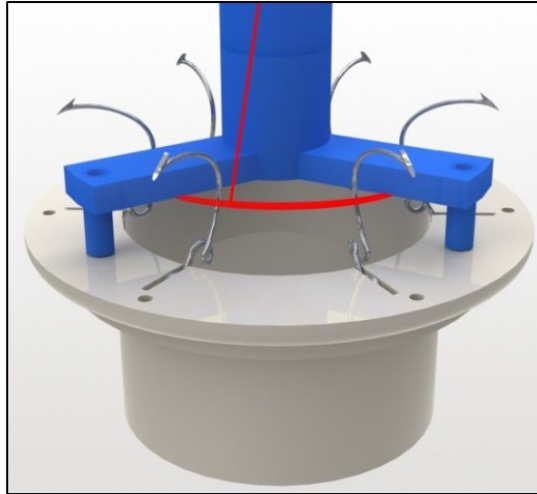
*Figure 68: Deployed Concept 7 shown in position with respect to (A) the aortic valve, (B) left ventricle, (C) left atrium, and (D) the mitral valve annulus. Original heart image source:*

*(66).*



*Figure 69: Metallic hook for Concept 7.*

While it would be possible to make the hooks from plastic, metal is preferred for strength and rigidity. In Figure 69, the hook's bottom loop enables rotation about an axis; the top loop is the end point of a suture line.

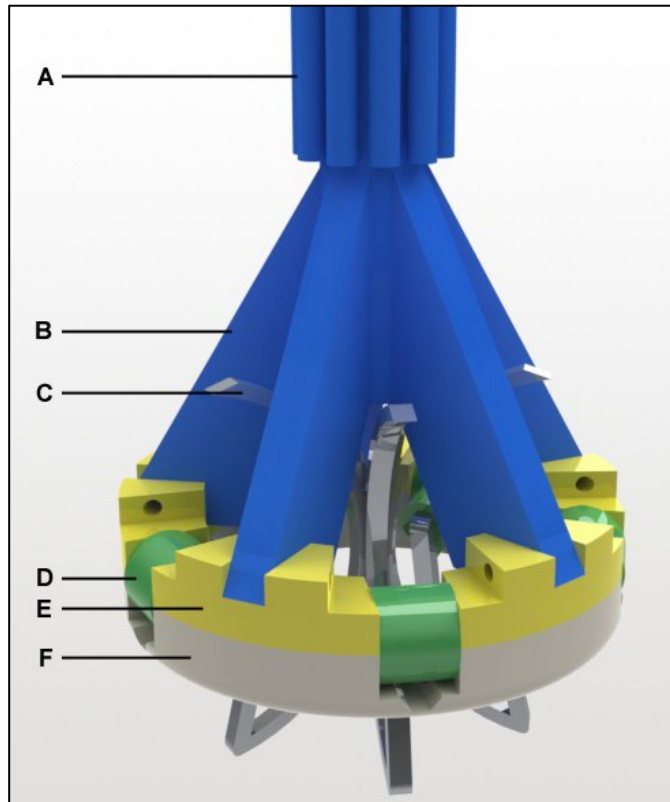


*Figure 70: Concept 7 safety suture encircling the hooks, to prevent unwanted deployment.*

As a safety feature, before the surgery, a loop using a suture line is made around all of the hooks (Figure 70), to prevent them from opening too early. Once the valve is inserted into the annulus, this suture line is cut and removed, and the hooks can be deployed.

Concept 7 has a number of advantages and disadvantages. Its main advantage is its simplicity, the potentially strong grip provided by the hooks, and the individual rotational control of each hook. It may be advantageous to make the hooks in different sizes, because the areas that are punctured along the perimeter of the mitral valve annulus are not uniform; however, this complicates the initial placement of the device in the annulus, as incorrect placement may result in the hooks puncturing the wrong locations. Therefore all six degrees-of-freedom of the NDI Aurora Mini 6 DOF sensor should be utilized which may increase surgery times. The main disadvantage of the concept is its lack of reversibility, as barbed hooks are difficult to remove. Alternatives such as barb-less hooks may prove advantageous. Other possible disadvantages include interference of the metallic hooks with the magnetic imaging equipment and tissue damage.

### 3.9 Concept 8: “Long hooks, two steps”

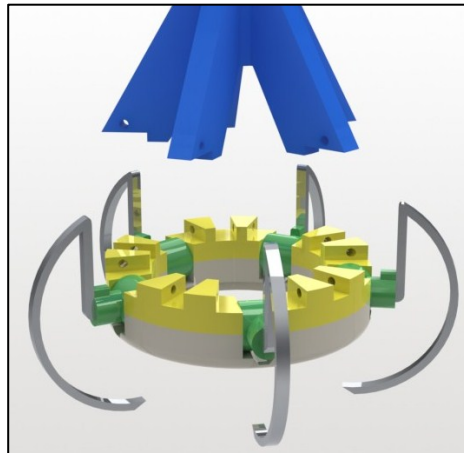


*Figure 71: Un-deployed Concept 8: "Long hooks, two steps", consisting of (A) suture guides placed along the holder, (B) base assembly holder, (C) custom metallic hooks, (D) hook rotating drum, (E) top plate of the base assembly, (F) bottom plate of the base assembly.*

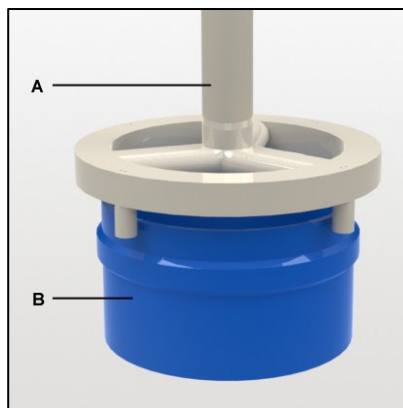
Similar to an earlier Concept 5, Concept 8: “Long hooks, two steps” shown in Figure 71 uses a two-step process based on custom hooks to penetrate the mitral valve annulus. It consists of a main holder, guides for the sutures, custom metallic hooks, drums that rotate the hooks and a base assembly that supports the holder and the drums.

The first step of the process consists in bringing an attachment base assembly into the mitral valve annulus. This base is fixed by means of custom rotating hooks. The surgeon

pulls on individual suture lines for each hook; the hooks then rotate following a circular path (ensuring that tissue is only penetrated in one spot and not torn) through the mitral valve annulus and its surrounding tissue. Then, the sutures holding the holder to the attachment base assembly are cut, and the assembly holder is removed. The deployed base assembly is shown in Figure 72 .

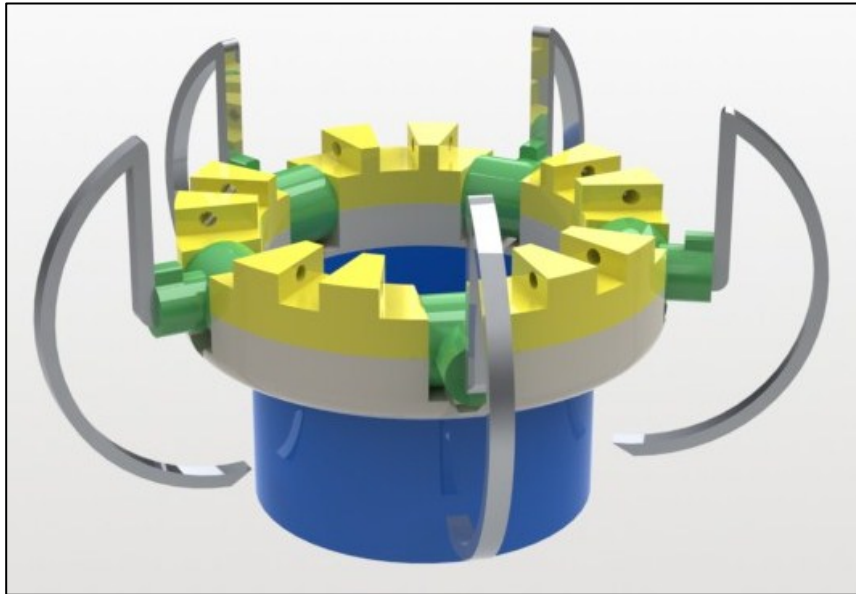


*Figure 72: Concept 8 completion of first step, showing deployed hooks and partially removed holder.*

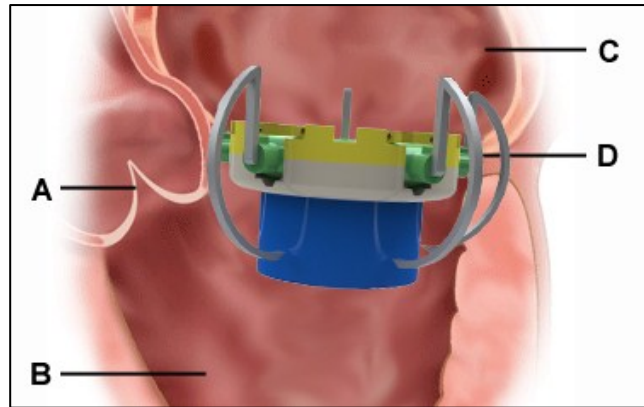


*Figure 73: Concept 8 valve holder assembly, similar to Concept 5, consisting of (A) a valve-only holder and (B) an On-X 25 mm valve. .*

The second step of the process consists in bringing the On-X 25 mm prosthetic mitral valve into the already fixed attachment base assembly. This is done by holding the prosthetic valve with a valve holder (Figure 73), guiding it by means of suture lines into the assembly (similar to Concept 5), with a final snap in place attachment mechanism securing the prosthetic valve to the base assembly. This means that the On-X 25 mm mitral valve must be modified to have a snap-type attachment. Once the prosthetic valve is attached, sutures attaching the holder to the valve are cut and removed to complete the procedure. The final deployed position is shown in Figure 74 and Figure 75.

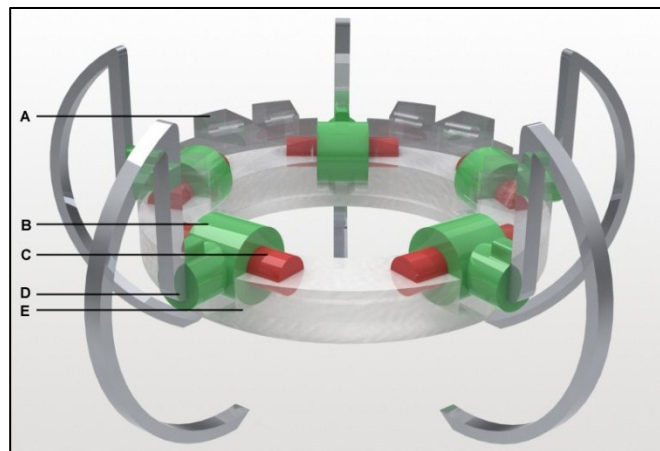


*Figure 74: Deployed Concept 8, showing hooks rotated into position, and valve prosthesis attached.*



*Figure 75: Deployed Concept 8 shown in position with respect to (A) the aortic valve, (B) left ventricle, (C) left atrium, and (D) the mitral valve annulus. Original heart image source:*

*(66).*



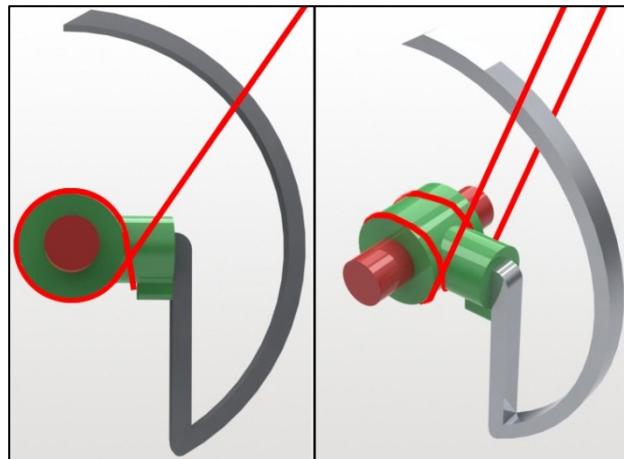
*Figure 76: Drum assembly in Concept 8, consisting of (A) upper base attachment, (B) rotator drum, (C) axis, (D) hook connection point, (E) lower base attachment (transparent).*

The rotating hook drum assembly shown in Figure 76 consists of an axis secured between the upper and lower base attachments about which the plastic rotator drum holding the hook rotates. The hooks' rectangular shape provides for a better connection with the

plastic drum rotators (Figure 76-C). A round hook cross-section would be prone to rotating within the plastic rotator.

A suture line forms a loop around the rotator drum head, runs below it inwards toward the ventricle and then upwards towards the surgeon's hands, as shown in Figure 77.

Methods for attaching the metallic hook to the plastic rotator include: epoxy glue, a simple force fit, or heating the plastic rotator until the melting point, force fitting the hook, and then letting the rotator cool down, ensuring a secure connection.

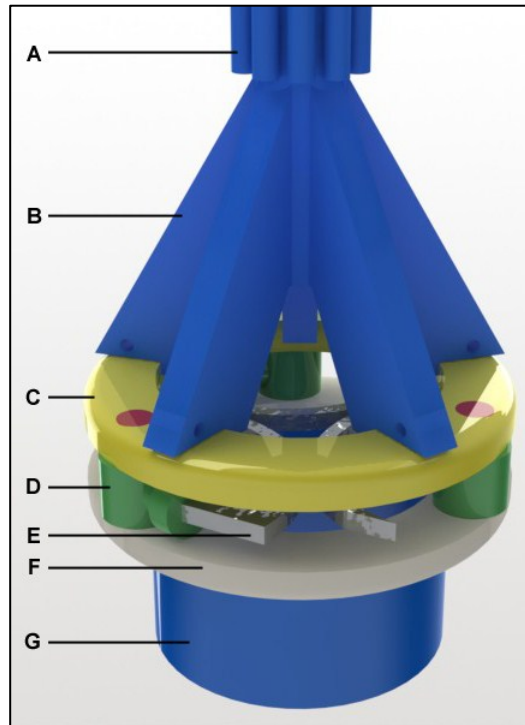


*Figure 77: Concept 8 rotator drum head, (left) side and (right) isometric view of how a suture line runs from the drum to the surgeon's hand.*

This concept's main advantage is that the custom designed hooks are quite large (larger than Concept 7), therefore are potentially able to provide good grip. Reversibility may be possible, as the hooks are not barbed; rotating them out of the mitral valve annulus successfully is a higher possibility than with barbed hooks. Barb-less hooks also cause less damage upon penetration, contributing to faster healing times.

The main disadvantage of this design comes from its two-step nature (a two-step system is required because the custom hooks are quite large and will otherwise interfere with the modified On-X 25 mm mitral valve): the surgery times will increase; navigating the prosthetic valve into the attachment base assembly is possible, but may prove to be more time consuming as all six degrees-of-freedom of the NDI Aurora Mini 6 DOF sensor must be utilized.

### 3.10 Concept 9: “Horizontal hooks”

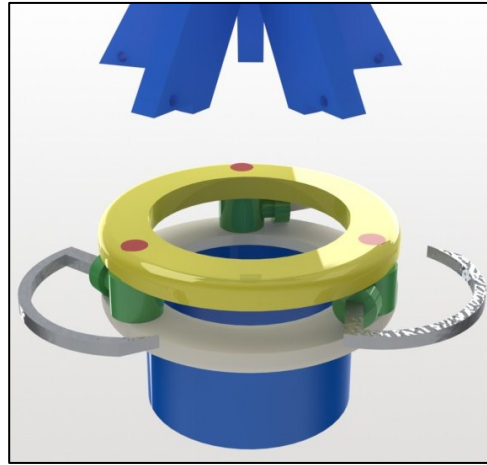


*Figure 78: Un-deployed view of Concept 9: "Horizontal hooks", consisting of (A) suture guides, (B) main holder, (C) top attachment, (D) rotating drum, (E) custom metallic hooks, (F) bottom attachment base, (G) On-X 25 mm mitral valve.*

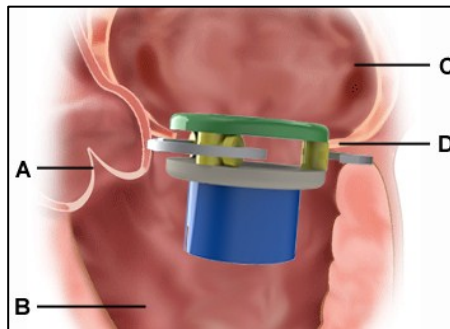
Concept 9: “Horizontal hooks” shown in Figure 78 is similar to Concept 8, except that the rotating hooks are now redesigned to be deployed horizontally. It consists of a main holder with suture line guides attached to it, a top and bottom attachments that support the rotating drums which hold the hooks, and a modified On-X 25 mm prosthetic mitral valve.

The surgeon brings the device into the mitral valve annulus, deploys the hooks horizontally outward by pulling on the suture lines. Once the assembly is in position and

secured, the sutures to the hooks and the holder are cut and the assembly is removed. A completely deployed assembly is shown in Figure 79 and Figure 80.



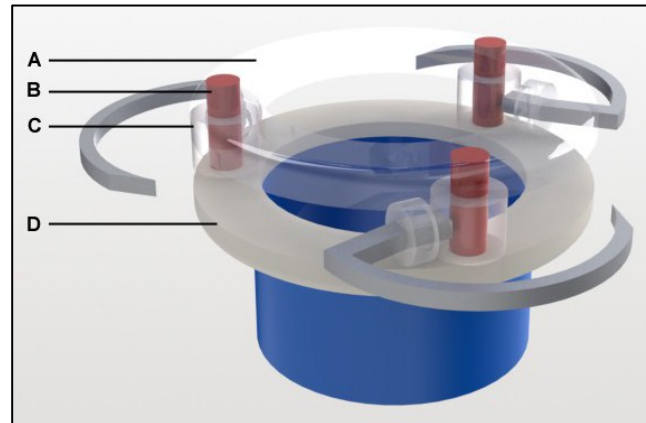
*Figure 79: Deployed Concept 9, showing hooks extended horizontally.*



*Figure 80: Deployed Concept 9 shown in position with respect to (A) the aortic valve, (B) left ventricle, (C) left atrium, and (D) the mitral valve annulus. Original heart image source: (66).*

Note that this is a one-step concept as compared to two-step Concept 8. Analogous to Concept 8 (Figure 77), the sutures run around the rotating drum (Figure 78), back inside the assembly and then towards the surgeon's hand.

The rotating drum assembly, shown in Figure 81, consists of an axis about which the plastic hook holder rotates (Figure 81). This axis is secured between the top and bottom attachment assemblies.

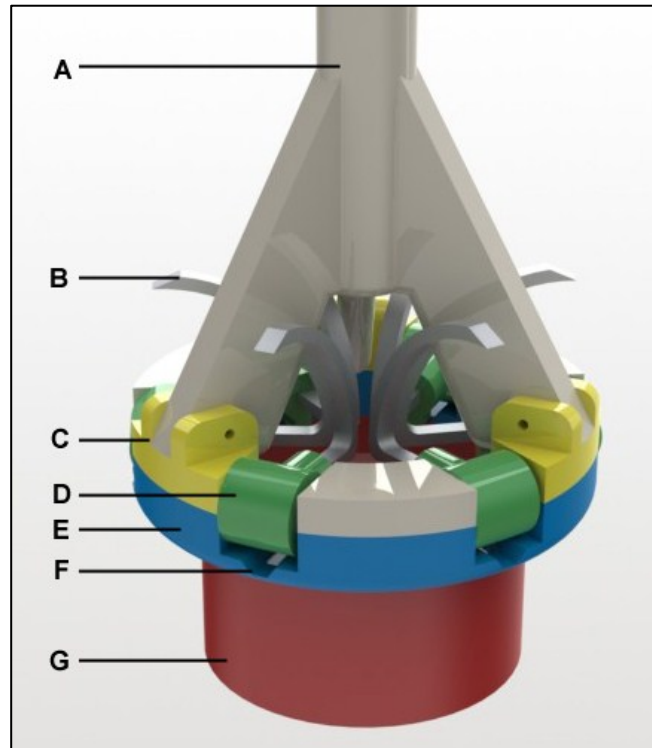


*Figure 81: Concept 9 drum assembly, consisting of: (A) top attachment, (B) an axis of rotation, (C) rotating drum, and a (D) bottom attachment.*

This concept's main advantage is that once the hooks are extended, their horizontal grip into the mitral valve annulus and its surrounding tissue will most likely prevent any vertical movement of the mitral valve prosthesis and the valve assembly. Other advantages include that reversibility is possible, and that barb-less hooks are less invasive than barbed ones.

The design of the hooks potentially needs to be tuned to different structures of tissue around the perimeter of the mitral valve annulus. This will require proper alignment and complicated initial navigation and placement of the assembly. Again all six degrees-of-freedom of the NDI Aurora Mini 6 DOF sensor will have to be utilized, hence prolonging surgery time.

### 3.11 Concept 10: “Advanced hooks”



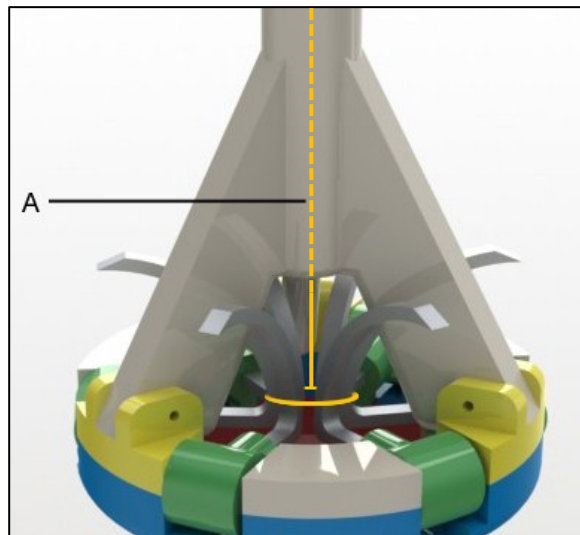
*Figure 82: Un-deployed Concept 10: "Advanced hooks", consisting of (A) main holder, (B) custom metallic hooks, (C) top attachment with slots to secure the main holder, (D) plastic rotator, (E) a lower attachment base, (F) cut-outs to guide the sutures, (G) and an On-X 25 mm mitral valve.*

Concept 10: “Advanced hooks” shown in Figure 82 is similar to Concept 8, except that the custom hooks have been redesigned to be shorter to allow for a single-step process and not to encroach on the prosthetic valve. This may reduce grip but is aimed at improving surgery times.

Concept 10 consists of a main holder, a top attachment base with slots for the main holder, a lower attachment base that connects to a modified On-X 25 mm mitral valve

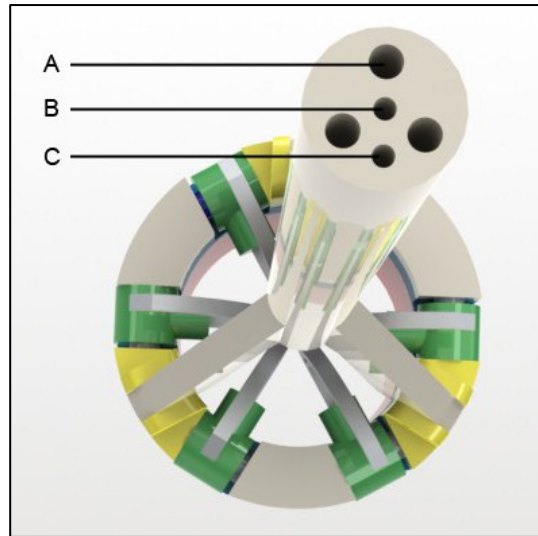
prosthesis and plastic rotator holding the custom metallic hooks. The original On-X 25 mm mitral valve must be modified to have a permanent connection to the lower attachment base.

The slots in the top attachment prevent the main holder from rotating about its longitudinal axis during the insertion phase. Holes of 0.8 mm diameter in the slots of the top attachment allow for pathways for the suture lines that secure the main holder to the top attachment. The holder has three legs that are fixed to the top attachment of the assembly, compared to five legs in Concepts 8 and 9, thus decreasing the number of sutures needed, and making the assembly less complicated to operate.



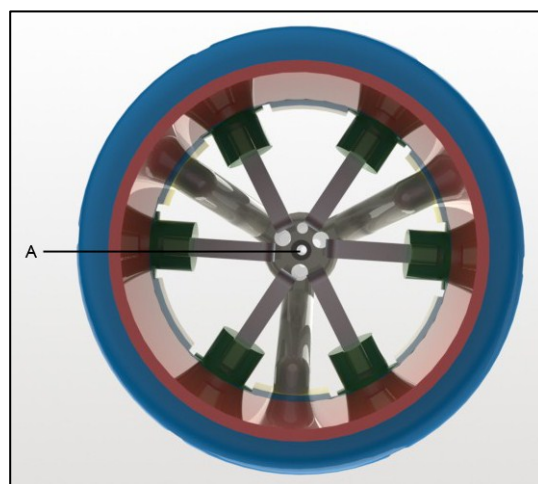
*Figure 83: Concept 10 safety suture, holding all of the hooks, to prevent unwanted deployment.*

As a safety measure, an extra suture line runs down to the hooks (Figure 83) and encircles them to prevent any unwanted deployment during initial positioning of the assembly into the mitral valve annulus.



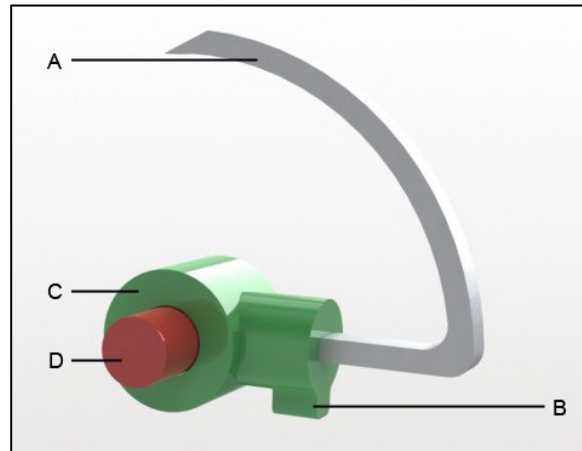
*Figure 84: Concept 10 main holder incorporates various pathways, (A) for the suture lines, (B) for the sensor wire, (C) and for the safety suture.*

The main holder incorporates five holes running down its longitudinal axis (Figure 84), three holes (1.5 mm diameter each) for the suture lines that activate the hooks and those that fix the holder to the top attachment, one central hole (1 mm diameter) for the sensor electrical wire, and one hole (1 mm diameter) for the safety suture.



*Figure 85: Concept 10 main holder incorporates (A) a slot for the tracking sensor.*

The sensor is located at the base of the main holder, fitted into a special slot and has a separate sensor wire pathway running longitudinally along the inside of the holder (Figure 85).



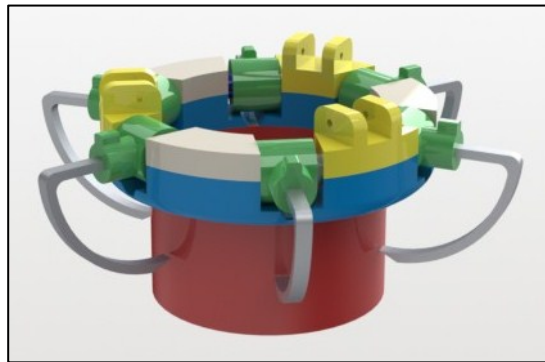
*Figure 86: Concept 8 rotator drum assembly, consisting of (A) custom metallic hooks, (B) tip to prevent slip of sutures, (C) plastic rotator, and (D) a supporting axis.*

Similarly to Concept 8, as shown in Figure 86, the rotator drum assembly consists of a plastic rotator with a rectangular slot, into which the custom metallic hooks are inserted. A rectangular slot is selected to prevent any unwanted rotation of the hook inside the plastic rotator. An axis secured by the top and bottom attachments enables the rotation of the hook. A small clearance is designed between the plastic rotator and the top/bottom attachments to facilitate the rotation.

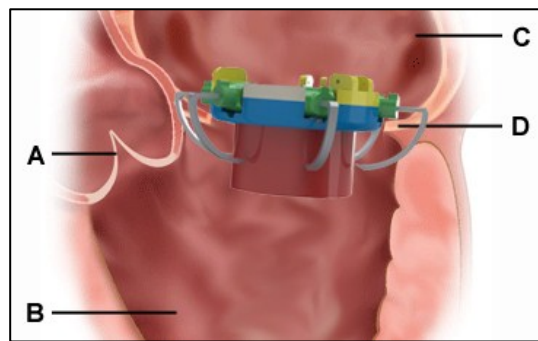
The principle of operation is similar to that of Concept 8 (Figure 77): the suture lines form a loop around the plastic rotators (Figure 86-C), run through the cut-outs of the lower base (Figure 82-F), and towards the surgeon's hand. Sharp changes of direction, as suture lines travel towards the surgeon, must be minimized. By pulling on individual suture lines,

individual deployment/control of each hook can be achieved. Protrusion on the plastic rotator (Figure 86-B) prevents the suture lines from slipping off the rotator.

The assembly is positioned in the mitral valve annulus, the safety suture line is cut and the surgeon is able to individually deploy the hooks into the annulus. Once the hooks are in position, the activation suture lines can be removed, along with the suture lines that secure the main holder to the top attachment base, thus releasing the main holder and completing the procedure. The deployed Concept 8 is shown in Figure 87 and Figure 88.



*Figure 87: Concept 10 deployed position, showing hooks rotated into position.*



*Figure 88: Deployed Concept 10 shown in position with respect to (A) the aortic valve, (B) left ventricle, (C) left atrium, and (D) the mitral valve annulus. Original heart image source:*

(66).

As mentioned before, this concept's main advantage is that shorter hooks allow for a single step process, possibly reducing surgery times as compared to a similar, but a two-step Concept 8. Other advantages may include good potential for reversibility; barb-less hooks are also less damaging to the tissue than barbed ones.

As in Concept 8, the shape of the hooks may require individual modifications as the structure around the mitral valve annulus is not uniform. Some hooks may need to be shorter or thinner than others; this may complicate navigation and potentially increase surgery time. The force required from the surgeon to deploy the hooks (and whether or not the sutures will be able to withstand that force) has to be determined by analysis and testing.

### 3.12 Decision analysis

As outlined in the problem definition, a number of design criteria have been set by the researchers at Robarts Research Institute to determine the best possible concept. These include the following criteria: ease of use, quality of grip around the entire mitral valve annulus, ease of manufacture, minimal interference with blood flow and heart structure, potential for reversibility, short surgery time, and reduced invasiveness of the concept.

All the proposed concepts are represented as C1 to C10 in Table 1. Each design criteria was weighted from 1 (least desirable) to 5 (most desirable) in the second row of Table 1. Evaluation of each design in each criterion category was done on a scale of 1 (poor) to 10 (excellent) as shown with bold block numbers in Table 1. The concept with the highest mark resulting from weighted performance with respect to the criteria was Concept 10.

*Table 1: Decision Analysis Matrix*

	Ease-of-use	Quality of grip around mitral valve annulus	Ease of manufacture	Minimal interference	Potential for reversibility	Short surgery time	Less invasive	SUM	#
	<b>3</b>	<b>4</b>	<b>3</b>	<b>5</b>	<b>4</b>	<b>4</b>	<b>2</b>		
C1	<b>4</b>	<b>2</b>	<b>2</b>	<b>4</b>	<b>5</b>	<b>8</b>	<b>6</b>		<b>8</b>
W1	12	8	6	20	20	32	12	110	
C2	<b>3</b>	<b>3</b>	<b>1</b>	<b>3</b>	<b>6</b>	<b>9</b>	<b>7</b>		<b>7</b>
W2	9	12	3	15	24	36	14	113	
C3	<b>10</b>	<b>1</b>	<b>5</b>	<b>1</b>	<b>1</b>	<b>10</b>	<b>10</b>		<b>6</b>
W3	30	4	15	5	4	40	20	118	
C4	<b>2</b>	<b>5</b>	<b>3</b>	<b>5</b>	<b>4</b>	<b>3</b>	<b>8</b>		<b>9</b>
W4	6	20	9	25	16	12	16	104	
C5	<b>1</b>	<b>6</b>	<b>6</b>	<b>2</b>	<b>2</b>	<b>1</b>	<b>5</b>		<b>10</b>
W5	3	24	18	10	8	4	10	77	
C6	<b>5</b>	<b>4</b>	<b>4</b>	<b>6</b>	<b>3</b>	<b>4</b>	<b>9</b>		<b>5</b>
W6	15	16	12	30	12	16	18	119	
C7	<b>9</b>	<b>7</b>	<b>7</b>	<b>10</b>	<b>7</b>	<b>5</b>	<b>1</b>		<b>3</b>
W7	27	28	21	50	28	20	2	176	
C8	<b>6</b>	<b>9</b>	<b>8</b>	<b>8</b>	<b>8</b>	<b>2</b>	<b>2</b>		<b>4</b>
W8	18	36	24	40	32	8	4	162	
C9	<b>7</b>	<b>10</b>	<b>9</b>	<b>7</b>	<b>9</b>	<b>6</b>	<b>3</b>		<b>2</b>
W9	21	40	27	35	36	24	6	189	
C10	<b>8</b>	<b>8</b>	<b>10</b>	<b>9</b>	<b>10</b>	<b>7</b>	<b>4</b>		<b>1</b>
W10	24	32	30	45	40	28	8	207	

Indeed, Concept 10: “Advanced Hooks” is easy to manufacture, has good reversibility capability, and may cause the least interference with blood flow or other structures of the heart. Though deployment may not be as fast as, for example, with Concept 3, independent control of deployment of each hook is highly advantageous. Concept 10 is more invasive than, for example, Concept 6, because of its hooks. However, changing the shape, size, and thickness of the hooks may reduce their invasiveness. Note that in this case, navigating the entire assembly into the mitral valve annulus is possible by utilizing the full capabilities of the NDI Aurora Mini 6 DOF sensor. Although it is difficult to assess the grip provided by the hooks without first building a prototype, it is anticipated that Concept 10 can be above average of the other concepts by customizing each individual hook.

Based upon the decision analysis matrix shown in Table 1, the discussions between myself and my supervisor with the researchers at the Robarts Research Institute, Concept 10: “Advanced hooks” was selected for further design development and prototyping.

## 4 Design Analysis

As noted earlier, it was determined that the force needed to puncture the tissues around the mitral valve annulus, including a design factor of 1.5, is approximately 3 N. Theoretical calculations, as well as finite element analysis were carried out to ensure that the design of Concept 10 was adequate to achieve such actuation force, before its prototype could be manufactured.

### 4.1 Theoretical calculations

A number of different analyses are presented below to verify the validity of Concept 10: “Advanced Hooks”, by subjecting it to maximum loads in different configurations, and verifying that the puncture forces that it can achieve are sufficient.

#### 4.1.1 Force resolution

Given a certain tensile force ( $F_H$ ) that is applied by the surgeon by pulling on the sutures, the objective is to solve for how much of that force is transferred down to the tip of the hooks. The resolved force at the tip of the hooks ( $F_{TIP}$ ) needs to be higher than 3 N to puncture the tissue and overcome any friction forces.

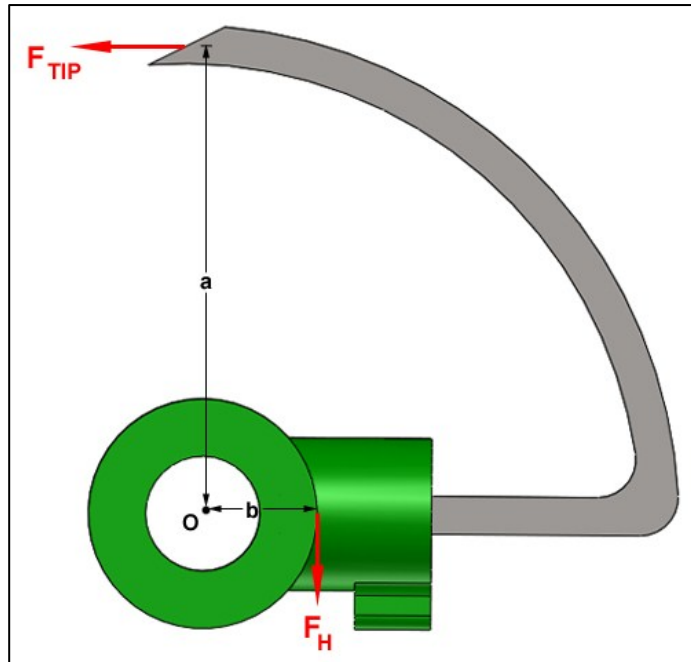


Figure 89: Resolution of the human force ( $F_H$ ) into the applied force ( $F_{TIP}$ ).

Figure 89 shows the plastic rotator and the metallic hook along with the applied forces. By assuming that the angular acceleration is zero (the angular velocity is constant), and neglecting friction forces, taking moments about point O in Figure 89, yields the equilibrium equation:

$$M_O = aF_{TIP} + bF_H = 0$$

Therefore, with  $a = 12.5$  mm and  $b = 3$  mm, the relationship between  $F_{TIP}$  and  $F_H$  is:  $F_{TIP} = 0.24F_H$ . It can be concluded that the minimum force that must be applied by the surgeon to overcome the 3 N puncture force is approximately 12.5 N. These calculations are based on a tri-pointed 1.1 mm surgical needle. Of course, the shape of the hook's tip plays a major role in determining the required penetration forces, and 12.5 N is taken as an indicative value only. Such value was deemed to be in the achievable range for the surgeon.

#### 4.1.2 Cantilever beam case

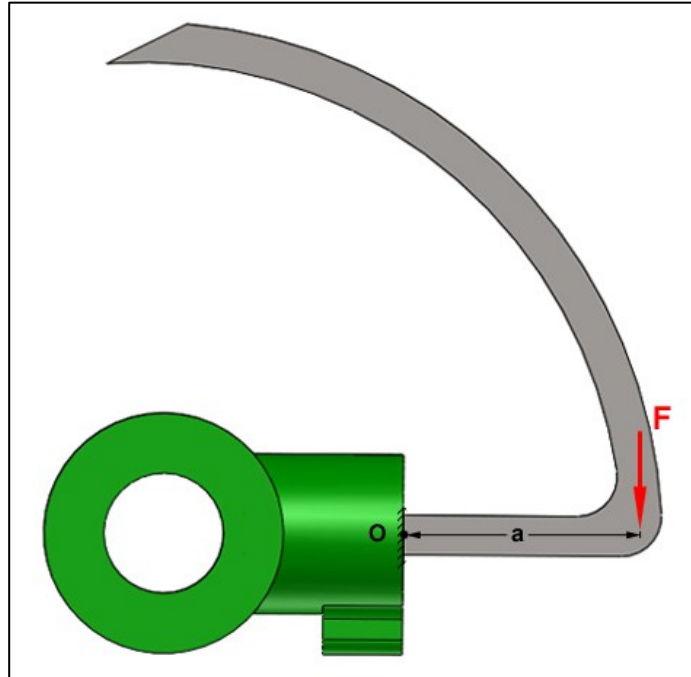


Figure 90: Cantilever end load case.

When a vertical force ( $F = 3 \text{ N}$ ) is acting on the horizontal section of the hook as shown in Figure 90, the reaction moment at point O is found to be:  $M_o = F \times a = 3 \times 6.477 = 0.0194 \text{ Nm}$ . The moment of inertia of the hook is given by:  $I = \frac{bh^3}{12}$ , with  $b = 0.0015 \text{ mm}$  and  $h = 0.001 \text{ m}$ . The maximum stress is therefore found to be:  $\sigma = \frac{Mc}{I} = \frac{(0.0194)(0.0005)}{1.25 \times 10^{-13}} = \pm 77.6 \text{ MPa}$  (67). This value is below the yield strength (290 MPa) of the stainless steel material to be used (68), as presented later.

### 4.1.3 Pure bending case

Another case is considered when a force ( $F = 3 \text{ N}$ ), as shown in Figure 91, is applied to the tip of the hook. The resultant stress distribution in cross-section “AA” and the deflection of the hook in the direction of the applied force is to be calculated.

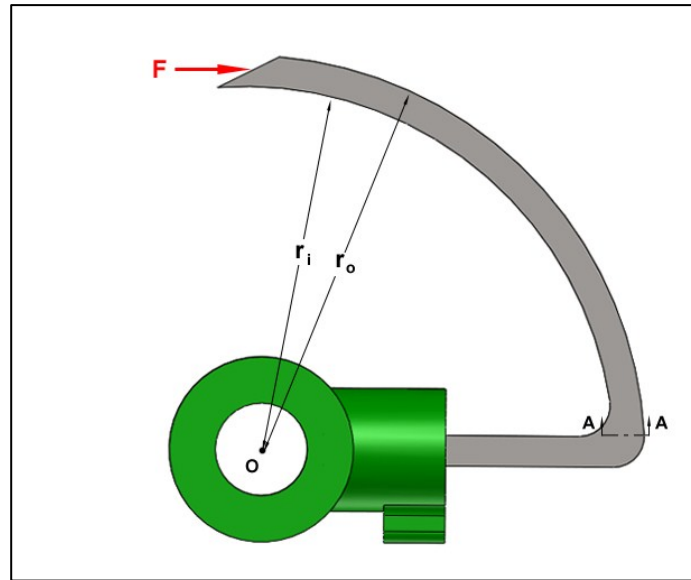


Figure 91: Pure bending case analysis.

The inside radius,  $r_i$  is 12 mm, and the outside radius,  $r_o$  13 mm. Therefore, the central radius ( $r_c$ ) is 12.5 mm. The height and the width of the hook's cross section are 1 mm and 1.5 mm respectively, giving a cross sectional area of  $1.5 \times 10^{-6} \text{ m}^2$ . The bending moment can be found as:  $M = 3 \times 0.0125 = 0.0375 \text{ Nm}$ . The radius of neutral axis is calculated as

follows:  $r_n = \frac{h}{\ln\left(\frac{r_o}{r_i}\right)} = 12.493 \text{ mm}$  (67); therefore the eccentricity ( $e = r_c - r_n$ ) is about

0.00667 mm. The stress distribution, ranging from the inner to outer fibers is calculated

according to the formula:  $\sigma = \frac{M(r_n - r)}{rAe}$ , where  $M$  is the bending moment,  $A$  is cross sectional area,  $e$  is eccentricity, and  $r$  is the radius at the point for which stress is calculated (67).

The maximum tensile stress, at the inside edge of the hook ( $r_i$ ) was found to be 156 MPa, the maximum compressive stress at the outside edge of the hook was 144 MPa, well below the yield strength of the material to be used. The bending stress results are illustrated in Figure 92.

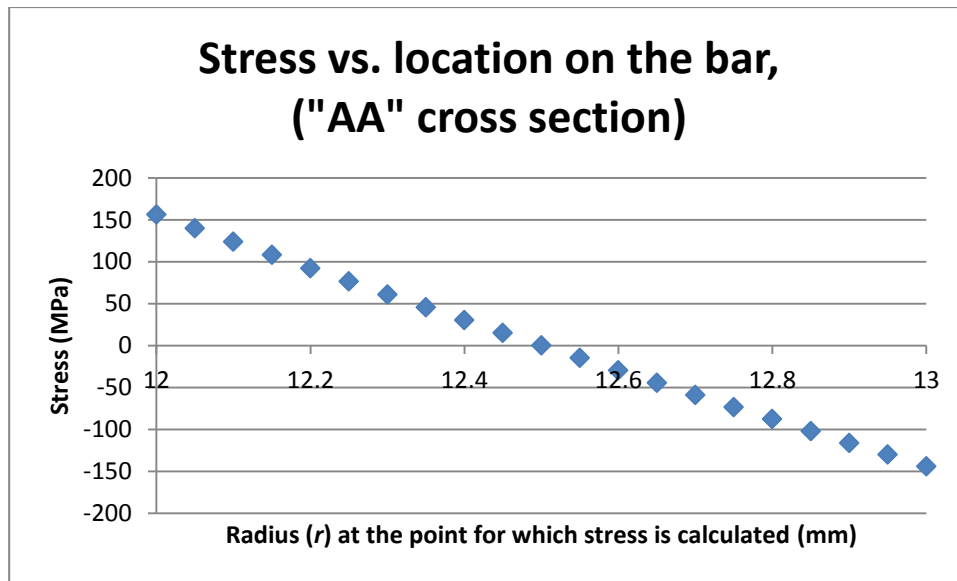
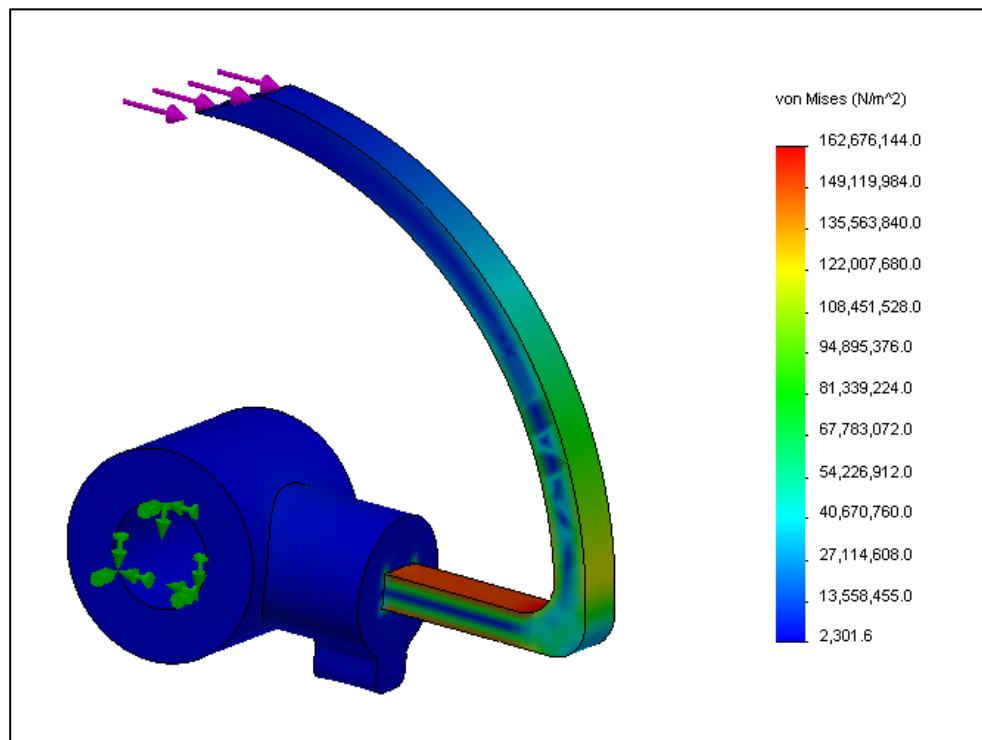


Figure 92: Pure bending case, stress results.

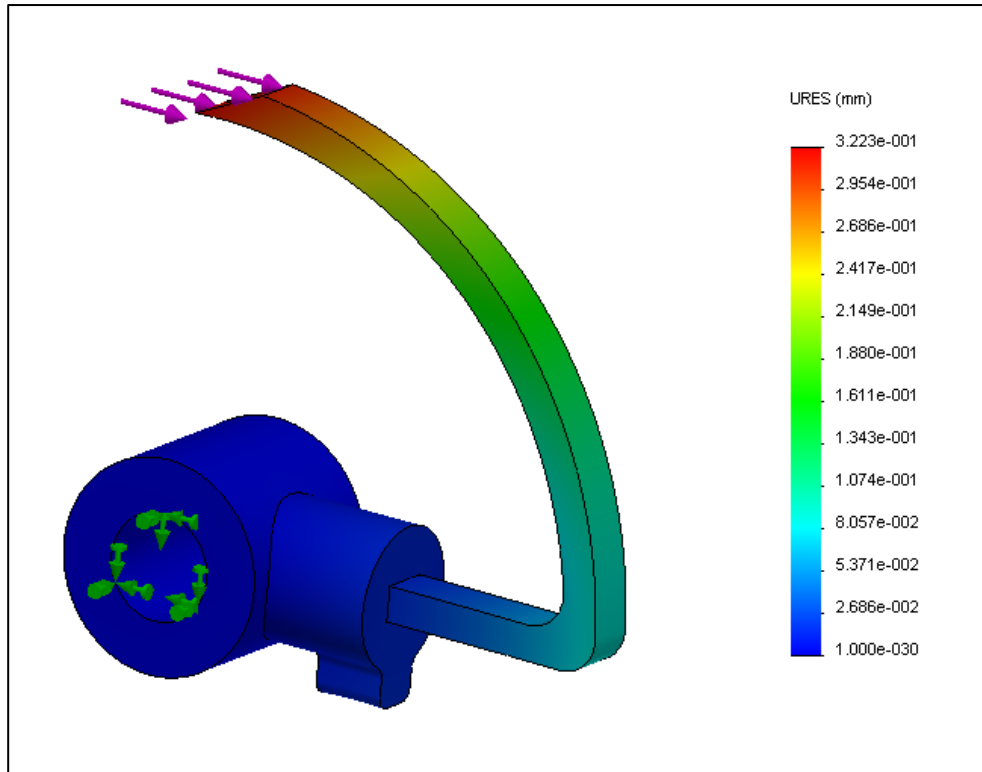
Castigliano's theorem was used to calculate the deflection of the hook in the direction of the applied force as shown in Figure 91. An approximation for the deflection given as  $\delta \approx \frac{\pi F r_c^3}{2EI}$  may be used (67). Given that  $E = 193$  GPa for the material to be used, and other values calculated as before, the maximum deflection is found to be approximately 0.38 mm.

## 4.2 Finite element simulations

Basic finite element simulations in SolidWorks software were done to verify the strength of concept 10. The plastic rotator was assumed fixed about its inner axis, as shown in Figure 93. The metallic hook was loaded with a force of 3 N at its tip. The von Mises stress results ( $\text{N/m}^2$ ) are presented in Figure 93, and the corresponding displacement results are presented in Figure 94.



*Figure 93: von Mises stress results gradient, with green arrows indicating the fixed conditions and purple arrows indicating the applied force.*



*Figure 94: Displacements gradient, with green arrows indicating the fixed conditions and purple arrows indicating the applied force.*

The maximum von Mises stress experienced was found to be 163 MPa, not exceeding the 290 MPa yield strength of the 316 stainless steel to be used (68). The displacements presented in Figure 94 were also adequate (maximum displacement generated of 0.32 mm); therefore the strength of the hook design was deemed sufficient. Differences between these results and those from hand calculations were minimal, confirming both approaches. It was then possible to proceed to prototyping.

### 4.3 Prototype 1 manufacturing

Plastic parts are needed for all the components except the hooks in Concept 10, because it is a required design criterion to reduce the interference with magnetic imaging equipment. The use of plastics is also very advantageous in biomedical applications since they offer superior design flexibility (compared to metals, ceramics, or glass). They are also much easier to manufacture, and meet the much needed biocompatibility requirements while maintaining mechanical performance (69). Metallic parts are needed for the anchoring mechanism.

For the manufacturing of plastic parts, ShapeWays Inc. was selected due to the costs savings and the convenience of simple online ordering. The manufacturing process used by ShapeWays is called selective laser sintering (SLS) (70). SLS uses plastic or metal layers of powder that are melted consecutively with a laser while “tracing out the required cross-section”; these successive layers form the required 3D shape (71).

The plastic material used by ShapeWays Inc. is PA 2200 (Nylon 12), a plastic offering good manufacturing detail, abrasion resistance, low water absorption, and good chemical resistance (70; 72; 73). PA 2200 is certified to be biocompatible according to EN ISO 10993-1 (74).

The tensile strength ( $\sigma_{UTS}$ ) of PA 2200 SLS is  $45 \pm 3$  MPa, and its tensile modulus ( $E$ ) is  $1700 \pm 150$  MPa (72). The variations in mechanical properties are due to the SLS process itself, as any two finished prototypes of the same 3D model will not be composed of identical consecutive layers of melted powder; therefore the mechanical properties will vary slightly (71).

The metallic hooks were manufactured by Tech-Etch. This company was selected due to significant cost savings offered. Tech-Etch specialize in a “photo etching process that produces intricate metal components with close tolerances” (75). Photo etching “involves the removal of metal from a continuous sheet on which a photomask has been deposited to protect some areas and allow others to be eroded” (76).

The metal used was 316 stainless steel, selected based on recommendation of John Moore (researcher at Robarts Research Institute, London, ON). 316 stainless steel offers higher corrosion resistance than conventional stainless steels, and is suitable for surgical and medical tools, as well as surgical implants; its mechanical properties are as follows: tensile strength of 558 MPa, yield strength of 290 MPa, and modulus of elasticity of 193 GPa (68).

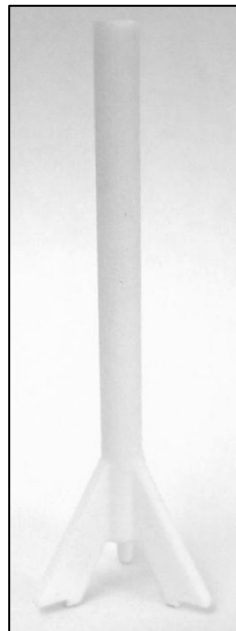
The first prototype of Concept 10 is shown un-deployed in Figure 95, and deployed in Figure 96. The main holder is shown in Figure 97.



*Figure 95: Prototype 1 of Concept 10: "Advanced hooks", un-deployed.*



*Figure 96: Prototype 1 of Concept 10: "Advanced hooks", deployed.*



*Figure 97: Prototype 1 of Concept 10: "Advanced Hooks" main holder view (Figure 82-A).*

## **4.4 Prototype 1 testing and results**

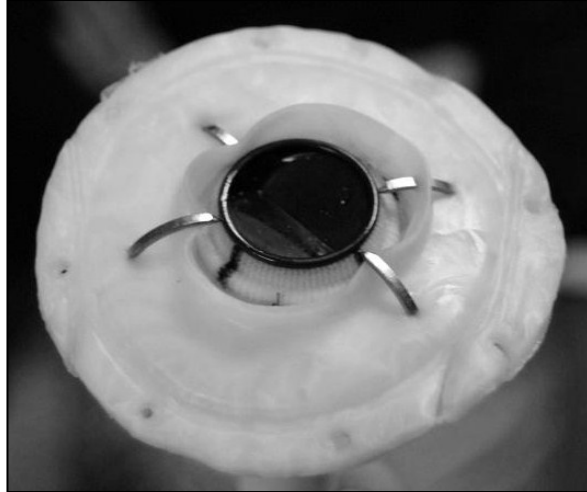
### **4.4.1 Test 1: Basic anchoring testing**

The purpose of this experiment was to test the basic performance of the anchoring mechanism of the intracardiac tool, to assess whether or not the grip on tissue was sufficiently strong to hold a prosthetic valve in place, and to make recommendation for any possible improvements in terms of anchor design, and the grip the anchors provide. As a first step, instead of using real tissues, a polyvinyl alcohol cryogel (PVA-C) membrane was used because it has material properties in the same range as real tissues. PVA-C is commonly used as a “tissue-mimicking material” and is suitable for magnetic resonance and ultrasound imaging (77).

### **4.4.2 Test 1: Results**

Test 1 was performed using the intracardiac tool with only one hook ready for deployment into the PVA-C membrane, with the PVA-C being held in place by a cylindrical support. The hook penetrated the surface and entered the PVA-C membrane over about 3-5 mm in depth, without completely puncturing the membrane. Additional penetration trials were made in London, ON, by the researchers at the Robarts Research Institute. As shown in Figure 98, four hooks were able to penetrate the PVA-C membrane; however, this was with great effort from the operator.

The results of Test 1 led to the following recommendation: the hooks should be made smaller and significantly thinner along their entire length while not compromising the hook’s strength.



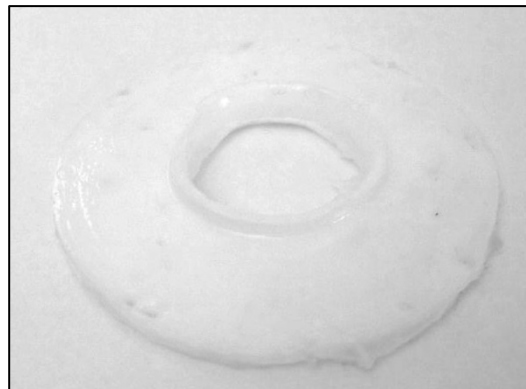
*Figure 98: Testing the penetration ability of the anchoring mechanisms.*

#### **4.4.3 Tests 2: Leak tests with a static water column**

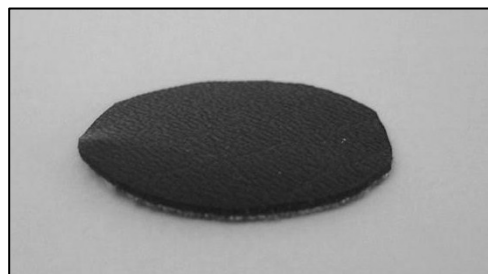
The goal of these tests was to evaluate the water-tightness allowed by the anchoring of the intracardiac device. The setup for these tests consisted of a plastic cylindrical support (Figure 99), PVA-C membrane with a circular opening to simulate the mitral valve annulus (Figure 100), a circular leather sheet to act as a closed mitral valve (Figure 101), and the intracardiac tool (Figure 102). The support included a detachable ring with screws to accommodate the PVA-C membrane.



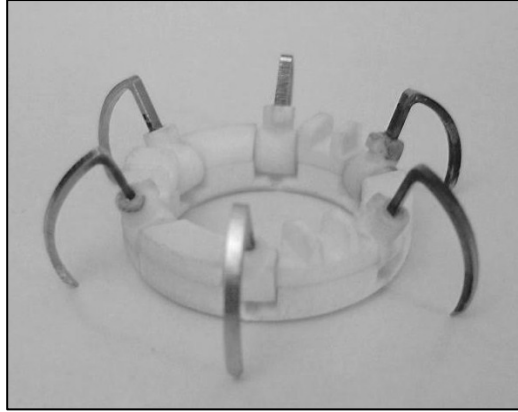
*Figure 99: Cylindrical support.*



*Figure 100: PVA-C membrane.*

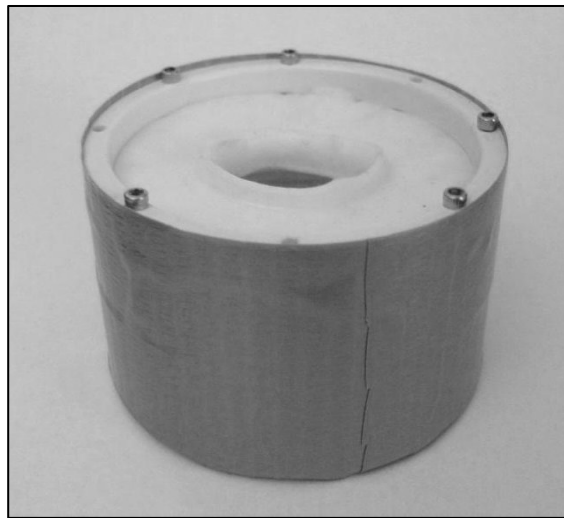


*Figure 101: Leather sheet.*



*Figure 102: Intracardiac tool.*

The PVA-C membrane was attached to the cylindrical support as shown in Figure 103, and wrapped around with tape to prevent any possible side leaks.



*Figure 103: PVA-C membrane attached to the plastic cylinder.*

The cylinder was filled with water, so as to form a column of water above the simulated mitral valve annulus. The water tried to leak through the attachment points.

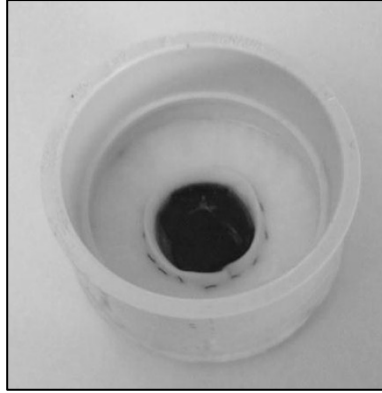
Two attachment conditions were tested. Firstly, the circular leather sheet was sutured to the PVA-C membrane, and the amount of leakage through the sutures between the leather sheet and the PVA-C membrane was measured (Test A). In Test B, the intracardiac tool was secured to the PVA-C membrane by means of its hooks; it was also sealed with tape to simulate a closed mitral valve. The leakage through the hook-anchoring points and the contact between the intracardiac tool and the PVA-C membrane was measured as well.

#### 4.4.4 Tests 2: Test A - results

Figure 104 shows the outside view of the setup for this test; the leather sheet was sutured onto the PVA-C membrane, with stitches approximately 2-5 mm apart. The PVA-C membrane was then attached into the cylindrical support. Figure 105 presents the inside view.



*Figure 104: Test A, outside view of the setup.*



*Figure 105: Test A, inside view.*



*Figure 106: Test A, sealed assembly, upside-down, outside view.*

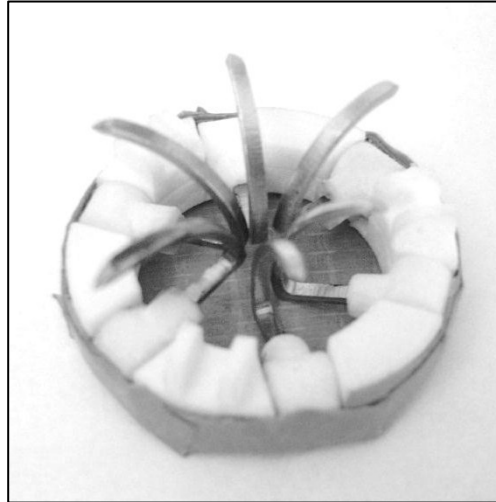
Figure 106 demonstrates the assembly wrapped in tape to prevent unwanted leakage from the sides; afterwards the cylinder was filled with about 80 ml of water and the total time until the water had drained was measured. Two trials were performed and the results are presented in Table 1.

*Table 2: Test A results*

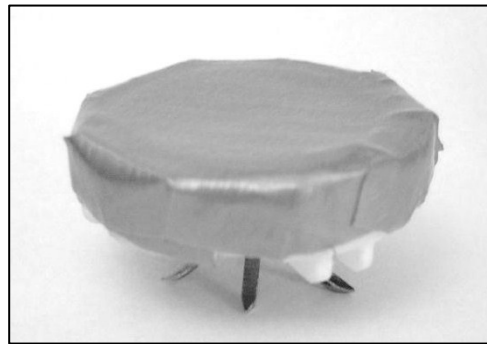
	Trial 1	Trial 2
Time until complete drainage	69 min	75 min

#### 4.4.5 Tests 2: Test B - results

Referring to Figure 107, the bottom portion of the intracardiac tool was sealed with tape to simulate a completely closed mitral valve.

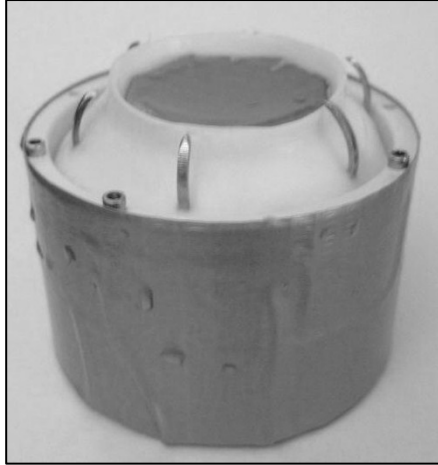


*Figure 107: Test B, intracardiac tool, sealed from the bottom with tape.*

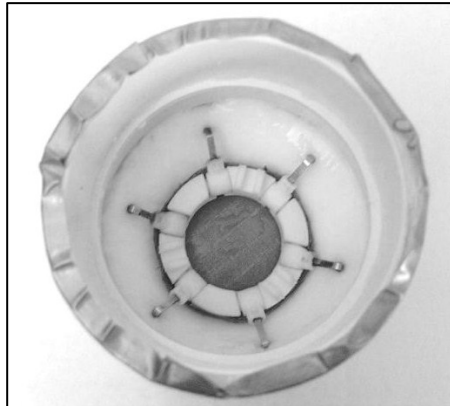


*Figure 108: Test B, upside-down view of sealed intracardiac tool.*

The tool was then anchored to the PVA-C membrane, using its hooks. Approximately 80 ml of water was added and time was measured till complete drainage.



*Figure 109: Test 2, Part B, upside-down view of the setup.*



*Figure 110: Test 2, Part B, inside view of the sealed intracardiac tool.*

Several trials were performed and results are presented in Table 2.

*Table 3: Test 2 - Part B results*

	Trial 1	Trial 2	Trial 3
Time until drainage	7.8 min	8.33 min	8.6 min

#### 4.4.6 Tests 2: Conclusions

By comparing the results reported in Table 2 and 3, it appears that using sutures instead of hooks as a means of attachment yielded considerably less leakage. This is probably due to more contact area and better contact pressure enforced by the sutures. The use of hooks as a means of attachment reduced the contact area and contact pressure between the intracardiac tool and the PVA-C membrane leading to more leakage.

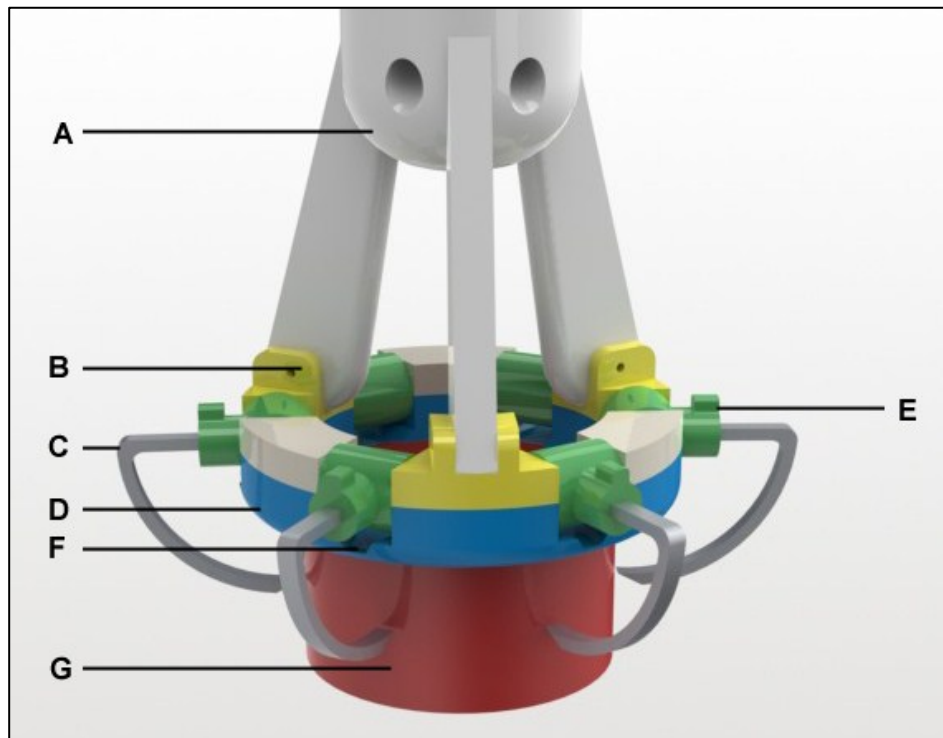
These tests demonstrated the need for several improvements of the design:

- The number of hooks should ideally be increased to the same number of sutures, but this is hardly an option because of limited space.
- The size of the hooks should be decreased. More specifically, the size should be reduced so that the hooks puncture as close to intracardiac tool as possible, and have less reach. This should ensure less leakage by creating better contact. This was also the recommendation from Test 1.

These proposed changes are aimed to better mirror the results obtained by using sutures as an attachment means.

#### 4.5 Prototype 2 design, and manufacturing

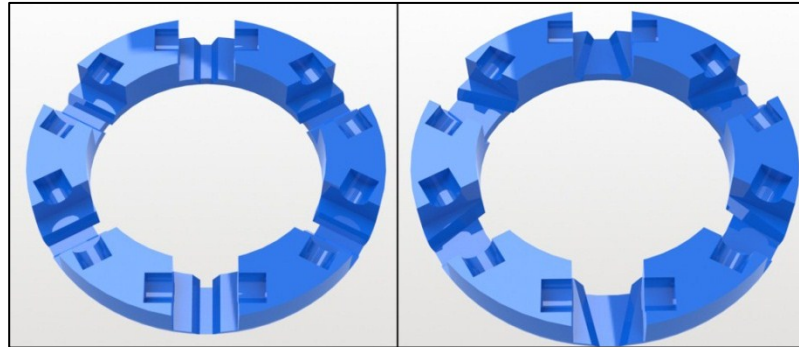
Concept 10: “Advanced hooks” was redesigned, as shown in Figure 111, based on the design deficiencies noted during operation of Prototype 1, and the unexpected deficiencies (such as tolerance problems and inadequate manufacturing of the main holder) encountered due to the SLS manufacturing process of Prototype 1.



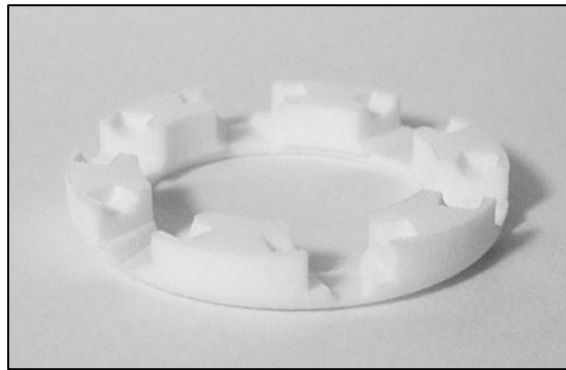
*Figure 111: Redesign of Concept 10: "Advanced hooks", consisting of (A) main holder, (B) top attachment with slots to secure the main holder, (C) custom metallic hooks rotated into position, (D) a lower attachment base, (E) plastic rotator, (F) cut-outs to guide the sutures, (G) On-X 25 mm mitral valve.*

As shown in Figure 112, the bottom attachment assembly was modified to better accommodate the suture lines running through it, by expanding the original cut-outs into

wider, less restrictive shapes. The manufactured bottom attachment plate is shown in Figure 113.



*Figure 112: (left) Prototype 1 of Concept 10 showing narrow cut-outs (Figure 111-F) for the suture lines, (right) which were modified to have a wider shape in Prototype 2.*



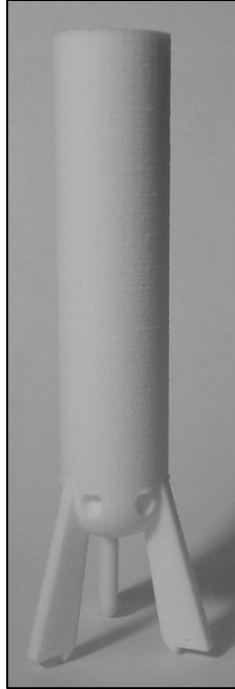
*Figure 113: Concept 10, Prototype 2 bottom attachment plate.*

The deficiencies in the SLS manufacturing process of Prototype 1 prompted the need to redesign the main holder to be much larger and taller in size, to have larger pathway openings for the suture lines, and to reduce any abrupt changes of direction in the path of the suture lines.



*Figure 114: Concept 10, Prototype 2 main holder.*

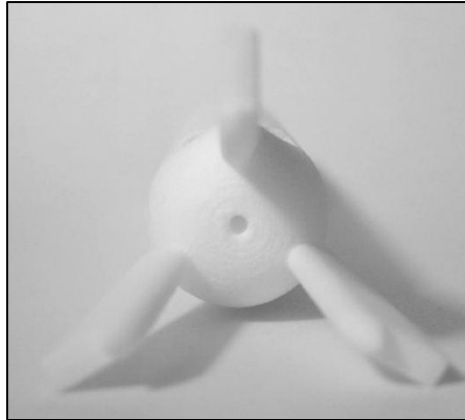
Prototype 1 had five holes running down its longitudinal axis (Figure 84). Prototype 2 was redesigned, as shown in Figure 114, to have a single central 8 mm diameter hole running along most of the main holder's shaft, and splitting into six 3.1 mm diameter holes (at a 45° angle) near the bottom. The manufactured Concept 10 Prototype 2 main holder is shown in Figure 115.



*Figure 115: Manufactured Concept 10, prototype 2 main holder.*

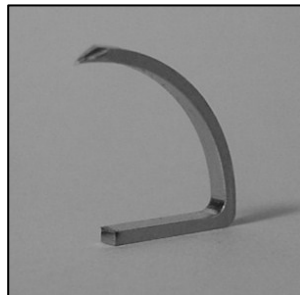
By increasing the rotator (Figure 111-E) size, small tolerances between the rotator and the top/bottom attachments (Figure 111-B) were also removed. After the prototype was built, filing ensured a good fit and easy rotation of the rotator. This allowed for more space for the sutures to hold on to, and prevented them from getting stuck between the rotator and the top/bottom attachments.

A single cut out was made at the base of the main holder for the sensor and its wire, as shown in Figure 116.



*Figure 116: Concept 10, prototype 2 main holder showing the sensor cut out.*

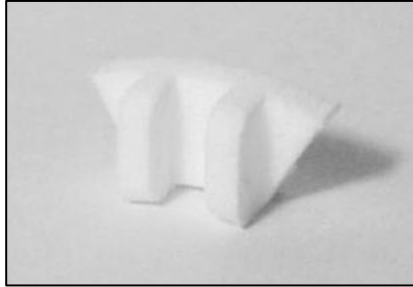
Custom 316 stainless steel hooks, as shown in Figure 117, have a fillet to reduce stress concentrations. This will allow for a smaller hook design to be implemented in the future. Recommendations stemming from Tests 1 and 2 called for the hooks to be redesigned, however, aside from some manual sharpening, the design of the hooks was unchanged due to the high manufacturing costs involved.



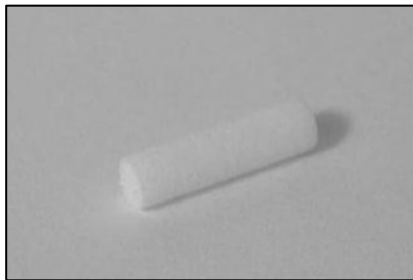
*Figure 117: Custom 316 stainless steel metal hook.*

Other parts manufactured for Prototype 2 included the top attachment with slots to secure the main holder (Figure 118), plastic rotators (Figure 119), the drum axis about which

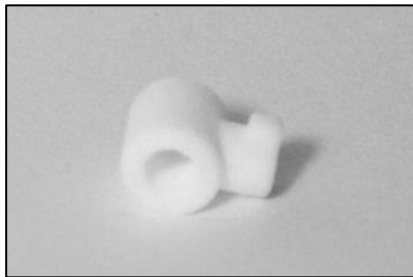
the plastic rotator rotate (Figure 120). All the parts for the entire assembly are shown in Figure 121.



*Figure 118: Concept 10, Prototype 2 top attachment with a slot to secure the main holder.*



*Figure 119: Manufactured Concept 10, prototype 2 drum axis.*



*Figure 120: Manufactured Concept 10, Prototype 2 plastic rotator.*



*Figure 121: All of the plastic parts manufactured for Concept 10, Prototype 2.*

The final, manufactured and assembled, prototype 2 is shown in Figure 122, with comparison to Prototype 1.



*Figure 122: Manufactured Concept 10, (left) Prototype 2, and (right) Prototype 1.*

## **4.6 Prototype 2 testing and results**

### **4.6.1 Test 3: Test in a dynamic surgical phantom**

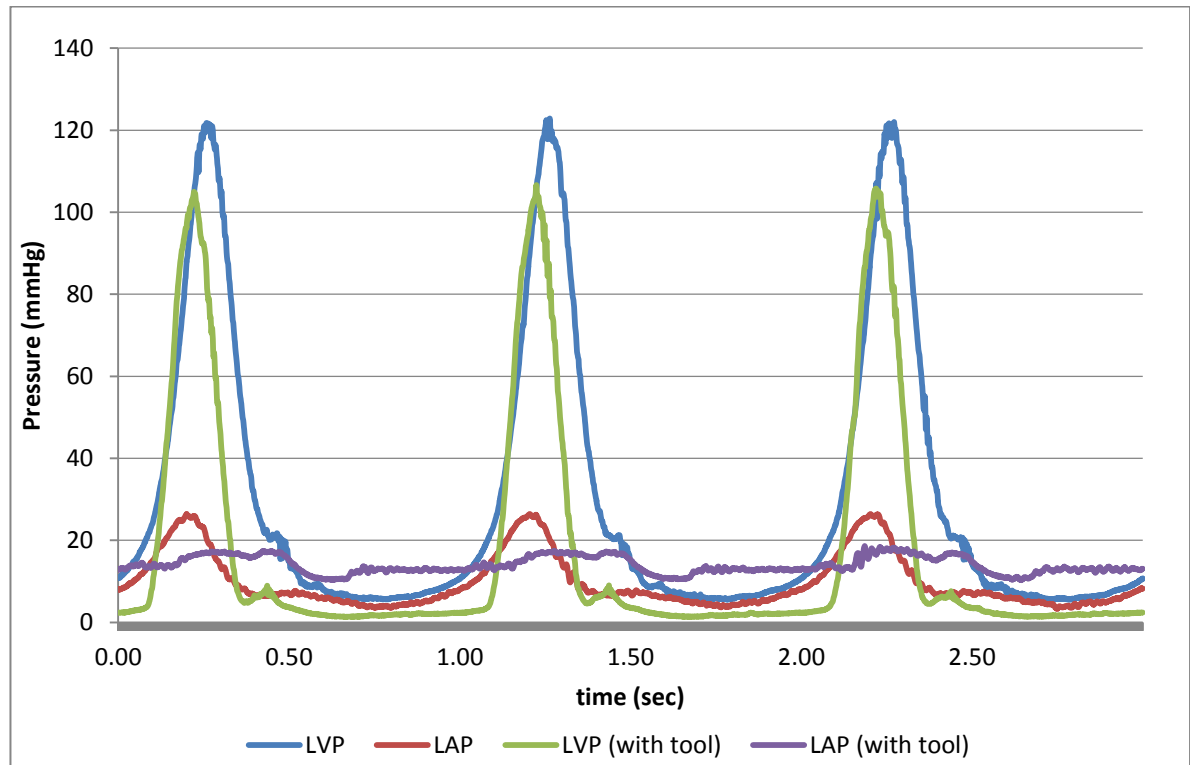
One of the specifications for the intracardiac tool design was to consider how much blood flow restriction the tool creates during its initial deployment. The initial deployment stage is defined as when the intracardiac tool is brought into close contact with the mitral valve annulus and the anchors are not yet inserted into the tissue. Therefore, the purpose of Test 3 was to compare the amount of blood flow between: the actual diastolic blood flow across a mitral valve, the diastolic blood flow in a dynamic surgical phantom across a mitral valve, and the diastolic blood flow in a phantom model with the intracardiac tool in its initial deployment stages.

The dynamic surgical phantom was developed at the Robarts Research Institute by Jonathan McLeod. Such equipment makes it possible to test the anchoring mechanisms of the intracardiac tool without using live animals (78). The phantom reproduces the conditions in a real heart by simulating the contraction and relaxation of the left ventricle. Therefore it can serve as a much more valuable tool to validate the efficiency of the intracardiac tool anchoring as opposed to a static phantom (78). A 40 percent glycerol water solution, pumped through a computer controlled Cardioflow 5000 MR gear pump, served as a standard blood replacement (78). Ultrasound (Philips iE33 system, with an X7-2t probe) was used to view the intracardiac tool during the procedure (78). No prosthetic valve was needed to simulate a fully open mitral valve as required in this test.

Pressures in the phantom left ventricle and the left atrium were measured during deployment of the intracardiac tool. Afterwards, the blood flow velocities were calculated

from the transvalvular pressure gradient according to the simplified Bernoulli's equation as presented in the literature review.

#### 4.6.2 Test 3: Pressure Results



*Figure 123: Test 3 pressure results comparing the left ventricle pressure (LVP), left atrium pressure (LAP), with the left ventricle/atrium pressures with intracardiac tool in position in the phantom.*

Without obstruction of the mitral valve Figure 123 shows the left ventricular pressure (LVP, in blue) and the left atrium pressure (LAP, in red) in the phantom. It is slightly inaccurate because a perfect model would have LAP higher than LVP by 3-5 mmHg. It also shows a negligible transvalvular pressure gradient for the short (approximately 0.6 – 0.8 sec) duration interval when the LVP almost coincides with LAP. However, the maximum

diastolic blood flow velocity in the phantom mitral valve, with an open orifice, was about 0.28 m/s as indicated by Jonathan McLeod, the designer of the phantom, confirming that the transvalvular pressure gradient was negligible, i.e. there was no significant obstruction.

Once the intracardiac tool was in position in the simulated mitral valve annulus, Figure 123 shows a transvalvular pressure gradient of about 10 mmHg, which would clinically be considered in the Grade 1 category (38). Figure 123 also shows a decrease in pressure in the left ventricle when the intracardiac tool was in position; this is believed to be due to unwanted fluid leakage.

*Table 4: Test 4 results.*

<b>Scenario</b>	<b>Actual diastolic blood flow velocity in mitral valve</b>	<b>Diastolic blood flow velocity in phantom mitral valve</b>	<b>Diastolic blood flow velocity in phantom model with the intracardiac tool in its initial deployment stage</b>
<b>Peak filling velocity</b>	0.9 m/s - 1.0 m/s in an average adult (36)	0.28 m/s (Maximum) 0.108 m/s (Average)	1.58 m/s

Based on the transvalvular pressure results of Figure 123, the diastolic blood flow velocity in the phantom model with the intracardiac tool in its initial deployment stage can be calculated at 1.58 m/s according to the simplified Bernoulli's equation. This velocity is approximately 60% higher than the actual diastole blood flow velocity in a real mitral valve, as indicated in Table 4. This may not be of great significance as the intracardiac tool is only in the mitral valve orifice for a limited time during the surgery; nonetheless, it would be desirable to minimize this discrepancy as much as possible.

## 5 Conclusions

The objective of this thesis was the design of an intracardiac tool to hold a prosthetic mitral valve, deliver it into the mitral valve annulus region, and anchor it in position. The intracardiac tool is to be used in conjunction with a universal cardiac introducer (UCI). The UCI ensures a safe connection to the heart and enables the use of specialized operating tools, so that an efficient, beating heart, surgery may be performed.

Before the design of an intracardiac tool was started, it was important to identify the motivations and challenges of the work. This entailed a review of the literature on the heart anatomy and physiology, the mitral valve and its surrounding tissues. Of importance, the heart's electrical pathways had to be well understood as any disruption to them may have dramatic consequences. Similarly, the geometry and nature of the dense fibrous cardiac skeleton needed attention to properly design the anchoring mechanism of the device.

The design of the anchoring mechanisms had to withstand the operating forces it was subjected to once in the mitral valve annulus. It was established that a systolic pressure gradient of about 110 mmHg (33) applied over the mitral valve cross sectional area created a force of about 10 N. It was also established that the anchoring device must occupy little space once in position, otherwise the diastolic pressure gradient between the left ventricle and the left atrium may increase and lead to ventricular hypertrophy (35).

The design of the anchoring mechanism had also to consider the forces necessary to puncture the tissues around the mitral valve annulus. These forces are difficult to assess due to the varied nature of the tissues. Moreover, they depend on the cross-section, sharpness,

and penetration velocity of the puncturing device. Based on the literature, it was estimated that a puncturing force of 3 N would be sufficient.

Review of the prior art on sutureless valves revealed that many valves that aim to minimize surgery times, and allow for less invasive procedures have been developed by a number of different companies. However, it was established that an essentially all-plastic device to deliver and anchor the mitral valve prosthesis was still to be designed.

Concepts were developed based on different ideas to deploy “leg extensions” that fit under the mitral valve annulus to hold the prosthetic valve in place. For lack of space and small actuators, the driving force in the deployment is provided by the surgeon’s hand by way of pulling on suture lines or turning shafts.

The design criteria outlined by the researchers at the Robarts Research Institute for this intracardiac tool, included ease of use, quality of grip, manufacturability, low interference with blood flow or magnetic field, reversibility, low invasiveness and short surgery times. Based on these criteria, Concept 10 was selected as the winning concept, and was used for further design analysis and prototyping.

The design analysis of the winning concept consisted of theoretical calculations, finite element simulations, and multiple tests of manufactured prototypes.

Recommendations from preliminary tests were to refine the design of the hooks, to reduce their cross-section, increase their sharpness and increase the number of hooks used. Other modifications to the original design were made to better accommodate and guide suture lines.

Preliminary testing of the tool for blood flow obstruction during deployment produced velocities approximately 60% higher than the real diastolic blood velocities in mitral valves.

While the feasibility of the proposed concept was established by the first preliminary tests that we carried out, two aspects of the design were identified for further improvements: the reduction of the leaks around the perimeter of the mitral valve after anchoring of the prosthesis, and the reduction of the obstruction to blood flow during deployment of the device. The first goal may be achieved by increasing the number of hooks to better mimic continuous sutures around the mitral valve. However, the size of these hooks must be well defined for strength and absence of interference between each other. More hooks also means more suture lines to activate them, which may become difficult as well. As the number of hooks is increased, proper care should be given to the second goal of reducing interference of the tool with the blood flow. Streamlining of the holder may help in this regard. With smaller metallic hooks, magnetic interference issues will be minimized even further, which may facilitate imaging and tool tracking. Moreover, smaller hooks will penetrate tissues more easily, and require less force from the surgeon to deploy them. If the surgeon can better feel how much resistance is provided by the tissues being punctured, better control and sensitivity are expected. The anchoring device will need to be tested to show whether or not it can withstand the approximate 10 N force applied on it in systole.

Aside from the short term goals outlined above, better performance of the anchoring mechanism against leakage may be achieved by better conforming the outline of the device to that of the required mitral valve annulus. In addition, the anchoring mechanism should

ideally be flexible to allow for the cyclic motions of the beating heart while maintaining its grip. It finally needs to allow the tissues to grow over and around it so that the prosthetic valve it carries can perform in nominal conditions.

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## **Appendix A: Cardiovascular diseases**

Below is a short glossary of the most common cardiovascular diseases.

### **Arrhythmia**

Arrhythmia is due to abnormal heart beats. The heart may beat too fast (tachycardia) or too slowly (bradycardia), or simply have irregular heartbeats. The heart's electrical impulses originate normally in the sinoatrial (SA) node; impulses originating elsewhere may cause arrhythmia (79; 80).

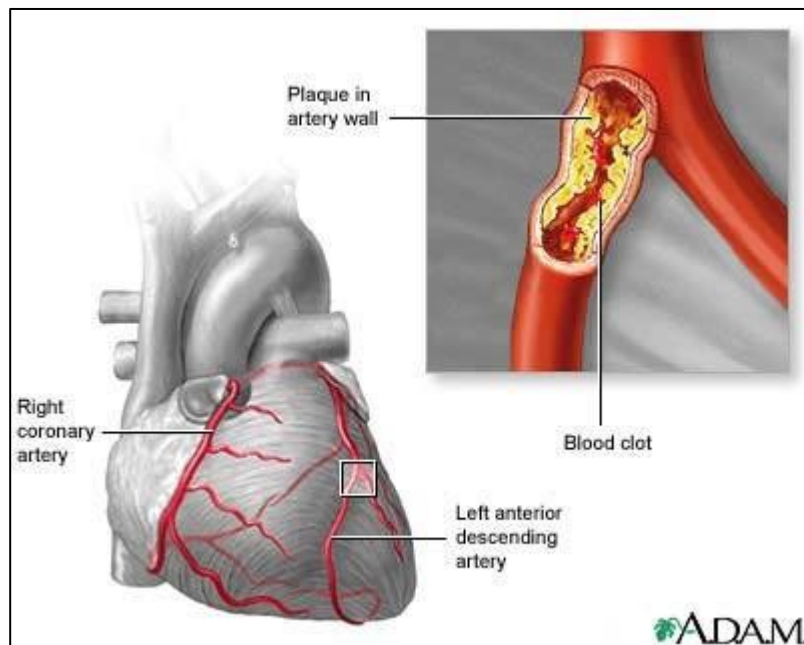
Many arrhythmias never cause any serious problems, however conditions such as angina, heart attack or failure, stroke and sudden death may occur (81; 80). Symptoms include heart palpitations, dizziness, sweating, shortness of breath, chest discomfort, and fainting (80).

There are multiple causes of arrhythmias. These include coronary artery disease, hypertension, congenital heart disease, valve disease, cardiomyopathy, or a past heart attack; other causes include caffeine, amphetamines and other medications (80; 81).

Treatment includes medication (anti-arrhythmic drugs, beta blockers to slow the heart, and blood thinners to prevent clots), surgical intervention (a pacemaker to regulate heartbeat, or in more serious cases, an implantable cardiac defibrillator), and lifestyle changes (e.g. quitting smoking, reducing alcohol, caffeine, stress, and having regular exercise) (80; 81).

## Atherosclerosis

As illustrated in Figure 124, atherosclerosis is a buildup of cholesterol, fat, or other substances that form hard plaques along the walls of arteries in general, and the coronary arteries in particular, that may lead to a blockage that diminishes the supply of oxygen and important nutrients to the heart (myocardial ischemia) (82; 83; 84). Most reported cases are in men over 50 and women over 60 years old (82). An obstruction of 60% will start to significantly interfere with the blood flow (84).



*Figure 124: Atherosclerosis. Source: (83)*

Even though this condition generally takes years to develop, the plaque may rupture in an instant causing blood to pool around the affect area, thereby increasing the blockage (stenosis) even further leading to a sudden reduction of blood flow through the artery (84). The result can be a myocardial infarction (84) or a cerebrovascular accident, depending on whether coronary arteries or cerebral arteries are blocked.

In general, reducing blood flow to the heart may lead to a number of symptoms, including: unstable angina (chest pains), nausea, heart palpitations, shortness of breath or myocardial infarction (83; 82).

There are numerous causes of atherosclerosis, including previous medical conditions (such as diabetes, hypertension, high cholesterol, or family history of heart disease), lifestyle choices (diets rich in saturated fats and cholesterol, heavy alcohol use, smoking, cocaine use, stress, obesity, and lack of exercise), as well as injuries sustained by the intima of the arteries (82; 84; 83).

Prevention plays an important factor and includes regular medical checks for blood pressure and cholesterol levels, making healthy changes in dietary habits (such as restricting the intake of saturated fats or cholesterol, limiting alcohol intake, and exercising regularly) or for more serious cases, cholesterol lowering medications (statins) or medications to reduce the risks of blood clots (such as Aspirin) (84; 82; 83).

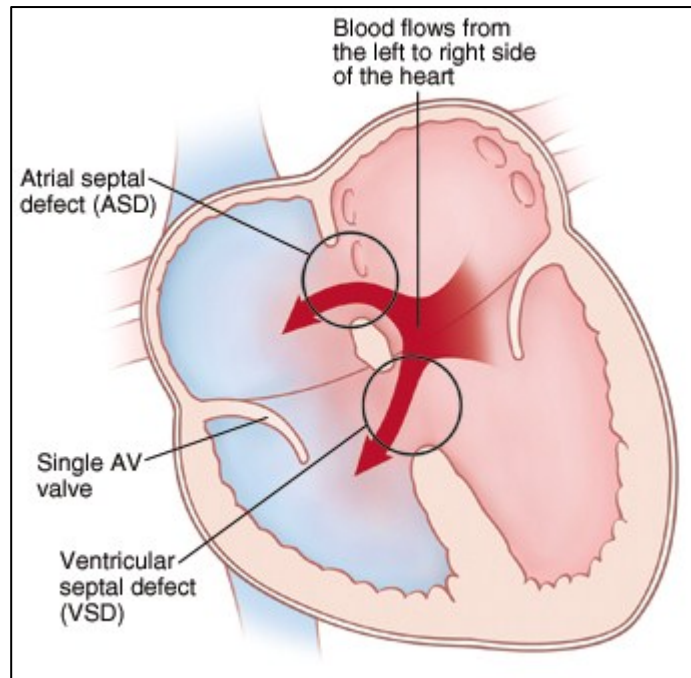
Treatment includes surgeries such as angioplasty, whereby a balloon is fed through a catheter and used to expand the arteries (85). Minimally invasive heart surgery may also be performed, whereby metallic stents are used to expand the arteries (83).

## **Congenital heart defects**

Congenital heart defects are complications that are present at birth. Approximately 0.8% of newborns in the United States and 1 - 1.25% in Canada have heart defects (86; 87). Causes may include inherited genetic conditions or exposure to certain medications in pregnant women (88). Occasionally congenital heart defects are also detected in adulthood due to emerging symptoms of heart defects that include shortness of breath, tiredness, heart murmurs or arrhythmias, and cyanosis (a blue discoloration of skin) (88; 89).

There are a number of different defects that can arise altering the blood flow in the differing parts of the heart, such as its walls, valves, veins and arteries (86). These defects range from simple complications that may never cause problems, to life threatening complications needing immediate surgery, or complications that require continuous medical attention into adulthood (86; 88).

Most common heart defects include: septal defects (ventricular septal or atrial septal defects, as shown in Figure 125), valve defects (incomplete closure, irregular shaped valves), or blood vessels defects (narrow or irregular blood vessels (88)). Referring to Figure 125, ventricular and atrial septal defects are essentially holes in the heart between the two atriums (atrial) or the two ventricles (ventricular), thus septal defects allow for improper mixture of oxygenated and deoxygenated blood (90). Valve defects include prolapse (for example, mitral valve prolapse is bulging of the valve back into left atrium), regurgitation (valve allows for leaks), and stenosis (narrowing of the valve) (90).



*Figure 125: AS and VS defects. Source: (91)*

Treatments vary according to the severity of the complications, and can range from medication to corrective surgery, with most patients undergoing surgery during childhood (89). Prescribed medications include beta blockers (slow down the heart), calcium channel blockers (relax blood vessels), warfarin (prevent blood clots), and diuretics (remove excess fluid) (88). Surgical procedures are commonly done through catheter intervention (88). More complicated congenital defects may require open heart surgery (88).

Owing to advances in medicine, over 90% of children with congenital heart disease now survive into adulthood (86). Over 1 million adults in the US live with some form of congenital heart disease (86). However adults still have certain lingering complications such as arrhythmias, hypertension, thrombosis, and are at risk for developing endocarditis or heart failures (89).

## Cardiomyopathy

Cardiomyopathy is a disease of the myocardium, the heart the muscles (92). It comprises such conditions as dilated cardiomyopathy, hypertrophic cardiomyopathy, and restrictive cardiomyopathy (92).

Dilated cardiomyopathy is the most common type of cardiomyopathy and occurs when a heart chamber becomes enlarged; the chamber then stretches and weakens the heart's walls; the weakened heart may also affect other major organs (92; 93; 94).

Hypertrophic cardiomyopathy is usually an inherited condition that occurs when the myocardium becomes thickened, asymmetrically, and forces the heart to work harder; severe cases of hypertrophic cardiomyopathy are often present in younger people, who may suddenly collapse or die during heavy exercise (95).

A rare condition called restrictive cardiomyopathy occurs when the heart walls become stiff and unable to relax or fill with blood, leading to electrical disorders (92). It may affect both ventricles causing inefficient pumping of blood (96). Restrictive cardiomyopathy often occurs after a heart transplant, but other causes include amyloidosis (deposition of abnormal amyloid protein in the heart (97)), scarring, iron overload, or diseases of the endocardium (96).

The symptoms of cardiomyopathy are similar to other heart diseases and usually develop slowly over time, however some symptoms may develop suddenly (94); they include shortness of breath during exercise or lying down, abnormal heart rhythms or palpitations, swelling of feet and ankles or abdomen, angina or dizziness, fatigue and

fainting; the symptoms may eventually progress to arrhythmias, pulmonary edema, heart attack or a heart failure in most patients (92; 93).

There are numerous causes of cardiomyopathy, including stress, inheritance (such as muscular dystrophy), congenital heart disease, autoimmune diseases (such as systemic lupus erythematosus, rheumatoid arthritis), poorly controlled high blood pressure, valve disease, infections of the heart (such as HIV infection, Chagas or Lyme disease) or a previous heart attack, diabetes, high usage of alcohol or certain drugs, vitamin deficiency (thiamine, calcium and magnesium), and even trace elements such as lead and mercury (92; 94).

Available treatments consist of medication therapies (medications such as captopril, enalapril, lisinopril to lower blood pressure, calcium channel blockers to relax blood vessels, diuretics such as thiazide or potassium-sparing diuretics to remove fluids), implantable devices (a pacemaker, cardioverter-defibrillator, or a left ventricular assist device (LVAD)), surgical intervention (myotomy-myectomy surgery, heart or valve transplants), and lifestyle changes such as diet and regular exercise (92; 94).

## Heart attack

Like all other muscles, the heart requires oxygenated blood for it to function normally. A heart attack or myocardial infarction is a condition when the heart lacks this oxygen-rich blood due to constricted coronary arteries (usually from buildup of cholesterol) (85). Cholesterol plaque buildup along the walls of the coronary arteries is a major contributor to a myocardial infarction (85). For still unknown reasons, these cholesterol plaques can crack causing the blood to clot around the affected area, thus effectively blocking the passage of blood (85). Since no blood is supplied by the blocked artery, the result is the death (necrosis) of the affected heart muscle cells (79).

The severity of the attack depends on which coronary artery was affected and the location of the blockage, as well as the degree of blockage (84). Medical attention is required immediately. Surprisingly, about half of the people suffering from a heart attack wait two hours or longer to seek medical treatment (79).

Symptoms of a heart attack include pressure, tightness, or pain in center chest area (most prominent symptom), pain in the shoulders, arms, or neck, shortness of breath, fainting, unusual heartbeats, and intense anxiety (79). A number of complications may also develop from a suffered heart attack. These include: cardiogenic shock, arrhythmias, heart failure, hypotension, angina, pericarditis, and mitral regurgitation (84).

## Hypertension

Hypertension or high blood pressure (HBP) is often labeled as a silent killer as it usually shows no symptoms (98). It is defined by the American Heart Association as a systolic pressure over 140 mmHg and diastolic over 90 mmHg (98). It is estimated that 24% of the adult population in the United States suffer from it (99). Although most of the time HBP shows no symptoms, in severe cases of an extremely elevated blood pressure, symptoms can include a headache, blurry vision, chest pains, nosebleeds, and ringing in the ears (99).

HBP may result in a number of serious conditions such as stroke (cerebral thrombosis, embolism, or hemorrhage (99)), aneurysms, kidney failure, vision problems (100; 98). It also greatly contributes to heart failure and atherosclerosis (98).

Risk factors for HBP increase in certain people with family history or ethnic background (e.g. African Americans have a higher risk) (98; 99). The causes of high blood pressure include excessive salt or alcohol intake, being overweight, stress, lack of exercise, kidney problems, certain medications, and hormonal disorders (100).

Treatment includes lifestyles changes such as a balanced diet, regular aerobic exercise, and quitting smoking (98). A number of medical treatment are available, such as diuretics (removes excess salt), beta blockers (slows the heart), alpha blockers (prevents tightening of blood vessels), and ACE inhibitors (relax blood vessels) (100).

## **Thrombosis**

A thrombus is defined as a blood clot in a blood vessel (101). When the clot gets detached from the vessel and floats away, it is then called an embolus, resulting in a condition called thrombosis (101). A myocardial infraction or a heart attack occurs when this blood clot may get lodged in the three main coronary arteries of the heart, blocking the supply of oxygen and nutrients, causing the affected area to stop working normally (102).

A clot may also develop due to atherosclerosis, a condition where coronary arteries have a buildup of fat and cholesterol that may suddenly crack and cause a blood clot to develop (102). A myocardial infraction may be caused by other means, and there is no clear answer as to how often thrombosis is the cause of it (103).

High cholesterol levels, smoking, family history of atherosclerosis, diabetes, lack of exercise and stress are believed to increase chances of developing thrombosis (103; 102).

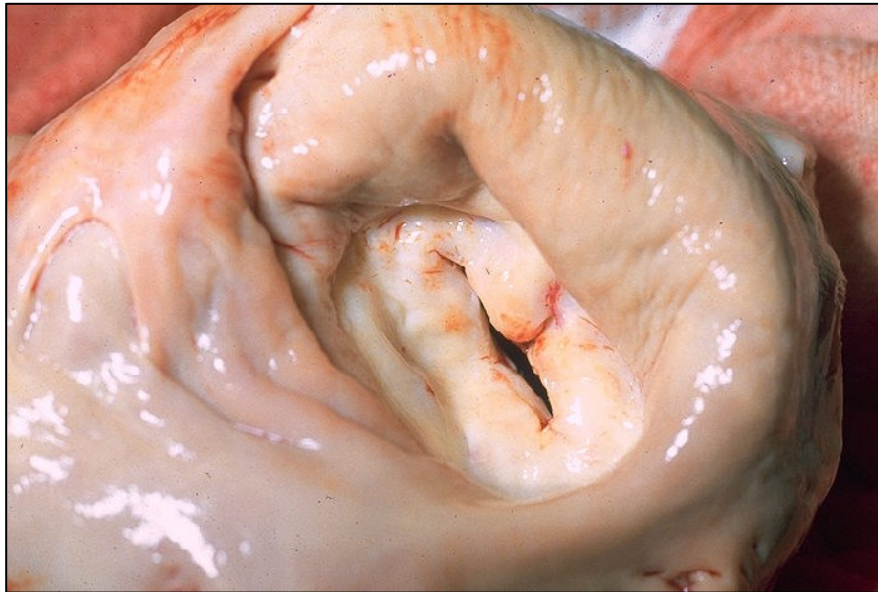
A number of different treatments are available to help recover from a heart attack, these include taking aspirin to prevent further clotting, drugs to dissolve clots, and surgical procedures such as coronary angioplasty or coronary artery bypass surgery (102).

## Appendix B: Mitral valve complications

### Stenosis

Any of the heart's four valves can suffer from stenosis (104). Stenosis is defined as “a narrowing or constriction of the diameter of a bodily passage or orifice” (104). More specifically, as shown in Figure 126, stenosis is the “incomplete opening of the mitral valve during diastole” caused by fusion of the leaflets' edges (105).

The normal area of the mitral valve is about 4-5 cm<sup>2</sup> (24). Symptoms of mitral valve stenosis develop when the area drops to less than 2.5 cm<sup>2</sup> (24). When the valve is constricted to just 1 cm<sup>2</sup> it is considered to be in critical condition (106). This constriction greatly reduces the blood flow from left atrium into the ventricle thus raising the working blood pressures (106).



*Figure 126: Mitral valve stenosis. Source: (107).*

The major cause of mitral valve stenosis is rheumatic fever; however, medical complications may only become apparent after 20 to 40 years when patients do not remember their history of fever (108; 106). Rheumatic fever is an inflammatory condition that can develop after a strep throat infection (streptococcus bacteria); it affects the joints, heart, brain and the skin, but it is not a common condition in the United States or Europe and cases of mitral valve stenosis due to rheumatic fever have decreased drastically over the last forty years (109; 110).

Other causes of stenosis include annular calcification (less than 3% of mitral stenosis cases), congenital (less than 1%), endocarditis, and metabolic diseases like Whipple's disease and Fabry's disease (110).

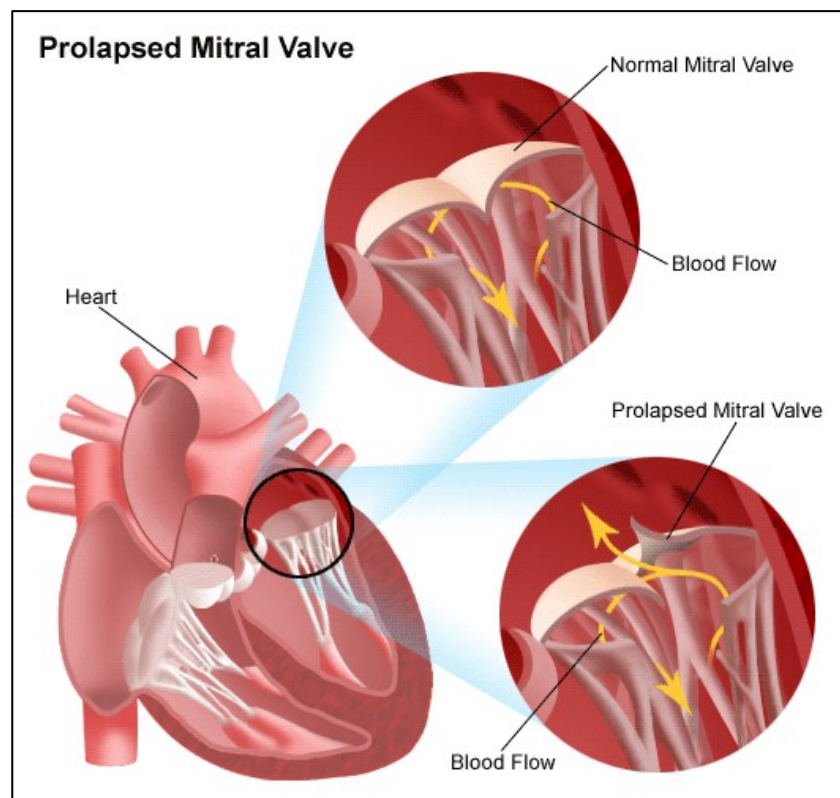
Symptoms of mitral valve stenosis are shortness of breath during exercising, swelling of the legs (108), a characteristic snapping sound after the second heart beat as well as symptoms of pulmonary congestion such as nocturnal paroxysmal dyspnea (a shortness of breath that awakens the patient during the night (111)) and orthopnea (breathlessness while lying down that is relieved when sitting or standing up (111)) (105). Atrial fibrillation also develops in approximately 40% of all patients with mitral valve stenosis (24), it is caused by the enlarged left atrium (due to the backing up of blood) that disturbs electrical pathways in the heart (112).

Stenosis can be treated through antibiotics to prevent further infections (during dental or surgical procedures to prevent endocarditis), diuretics, and medical control of atrial fibrillation (108), and anticoagulation medicine to prevent strokes (106). Surgeries include balloon catheterization whereby an expanding balloon can re-open the affected valve, open

heart surgery to replace the valve (108), or valvotomy (surgically enlarging the valve by manually separating of the commissures) (106). If stenosis is left untreated, stenosis may lead to right heart failure, pulmonary hypertension or pulmonary congestion (105), atrial fibrillation, and the development of thrombi that may dislodge and lead to stroke.

## Prolapse & regurgitation

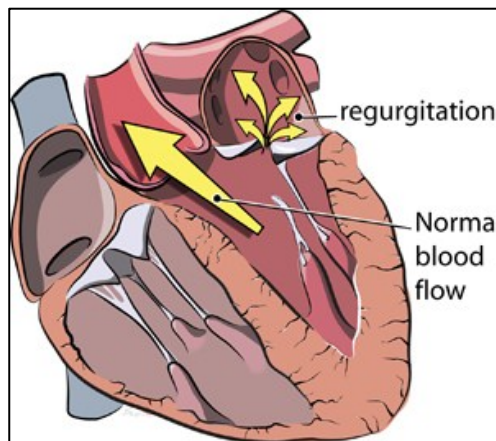
Mitral valve prolapse (MVP) is defined as a condition when one or both leaflets of the mitral valve project back into the left atrium during systole, and this projection prevents the leaflets from making a tight seal with each other (113). Although 10-20% of the population is estimated to have this condition, there are however usually no evident symptoms and no increased chances of a stroke, fibrillation or sudden death (very rare, less than 1% (24)), enabling these people to live normal and active lives (108; 113). However, some people may develop symptoms of prolapse such as palpitations, chest pain, fatigue, difficulty breathing and shortness of breath when lying down (114).



*Figure 127: Mitral valve prolapse. Source: (115).*

In a small number of people with mitral valve prolapse, this bulging-back of the mitral valve into the left atrium can cause mitral valve regurgitation, a condition where some blood leaks back into the left atrium during systole (113). However mitral valve prolapse does not necessarily mean regurgitation will also be present, and most people never develop this backflow (113). Regurgitation may also result from ruptured chordae tendineae, ruptured papillary muscles, or myxomatous degeneration of the mitral valve leaflets (106).

Numerous diseases and complications can lead to regurgitation. These include primary conditions: prolapse, rheumatic fever, endocarditis (a major cause of regurgitation (24)), congenital lesions, annular calcification (110; 114). Secondary conditions include: coronary artery disease, Marfan's syndrome (long and redundant anterior mitral leaflet), Ehlers-Danlos syndrome, polycystic kidney disease, dilated cardiomyopathy, endomyocardial fibrosis (110; 114). Other conditions include systemic lupus erythematosus, radiation therapy, surgical trauma, scleroderma, rheumatoid arthritis, amyloidosis (110; 114).



*Figure 128: Mitral valve regurgitation. Source: (116).*

Symptoms of regurgitation include shortness of breath, palpitations or abnormal heart beat (arrhythmias or fibrillation), a fourth heart sound (24), chest pain, general fatigue, and pulmonary oedema (due to pulmonary congestion (24)) (113; 106).

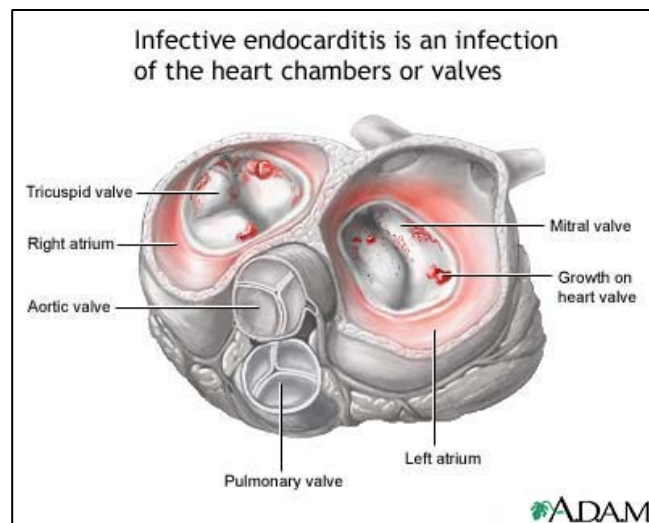
Initial diagnosis is made by echocardiography with Doppler examination to determine the severity of regurgitation (106), chest x-ray or MRI. Treatment of mitral valve prolapse is often not required, but if necessary medication is prescribed (ACE inhibitors, and anticoagulants to prevent stroke (106)) or heart surgery if it is required to repair or replace the complete valve or the valve annulus if the conditions worsen (113; 114). To reduce pulmonary congestion, nitroprusside or dobutamine may be used (24).

If left untreated, regurgitation may increase and lead to a higher chance of infectious endocarditis, stroke, arrhythmias, enlarged left ventricle (112) and higher working pressures (114).

## Endocarditis

Endocarditis is a bacterial (mainly streptococci, staphylococci, and enterococci) infection of the heart, more specifically it is an infection of the heart valves, chordae tendinae, heart's lining (endocarditis) and very rarely the heart muscle (108; 117; 118). As shown in Figure 129, endocarditis is more commonly an infection of an already diseased valve (118) or of an already abnormal valve (117). In healthy hearts, endocarditis is very uncommon (119). In the United States, the incidence of endocarditis accounts for approximately less than 0.5% of all hospital admissions (110).

With regards to the valves, endocarditis may cause the following complications: thrombotic masses on the valves (which may dislodge and cause a stroke), tears of the leaflets or chordae, and abscesses around the mitral valve ring (118).



*Figure 129: Endocarditis affecting the heart valves. Source: (120).*

Certain conditions may leave subjects more susceptible to endocarditis. They include: history of heart disease (septal defect may spread infection from one side of the

heart to the other (118)), artificial or weakened heart valves, diabetes, HIV, injection drug use, and prior valve or dental surgery (108; 117).

Symptoms of endocarditis may be sudden or develop gradually. They include: high fever (most common symptom), stroke, skin or joint infections, heart failure, pneumonia, general weakness, fatigue, abnormal urine color, excessive sweating, splinter hemorrhages under the nails, joint or muscle pains, weight loss without dieting, and a tender spleen (108; 117; 119; 118).

Endocarditis is commonly treated with antibiotics (intravenously, or long term therapy for up to six weeks (117)). Additionally, it can also be prevented with antibiotics in more susceptible patients who have a prior history of endocarditis, an artificial heart valve, regurgitation, or heart disease (108). Surgery is usually only necessary when the infection may lead to stroke, or damage to the heart or the organs becomes excessive (117). However, improvements in surgical techniques have also led to better treatment therapies (110). To help alleviate the symptoms, patients are recommended to keep a balanced nutrition with a diet consisting of fruits and vegetables including herbs, and exercise moderately (121).